Received: 8 May 2023 | Revised: 18 July 2023 | Accepted: 25 July 2023

DOI: 10.1111/jsr.14011

RESEARCH ARTICLE

Idiopathic hypersomnia years after the diagnosis

Karel Šonka[1] | Eva Feketeová[2] | Soňa Nevšímalová[1] | Eszter Maurovich Horvat[1] | Iva Příhodová[1] | Simona Dostálová[1] | Karolína Galušková[1] | Martin Milata[1] | Jitka Bušková[3] | Marek Susta[4]

[1]Department of Neurology and Centre of Clinical Neuroscience, First Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic

[2]Department of Neurology, Faculty of Medicine, University of P.J. Šafárik and University Hospital of L. Pasteur, Košice, Slovak Republic

[3]National Institute of Mental Health, Klecany and Third Faculty of Medicine, Charles University, Prague, Czech Republic

[4]St. Elisabeth University, Bratislava, Slovak Republic

Correspondence
Karel Šonka, Department of Neurology and Centre of Clinical Neuroscience, Charles University in Prague, First Faculty of Medicine and General University Hospital, Prague, Czech Republic, Katerinská 30, 128 21 Prague 2, Czech Republic.
Email: ksonka@lf1.cuni.cz

Funding information
Charles University Cooperatio program in neuroscience; Ministry of Health of the Czech Republic, Grant/Award Number: NU20-04-00088

Summary

Little attention has been paid to the long-term development of idiopathic hypersomnia symptoms and idiopathic hypersomnia comorbidities. The aim of this study was to describe the general health of patients with idiopathic hypersomnia years after the initial diagnosis, focusing on current subjective hypersomnolence and the presence of its other possible causes. Adult patients diagnosed with idiopathic hypersomnia ≥ 3 years ago at sleep centres in Prague and Kosice were invited to participate in this study. A total of 60 patients were examined (age 47.3 ± SD = 13.2 years, 66.7% women). In all participants, their hypersomnolence could not be explained by any other cause but idiopathic hypersomnia at the time of diagnosis. The mean duration of follow-up was 9.8 + 8.0 years. Fifty patients (83%) reported persisting hypersomnolence, but only 33 (55%) had no other disease that could also explain the patient's excessive daytime sleepiness and/or prolonged sleep. In two patients (3%), the diagnosis in the meantime had changed to narcolepsy type 2, and 15 patients (25%) had developed a disease or diseases potentially causing hypersomnolence since the initial diagnosis. Complete hypersomnolence resolution without stimulant treatment lasting longer than 6 months was reported by 10 patients (17%). To conclude, in a longer interval from the diagnosis of idiopathic hypersomnia, hypersomnolence may disappear or may theoretically be explained by another newly developed disease, or the diagnosis may be changed to narcolepsy type 2. Thus, after 9.8 years, only 55% of the examined patients with idiopathic hypersomnia had a typical clinical picture of idiopathic hypersomnia without doubts about the cause of the current hypersomnolence.

KEYWORDS
comorbidity, depression, diagnosing, follow-up, hypersomnolence, idiopathic hypersomnia

1 | INTRODUCTION

Idiopathic hypersomnia (IH) is a rare neurological disease whose main symptom is hypersomnolence, which includes excessive daytime sleepiness and excessive amounts of sleep (extended nocturnal sleep and long naps, together called hypersomnia; Billiard & Sonka, 2022; Dauvilliers et al., 2022; Ohayon, 2008; Trotti, 2017a). The current International Classification of Sleep Disorders (3rd edition) (ICSD-3)

ranges IH in the group of Central Disorders of Hypersomnolence whose primary complaint is the hypersomnolence not caused by disturbed nocturnal sleep or maladjusted circadian rhythms (American Academy of Sleep Medicine, 2014), and the obligatory diagnostic criteria of IH according to ICSD-3 are listed in Table 1. The previous 2nd edition of the International Classification of Sleep Disorders (ICSD-2; American Academy of Sleep Medicine, 2005) divided IH into two disorders: IH with long sleep time (LST); and IH without LST. According to the ICSD-2, the characteristic criterion of IH with LST was an extension of the main sleep period to more than 10 hr. For IH without LST, nocturnal polysomnography (PSG) had to demonstrate the main sleep duration of 6–10 hr and a mean sleep latency of ≤ 8 min on the following day of Multiple Sleep Latency Test (MSLT; American Academy of Sleep Medicine, 2005). Thus, the diagnostic criteria of IH according to ICSD-2 (both forms combined) and ICSD-3 are nearly identical, including the criterion that the hypersomnolence should not be better explained by another aetiology (American Academy of Sleep Medicine, 2005; American Academy of Sleep Medicine, 2014; Billiard & Sonka, 2022).

The knowledge of IH aetiopathogenesis is limited, and its basic principles are still unknown (Dauvilliers et al., 2022; Trotti, 2017a). Treatment of IH is symptomatic. Alerting agents (central stimulants and other wake-promoting agents) mostly developed for the treatment of narcolepsy were for a long time the only option for the hypersomnolence treatment in IH. The efficacy of drugs against sleepiness in IH was assessed only by academic trials (Arnulf et al., 2022; Arnulf et al., 2023; Dauvilliers et al., 2022; Evangelista et al., 2018; Inoue et al., 2021; Leu-Semenescu et al., 2014; Mayer et al., 2015; Trotti et al., 2015) and until 2021, standard randomized control studies and long-term drug trials in patients with IH were completely lacking. The off-label pharmacological treatment of IH makes it less accessible. The information on the long-term clinical course of hypersomnolence in IH is limited. We recently presented that subjects who were previously diagnosed with IH and still suffered from hypersomnolence retained their affiliation to LST and non-LST forms of IH after a follow-up of 5.4 ± 5.2 years (Nevsimalova et al., 2021). IH is considered a lifelong illness, but individual remissions were reported in several series (Anderson et al., 2007; Bassetti & Aldrich, 1997; Billiard et al., 1998; Bruck & Parkes, 1996; Kim et al., 2016).

The aim of this study was to assess the clinical status of patients previously diagnosed with IH, with special attention to the general clinical picture, other diseases, persistent sleepiness, and other circumstances indicating conformity or non-conformity with the diagnostic criteria for IH.

TABLE 1 The obligatory diagnostic criteria of IH according to the ICSD-3, 2014

A.	Daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months
B.	No cataplexy
C.	Fewer than two sleep-onset REM periods or no sleep-onset REM periods on MSLT and on the preceding night PSG
D.	Mean sleep latency of ≤ 8 min on MSLT and/or total 24-hr sleep time ≥ 660 min
E.	The exclusion of insufficient sleep syndrome
F.	The hypersomnolence and/or MSLT findings are not better explained by another sleep disorder, other medical or psychiatric disorder, or use of drugs or medications

Abbreviations: MSLT, multiple sleep latency test; PSG, polysomnography; REM, rapid eye movement.

