Sleep Medicine 93 (2022) 84–89

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

The association of saccadic abnormalities with rem sleep in patients with Huntington's disease

Jagadish Annapureddy [a, 1], Somdattaa Ray [a, 1], Nitish Kamble [a], Gulshan Kumar [b], Pramod Kumar Pal [a], Seshagiri DV [a], Sanjeev Jain [c], Bindu Kutty [b], Ravi Yadav [a, *]

[a] Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka, 560029, India
[b] Neurophysiology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka, 560029, India
[c] Molecular Genetics Laboratory, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru, Karnataka, 560029, India

ARTICLE INFO

Article history:
Received 19 July 2021
Received in revised form
8 October 2021
Accepted 31 October 2021
Available online 12 November 2021

Keywords:
HD
Sleep
Extra ocular movements
REM sleep

ABSTRACT

Background: Huntington's disease (HD) is a progressive neurodegenerative disorder characterised by chorea, cognitive impairment, psychiatric and behavioral disturbances. Sleep disturbances including reduced REM sleep have been observed in HD.
Objectives: The aim of the study was to study the polysomnography findings in HD and to assess whether oculomotor abnormalities are associated with poor REM sleep.
Methods: Twenty-nine genetically confirmed HD patients underwent clinical evaluation including extraocular movement and OKN examination. Twenty-six patients and 15 controls underwent overnight video polysomnography (VPSG).
Results: VPSG of 23 HD patients and 13 controls were considered for analysis. Compared to controls, HD patients had higher median wake period and higher WASO percentage ($p = 0.005$). REM sleep percentage was reduced significantly in HD in comparison to controls ($p < 0.001$). Out of 23 patients, only two patients had REM sleep above 20% while 14 patients had REM sleep percentage less than 15%. Poor horizontal OKN (grades 2 and 3) was associated with the presence of low REM sleep percentage (REM sleep less than 15%) ($p = 0.02$). Low REM sleep was also associated with severe illness (UHDRS) ($p = 0.038$).
Conclusion: An association between decreased REM sleep and OKN abnormalities indicate that EOM abnormalities seen in HD could lead to errors in scoring REM sleep. To understand the actual degree of decreased REM sleep percentage will require additional parameters in AASM guidelines to score REM sleep in patients with EOM abnormalities like that seen in HD.

1. Introduction

Huntington's disease (HD) is a progressive neurodegenerative disorder which is inherited in an autosomal dominant fashion with CAG trinucleotide repeats on chromosome four [1]. Clinical features seen in HD are motor disturbances including chorea, cognitive, psychiatric and behavioral disturbances. In addition, sleep disturbances have also been reported in HD.

Sleep disturbances have been self reported by 87.8% of the patients with HD out of which 52.7% of the patients reported it as a significant contributor of overall morbidity, requiring medical help for the same [1]. Sleep disturbances included frequent night time awakenings, early morning awakenings, excessive daytime sleepiness, periodic limb movements and restless leg movements [1]. Compared to clinical scales, polysomnography (PSG) studies have proven to be more sensitive in detecting sleep abnormalities in HD [2]. PSG studies have revealed that sleep disturbances are one of the earliest manifestations of premanifest HD carriers [3]. PSG features in HD patients include increased duration of stage 1 sleep, decreased REM sleep duration, fragmented sleep, increased wake after sleep onset (WASO) [3,4]. Sleep quality tend to worsen as the disease progresses from premanifest to manifest stage [3].

* Corresponding author. Department of Neurology, National Institute of Mental Health & Neurosciences (NIMHANS), Hosur Road, Bengaluru, 560029, Karnataka, India. Fax: +91 80 26562829.
E-mail address: docravi20@yahoo.com (R. Yadav).
[1] Both authors have contributed equally to the manuscript.

https://doi.org/10.1016/j.sleep.2021.10.035
1389-9457/

Apart from HD, decreased REM sleep has been observed in many other movement disorders including Parkinson's disease [5], cervical dystonia [6] and SCA [7]. Reduced eye movements in SCA can lead to challenges in reporting REM sleep stage [7]. Similar, to SCA, HD has progressive impairment of saccades and pursuits with advancement of the disease. Hence, it is likely that the reduced REM sleep in HD may be linked to reduced eye movements.

