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PREVALENCE OF SLEEP DISORDERS IN ADULTS WITH DOWN SYNDROME: A COMPARATIVE STUDY OF SELF-REPORTED, ACTIGRAPHIC AND POLYGRAPHIC

FINDINGS

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Disclosure Statement

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ABSTRACT

Study Objectives: Sleep problems are often undetected in adults with Down syndrome (DS). Our objective was to determine the prevalence of sleep disorders in adults with DS through self-reported and objective sleep measures.

Methods: We performed a community-based cross-sectional study of 54 adults with DS not referred for sleep disorders. Two polysomnography (PSG) sleep studies were performed. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI); daytime sleepiness was evaluated using the Epworth Sleepiness Scale (ESS) and the risk for the sleep apnea syndrome (OSA) was identified using the Berlin Questionnaire (BQ). Participants' sleep/wake pattern was assessed from sleep diaries and by wrist actigraphy. PSQI, ESS, and PSG measures were compared with 35 sex-, age-, and body mass index-matched patients in the control groups.

Results: In PSG measures, adults with DS showed lower sleep efficiency (69 ± 17.7 versus 81.6 ± 11 ; $P < .001$), less rapid eye movement sleep (9.4 ± 5.8 versus 19.4 ± 5.1 ; $P < .001$), a higher prevalence of OSA (78% versus 14%; $P < .001$), and a higher apnea-hypopnea index (23.5 ± 24.5 versus 3.8 ± 10.5 ; $P < .001$) than patients in the control group. In the DS group, the questionnaires (mean PSQI 3.7 ± 2.9 ; mean ESS 6.3 ± 4.5 and mean BQ 1 ± 0) did not reflect the sleep disturbances detected on the PSG. Actigraphy data recorded daytime sleep that was not self-reported (118.2 ± 104.2 minutes).

Conclusions: Adults with DS show severe sleep disruption and a high prevalence of OSA, undetected by self-reported sleep measures. Actigraphy, PSG, and validated simplified devices for screening OSA should be routinely recommended for this population because treatment of sleep disorders can contribute to healthy aging.

Keywords: actigraphy, aging, Down syndrome, obstructive sleep apnea, polysomnography, self-reported sleep quality, sleep disruption

BRIEF SUMMARY

Current Knowledge/Study Rationale: The few studies to date on sleep disorders in adults with Down syndrome (DS) are mainly descriptive, based on self-reported measures only, and performed in small samples. Objective polysomnography and actigraphy studies in this setting are therefore lacking. This study determined the prevalence of sleep disorders in adults with DS using both self-reported and objective sleep measures.

Study Impact: This is an objective, community-based sleep study conducted in a large sample of adults with DS. Although the participants were not referred for sleep disorders, we observed a high prevalence of sleep disruption, obstructive sleep apnea, and napping during the day. These findings were not detected by current self-reported sleep measures or reported by caregivers.

INTRODUCTION

Life expectancy for patients with Down syndrome (DS) has increased dramatically in recent years and is now over 60 years in developed countries.¹ This advance is largely because of improvements in medical care provided for associated comorbidities. Treatment of sleep disorders in patients with DS may further help improve cognition, general health, and quality of life for this population.^{2,3} However, consensus based sleep guidelines for adults with DS are lacking. Sleep problems are commonly reported in the DS population, but unlike for children with DS,⁴⁻⁷ data on the prevalence, severity, and health consequences of sleep disorders in adults with DS are scarce.⁸ Most previous studies have been descriptive and based on small samples using self-reported sleep measures in cohorts with mixed intellectual disabilities.^{3,9} These reports, based on caregiver ratings, display a wide range in the prevalence of sleep disorders: the prevalence of sleep apnea ranges from 13.3% to 40% and behavioral sleep disturbances range from 22.7% to 60%.^{3,10,11} However, in the adult population, these figures, which are based on clinical reports and self-reported sleep measures, may be underestimated when compared to objective sleep data, as is the case in the pediatric DS population.⁶

To our knowledge, only two previous studies have objectively evaluated sleep in adults with DS using full polysomnography (PSG), the standard reference technique for diagnosing sleep disorders. Both studies evidenced a high prevalence of obstructive sleep apnea (OSA).^{12,13} In these studies, however, sample size was small, adults with DS were relatively young (12 and 6 participants with a median age of 33 and 35 years, respectively),^{12,13} sex differences were not taken into account, and participants were assessed only for OSA. Recently, the Adult Health Care Workgroup of the Down Syndrome Medical Interest Group USA (DSMIG-USA) identified sleep apnea as a co-occurring medical condition and paid special attention to adults with DS, though the resulting data are somewhat sparse because of the small size and selection bias of the studied samples.¹⁵ The group highlighted the need to confirm these objective sleep findings in a larger, community-based population of adults with DS in order to generalize sleep data and develop specific screening and treatment guidelines for OSA.