2 | PATIENTS AND METHODS

Patients were recruited in two sleep and wake centres in neurological departments in tertiary university hospitals in Prague (Czech Republic) and Košice (Slovak Republic) in 2019–2022. The conditions of recruitment were as follows. (a) The diagnosis of IH according to the diagnostic criteria valid at the time of diagnosis (American Academy of Sleep Medicine, 2005; American Academy of Sleep Medicine, 2014). The first diagnostic work-up of IH included a complete sleep examination by a neurologist certified in sleep medicine, night video PSG, and next-day MSLT. The LST variant of IH was proved/excluded by 10 days of actigraphy and/or by 22 hr of PSG recording after MSLT (Vernet & Arnulf, 2009). (b) The secondary reason for hypersomnolence was excluded at the time of diagnosis—especially no sleep restriction, apnea–hypopnea index (AHI) < 10, and periodic leg movements index < 15. (c) IH was a unique sleep disorder diagnosis at the time of diagnosis. (d) Hypocretin-1 level in the cerebrospinal fluid (if assessed) > 110 pg ml^{-1}. (e) No medication potentially affecting sleep and wakefulness at the time of diagnosis. (f) The adult age at the time of the study. (g) The interval from the diagnosis to the study examination ≥ 3 years. (h) Willingness to come personally to the sleep centre and to participate in the study. Subsequent treatment, type of medical care, and HLA typing were not relevant for inclusion.

We found in our archives records of 76 patients meeting the above-mentioned criteria. The contact with 16 subjects was lost (Table S1). All remaining subjects (50 in Prague, 10 in Košice) agreed to participate in the study. Six patients from the Prague group were diagnosed with IH before 2005, the year of ICSD-2 publication; and the compliance with the diagnostic criteria of IH according to ICSD-2 at the time of their diagnosis was retrospectively carefully checked. The assessment of hypocretin-1 level in the cerebrospinal fluid was performed in 11 patients. Seventeen subjects underwent at the time of diagnosis 22-hr-long PSG recording after MSLT. We merged patients diagnosed with IH with LST according to ICSD-2 and patients with a 24-hr sleep time ≥ 660 min diagnosed according to ICSD-3 in one group labelled IH with LST.

The study procedure included a standard in-person clinical examination (interview and basic physical examination) taking into account reports from our departments and other physicians (if available) and sleep studies if they were performed during the follow-up. New PSG and MSLT were not performed. The study examination aimed: (a) to record/diagnose new psychiatric, neurological and medical diseases; (b) to record new drug and substance intake history; (c) to assess by detailed interview the symptoms of IH including sleep drunkenness (Trotti, 2017b); and

(d) to search for other sleep disorders. The participants rated their sleepiness using Epworth Sleepiness Scale (ESS; Johns, 1991).

Twenty-six subjects underwent a second PSG (in 22 followed by MSLT) in the interval between the initial diagnosis and the study examination. The reasons for the second PSG were heterogenous: 10 times verification of the diagnosis asked by treating physicians or by medical insurance, 10 times exclusion of sleep-related breathing disorder, and six times suspicion on narcolepsy. The delay between the diagnostic PSG and MSLT and the second PSG was on average 6.7 years (SD = 7.2), with a broad range of 1–34 years. Newly discovered sleep diseases were diagnosed according to ICSD-3 (American Academy of Sleep Medicine, 2014).

Detected comorbidities were exploited in detail, and later were grouped according to the affected system (e.g. respiratory diseases) or part of the body (e.g. headache). The somatic diseases surveyed, namely hypertension, diabetes, thyroid disease, autoimmune diseases, gastrointestinal diseases, respiratory diseases and malignancies, were later aggregated into a single item (somatic diseases aggregated). Information on autonomic system disorders is not included because the subjective information obtained was not considered sufficiently valid.

Remission of hypersomnolence was defined as the absence of subjective symptoms of hypersomnolence (excessive daytime sleepiness, night sleep duration > 9 hr, sleep inertia) without medication for at least 6 months (the "Recovered" group).

For patients in the study who still suffered from hypersomnolence, we investigated whether they still met the criterion of the absence of another condition that could explain the hypersomnia better (the "Undisputed IH" group).

Subjects with hypersomnolence that could theoretically (according to the experienced clinician's opinion) be much better (more likely) explained by another cause constituted the "Multiple Plausible Causes of Hypersomnolence" group. Subjects rediagnosed with type 2 narcolepsy (NT2) were not included in this group because their hypersomnolence is no longer considered IH. The flowchart and decision tree is shown in Figure 1. We stress that all subjects included in the study had at the time of diagnosis no other condition potentially explaining the hypersomnolence. All these conditions appeared during the follow-up.

The study was approved by the Ethics Committee of the General University Hospital in Prague (opinion number—1264/18S-IV) and the Ethics Committee of the L. Pasteur University Hospital in Kosice (2022/EK/10080). Patients agreed to participate in the study by signing informed consent. The data that support the findings of this study are available from the corresponding author upon reasonable request.

The primary statistical processing of the data obtained using SPSS software (by IBM) confirmed the absence of normal distribution for the scale variables, so a non-parametric method with post hoc Dunn's test was used to reduce the risk of type 1 error. The source dataset was dominated by nominal variables, and chi-square with post hoc Fisher's exact test was used to compare the datasets. In all cases, two groups were always compared with each other; a pooled test (K-independent samples) was performed to clearly distinguish the origin of any statistically significant differences between groups.

3 | RESULTS

3.1 | All participants—general information and details on sleep and sleep disturbances

Women represented 66.7% of participants; 33.3% of participants were males including two transsexuals female to male. The average age of all groups was 47.3 (SD = ± 13.2) years. Forty-five percent of patients were formerly diagnosed with IH with LST. The symptoms started at the age of 25.8 (± 13.5) years, and the diagnosis of IH was stated at the age of 37.5 (± 10.9) years; 33.4% of patients reported a first-degree family member suffering from hypersomnolence. HLA DQB1*0602 haplotype was found in 27.3% of patients.

Whole-life experience of sleep drunkenness was reported by 60% of subjects, sleep paralysis by 18.3%, and sleep-related hallucinations by 15%. Other parasomnias were present in 8.3% of participants—one participant had nightmares sometimes accompanied by sleep paralysis, one participant had somnambulism, three participants taking antidepressants had probable rapid eye movement (REM) sleep behaviour disorder, and the participant rediagnosed to NT2 had a REM sleep behaviour disorder confirmed using PSG. Restless legs syndrome (RLS) was diagnosed in 15 subjects (25%) three of them were on the treatment, and obstructive sleep apnea (OSA; AHI ≥ 15) was objectively documented in four subjects (6.7%). Three were at the time of the study on continuous positive airway pressure (CPAP)—one with good compliance and two with insufficient compliance. None reported a sleepiness change on CPAP.

There was 51.7% of patients who were ever treated by stimulants and/or wake-promoting agents: modafinil (32 patients), methylphenidate (29 patients), dexamphetamine (one patient), bupropion (six subjects), phenmetrazine/dexphenmetrazine (two subjects), pitolisant (two subjects); 38.3% of patients were treated at the time of the study (modafinil, methylphenidate, bupropion and pitolisant).