In HD, few PSG based studies are available with limited sample size and variable results. Moreover, there are no studies evaluating the sleep architecture abnormalities in relation to eye movement abnormalities. The aim of the study was to study the REM sleep and correlate with optokinetic nystagmus (OKN) abnormalities in patients with HD. We hypothesized that low REM sleep correlated with impaired eye movements and OKN.

2. Methods

The study was a cross-sectional case control study done at the Department of Neurology, National Institute of Mental Health and Neurological Sciences (NIMHANS) Bangalore, India from December 2017 to October 2019. Ethical approval was obtained from Institutional Ethics committee (NIMH/DO/IEC (BS and NSDIV)/2017–2018/3.05/1.1.2018). HD patients who visited outpatient services and agreed to participate in the study were included after taking the informed consent, hence conforming to the declaration of Helsinki.

After obtaining sociodemographic details, clinical details including family history and details of medication were enquired. Clinical examination was focused on eye movement examination. Extra ocular movements (EOM) were examined for gaze restriction with detail towards saccades and pursuits. Patients were also subjected to optokinetic nystagmus (OKN) evaluation using OKN tape. OKN testing provides an integrated measure of saccade testing contralateral to the direction of target and pursuit testing ipsilateral to the direction of target [8]. The OKN tape has black rectangles measuring 12.9 cm^2 (2 × 2 inches), separated by two inches, on a 90 cm long white cloth. EOM were graded as–normal, appearance of sclera on lateral gaze: mild gaze palsy, near total restriction of gaze: minimal to absent extra ocular movements. Intermediate gaze restriction was considered when extra ocular movement restriction was partial. Findings on OKN analysis were graded as–normal (0), moderate decrease in OKN amplitude (1) severe decrease in OKN amplitude (2), absent OKN (3) [9].

The severity of the HD was assessed using the Unified Huntington's Disease Rating Scale (UHDRS) [10].Patients with UHDRS score of ≤25 were considered to have mild disease while patients with score of ≥26 were considered to have severe disease [11]. Total functional capacity (TFC) was also assessed among patients with HD. Patients with mild disease had a score of 11–13, moderate disease had a score of 7–10 and severe disease had a score of 3–6 [12]. Patients were evaluated for REM behavior disorder (RBD) using Mayo sleep questionnaire [13], restless leg syndrome (RLS) using RLS criteria and the International RLS study group rating scale [14], excessive daytime sleepiness using Epworth Sleepiness Scale (ESS) [15], sleep quality using Pittsburgh Sleep Quality Index (PSQI) [16], depression using Hamilton depression scale (HAM- D) [17], anxiety using Hamilton anxiety scale (HAM-A) [18]. Patients with PSQI greater than five were considered as poor sleepers, ESS greater than ten were considered to have excessive daytime sleepiness, HAM-A scores greater than 14 were considered to have anxiety. For depression, the following was the cut off-no depression (0–7), mild depression (8–16), moderate depression (17–23), and severe depression (≥24). For self esteem, following was the cut off: low self esteem (0–15), normal self esteem (15–25), high self esteem (25–30). We recruited age and gender matched healthy controls who provided consent to undergo assessment by questionnaire and video polysomnography.

2.1. Polysomnography

Overnight video PSG was obtained in a sleep laboratory at NIMHANS using the system SOMNOmedic GmBH, Germany®. PSG was performed as per the guidelines laid down by the American Academy of Sleep Medicine (AASM) (2017) [19]. Patients were instructed to stop medication three days before polysomnography. Patients and controls were advised to refrain from mid-day naps and caffeine prior to the night of scheduled PSG. The PSG was recorded during patients' regular sleeping hours. Recording was performed between 9.30 and 11.30 pm to 6–7 am.