The objective of the current study was to characterize and determine the prevalence of sleep disorders in a large, community-based sample of adult participants with DS and to compare the results obtained with self-reported and objective sleep measures.

METHODS

Study design and participants

Participants with DS were included from the Down Alzheimer Barcelona Neuroimaging Initiative (DABNI), a research program developed by the Barcelona Down Medical Center (BDMC) of the Catalan Down Syndrome Foundation together with Hospital de la Santa Creu i Sant Pau in Barcelona (HSCSP).^{15,16}

The BDMC is a non-profit organization that provides medical and social support to people with DS in Catalonia. Its active database includes more than 2,000 individuals. The BDMC and HSCP have jointly developed two projects: the Health Plan for Adults with DS to screen for medical comorbidities and DABNI17 and a research initiative for the study of Alzheimer disease in patients with DS. The former of these two projects, the Health Plan for Adults with DS, is population based and it includes more than 500 individuals. From September 2014 to June 2016, when the data for the current manuscript were collected, 380 participants participated in the DABNI research project, 54 of whom agreed to participate in the additional sleep study.

All participants underwent a full medical, neurological, and neuropsychological evaluation. A sleep specialist explained the study in detail to all participants with DS and their legal tutors prior to their inclusion in the study. Written informed consent was obtained from all parents or legal caregivers and assent was acquired from the participant. The study was approved by the local ethics committee following the principles stated in the Declaration of Helsinki.

Inclusion criteria were good general condition, age older than 18 years, and ability to understand and accept the study procedures. We included only participants with mild to moderate mental retardation according to International Classification of Diseases, Tenth Edition criteria (Intelligence Quotient scores > 34). Exclusion criteria were severe mental retardation, history of conditions that could affect brain structure or function (such as stroke or traumatic brain injury), and the use of new psychoactive drugs in the 3 months preceding the sleep studies. Sleep complaints were not considered in the inclusion criteria.

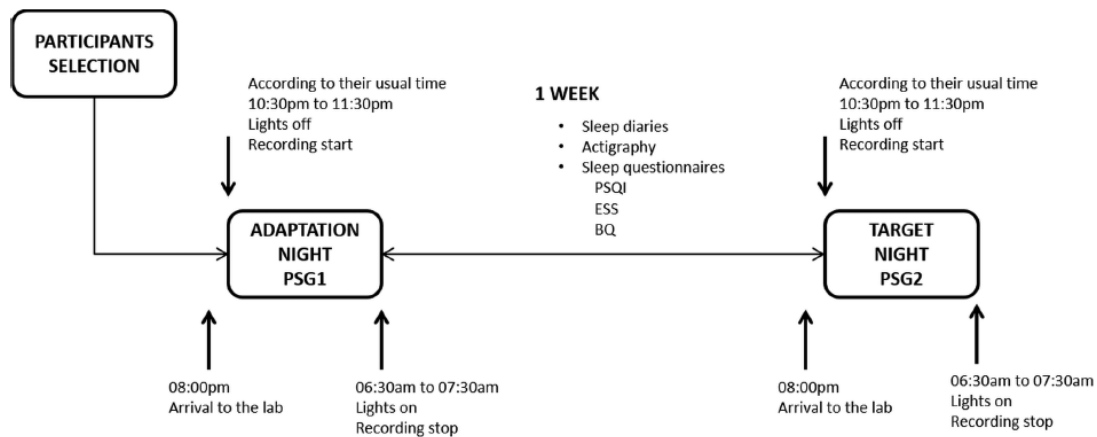
A control group matched for age, sex and body mass index (BMI) was selected retrospectively from a pool of volunteers from the general population who had performed nocturnal PSG in the sleep laboratory at the Drug Research Center of the Research Institute at Hospital de la Santa Creu i Sant Pau. The medical history of these participants was recorded and all had physical and neurological examinations before the PSG. We excluded participants with a history of chronic medical disorders such as chronic obstructive pulmonary disease,

uncontrolled diabetes, cardiovascular disease, or psychiatric disorders. Participants under treatment for sleep disorders and those with any neurodegenerative diseases or with neurological conditions that could affect brain function, such as stroke, were also excluded.