3.2 | All participants—comorbidities not related to sleep with detailed information on new diagnoses

The most common group of diseases was mental disorders. Mood disorders (in all cases diagnosed by a psychiatrist) were reported by 26 patients (depression in all but one case of bipolar disorder); 23.3% of patients were currently (for more than 6 months) on antidepressant treatment. Not all patients who reported depression were currently clinically depressed, but 10 subjects from this group were considered severely depressed at the time of the study, most of them taking drugs affecting wakefulness. A patient with bipolar disorder was not asymptomatic despite substantial pharmacotherapy. Mood disorders had required hospitalization in the past in four patients, in some cases repeatedly. The prevalence of anxiety (not always diagnosed by a psychiatrist) was 25.0%. One subject suffered from anorexia nervosa at a young age (before IH was diagnosed), and his body mass index (BMI) had been stable but low for many years (currently 17.6 $kg\ m^{-2}$).

Regarding neurological diseases, 35% of the patients reported headaches (four reported migraine without aura, two migraine with

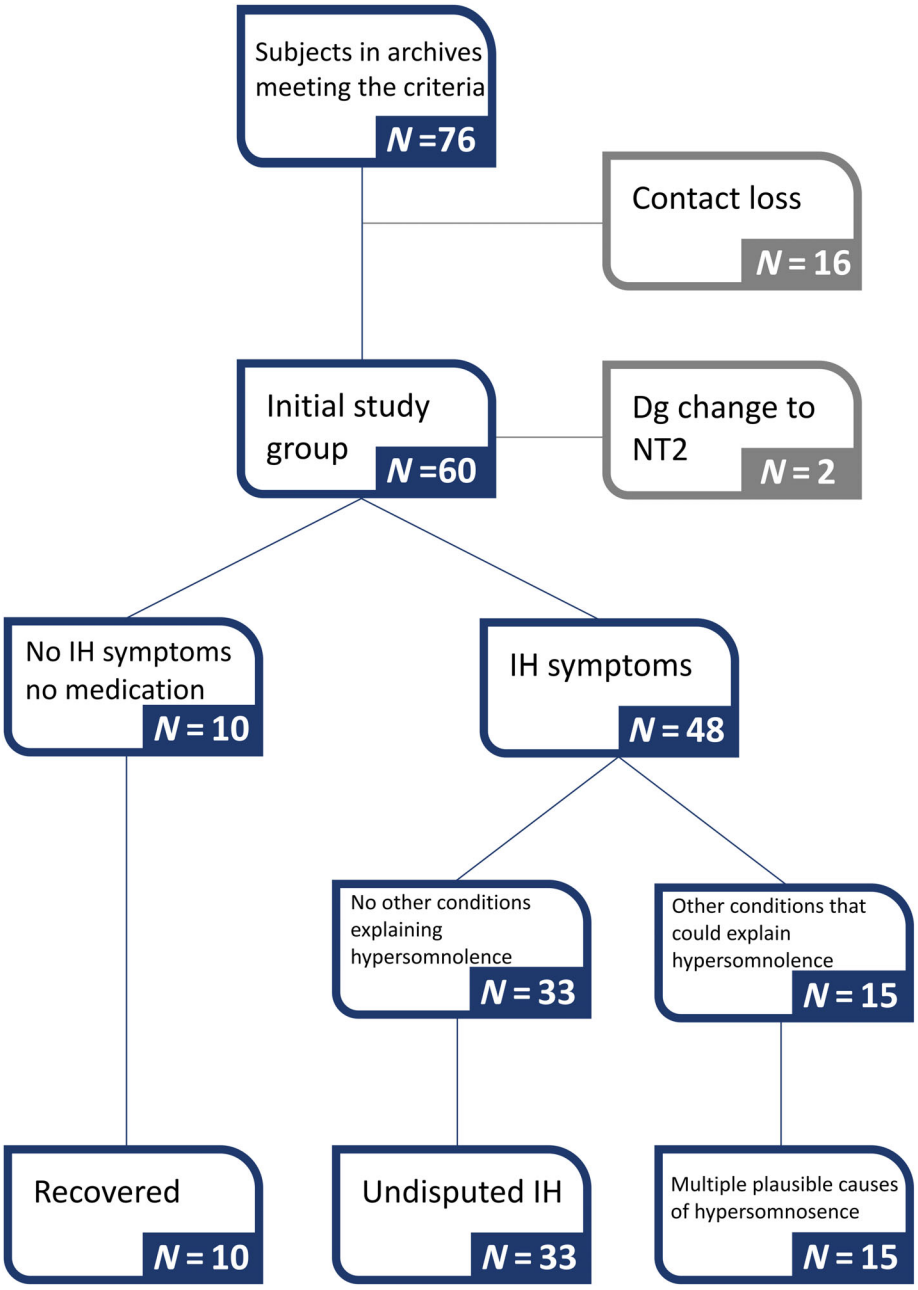

FIGURE 1 The flowchart and decision tree. IH, idiopathic hypersomnia.

aura—one of them experienced an attack of headache with hemiparesis; 11 subjects had a history of tension headache and four subjects reported sleepiness-induced headache in situations where they could not take a nap), and three patients had head trauma (all mild concussions). Central nervous system infection was reported by five patients (two mild tick encephalitis after the IH onset, four mild viral encephalomeningitis many years before the onset of hypersomnolence), one patient suffered from essential tremor, and one reported unilateral masticatory muscle dystonia treated with botulinum toxin. Four subjects had a history of functional movement disorder, and one was diagnosed with a mixed dissociative disorder.

An overall serious infection other than Covid 19 was reported by seven patients (Lyme disease four times, toxoplasmosis once, mononucleosis twice, and Hong Kong influenza once). Four participants had experienced Covid 19—three mild forms, one was hospitalized but not artificially ventilated. Malignancy was reported by one patient. Rheumatological diseases were reported by 10 patients, two of whom reported rheumatoid arthritis. Hypertension was diagnosed in 25.0%, 10% reported cardiac disease (no cases of myocardial infarction), 10.0% diabetes, 23.3% well-controlled thyroid disease, 35.0% had gastrointestinal disease, 16.7% autoimmune disease (no cases of neurological autoimmunity) and 21.7% respiratory disease. Significant urological and gynaecological diseases were not recorded.

The current mean BMI of all participants was 26.2 (± 5.2) kg m^{-2}, and 35% of subjects were obese (BMI > 30 kg m^{-2}).

Current regular alcohol consumption was reported by 30.0% (all moderate) of the participants, and 36.7% were smokers.