Electroencephalography- Patients were connected with electrodes (monopolar based gold disc electrodes-grass electrodes, Natus neurology®) connected over scalp-Fp1, Fp2, F3, F4, C3, C4, T3, T4, O1, O2, the ground electrode at Fz and reference electrodes at FpZ. M1, M2 electrodes were placed as references during offline analysis. Electro oculogram (EOG) electrodes were placed 1 cm horizontal and 1 cm vertically above and below the outer canthi of left and right eye. Three electromyogram (EMG) electrodes were placed-one electrode 1 cm above the inferior edge of mandible at midline and other two electrodes were placed 2 cm horizontal and 2 cm vertically away from either side of midline. The EOG and EMG derivations were in accordance with AASM 2017 guidelines [19]. The electrodes were placed according to the 10–20 international system for electrode placement. Channels recording ECG, airflow sensors, chest and abdominal motion, oxygen saturation, bilateral tibialis electromyogram, were also placed. Before acquisition of data, impedance was maintained below 5 KΩ.

2.2. Sleep data scoring and analysis

The acquired sleep data was converted into European Data Format (EDF) and was analyzed in Polyman software version 1.15. The data was scored manually by the author and independently by another senior researcher. The sleep data was analysed based on sleep scoring guidelines AASM 2017 [19]. The PSG recording was scored for sleep stages- NREM stage 1(N1), stage 2 (N2), stage 3(N3) and REM sleep, and for respiratory abnormalities such as apnea or hypopnea. Sleep variables that were assessed included total sleep time (TST), sleep efficiency, WASO, percentage of TST spent in NREM stages 1,2,3 and REM sleep and REM sleep latency.

Based on EEG features and electro-oculogram findings, REM sleep was scored. REM sleep was considered to have terminated when there is transition to wakefulness or N3, majority of epoch satisfies criteria for N2 in the absence of rapid eye movements (REM), arousal followed by low amplitude mixed frequency waveforms with slow eye movements [19].

3. Statistical analysis

The data was entered into an MS excel sheet and data was analysed using SPSS version 20. Descriptive statistics were expressed in the form of frequency, percentage and mean ± standard deviation. Normal distribution for all the variables was tested using Shapiros-Wilks' test. Independent T-test and Mann–Whitney U test were used for continuous variables following normal and skewed distribution, respectively. Based on the distribution, either Kruskal–Wallis test or One-way ANOVA were used for comparison between the groups. To compare the differences in normal and low REM sleep among patients with normal and abnormal OKN, Fisher's exact test was used. The level of significance (p value) was placed at 0.05.

4. Results

4.1. Demographic and clinical details

Twenty-nine patients and 15 healthy controls were recruited into this study. The mean age of patients were 39.72 ± 10.3 years (range 16–69 years) and that of controls were 31.06 ± 5.836 years (range 25–42 years) (Table 1). Out of the 29 patients, 9(31.03%) were female and 20(68.97%) were male. The severity of the disease was classified according to TFC. Based on TFC, mild HD was observed in 9(31.03%) patients, moderate HD in 16 (55.17%) patients and severe HD in 4 (13.79%) patients. Family history was present in 26 out of 29 patients and three patients had sporadic onset.

The details of non-motor symptoms in HD are elaborated in Table 1. Sleep impairment was found in all patients with severe HD, while it was reported by 3(33%) out of nine patients with mild HD. Mild anxiety and depression was reported by 7 (24%) and 8 (27.5%) patients, respectively. REM behavior disorder was reported in five patients. There was a significant positive correlation between PSQI, ESS, HAM -D with UHDRS, duration of illness in our study.

Patients were treated with variety of drugs such as lithium, valproate, haloperidol, aripiprazole, amantadine, escitalopram, carbamazepine, tetrabenazine and clonazepam. Ten (33%) patients were on medication to treat dyskinesia and other movement disorders while 18 (62%) patients required medication for psychiatric disturbances.

4.2. Eye movement abnormalities-

The eye movement abnormalities have been discussed in Table 2. As the severity of disease increased, the degree of severity of involvement of saccades and pursuit also increased. In all grades of severity of the disease, saccades were more affected than pursuits. The vertical direction was slightly more involved than the horizontal direction.