Sleep Evaluation

All participants with DS underwent a full sleep evaluation. This included a sleep interview with a sleep specialist, and a self-reported and objective evaluation of nocturnal sleep and the circadian sleep-wake cycle. Nocturnal sleep was studied objectively by means of two full video PSG studies performed 1 week apart. Sleep/wake cycles were collected via sleep diaries and actigraphy was conducted in between the two PSG studies. Figure 1 shows an outline of the procedure.

Figure 1



BQ = Berlin Questionnaire, ESS = Epworth Sleepiness Scale, PSG = polysomnography, PSQI = Pittsburgh Sleep Quality Index.

Subjective sleep questionnaires

All participants were given a notebook that included sleep questionnaires and sleep diaries to be completed by the caregivers. The sleep questionnaires included the validated Spanish version of the following scales: the Pittsburgh Sleep Quality Index (PSQI) to assess patients' self-reports of sleep quality;¹⁸ the Epworth Sleepiness Scale (ESS) to evaluate somnolence (with a modification of the last question about the DS person as a passenger in a car while stopped for a few minutes in traffic);²⁹ and the Berlin Questionnaire (BQ) to identify participants at risk for the sleep apnea syndrome.^{20,21}

Actigraphy and sleep diaries

During the week between the two PSG studies, participants wore a wrist actigraph (Actigraph, Actilife 5). They also completed a sleep diary with daily reports about quality of

sleep and sleep initiation, and maintenance variables: bedtime, wake time, sleep latency (SL), and wake after sleep onset (WASO).

Nocturnal polysomnography (PSG)

Sleep *recordings* were performed in individual, sound-attenuated, temperature-regulated rooms in the sleep laboratory at our sleep unit. Participants were continuously supervised by qualified technical staff and were recorded on video/audio with the use of an infrared camera. PSG tests were started at their median bedtime as defined by the prospective diary collection, with a recording time of 8 hours. To minimize PSG-related disturbances, the first PSG session was an adaptation night to familiarize participants with the laboratory and recording procedures. The second PSG was the target night from which results were obtained for the final sleep evaluations. The morning after each of the two PSG nights, all participants completed a questionnaire about their sleep quality in the laboratory. We compared this questionnaire with their usual reported sleep quality at home.

PSG sleep data were acquired by means of the Compumedics E Series System (Compumedics, Victoria, Australia). All-night video PSG-recordings included: (1) 19 electroencephalography channels referenced to averaged mastoid electrodes (A1-A2) according to the international 10–20 system; (2) 2 electrooculographic channels; (3) 4 surface electromyographic channels: 2 from the mentalis, 1 from the right anterior tibialis and 1 from the left anterior tibialis in lower limbs; and (4) 6 channels to monitor respiratory function: 1 for oximetry, 2 for oronasal airflow using a thermistor and nasal cannula, 2 to record thoracoabdominal movements by inductance plethysmography, and a microphone at the suprasternal notch to detect snoring.

Sleep stages were visually scored for 30-second epochs according to the guidelines of the American Academy of Sleep Medicine (AASM).²² Profusion Sleep Software was used (Compumedics PSG3 version 3.4). Scoring was performed by an experienced sleep technologist and later reviewed by an accredited sleep somnologist.

Arousals were defined using AASM criteria. Respiratory variables included the apnea-hypopnea index (AHI), defined as the sum of all apneas (> 90% reduction in airflow for > 10 seconds) and all hypopneas (airflow reduction greater than 30% for at least 10 seconds with an oxygen saturation decrease of approximately 3% or a cortical awakening) per hour of sleep, and mean oxygen saturation during the night (SpO₂).²³

Periodic limb movements and abnormal rapid eye movement (REM) sleep behavior disorder were defined according to the International Classification of Sleep Disorders.²⁴

Sleep data from the control group were obtained retrospectively. The control group underwent a 1-night PSG study performed using the same monitoring techniques as the DS group and ESS and PSQI scores were obtained. This group did not provide actigraphy data or answer the BQ.