3.3 | Current compliance with the diagnostic criteria

In a total of 27 patients (45%), the diagnostic criteria were no longer met or there was serious doubt as to whether the patients would have met them if the criteria had been applied strictly without knowledge of the patient's previous IH history. Two subjects were re-evaluated between the initial diagnosis of IH and the study examination and their diagnosis were changed to narcolepsy type 2 due to ≥2 sleep onset REM periods (SOREMPs) on de novo nocturnal PSG and MSLT (these subjects are not included in the following comparisons). Ten subjects (17%) reported that their hypersomnolence had resolved and all were stimulant-free at the time of the study and 6 months prior to the study (the "Recovered" group). The 15 subjects (25%) who still reported hypersomnolence had clinically significant comorbidity(s) at the time of the study (Table S2) that, without prior knowledge of the IH diagnosis, may "better explain hypersomnolence than IH" (the "Multiple Plausible Causes of Hypersomnolence" group). We divided the common comorbidities considered more likely or a better explanation for hypersomnolence into three categories (most patients had multiple diseases with the potential to cause hypersomnolence and are represented in more than one category). The first category (11 subjects)—severe depression or bipolar disorder, in some patients in combination with other psychiatric disorders. The second category (seven subjects)—serious medical illnesses that are currently in a severe/significant clinical state, usually multiple and causing night-time sleep disturbances—severe chronic obstructive pulmonary disease, heart failure, chronic musculoskeletal pain and others; often combined. The third category (six persons)—severe primary nocturnal sleep disorders without effective/successful treatment—OSA (three persons) and severe RLS with or without periodic limb movements in sleep (three persons, all subjectively perceived sleep initiation and continuity disturbances). Subjects with OSA were not adequately treated with CPAP, either because of refusal of treatment or non-compliance with the treatment regimen. RLS in the above-mentioned three patients was not effectively treated at the time of the study; one subject with RLS was on treatment with a selective serotonin reuptake inhibitor. It is worth noting that all of the disorders considered to be the likely another cause of hypersomnolence occurred after the diagnosis of IH.

Thirty-three patients (55%) reported hypersomnolence with no other possible cause and therefore clearly continued to meet the diagnostic criteria for IH (the "Undisputed IH" group).

3.4 | Differences between groups recovered, undisputed IH and multiple plausible causes of hypersomnolence

There were no significant differences between the groups in the age of onset of symptoms, age of diagnosis and male/female ratio (one transsexual man was included in the Undisputed IH group and the other in the Multiple Plausible Causes of Hypersomnolence). Patients in the Undisputed IH group were followed for a shorter time than those who recovered. The percentage of HLA DQB1 * 0602 carriers did not differ. The LST form was similarly represented in all three groups. Persons in the Recovered group evaluated the ESS lower than those in the other two groups. Because no one in the Recovered group was taking stimulants by definition, the Recovered group had a significantly lower proportion of participants currently taking stimulants compared with the other groups (Table 2).

Regarding comorbidities, the most important result is the higher lifetime prevalence of depression, anxiety and cumulative psychiatric illness in the Multiple Plausible Causes of Hypersomnolence group compared with the other two groups. Treatment with antidepressants was more frequently reported by persons in the Multiple Plausible Causes of Hypersomnolence group compared with those in the Undisputed IH group (Table 3).

Patients in the Multiple Plausible Causes of Hypersomnolence group had a higher BMI than patients in the Undisputed IH group. Patients in the Multiple Plausible Causes of Hypersomnolence group reported headaches at a higher rate than patients who recovered. Other comorbidities did not differ in the medical history of patients in the three groups, even when somatic comorbidities were aggregated as a single item (Table 3). Diseases not listed in Table 3 were rarely present in the study groups. This also applies to functional movement disorder—two patients fell into the Undisputed IH group and two into the Multiple Plausible Causes of Hypersomnolence group. OSA was present in the Multiple Plausible Causes of Hypersomnolence group only. Other sleep disorders or symptoms were represented in all three groups.

3.5 | Analysis of factors influencing patient allocation to one of three predefined groups

Despite the low number, we decided to perform a factor analysis (Gaskin & Happell, 2014) of the groups, which by definition could only be performed on the complete data available for 58 patients. Eigenvalues of the correlation matrices were used to determine the number of factors of interest. The primary Varimax rotated component output matrices contained cross-loadings but, after several iterations, pure rotated output matrices without cross-loadings were obtained. The number of factors and the variable contribution varied across groups. Two factors were identified in the group Recovered, a diagnosis of a long night's sleep and somatic problems contributed to the first factor, while lifelong stimulant use and smoking contributed to the second. For group Undisputed IH, three factors were identified. The first can be described as psychiatric, contributed by psychiatric disorders and psychiatric medication; the second, sleep-related, contributed by the presence of the LST form of IH and sleep drunkenness; and the third factor, more generally neurological, loaded by RLS and the presence of the HLA DQB1 * 0602 allele. In group Multiple Plausible Causes of Hypersomnolence, four factors were identified with contributing factors distinctly different from group Undisputed IH. The first factor included RLS and smoking, the second somatic and psychiatric diseases, the third only the presence of the HLA DQB1 * 0602 allele, and the fourth only the presence of LST IH form.

TABLE 2 IH and sleep history, sleep symptoms and disorders, and current ESS

			Persisting hypersomnolence (except two subjects rediagnosed to NT2)		Between groups comparisons		
	All participants	Recovered	Undisputed IH	MPCH	Recovered versus Undisputed IH	Undisputed IH versus MPCH	Recovered versus MPCH
N	60 (100%)	10 (100%)	33 (100%)	15 (100%)			
Age at the study (years)	47.3 (± 13.2)	49.8 (± 13.7)	44.0 (± 12.9)	51.1 (± 12.9)	n.s.	n.s.	n.s.
Females, *n* (%)	40 (66.7%)	6 (60%)	22 (66.7%)	11 (73.3%)	n.s.	n.s.	n.s.
IH with LST *n* (%)	27 (45%)	4 (40%)	15 (45.5%)	7 (46.7%)	n.s.	n.s.	n.s.
Age at the symptoms onset, years	25.8 (± 13.5)	26.5 (± 17.0)	25.4 (± 13.5)	26.3 (± 12.2)	n.s.	n.s.	n.s.
Age at diagnosis, years	37.5 (± 10.9)	39.9 (± 13.2)	36.4 (± 11.7)	38,7 (± 7.0)	n.s.	n.s.	n.s.
Duration of the follow-up, years	9.8 (± 8.0)	9.9 (± 3.6)	7.6 (± 5.6)	12.4 (± 11.1)	**0.015**	n.s.	n.s.
HLA DQB1 * 0602, *n* positive/*n* examined (%)	15/55 (27.3%)	1/9 (11.1%)	9/31 (29%)	3/13 (23.1%)	n.s.	n.s.	n.s.
Familial history of EDS, *n* (%)	20 (33.4%)	3 (30%)	9 (27.3%)	5 (33.3%)	n.s.	n.s.	n.s.
Whole-life sleep drunkenness, *n* (%)	36 (60%)	4 (40%)	20 (60.6%)	10 (66.7%)	n.s.	n.s.	n.s.
RLS, *n* (%)	15 (25%)	1 (10%)	7 (21.2%)	7 (46.7%)	n.s.	n.s.	n.s.
Sleep apnea, *n* (%)	4 (6,7%)	0	0	4 (26.7%)	n.s.	**0.007**	n.s.
Whole-life stimulants, *n* (%)	31 (51.7%)	4 (40%)	17 (51.5%)	8 (53.3)	n.s.	n.s.	n.s.
Currently stimulants, *n* (%)	23 (38.3%)	0	15 (45.5%)	6 (40%)	**0.019**	n.s.	0.051
Current ESS	13.2 (±5.1)	7.2 (±4.3)	13,5 (±4.1)	17.7 (±3,5)	**0.000**	n.s.	**0.000**

Note: Bold values indicate the significance $p < 0.05$.
Abbreviations: EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; IH, idiopathic hypersomnia; LST, long sleep time; MPCH, Multiple Plausible Causes of Hypersomnolence; *n*, number; n.s., non-significant; NT2, narcolepsy type 2, RLS, restless legs syndrome.