The details of OKN findings are given in Table 2. OKN was impaired in both vertical and horizontal directions in HD cases. OKN was affected in all severely affected cases of HD. OKN was completely absent in 13% of HD patients.

4.3. Results of video PSG

After informed consent, 26 HD patients and 15 patients underwent Video-PSG. Two control PSG and three HD PSG were excluded from analysis in view of markedly low sleep efficiency. The total sleep duration was similar between the groups. Average sleep efficiency was reduced in HD compared to controls ($p < 0.001$). Sleep architecture of HD patients deviated grossly from the normal patients in most parameters.

4.4. Sleep parameters

HD patients had higher median wake period and higher WASO percentage than control population ($p = 0.005$) (Table 3). Significantly higher percentage of N2 sleep was found among patients with HD. In addition, HD patients had significantly high number of stage transitions in sleep in comparison to controls ($p = 0.007$). Sleep arousals were slightly more in HD patients than in controls that failed to reach statistical significance.

4.5. REM sleep

REM sleep percentage was reduced significantly in HD in comparison to controls ($p < 0.001$). REM sleep was absent in two HD patients. Mean REM sleep percentage was 11.68 ± 6.9%. Out of 23 patients, only two patients had REM sleep above 20% while 14 patients had REM sleep percentage less than 15%. Five patients had REM sleep without atonia (RSWA) in their video PSG (confirmed by AASM criteria) that correlated with the presence of RBD as evident in questionnaire.

Poor horizontal OKN (grades 2 and 3) was associated with the presence of low REM sleep percentage (REM sleep less than 15%) ($p = 0.02$). Low REM sleep was also associated with severe illness (UHDRS>25) ($p = 0.038$). However, low REM sleep had no association with poor vertical OKN, TFC or CAG repeats.

4.6. Apnoea

Compared to controls, higher number of HD patients were observed to have obstructive sleep apnea. Mild apnea (AHI:5–15) and moderate apnea (AHI: 16–30) were observed in two patients with HD in each group. Hypopnea and apnea was reported in four controls too but AHI was less than five in these controls. Neither central nor mixed apnoea were reported in cases or controls. Hence, overall apnoea-hypopnoea index was more in cases than in controls (supplementary table).

5. Discussion

Using validated questionnaires that were further complemented with video PSG, we found significant sleep disturbances and other nonmotor symptoms in HD. To the best of our knowledge, this is the first study to systematically assess OKN abnormalities among HD patients with decreased percentage of REM sleep. We could establish an association between poor extraocular movements and decreased REM sleep in video PSG. Our study also showed an association of decreased REM sleep with increasing severity of disease, that is concordant with the fact that the gaze abnormalities continue to worsen with increasing severity of HD.

Table 1
Demographic details and frequency of non-motor symptoms in mild, moderate and severe HD.

	Mild HD (11–13) N = (9/29)	Moderate HD (7–10) (N = 16/29)	Severe HD (3–6) N = (4/29)	P value
Age at onset (years)	29 ± 10.2	36 ± 10.8	35 ± 4.6	0.3
Duration of illness (years)	4.2 ± 2.0	6.6 ± 3.5	12 ± 2.6	0.04*
CAG repeats	46.8	44.4	45.3	0.376
UHDRS-M	20.8 ± 12.0	32.5 ± 15.5	80 ± 16.3	<0.001*
PSQI >5	3/9 (33.3%)	10/16(62.5%)	4/4 (100%)	0.006*
ESS >10	0/9 (0%)	6/16 (37.5%)	2/4 (50%)	0.5
RBDSQ >5	3/9 (33.3%)	2/16 (12.5%)	0/4 (0%)	0.05*
HAM-A > 14	2/9 (22.2%)	2/16 (12.5%)	3/4 (75%)	0.07
HAM-D > 7	1/9 (11.1%)	4/16 (25%)	3/4 (75%)	0.004*

PSQI- Pittsburg sleep quality index, ESS- Epsworth sleepiness scale, RBDSQ- REM sleep behavioural disorder sleep questionnaire, HAM-A and HAM-D Hamilton Anxiety and depression rating scale, HD- Huntington's disease.
Mild, moderate and severe HD grading done based on total functional capacity score(TFC).