Statistical Analyses

Statistical analyses were performed using SPSS version 23 software (IBM Corp., Armonk, New York, United States). Demographics and sleep scores were compared between groups by means of t tests for repeated measures. The statistical threshold was set at .05. To assess the differences between the various sleep techniques performed in participants with DS, general lineal models with one within-participant factor (techniques, three levels) were applied separately to each sleep variable. For all variables, results were pair-compared by means of the t test for repeated measures if required. Greenhouse-Geisser correction was used. The Pearson correlation was applied to evaluate the relationship between sleep variables.

RESULTS

Participant characteristics

Table 1 shows the participants' demographic characteristics.

Table 1—Demographic characteristics of study participants with Down syndrome and in the control group.

	DS (n = 47)	Controls (n = 35)
Age, mean (SD), years	39.6 (12.4)	39.2 (12.9)
Male sex, n (%)	29.0 (61.7)	20.0 (57.1)
BMI, mean (SD), kg/m ²	26.8 (4.1)	25.4 (4.3)
Dementia	5.0 (10.6)	0.0 (0.0)
Hypothyroid, n (%)	18.0 (38.3)	0.0 (0.0)
Hypertension, n (%)	1.0 (2.1)	2.0 (5.7)
Cardiovascular disease, n (%)	2.0 (4.3)	0.0 (0.0)

BMI = body mass index, DS = Down syndrome, SD = standard deviation.

The mean age of participants with DS was 39.6 (range 20–62 years). Ten participants were obese (BMI > 30 kg/m²), 19 were overweight, and 18 had a normal BMI (BMI 18 to < 25 kg/m²).

The oropharyngeal examination showed 6 participants (12.7%) had a Mallampati class III airway and 41 participants (87.2%) had a Mallampati class IV airway. Four had undergone adenoidectomy, and one had undergone tongue reduction. Clinically, 17 participants presented a nonclinically significant heart murmur and 2 participants had undergone surgery for a congenital heart defect with minimal residual cardiac insufficiency. Five patients were being treated with levothyroxine, 12 with antidepressants, 2 with benzodiazepines, 5 with antipsychotics, 1 with gabapentin, and 1 with topiramate. Twelve participants were medication free. There were no significant differences in the sociodemographic variables in sleep measures (except for the periodic limb movement index in PSG data; see next paragraphs) among participants with DS on antidepressant medication and those who were not taking antidepressants (Table S1 in the supplemental material). Six adults with DS had Alzheimer disease dementia, but their exclusion did not change the results (Table S2 in the supplemental material).

Forty participants (85.1%) lived at home with a family member, 4 (8.5%) lived in an independent but supervised apartment, and 3 (6.4%) lived in a nursing home. Thirty-five individuals in the control group were recruited from the sleep laboratory database. No statistically significant differences were observed between the DS group and control group regarding mean age: 39.2 years (range 18–71) ($P = .89$). Neither were statistically significant differences found regarding mean BMI: 25.4 (20–35.1) kg/m², ($P = .14$).

Table 2—Scores for the sleep questionnaires in participants with Down syndrome and in the control group.

Questionnaire	DS (n = 47)	Controls (n = 35)
PSQI	3.7 (2.9) **	5.7 (2.8)
ESS	6.3 (4.5) *	8.8 (5.8)
BQ	1.0 (0.0)	NA

Data are presented as mean (standard deviation). Asterisks indicate statistical significance: * = $P < .05$, ** = $P < .01$. BQ = Berlin Questionnaire, DS = Down syndrome, ESS = Epworth Sleepiness Scale, NA = not available, PSQI = Pittsburgh Sleep Quality Index.

Subjective sleep data

Sleep questionnaires were appropriately completed by caregivers for 40 participants with DS. Compared to patients in the control group, participants with DS had significantly lower ESS ($P = .04$) and PSQI ($P = .002$) scores. Table 2 shows the mean global sleep questionnaire scores for both groups. In the DS group, the mean values of all self-reported sleep measures were within normal limits: (1) ESS suggested somnolence ($ESS > 10$) in 8 participants (17.0%) but no participants presented severe somnolence ($ESS > 16$); (2) PSQI suggested sleep disorders ($PSQI > 5$) in 9 participants (19.2%); and (3) BQ suggested sleep apneas in 2 participants (4.3 %).

In the control group, the mean ESS score was within the normal range ($ESS < 10$). The mean PSQI score was slightly above the pathological score ($PSQI > 5$) but it was within the range described in previous large scale PSQI normative studies in the general population.²⁵

No statistical differences between males and females were observed for any of these variables in either group.