4 | DISCUSSION

We believe that the important contribution of the study is the description of patients' clinical status years after diagnosis despite no new PSG and MSLT at the follow-ups were performed. We confirmed previous rare reports (based also only on subjective reports) that hypersomnolence in IH may disappear, although IH was first described as a chronic unremitting disease (Roth, 1976). Both forms of IH (with and without LST) can resolve, as reported by Kim et al. (2016). In those who recovered, no unusual clinical features were found in their history except for a low prevalence of psychiatric disorders that occurred after the initial diagnosis. The factor analysis performed in this study also did not detect a clinically significant phenotype of a remission candidate.

Our IH remission rate (17%) is among the lower ones, but previous reports of recovery from IH hypersomnolence have certain limitations (old-fashioned diagnostic methods, inadequate description of treatment status, a short follow-up period, or a follow-up performed over the phone). A recent study by Kim et al. retrospectively analysed a 5-year follow-up of 24 subjects with IH diagnosed solely based on MSLT latency and found a remission rate (defined similarly to our study) of 32.5%. Their study participants with and without remission showed no differences (Kim et al., 2016). Bassetti and Aldrich analysed 35 patients with IH followed for more than 1 year and found improvement in nine (26%; Bassetti & Aldrich, 1997). In the group reported by Anderson et al., "spontaneous improvement" was noted in 14% after 3.4 ± 2.2 years of follow-up (Anderson et al., 2007).

Our two earlier studies evaluating smaller and partially overlapping Prague IH patients had different aims (they did not focus on symptom resolution), and included younger patient cohorts with a shorter interval since diagnosis and did not assess rates of recovery (Nevsimalova et al., 2021; Susta et al., 2022). The natural course of IH and all possible real-world influences were the subjects of a dynamic simulation model that achieved 76.1% convergence with the observed natural course of the disease (Susta et al., 2022).

The reason for IH remission and the clinical phenotype of future recovery awaits large prospective studies as well as better IH phenotyping.

4.1 | Instability of the diagnosis of IH versus NT2

The change of IH diagnosis to NT2 in two patients from our sample is not surprising, because the difference between these two hypersomnias is based solely on the number of SOREMPs in MSLT and there is low MSLT test-retest reliability in narcolepsy type 2 and IH (Lopez et al., 2017; Ruoff et al., 2018; Trotti et al., 2013), and there are suggestions that IH and NT2 may at least partially merge in one disease (Fronczek et al., 2020; Lammers et al., 2020).

TABLE 3 Whole-life major comorbidities and BMI

			Persisting hypersomnolence (except 2 subjects rediagnosed to NT2)		Between groups comparisons		
	All participants	Recovered	Undisputed IH	MPCH	Recovered versus Undisputed IH	Undisputed IH versus MPCH	Recovered versus MPCH
N	60 (100%)	10 (100%)	33 (100%)	15 (100%)			
Current BMI	26.2 (± 5.2)	27.1 (± 5.9)	25.2 (± 4.5)	28.6 (± 6.3)	n.s.	**0.035**	n.s.
Current BMI > 30 kg m^{-2}, *n* (%)	21 (35%)	3 (30%)	9 (27.3%)	9 (60%)	n.s.	n.s.	n.s.
Life prevalence depression + BD, *n* (%)	26 (43.3%)	3 (30%)	11 (33.3%)	11 (73.3%)	n.s.	**0.014**	**0.049**
Life prevalence anxiety, *n* (%)	15 (25%)	1 (10%)	5 (15.2%)	8 (53.3%)	n.s.	**0.012**	**0.040**
Antidepressants, *n* (%)	14 (23.3%)	1 (10%)	5 (15.2%)	7 (46.7%)	n.s.	**0.031**	n.s.
Life prevalence psychiatric diseases aggregated, *n* (%)	32 (53.3%)	4 (40%)	13 (39.4%)	14 (93.3%)	n.s.	**0.000**	**0.007**
Headache, *n* (%)	21 (35%)	1 (10%)	10 (30.3%)	9 (60%)	n.s.	n.s.	**0.034**
Hypertension, *n* (%)	15 (25%)	5 (50%)	5 (15.2%)	5 (33.3%)	**0.036**	n.s.	n.s.
Diabetes, *n* (%)	6 (10%)	3 (30%)	2 (6.1%)	1 (6.7%)	n.s.	n.s.	n.s.
Thyreopathy, *n* (%)	14 (23.3%)	0	8 (24.2%)	6 (40%)	n.s.	n.s.	n.s.
Gastrointestinal diseases, *n* (%)	21 (35%)	4 (40%)	12 (36.4%)	5 (33.3%)	n.s.	n.s.	n.s.
Autoimmune diseases, *n* (%)	10 (16.7%)	2 (20%)	6 (18.2)	1 (6.7%)	n.s.	n.s.	n.s.
Respiratory diseases, *n* (%)	13 (21.7%)	4 (40%)	6 (18.2)	5 (33.3%)	n.s.	n.s.	n.s.
Important infections, *n* (%)	14 (23.3%)	3 (30%)	5 (15.2)	6 (40%)	n.s.	n.s.	n.s.
Smoking, *n* (%)	22 (36.7%)	4 (40%)	11 (33.3%)	6 (40%)	n.s.	n.s.	n.s.
Somatic diseases aggregated, *n* (%)	41 (68.3)	9 (90%)	22 (66.7%)	10 (66.7%)	n.s.	n.s.	n.s.

Note: Bold values indicate the significance $p < 0.05$.
Abbreviations: BD, bipolar disorder; BMI, body mass index, IH, idiopathic hypersomnia; MPCH, Multiple Plausible Causes of Hypersomnolence; *n*, number; n.s., non-significant; NT2, narcolepsy type 2.

4.2 | Comorbidities

The occurrence of OSA in late middle-aged patients with IH does not go out of the larger range of the population. The HypnoLaus study on an unselected group in the age range of 40–85 years using standard examination and diagnostic criteria determined the prevalence of sleep apnea according to AHI ≥ 15 in 23.4% of women and in 49.7% of men (Heinzer et al., 2015). Similar results were obtained in the study of Czechs above 50 years without any sleep disorder symptoms (Dostálová et al., 2020). Participants of our study are from this point underdiagnosed because only a part underwent a new night recording. The previous diagnosis of IH may prevent the suspicion of sleep apnea. Surprisingly high is the proportion of untreated and not efficiently treated patients with OSA (75%), which may be explained by the low or no subjective improvement in OSA treatment in patients with hypersomnolence.