Table 2
Extra ocular movement impairment in mild, moderate and severe HD.

	All HD patients (N = 29)	Mild HD (N = 9/29)	Moderate HD (N = 16/29)	Severe HD (N = 4/29)	Controls (15)
Gaze palsy	19(65.5%)	3(33%)	12(75%)	4 (100%)	0
Slow saccades	25(86%)	6(67%)	15(93%)	4(100%)	0
Broken pursuits	19(65.5%)	3(33%)	12(75%)	4(100%)	0
Vertical OKN (Impaired)					
Mild OKN impairment (1)	8(27.6%)	4(44.4%)	4(25%)	0(0%)	1.6%)
Moderate OKN impairment (2)	9(31%)	3(33.3%)	6(37.5%)	0(0%)	0(0%)
Severe OKN impairment (3)	9(31%)	0(0%)	5(31.3%)	4(100%)	0(0%)
Horizontal OKN					
Mild OKN impairment (1)	14(48.3%)	6(66.7%)	8(50%)	0(0%)	1(6.6%)
Moderate OKN impairment (2)	8(27.6%)	0(0%)	6(37.5%)	2(50%)	0(0%)
Severe OKN impairment (3)	2(6.9%)	0(0%)	0(0%)	2(50%)	0(0%)

Table 3
Comparison of various sleep parameters between HD and controls.

VPSG parameter	HD Cases	Controls	P Value
Total recording duration (minutes)	514.5(448.5–555)	473.5(425–527)	0.649
Total sleep duration(minutes)	476 (381–525.5)	467(404–504.3)	0.948
Sleep onset latency (minutes)	28 (9–43)	10 (4.75–28)	0.214
Wake duration (minutes)	155(92.5–225)	90(60.3–109.8)	0.005*
WASO duration (minutes)	122.5(68.5–217.5)	84.5(33.3–101.8)	0.60
WASO (Percentage)	30.8(16.6–43.7)	16.6(7.8–19.7)	0.005*
Sleep efficiency (Percentage)	65.8(55.7–79.3)	80.9(76.6–85.9)	<0.001*
Stage N1 Latency (minutes)	25(8–72.5)	20.5(8.5–57.5)	0.673
Stage N2 Latency (minutes)	28(9–43.5)	20.5(8–34.5)	0.537
Stage N3 Latency (minutes)	58.75(21.5,-124.8)	11.5(5–17.25)	<0.001*
Stage REM Latency (minutes)	158.25 (88.3–246)	87.5 (59.5–114.7)	0.006*
Stage N1duration (minutes)	12.5(5–29.5)	3.5(2.5–6.3)	0.795
Stage N2 duration (minutes)	159.5(134.5–219)	52(46.9–55.4)	0.131
Stage N3 duration (minutes)	51.5(18.5–82.5)	20.9(14.6–26.2)	0.022*
Stage REM duration (minutes)	29.5(18–58)	22.4(20.2–25.4)	<0.001*
Stage N1 Percentage	4.7(2.6–12.5)	3.5(2.5–6.3)	0.379
Stage N2 Percentage	60.8(52.8–77.1)	52(46.9,55.4)	0.006*
Stage N3 Percentage	17.9(6.7–24.4)	20.9(14.6,26.2)	0.214
Stage REM Percentage	12.8(5.5–16.7)	22.4(20.2,25.4)	<0.001*

WASO- wake after sleep onset, VPSG-video polysomnography, N1- NREM (non rapid eye movement) stage1, N2- NREM stage 2, N3- NREM stage 3, REM - rapid eye movement.