Sleep diary data

Table 3 shows sleep initiation and maintenance parameters from sleep diaries from participants with DS. The sleep diaries showed normal SL (< 20 minutes) and normal sleep efficiency (SE; $> 90\%$). Two participants had an SL longer than 30 minutes, and 10 participants had an SE under 85%.

Table 3—Comparison of sleep initiation and maintenance variables between sleep diary, actigraphy, and polysomnography in participants with Down syndrome.

Sleep Parameters	Sleep Diary (D)	Actigraphy (A)	Polysomnography (P)	mANOVA
TIB (minutes)	542.4 (61.4)	536.1 (50.2)	483.0 (8.6)	D:P**, A:P**
SL (minutes)	15.5 (10.4)	26.2 (20.2)	26.1 (20.2)	D:P*, D:A**
TST (minutes)	501.7 (70.3)	383.9 (72.4)	340.9 (84.1)	D:P**, D:A**, P:A*
WASO (minutes)	28.5 (41.6)	125.7 (64.0)	103.9 (75.7)	D:P**, D:A**, P:A*
SE (%)	92.1 (8.4)	71.8 (12.0)	70.7 (17.3)	D:P**, D:A**

Data are presented as mean (standard deviation). Symbols indicate statistical significance: + = $P < .10$, * = $P < .05$, ** = $P < .01$ for comparisons between sleep diary (D), actigraphy (A), and polysomnography (P). mANOVA = multivariate analysis of variance, SE = sleep efficiency ($100 \times [TST / TIB]$), SL = sleep latency (time from lights out to the first minute of stage N2 sleep), TIB = time in bed (time from lights out to lights on), TST = total sleep time (TIB minus time spent awake), WASO = wake after sleep onset (TIB minus SL and TST).

Actigraphy data

The wrist actigraphy results from the participants with DS, presented in Table 3, show a mean SL slightly above the normal range (> 20 minutes), with reduced SE (< 85%). Mean daytime napping was 118.2 ± 104.2 minutes. Estimated total sleep time (TST) over 24 hours (mean nocturnal TST + mean daytime napping) obtained by actigraphy data was 501 minutes (383.9 and 118 minutes, respectively).

Polysomnography data

Seven of the initial 54 participants with DS did not complete the second PSG night. Full PSG data from both nights were obtained for the remaining 47 adults. PSG was well tolerated, though participants had difficulty sleeping the first night. We observed differences in maintenance of sleep variables between the two nighttime PSG tests. Sleep efficiency on the second night increased 4.2% on average compared with the first night, but this difference did not reach statistical significance ($P = .15$). On the second night, 25 participants with DS (53.2%) presented prolonged SL (> 20 minutes) and 18 (38.3%) had an early awakening with a mean early wake time of 9.2 minutes (range 0–115). Sleep efficiency was under 85% in 74.5% of the participants. Sleep quality on both PSG nights was scored by the participants as similar to that at home.

Sleep initiation and maintenance variables

Results from the three sleep monitoring techniques performed in participants with DS regarding sleep initiation and maintenance differed significantly, as shown in Table 3. Time in bed, TST, and SE were significantly higher in the sleep diary than in the actigraphy and nighttime PSG data. SE was lower in only 35.3% of participants according to their sleep diaries, compared to 87.8% according to actigraphy and 74.5% according to PSG data. Similarly, SL and WASO were significantly lower in sleep diaries than in actigraphy and PSG data.

Sleep architecture variables

Compared to patients in the control group, participants with DS showed a decrease in TST and in SE, and an increase in SL, REM, SL, and WASO, as shown in Table 4.

Participants with DS also showed significantly higher percentages of stage N1 and N3 sleep, and more decreases in REM sleep than those in the control group. Specifically, in participants with DS, the percentage of REM sleep was under 20% in all but 1 participant, and 3 participants did not experience REM sleep. We found no significant differences in the mean REM percentage between those who were taking antidepressants and those who were not ($P = .358$). We did not find any correlation between the percentage of REM sleep and age

($P = .68$). The arousal index score was higher in the DS group than in the control group, mainly because of a higher AHI in the DS group.

Men with DS had a significantly higher percentage of stage N1 sleep than women with DS ($P = .001$). In the control group, women had a significantly longer SL (31.5 ± 21) than men (16.7 ± 11.16) ($P = .018$).

Table 4—Polysomnographic findings for study participants with Down syndrome and in the control group.