The prevalence of RLS in the general Euro-American population was found in 2.7% up to 11%, increasing with age and affecting more women (Allen et al., 2005; Berger et al., 2004), thus the RLS prevalence in our IH cohort is higher and extremely high in the Multiple Plausible Causes of Hypersomnolence group. This may be at least partially explained by the fact that the patients in this group suffer from serious diseases. According to the recent concept, RLS occurs more frequently in important diseases without any direct aetiological link with RLS, and these diseases are supposed to trigger the manifestation of RLS symptoms in people with a low genetic disposition (Trenkwalder et al., 2016). This may be the case in our patients from the Multiple Plausible Causes of Hypersomnolence group. The patients in the Multiple Plausible Causes of Hypersomnolence group were also frequently exposed to antidepressants, which may facilitate RLS (Winkelman, 2022). Nevertheless, the occurrence of RLS and periodic limb movements in sleep in older IH subjects should be studied systematically.

At least one psychiatric illness was reported by 53.3% of patients, and 43.3% reported depression or bipolar disorder with severe depression. A recent meta-analysis of cross-sectional studies on the prevalence of depression and depressive symptoms among outpatients found an overall pooled prevalence of depression or depressive symptoms of 27.0%. Studies originating from neurology departments had a mean of 35% with a 95% confidence interval of 30%–40% (Wang et al., 2017), which is lower than the prevalence in our sample. The prevalence rates can only be superficially compared because we

are considering lifetime occurrence of depression; on the other hand, we may have missed some cases that were not reported due to psychiatric stigma and cases of depression that were not examined by a psychiatrist. The prevalence of depression in IH is high, this fact has been reported by several authors (Galuskova & Sonka, 2021), and it is a difficult clinical decision whether a case should be diagnosed as IH or depression with hypersomnia (Buskova et al., 2022). The question still remains to what extent mood disorders are related to the biological background of IH and to what extent they are a psychophysiological consequence of IH and are biologically independent disorders. The same uncertainty of causality with IH applies to the finding of anxiety in 25% of our sample, which is higher than the prevalence of anxiety of 7.4% found in one large national study (Kagstrom et al., 2019) and compared with the 10%–14% reported in a recent large review (Penninx et al., 2021). Anxiety is also comorbid with many disorders, including depression, and affects more women (Penninx et al., 2021). Unlike depression, the diagnosis of anxiety has not been in all cases established by a psychiatrist and, on the other hand, mild forms were perhaps overlooked in our study. Another unresolved question is whether antidepressant treatment can prevent the finding that IH tends to disappear. Based on a careful description of the symptoms and their history, and on the antidepressants used (venlafaxine, sertraline, fluoxetine, bupropion and escitalopram, all at standard or low doses), we hypothesize that the five patients taking antidepressants in the group with undisputed IH still had true IH hypersomnolence.

The prevalence of other illnesses besides psychiatric and sleep-related ones could not be analysed in detail because we were mostly dependent on information provided by the patient. The study by Nevsimalova et al. (2021) provides more details on comorbidities with similar general results. We consider important the information that comorbidities, except for psychiatric comorbidities, do not exceed the normal range of prevalence in the general population and thus do not help to clarify the pathophysiology of IH.

4.3 | Failure to meet diagnostic criteria years after the diagnosis

Our results show that a quarter of patients who have been diagnosed with IH in the past are still sleepy, but currently have another new disease or diseases that can induce hypersomnolence (in all cases these new diseases were clinically very significant). Sensu stricto, in such cases, the patient should be labelled with a second diagnosis besides IH—hypersomnia caused by a medical disorder or hypersomnia caused by medication, or hypersomnia associated with a psychiatric disorder—according to ICSD-3 (American Academy of Sleep Medicine, 2014). It probably does not work like that in real life but, more importantly, the first-time-consulted sleepy patient who theoretically suffers from IH and at the same time has another disease well known to cause hypersomnolence (OSA, depression, night sleep disruption due to nocturnal asthma, pain, etc.) will never receive an IH designation because the criterion requiring that "the hypersomnolence and/or the findings on the MSLT are not better explained by another sleep disorder, another medical or psychiatric disorder, or drug or medication use" is not met and, in real medicine, no physician will consider IH in front of such a patient because the reason for the hypersomnolence other than IH seems obvious. This may have practical relevance to the persistence of sleepiness in well-treated diseases thought to cause sleepiness; for example, persistent sleepiness in OSA (Javaheri & Javaheri, 2020). Also, the lower likelihood of an IH diagnosis in persons with other diseases may partly explain why we believe that IH usually begins in young adulthood (Billiard et al., 1998). Thus, we need an independent strong biomarker of IH allowing the diagnosis and confirmation of IH even in the presence of other diseases potentially causing hypersomnolence.

4.4 | Limitations

The study has several limitations. First, the study is not prospective, and information concerning comorbidities is based mostly on the information provided by patients. Second, the new nocturnal PSG and MSLT were not part of the study, and only 26 subjects underwent the new PSG independently in this study. One can speculate that the new nocturnal recording could reveal more OSA and more subjects with other nocturnal sleep imperfections and raise even more questions. Third, the study sample is small (despite being one of the largest in IH research), which is due to the low prevalence of IH. The selection bias is not excluded because we do not know the clinical status of patients who were not contacted and who were not included as they did not meet the study criteria. Fourth, the degree of influence of other diseases on hypersomnolence was not analysed because it was neither feasible nor the aim of this study. Fifth, the study does not report PSG and MSLT values at the time of initial diagnosis because some of these were obtained more than 20 years ago and detailed results of these tests could not be traced.

5 | CONCLUSION

Symptoms of IH are present in the majority of patients even after years of duration and, in more than half of them, there was no doubt that the diagnostic criteria are still met.

One-sixth of the patients have lost hypersomnolence and are free of waking supportive treatment. A quarter of patients suffer from hypersomnia attributable to other newly diagnosed diseases. If these patients had not been diagnosed with IH in the past, IH would probably not even be considered at present.

The study does not question IH as a separate nosological entity, it seeks to deepen the understanding of this disease, and in the context of the presented results points out possible implications of the current diagnostic approach. The last criterion of ICSD-3, which requires the absence of other diseases causing sleepiness, thus narrows the group of patients in whom the diagnosis can be made to otherwise healthy persons. The study highlights the importance of regular follow-up of patients with IH in terms of the nature of sleep–wake disorders and from a psychiatric perspective.

AUTHOR CONTRIBUTIONS

Karel Šonka: Conceptualization; investigation; funding acquisition; writing – original draft; methodology; validation; writing – review and editing; project administration. **Eva Feketeová:** Conceptualization; investigation; writing – original draft; validation; writing – review and editing; methodology. **Soňa Nevšímalová:** Conceptualization; investigation; validation; writing – review and editing. **Eszter Maurovich Horvat:** Investigation; writing – review and editing. **Iva Příhodová:** Conceptualization; investigation; validation; writing – review and editing. **Simona Dostálová:** Investigation; validation; writing – review and editing. **Karolína Galušková:** Investigation; writing – review and editing. **Martin Milata:** Investigation; writing – review and editing; software. **Jitka Bušková:** Investigation; validation; writing – review and editing. **Marek Susta:** Conceptualization; methodology; validation; writing – review and editing; formal analysis; software.