In this study, sleep impairment was reported by 68% of the patients with HD. All patients with severe HD reported sleep impairment whereas only 33.3% patients with mild HD reported sleep disturbances. Mild anxiety and depression were reported in 24% and 27.5% of the patients, respectively. The incidence of anxiety in HD has been reported between 12.5% and 71% while a higher incidence of depression has been reported in other studies [20]. Excessive daytime sleepiness and RBD was reported in 27.5% and 17.2% of our patients respectively that is in line with the findings of earlier studies [4,11]. A higher proportion of patients with poor sleep, excessive daytime sleepiness, anxiety and depression had severe disease. The finding of sleep impairment and depression with increasing severity of HD is in concordance with previous studies [20–22]. A higher proportion of patients with RBD had mild disease in our study. This finding is in line with the other studies where RBD has been reported by patients with mild and moderate HD [11,21].

In agreement with previous studies [3,4,11,23], PSG findings in our study included markedly decreased sleep efficiency, increased WASO, and decreased REM sleep with normal sleep latency, indicative of disturbance of sleep maintenance. In addition, increased sleep arousal and increased sleep transition were observed in our HD patients. Patients also spent significantly less time in deeper stages of sleep (N3). Reduced REM sleep has been reported in almost all the PSG studies in HD. In a study by Carla Piano et al., the mean REM sleep percentage was less than 10% [4]. In our study, two patients had absent REM sleep. Similar findings have been reported in other studies [4,11]. In our study, one of the two patients with absent REM sleep had severely impaired EOM, while the other patient had mild EOM abnormality. It has been earlier demonstrated earlier that restricted EOM, as seen in SCA, was associated with decreased REM sleep [24]. We inferred that similar postulate could explain our finding of decreased REM sleep in patients with HD who also have supranuclear gaze impairment. Moreover, both disorders being a trinucleotide repeat disorder might have a similar pathological basis for supranuclear gaze involvement.

Defects in initiation and maintenance of saccades is due to dysfunction in basal ganglia and frontal lobes while saccade velocity disturbance is secondary to pathology of input commands to brainstem, brainstem itself or its output to premotor cortex [25]. Saccades and rapid eye movements both require a higher velocity for execution. Slowing of saccadic velocity might pose difficulty in executing rapid eye movement during REM sleep in PSG. Kimura et al. postulated that brainstem lesions leading to horizontal restriction of extra ocular movements during wakefulness, might also impede conjugate rapid eye movements during REM sleep [26]. Progressive supranuclear palsy, a progressive degenerative disorder is also characterised by severely reduced REM sleep [27]. Extensive pontine involvement with destruction of pontine tegmentum has been shown to be associated with severely decreased or even absent REM sleep [28,29]. Additional disturbances of sleep wake cycle have been observed in patient with pontine lesions [30]. REM sleep abnormalities have been observed in other degenerative diseases with relatively less EOM impairment. Basal forebrain's cholinergic neurons contribute to cerebral activation during REM sleep, that gets impaired in Alzeihmer's disease, leading to poor REM sleep [31]. In PD, brainstem nuclei degeneration (particularly pedunculopontine nuclei) impedes thalamocortical activation leading to disrupted NREM and REM sleep [32]. Progressive loss of REM on cells in pons with REM off cells escaping the degenerative process was purported by Tuin et al. to explain low REM sleep in SCA [24].

Rapid eye movements in adults are mainly horizontal while it is vertical in infants [33] but few authors have suggested that the direction of rapid eye movements in REM sleep could be vertical

[34]. In patients with voluntary gaze abnormalities, the direction of rapid eye movements changed to the direction of eye movements that could be elicited on command during wakefulness [33]. Yet, patients with vertical gaze palsy [33] as well as horizontal gaze palsy were reported to have severely decreased and even absent REM sleep [28]. In our study, decreased REM sleep was associated with restriction in horizontal OKN, rather than vertical OKN.