Sleep Variables	DS (n = 47)	Controls (n = 35)
TST (minutes)	337.9 (88.1)**	395.8 (44.5)
SE (%)	69.7 (17.7)**	81.6 (11.0)
WASO (minutes)	101.9 (73.3)**	55.5 (31.4)
SL (minutes)	39.3 (49.6)**	23.0 (17.5)
REM sleep latency (minutes)	186.7 (82.0)**	112.8 (50.9)
Stage N1 sleep (%TST)	8.1 (6.1)*	5.4 (3.5)
Stage N2 sleep (%TST)	48.3 (10.9)	47.7 (9.2)
Stage N3 sleep (%TST)	33.8 (12.8)*	27.9 (7.5)
Stage R sleep (%TST)	9.4 (5.8)**	19.4 (5.1)
AHI (events/h)	23.5 (24.5)**	3.8 (10.5)
AHI REM sleep (events/h)	23.1 (25.8)**	4.2 (9.0)
AHI NREM sleep (events/h)	22.9 (25.1)**	3.5 (10.5)
OAI (events/h)	5.04 (12.3)**	0.3 (1.3)
HI (events/h)	17.1(19.4)**	3.3 (9.3)
CAI (events/h)	0.2 (1.1)**	0.0 (0)
Basal wake O ₂ Sat (%)	95.7 (1.9)+	95.2 (5.2)
ODI-3% (events/h)	22.7 (25.2)**	3.0 (9.8)
Saturations below 90% (events/h)	7.33 (13.1)**	1.3 (4.8)
Respiratory arousal index (events/h)	16.3 (16.4)**	3.5 (9.6)
Total arousal index (events/h)	19.7 (15.5)**	6.1 (9.7)
PLMI (events/h)	5.7 (11.0)	3.5 (7.3)

Data are presented as mean (standard deviation). Symbols indicate statistical significance: + = $P < .10$, * = $P < .05$, ** = $P < .01$. AHI = apnea-hypopnea index, CAI = central apnea index, DS = Down syndrome, HI = hypopnea index, NREM = non-rapid eye movement, OAI = obstructive apnea index, ODI-3% = oxygen desaturation index, PLMI = periodic limb movement index, REM = rapid eye movement, SE = sleep efficiency, SL = sleep latency.

Sleep respiratory variables

Compared with the control group, participants with DS presented more sleep respiratory alterations, with a higher AHI and greater decreases in oxygen saturation during sleep (Table 4). These differences remained significant after age, sex, and BMI were included as covariates in the model. The median AHI adjusted for the covariables age, sex, and BMI was 22.81 in the DS group and 5.46 in the control group.

Thirty-four participants with DS (78.7%) and five patients in the control group (14%) had OSA. OSA was severe in 15 participants with DS (AHI > 30 events/h), moderate in 8 (AHI < 15–29.99 events/h), and mild in 11 (AHI 5–14.99 events/h). We did not find central

sleep apnea syndrome (> 5 events/h) or periodic breathing disorder in any participants. In the control group, OSA was moderate in one participant and mild in four participants.

In both groups, the AHI correlated positively with WASO, stage N2 sleep, number of shift changes, oxygen desaturation index, and total arousal, and inversely with stage N3 sleep and basal and minimal oxygen saturation during sleep ($P < .001$). In the group with DS we found a significant correlation between AHI and BMI ($r = .5$, $P < .001$), but only a tendency toward a correlation between AHI and age ($r = .26$, $P = .07$), sex, and percentage of REM sleep ($r = -.04$, $P = .75$). We did not find any correlation between AHI and the self-reported sleep questionnaires, though we did observe a negative correlation between stage N3 sleep and ESS scores ($r = -.348$, $P = .017$).

In the control group, the AHI score correlated with age ($P < .001$, $r = .58$), but not with BMI ($P = .12$, $r = .27$).

Abnormal behaviors during sleep and sleep-related movement disorders

Two participants reported nightmares but these were not reflected in the PSG recordings. Twenty experienced sleep talking; this occurred mainly during superficial non-rapid eye movement stages and was generally incomprehensible. In 3 of the 47 participants, some isolated movements during REM sleep were observed. However, no episodes fulfilled the diagnostic criteria for sleepwalking, REM sleep behavior disorder, or epileptic seizures. Repetitive swallowing and chewing movements, without bruxism features, were observed in five participants during wake time and also during sleep time on the PSG. No self-reported clinical symptoms suggestive of restless leg syndrome were reported by the participants. Periodic limb movements (> 5 events/h) were present in 10 participants and only 1 participant had more than 15 events/h. Individuals with DS not taking antidepressant medication had higher periodic limb movements and higher periodic limb movement arousal index scores than those taking antidepressant medication (Table S1).