ACKNOWLEDGEMENTS

The study was supported by Ministry of Health of the Czech Republic, grant number NU20-04-00088. Karel Šonka, Soňa Nevšímalová, Iva Příhodová, Simona Dostálová, Martin Milata and Karolína Galušková are supported by Charles University Cooperation program in neuroscience.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Karel Šonka https://orcid.org/0000-0001-5773-9656
Eva Feketeová https://orcid.org/0000-0002-7746-3797
Soňa Nevšímalová https://orcid.org/0000-0003-0083-3742
Eszter Maurovich Horvat https://orcid.org/0009-0008-5784-0947
Iva Příhodová https://orcid.org/0000-0002-3327-5487
Simona Dostálová https://orcid.org/0000-0002-4421-9958
Karolína Galušková https://orcid.org/0000-0002-9313-4571
Martin Milata https://orcid.org/0009-0001-9982-6421
Jitka Bušková https://orcid.org/0000-0001-8590-8031
Marek Susta https://orcid.org/0000-0003-2544-4751

REFERENCES

Allen, R. P., Walters, A. S., Montplaisir, J., Hening, W., Myers, A., Bell, T. J., & Ferini-Strambi, L. (2005). Restless legs syndrome prevalence and impact: REST general population study. *Archives of Internal Medicine*, *165*(11), 1286–1292. https://doi.org/10.1001/archinte.165.11.1286

American Academy of Sleep Medicine (2005). International classification of sleep disorders. 2nd ed.: *Diagnostic and coding manual*. American Academy of Sleep Medicine.

American Academy of Sleep Medicine (Ed.). (2014). *International classification of sleep disorders* (3rd ed.). American Academy of Sleep Medicine.

Anderson, K. N., Pilsworth, S., Sharples, L. D., Smith, I. E., & Shneerson, J. M. (2007). Idiopathic hypersomnia: A study of 77 cases. *Sleep*, *30*(10), 1274–1281. https://doi.org/10.1093/sleep/30.10.1274

Arnulf, I., Leu-Semenescu, S., & Dodet, P. (2022). Precision medicine for idiopathic hypersomnia. *Sleep Medicine Clinics*, *17*(3), 379–398. https://doi.org/10.1016/j.jsmc.2022.06.016

Arnulf, I., Thomas, R., Roy, A., & Dauvilliers, Y. (2023). Update on the treatment of idiopathic hypersomnia: Progress, challenges, and expert opinion. *Sleep Medicine Reviews*, *69*, 101766. https://doi.org/10.1016/j.smrv.2023.101766

Bassetti, C., & Aldrich, M. S. (1997). Idiopathic hypersomnia. A series of 42 patients. *Brain*, *120*(Pt 8), 1423–1435. https://doi.org/10.1093/brain/120.8.1423

Berger, K., Luedemann, J., Trenkwalder, C., John, U., & Kessler, C. (2004). Sex and the risk of restless legs syndrome in the general population. *Archives of Internal Medicine*, *164*(2), 196–202. https://doi.org/10.1001/archinte.164.2.196

Billiard, M., Merle, C., Carlander, B., Ondze, B., Alvarez, D., & Besset, A. (1998). Idiopathic hypersomnia. *Psychiatry and Clinical Neurosciences*, *52*(2), 125–129. https://doi.org/10.1111/j.1440-1819.1998.tb00987.x

Billiard, M., & Sonka, K. (2022). Idiopathic hypersomnia: Historical account, critical review of current tests and criteria, diagnostic evaluation in the absence of biological markers and robust electrophysiological diagnostic criteria. *Nature and Science of Sleep*, *14*, 311–322. https://doi.org/10.2147/NSS.S266090

Bruck, D., & Parkes, J. D. (1996). A comparison of idiopathic hypersomnia and narcolepsy-cataplexy using self report measures and sleep diary data. *Journal of Neurology, Neurosurgery, and Psychiatry*, *60*(5), 576–578. https://doi.org/10.1136/jnnp.60.5.576

Buskova, J., Novak, T., Miletinova, E., Kralova, R., Kost Alova, J., Klikova, M., & Veldova, K. (2022). Self-reported symptoms and objective measures in idiopathic hypersomnia and hypersomnia associated with psychiatric disorders: A prospective cross-sectional study. *Journal of Clinical Sleep Medicine*, *18*(3), 713–720. https://doi.org/10.5664/jcsm.9702

Dauvilliers, Y., Bogan, R. K., Arnulf, I., Scammell, T. E., St Louis, E. K., & Thorpy, M. J. (2022). Clinical considerations for the diagnosis of idiopathic hypersomnia. *Sleep Medicine Reviews*, *66*, 101709. https://doi.org/10.1016/j.smrv.2022.101709

Dostálová, S., Šusta, M., Nepožitek, J., Peřinová, P., Příhodová, I., Ibarburu Lorenzo y Losada, V., DallAntonia, I., Bezdicek, O., Nikolai, T., & Šonka, K. (2020). Polysomnographic findings in individuals over 50 years of age lacking subjective signs of sleep disturbance (In Czech). *Ceska a Slovenska Neurologie a Neurochirurgie*, *83*, 57–63.

Evangelista, E., Lopez, R., & Dauvilliers, Y. (2018). Update on treatment for idiopathic hypersomnia. *Expert Opinion on Investigational Drugs*, *27*(2), 187–192. https://doi.org/10.1080/13543784.2018.1417385

Fronczek, R., Arnulf, I., Baumann, C. R., Maski, K., Pizza, F., & Trotti, L. M. (2020). To split or to lump? Classifying the central disorders of hypersomnolence. *Sleep*, *43*(8), zsaa044. https://doi.org/10.1093/sleep/zsaa044

Galuskova, K., & Sonka, K. (2021). Idiopathic hypersomnia and depression, the challenge for clinicians and researchers. *Prague Medical Report*, *122*(3), 127–139. https://doi.org/10.14712/23362936.2021.13

Gaskin, C. J., & Happell, B. (2014). On exploratory factor analysis: A review of recent evidence, an assessment of current practice, and recommendations for future use. *International Journal of Nursing Studies*, *51*(3), 511–521. https://doi.org/10.1016/j.ijnurstu.2013.10.005

Heinzer, R., Vat, S., Marques-Vidal, P., Marti-Soler, H., Andries, D., Tobback, N., Mooser, V., Preisig, M., Malhotra, A., Waeber, G., Vollenweider, P., & Haba-Rubio, J. (2015). Prevalence of sleep-disordered breathing in the general population: The HypnoLaus study. *The Lancet Respiratory Medicine*, *3*(4), 310–318. https://doi.org/10.1016/S2213-2600(15)00043-0