It may be emphasized that REM sleep may not be so severely abolished as it may appear. This is evident by the presence of features of REM sleep such as saw tooth waves and low amplitude mixed frequency in absence of rapid eye movement in sleep [33]. Hence, an inference can be drawn that restricted EOM may lead to decreased rapid eye movement during REM sleep. This implies that during REM sleep scoring, reliability on one of the two major determinants of REM sleep scoring (rapid eye movement), suffers in the light of extra ocular movement impairment. Given that rapid eye movement is one of the essential criteria to identify REM sleep in PSG according to AASM guidelines [19], additional parameters are essential in conditions where EOM abnormalities may falsely lead to low REM sleep scoring [7]. Only then we will be able to ascertain, to what degree can we solely attribute low REM sleep percentage to EOM abnormalities. Similar findings were noted in our study. However, the mere restriction of EOM may fail to completely explain decreased REM sleep. Earlier studies have shown that the presence of voluntary gaze abnormalities appear to be mandatory for affecting rapid eye movement even if reflex EOM is normal [33]. The reverse is true in premanifest HD where reflex EOM are affected with normal voluntary gaze, but these patients also have poor REM sleep [11]. Hence, poor REM sleep may be observed in HD even before the development of voluntary gaze abnormalities, as seen in premanifest HD. Challenges in REM sleep scoring in HD is compounded by the relatively higher chin tone in EMG observed in a previous study [11]. Thus, generators of REM sleep and saccades may have a common substrate or lie in close proximity in brainstem. This could explain low REM sleep due to concurrent impairment of REM centres and poor REM sleep detection due to EOM involvement in brainstem lesions and HD.

Many other theories can explain the mechanism of poor REM sleep in HD. Pathological affliction of REM sleep generators in brainstem by the mutant huntingtin protein could be plausible cause. Moreover, relative lack of atonia during REM sleep have been observed in patients with HD. This indicates probable neuronal loss in areas controlling atonia during REM sleep such as locus coerulus, hypothalamus, pedunculopontine region and parvo magnocellularis in medulla [11]. In HD, pathological abnormalities have been noted in locus coerulus and hypothalamus [35]. In HD, cerebral metabolic activity is impaired that could also lead to a disturbance in REM sleep mechanism [11]. Circadian rhythm disturbances have been reported in HD that originates from pathology of suprachiasmatic nucleus (SCN) in HD [36]. Although sleep wake cycle is regulated by SCN, its pathology is less likely to explain poor REM sleep percentage since duration of REM sleep is governed by homeostatic mechanisms. SCN lesions have been found to be associated with delayed transition to REM sleep [37] that may explain increased REM sleep latency in our study.

The major limitation of the study was the small sample size, leading to the study largely being a descriptive study. All the patients and controls underwent only one night PSG that could lead to first night effect, thus affecting PSG results. A subjective analysis of eye movements using electro-oculography and details of REM sleep without REMs could have highlighted more details regarding REM sleep abnormalities in HD. These limitations were balanced by the study of OKN and application of video PSG in genetically confirmed individuals with HD.

This study adds to the existing literature regarding the PSG abnormalities in HD. Gaze abnormalities in HD leads to errors in identification of REM sleep and may falsely lead to decreased REM sleep percentage recorded in HD. However, pathological studies in HD patients will be essential to determine the pathological substrate of poor REM sleep. To understand whether REM sleep is indeed low in HD, we will require additional REM sleep parameters to be considered for REM sleep scoring in PSG of patients with EOM abnormalities like that seen in HD.

Source of funding

Golden Jubilee Fund of Department of Neurology, National Institute of Mental Health and Neurosciences, Bengaluru, India.

Compliance with ethical standards

Ethical approval for the study was provided by Institutional ethical board, hence fulfilling the ethical standards laid down in the Declaration of Helsinki for research on human subjects. Informed consent was taken from all the study participants.

Author contribution

Jagadish Annapureddy- Conceptualization, Resources, Methodology. Investigation; Somdattaa Ray – Resources, Visualisation, Methodology, Validation, Writing – original draft and review; Nitish Kamble- Resources; Bindu Kutty- Conceptualisation, Supervision; Pramod Kumar Pal-Conceptualisation, Supervision; Seshagiri DV- Resources, Seshagiri DV- Resources, Sanjeev Jain-Resources, Gulshan Kumar2 PhD Ravi Yadav- Conceptualisation, Visualisation, writing review, Supervision

Conflict of interest

None of the authors have any financial disclosure to make or have any conflict of interest.

The ICMJE Uniform Disclosffigure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2021.10.035.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2021.10.035.

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