DISCUSSION

The results of this study suggest that adults with DS have severe sleep disorders that are not detected by current self-reported sleep measures or reported by caregivers. Although the participants with DS were not referred because of suspicion of a sleep disorder, 74.5% had poor SE and 78% had OSA. The actigraphy data also recorded lower SE and higher napping than that reported in the sleep diaries by the caregivers.

A major finding in this study is that the self-reported sleep questionnaires did not reflect the sleep disturbances in this population. One reason could be that the questionnaires reflect the caregivers' perceptions and are therefore subjective. As validated questionnaire-based tools to screen for sleep disturbances in adults with DS are lacking, we used the same questionnaires as in the control group.

The PSQI sleep questionnaire excluded the presence of sleep disorders and indicated good sleep quality. Self-reported sleep quality has been related to the amount of slow wave sleep (SWS, or stage N3 sleep).²⁶ We did not, however, find any correlation between SWS and PSQI scores, but PSQI scores did correlate with the sleep diaries ($P = .004$, $r = -.447$), as has been shown in the general population.²⁷ More surprisingly, the Berlin questionnaire, which has proved highly sensitive in detecting OSA in the general population,²⁸ classified the possibility of participants with DS having sleep apneas as low. This suggests caregivers may underreport snoring and fatigue, the typical signs of OSA, in this population. The adapted ESS also failed to detect somnolence in the DS group, as in previous studies.^{10,29} We speculate that the DS caregiver does not generally recognize sleepiness and frequently attributes quiescent states to aging or normal apathy.

Participants did not report problems in their sleep diaries regarding falling to sleep or staying asleep. Although they spent a median of 9 hours in bed, 1 hour more than their age-matched general population,³⁰ this longer time in bed did not increase awakenings during the night or reduce self-reported SE. However, participants and their caregivers overestimated TST and sleep quality, most likely because sleep disturbances are perceived in cases of nocturnal agitation but not during peaceful insomnia, as in the general population. Conversely, when evaluated with objective measures, almost all participants presented with problems initiating and maintaining sleep.

The decrease in nocturnal TST detected from PSG data could be partially explained by the daytime napping suggested by actigraphy data and the consequent reduction in sleep homeostatic pressure.³¹ Indeed, PSG data alone could underestimate the TST. We observed a discrepancy between the absence of self-reported daytime naps and the long daytime sleep that was detected by actigraphy data (results not shown). Nevertheless, other objective

measures of sleepiness, such as the Multiple Sleep Latency Test, should be performed to differentiate real sleep from periods of quiet restfulness to obtain a more accurate estimate of the total amount of sleep time over 24 hours, and to compare this with that in the general population.³⁰ Nocturnal TST was nevertheless reduced even in individuals who did not nap. In addition to the structural brain anomalies associated with DS, disturbances in the cholinergic and serotonergic systems and deterioration of the cholinergic basal forebrain neuronal function may also affect the sleep/wake pattern.³² Specifically, a decrease in TST in people with DS could also be related to variants of the human clock gene in circadian rhythm sleep. Recently published data from DS mouse models expressing sleep-related phenotypes comparable with rest/activity patterns in participants with DS might be helpful in future research.³³

Aging in the general population is associated with a physiological decrease in SWS and REM sleep as sleep becomes more fragmented,³⁰ with a notable reduction in REM sleep in Alzheimer disease.³⁴ Senescence in individuals with DS occurs earlier than in the general population.³⁵ The PSG results in our study suggest a premature sleep aging process in DS, with chronological age not matching physiological age, and changes in sleep patterns appearing earlier than in the general population. Moreover, presenile-onset Alzheimer disease will develop in most people with DS. Dementia is associated with more sleep disturbances than expected with normal aging in the general population.³⁶ Similar data, however, are not yet available for participants with DS. Further studies are necessary to assess the impact of Alzheimer disease on sleep in the DS population.