Inoue, Y., Tabata, T., & Tsukimori, N. (2021). Efficacy and safety of modafinil in patients with idiopathic hypersomnia without long sleep time: A multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study. *Sleep Medicine*, *80*, 315–321. https://doi.org/10.1016/j.sleep.2021.01.018

Javaheri, S., & Javaheri, S. (2020). Update on persistent excessive daytime sleepiness in OSA. *Chest*, *158*(2), 776–786. https://doi.org/10.1016/j.chest.2020.02.036

Johns, M. W. (1991). A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep*, *14*(6), 540–545. https://doi.org/10.1093/sleep/14.6.540

Kagstrom, A., Alexova, A., Tuskova, E., Csajbok, Z., Schomerus, G., Formanek, T., Mladá, K., Winkler, P., & Cermakova, P. (2019). The treatment gap for mental disorders and associated factors in The Czech Republic. *European Psychiatry*, *59*, 37–43. https://doi.org/10.1016/j.eurpsy.2019.04.003

Kim, T., Lee, J. H., Lee, C. S., & Yoon, I. Y. (2016). Different fates of excessive daytime sleepiness: Survival analysis for remission. *Acta Neurologica Scandinavica*, *134*(1), 35–41. https://doi.org/10.1111/ane.12504

Lammers, G. J., Bassetti, C. L. A., Dolenc-Groselj, L., Jennum, P. J., Kallweit, U., Khatami, R., Lecendreux, M., Manconi, M., Mayer, G., Partinen, M., Plazzi, G., & Dauvilliers, Y. (2020). Diagnosis of central disorders of hypersomnolence: A reappraisal by European experts. *Sleep Medicine Reviews*, *52*, 101306. https://doi.org/10.1016/j.smrv.2020.101306

Leu-Semenescu, S., Nittur, N., Golmard, J. L., & Arnulf, I. (2014). Effects of pitolisant, a histamine H3 inverse agonist, in drug-resistant idiopathic and symptomatic hypersomnia: A chart review. *Sleep Medicine*, *15*(6), 681–687. https://doi.org/10.1016/j.sleep.2014.01.021

Lopez, R., Doukkali, A., Barateau, L., Evangelista, E., Chenini, S., Jaussent, I., & Dauvilliers, Y. (2017). Test-retest reliability of the multiple sleep latency test in central disorders of Hypersomnolence. *Sleep*, *40*(12), zsx164. https://doi.org/10.1093/sleep/zsx164

Mayer, G., Benes, H., Young, P., Bitterlich, M., & Rodenbeck, A. (2015). Modafinil in the treatment of idiopathic hypersomnia without long sleep time—A randomized, double-blind, placebo-controlled study. *Journal of Sleep Research*, *24*(1), 74–81. https://doi.org/10.1111/jsr.12201

Nevsimalova, S., Susta, M., Prihodova, I., Horvat, E. M., Milata, M., & Sonka, K. (2021). Idiopathic hypersomnia: A homogeneous or heterogeneous disease? *Sleep Medicine*, *80*, 86–91. https://doi.org/10.1016/j.sleep.2021.01.031

Ohayon, M. M. (2008). From wakefulness to excessive sleepiness: What we know and still need to know. *Sleep Medicine Reviews*, *12*(2), 129–141. https://doi.org/10.1016/j.smrv.2008.01.001

Penninx, B. W., Pine, D. S., Holmes, E. A., & Reif, A. (2021). Anxiety disorders. *Lancet*, *397*(10277), 914–927. https://doi.org/10.1016/S0140-6736(21)00359-7

Roth, B. (1976). Narcolepsy and hypersomnia: Review and classification of 642 personally observed cases. *Schweizer Archiv für Neurologie, Neurochirurgie Und Psychiatrie*, *119*(1), 31–41.

Ruoff, C., Pizza, F., Trotti, L. M., Sonka, K., Vandi, S., Cheung, J., Pinto, S., Einen, M., Simakajornboon, N., Han, F., Peppard, P., Nevsimalova, S., Plazzi, G., Rye, D., & Mignot, E. (2018). The MSLT is repeatable in narcolepsy type 1 but not narcolepsy type 2: A retrospective patient study. *Journal of Clinical Sleep Medicine*, *14*(1), 65–74. https://doi.org/10.5664/jcsm.6882

Susta, M., Sonka, K., Bizik, G., Petranek, S., & Nevsimalova, S. (2022). Idiopathic hypersomnia-a dynamic simulation model. *Frontiers in Neurology*, *13*, 902637. https://doi.org/10.3389/fneur.2022.902637

Trenkwalder, C., Allen, R., Hogl, B., Paulus, W., & Winkelmann, J. (2016). Restless legs syndrome associated with major diseases: A systematic review and new concept. *Neurology*, *86*(14), 1336–1343. https://doi.org/10.1212/WNL.0000000000002542

Trotti, L. M. (2017a). Idiopathic hypersomnia. *Sleep Medicine Clinics*, *12*(3), 331–344. https://doi.org/10.1016/j.jsmc.2017.03.009

Trotti, L. M. (2017b). Waking up is the hardest thing I do all day: Sleep inertia and sleep drunkenness. *Sleep Medicine Reviews*, *35*, 76–84. https://doi.org/10.1016/j.smrv.2016.08.005

Trotti, L. M., Saini, P., Bliwise, D. L., Freeman, A. A., Jenkins, A., & Rye, D. B. (2015). Clarithromycin in gamma-aminobutyric acid-related hypersomnolence: A randomized, crossover trial. *Annals of Neurology*, *78*(3), 454–465. https://doi.org/10.1002/ana.24459

Trotti, L. M., Staab, B. A., & Rye, D. B. (2013). Test-retest reliability of the multiple sleep latency test in narcolepsy without cataplexy and idiopathic hypersomnia. *Journal of Clinical Sleep Medicine*, *9*(8), 789–795. https://doi.org/10.5664/jcsm.2922

Vernet, C., & Arnulf, I. (2009). Idiopathic hypersomnia with and without long sleep time: A controlled series of 75 patients. *Sleep*, *32*(6), 753–759. https://doi.org/10.1093/sleep/32.6.753

Wang, J., Wu, X., Lai, W., Long, E., Zhang, X., Li, W., Zhu, Y., Chen, C., Zhong, X., Liu, Z., Wang, D., & Lin, H. (2017). Prevalence of depression and depressive symptoms among outpatients: A systematic review and meta-analysis. *BMJ Open*, *7*(8), e017173. https://doi.org/10.1136/bmjopen-2017-017173

Winkelman, J. W. (2022). Treating severe refractory and augmented restless legs syndrome. *Chest*, *162*(3), 693–700. https://doi.org/10.1016/j.chest.2022.05.014

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Šonka, K., Feketeová, E., Nevšímalová, S., Horvat, E. M., Příhodová, I., Dostálová, S., Galušková, K., Milata, M., Bušková, J., & Susta, M. (2023). Idiopathic hypersomnia years after the diagnosis. *Journal of Sleep Research*, e14011. https://doi.org/10.1111/jsr.14011