In line with previous objective data^{12,13} we found that OSA was the main sleep disturbance in the DS population (78%). This figure is considerably higher than the 14% in the control group, which was also in line with the prevalence in the general population.³⁷

We observed only a tendency for correlation between OSA and age in our DS group. It did not reach the significance reported in children with DS^{4,6} or in the general population,³⁷ but this may be caused by the lower power of our sample. We did observe a relationship between OSA and BMI, as commonly reported in the general population³⁸ and in participants with DS.^{12,13} Aging in DS is associated with hypothyroidism and obesity, both of which are known risk factors for OSA.³⁹ Both of these conditions worsen the upper airway narrowing that is present from infancy in participants with DS due to their craniofacial and functional abnormalities.^{6,7} Further studies may determine whether dietary control or weight loss through exercise in adults with DS prevents or decreases OSA severity, as measured by reductions in the AHI and observed in the general population.³⁹

Another point of note is that the participants in our study had not been referred because of suspicion of OSA. Our findings show that the prevalence of sleep apnea in adults with DS is high whether or not they are referred for suspected OSA. These data stress the need for a change in clinical practice and for routine PSG screening for sleep apnea in adults with DS.

We recorded few abnormal motor behaviors during sleep. The most frequent event was sleeptalking. Despite the relative increase in slow wave sleep, we found no episodes of non-rapid eye movement-related parasomnia or REM sleep behavior disorder in the short periods of REM sleep recorded. Periodic limb movements during sleep were infrequent in our findings.

Our results have several clinical implications. First, they indicate that sleep problems are underrecognized by patients and caregivers. This could be because they are masked by the patients' global intellectual disability, because they are chronically present, or because they are accepted by caregivers as part of the aging process. Second, most of our participants with DS had severe OSA, a disorder associated with a higher risk of mortality.⁴⁰ Although the average life expectancy has increased dramatically for people with DS in recent years, it is still 20 years less than that for the general population.³⁵ Monitoring treatable OSA risk factors and early detection and correction of OSA could help minimize derived comorbidities and improve life expectancy. Sleep disturbances in adults with DS may have a greater effect on physical, mental, and emotional health than in the general population,^{2,8,41} leading to a higher incidence of daytime behavioral problems, an increased risk of accidents, and more visits to physicians.³ Third, our results highlight the need to design questionnaires to specifically screen for sleep disturbances in adults with DS. Nevertheless, until such scales or other more practical screening approaches are available,⁴² we suggest PSG be routinely recommended in this population. Fourth, these sleep-based data may be useful for developing guidelines and programs for the prevention, screening, and treatment of sleep disorders in the adult DS population. Treating sleep disorders may improve cognition and quality of life in adults with DS,⁴³ helping them to achieve their full potential in terms of mental and physical health as they age.

This study has three main limitations: the absence of actigraphy and sleep diaries in the control sample, the limited sample size, and the inclusion of both premenopausal and postmenopausal women. The availability of actigraphy and sleep diaries would have allowed evaluation of the differences in the sleep-wake pattern between the DS group and the general population. Validation of actigraphy data through comparison with PSG data in the adult DS population is still needed. Larger studies are also required to compare the results of PSG, actigraphy, and sleep diaries in the DS population in order to validate their usefulness in detecting sleep disorders, as has been demonstrated for the general population.⁴⁴ Regarding

the limited sample size, this may have limited the power to establish significant differences in some variables. Finally, postmenopausal women in the general population have a higher risk of the development of OSA,⁴⁵ but although we did not perform any specific determinations of sex hormones, we found no notable sex difference for any of the sleep variables analyzed.

Our study also has several strengths. It compares self-reported and objective sleep measures in a large sample of adults with DS, and there was no bias toward sleep disorders. Furthermore, we performed a complete PSG adaptation night, which allowed us to achieve higher SE on the second PSG night. Finally, the actigraphy recordings collected over 7 days provided further information about habitual sleep-wake patterns.

In conclusion, we found a high prevalence of sleep disorders in adults with DS. Seventy-four percent of the adults showed poor SE and 78% had OSA that was not detected by current self-reported sleep measures. OSA was severe in 30% of the participants. These findings support the notion that the adult DS population should undergo routine objective screening methods for sleep disturbances as adequate treatment might promote healthy aging.

ABBREVIATIONS

AHI, apnea-hypopnea index

BQ, Berlin Questionnaire

DS, Down syndrome

ESS, Epworth Sleepiness Scale

OSA, obstructive sleep apnea

PSG, polysomnography

PSQI, Pittsburgh Sleep Quality Index

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