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Cannabis use, sleep and mood disturbances among persons with epilepsy – A clinical and polysomnography study from a Canadian tertiary care epilepsy center

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ABSTRACT

Objective: Interest in anti-seizure properties of cannabinoids is increasing, with the rise in prevalence of recreational and medical cannabis use, especially across Canada. In a recent study on people with epilepsy (PWE), cannabis use showed a strong association with poor psychosocial health. Sleep and mood comorbidities are highly prevalent in epilepsy, and are common motivations for cannabis use. The primary objective of this study was to assess demographic, subjective and objectively assessed sleep quality and mood related differences among PWE who regularly use cannabis compared to those who do not.

Methods: Consecutive consenting patients with a confirmed epilepsy diagnosis, admitted to our Epilepsy Monitoring Unit, over a 3-year period (2019–2022) were enrolled. Detailed epilepsy-related data and self-reported sleep [Pittsburgh Sleep quality index (PSQI)], Epworth Sleepiness Scale (ESS)], mood [(Beck's Depression Inventory (BDI) and Beck's Anxiety inventory (BAI)] and cannabis use related data were collected. Overnight polysomnography (PSG) was conducted on the first night of admission, with simultaneous 18-channel video-EEG. Sleep (PSG) scoring followed American Academy of Sleep Medicine guidelines by a scorer blinded to clinical details.

Results: Among 51 patients with similar seizure control, 25 (13 F) reported cannabis use (mean age 36.3±14.8 years) and were significantly younger than 26 (18 F) non-users (mean age 48.3±15 years). Cannabis users had significantly better subjective sleep quality (mean PSQI scores 7.2±2.9 vs 10.2±5.2 respectively). Most patients endorsed sleepiness (Cannabis users with ESS scores greater than 10; 91.3 %, 77.3 % in non-users) and moderate to extreme depression (BDI) scores. No significant differences were observed in objective sleep parameters. BDI score significantly predicted PSQI and ESS scores on multiple logistic regression analysis.

Significance: Despite a significant age difference, self-reported sleep quality is better among PWE who report regular cannabis use compared to non-users. However, there is no significant difference in objective sleep quantity and quality from PSG between the two groups. Additionally, severity of depressive symptoms is a significant predictor of sleep quality and of excessive daytime sleepiness among PWE.

1. Introduction

Epilepsy is a common neurological condition with a point prevalence of 6.38 per 1000 persons (Fiest et al., 2017). While seizure freedom remains the main goal of epilepsy treatment, there are multiple non-seizure morbidities, that may impact quality of life among people with epilepsy (PWE), in the form of psychiatric, (Desai et al., 2010) sleep related, (Zanzmera et al., 2012) as well as cognitive, endocrine

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abnormalities and medication-related adverse effects (Keezer et al., 2016).

There is growing evidence favoring the effectiveness of cannabinoids in seizure control among patients with epilepsy syndromes like Dravet's and Lennox-Gastaut syndrome (Devinsky et al., 2017, 2018). This has enhanced interest in the anti-seizure properties of cannabinoids. At the same time, the prevalence of recreational cannabis use has risen over the last decade, across Canada, especially among adult populations (Vignault et al., 2021). Canada, on October 17, 2018, formally legalized the cultivation, possession, acquisition, and consumption of cannabis and its by-products, making Canada the second country in the world, after Uruguay, to formally legalize it and the first G7 and G20 nation to do so. In light of limited evidence regarding the anti-seizure properties of cannabinoids, general interest in the use of recreational cannabis among PWE, has the potential to rise steadily, and highlights the urgent need for research.

However, there is a paucity of literature on the differences in seizure control, neuropsychiatric co-morbidities and sleep quality in epilepsy populations using recreational or medical cannabis. One recent study demonstrated a strong association between cannabis use and poor psychosocial health (Urits et al., 2020). Recently, in a Canadian nationwide survey-based study, Esmonde-White, C and colleagues found 55.9 % PWE participants reported marijuana use, the majority having started it for recreational purpose (Esmonde-White et al., 2023).

Among PWE, sleep remains an important component of quality of life and is also closely connected with cognition, mood, and behavior. Sleep problems can be an important motive for people to initiate cannabis use, without much evidence to support its effectiveness (Esmonde-White et al., 2023). In a study on patterns and motives of cannabis use, nearly half the participants used cannabis for insomnia (range 32 %-58 %); (Haug et al., 2017) while subjective and polysomnographic assessment among treatment-seeking cannabis users has demonstrated that nearly one third had delayed sleep initiation, with poor sleep maintenance and sleep efficiency among more than half of them (Pacek et al., 2017). There is a growing need for in depth evaluation of sleep and overall quality of life among PWE, who are cannabis users.

Comprehensive subjective as well as objective evaluation of sleep and quality of life among PWE who are cannabis users, would generate important knowledge. This knowledge could aid in the development of future guidelines for monitoring PWE using cannabis and for utilizing cannabinoids in seizure control treatment. The current study examines the use of whole cannabis, which includes additional compounds such as terpenes (Sommano et al., 2020). These compounds can interact with one another and produce distinct effects which might differ from that of pure CBD or THC. With this information in the background, the current study was designed to capture the real-life impact of cannabis use on sleep among PWE. The primary objective of this study was to assess demographic, subjective and objectively assessed sleep quality and mood related differences among PWE who regularly use cannabis compared to those who do not.

2. Materials and methods

This study was a prospective cross-sectional study conducted between 2019 and 2022 at a tertiary care Canadian comprehensive Epilepsy referral center. The manuscript was prepared in line with the STROBE guidelines for cross-sectional studies. Consecutive consenting adult patients with a diagnosis of epilepsy confirmed by an epileptologist or neurologist formed the study population.

Patients admitted to the Epilepsy monitoring unit (EMU) for two nights or more and not undergoing sleep deprivation, were included in the study, after obtaining informed consent. Patients with severe neurological (encephalitis, recent stroke, multiple sclerosis, neurodegenerative disorders), medical (heart failure, malignancy, severe hematological and immunological conditions) and psychiatric (previously diagnosed, uncontrolled schizophrenia or other psychoses) co-morbidities, were excluded. Patients with polysubstance abuse disorder were excluded. Pregnant women were also excluded.

Considering prevalence of cannabis use among proposed study population as approximately 20 % (9) and prevalence of sleep abnormalities among cannabis users to be approximately 45 % (10), the sample needed for a power of 80 % and confidence level of 95 % was calculated to be 46 in each group (cannabis users and non-users) for detecting a statistically significant difference between groups. However, this being a pilot study and with a reduction in number of patients undergoing evaluation in the EMU due to the start of the COVID-19 pandemic, feasibility reassessment was done with a revised strategy to include as many patients as feasible within the study period. In addition, during the initial year of recruitment, it was also clear that the prevalence of cannabis use among eligible participants was much higher than proposed at the time of sample size calculation, thus keeping the study with a smaller sample size still adequately powered.

2.1. Methodology

Diagnosis of epilepsy was based on the most recent definition of epilepsy proposed by the International League Against Epilepsy (Fisher et al., 2014). The diagnosis was confirmed by at least one staff epileptologist/neurologist.

Approval from the Queen's University Institutional ethics committee (HSREB) was obtained prior to initiation of the study.

Patients scheduled for EMU evaluation were contacted via telephone in advance and a participant information sheet regarding study details was emailed to them. Selection bias was addressed by consecutively enrolling all eligible patients. A detailed verbal or in-person informed consent was obtained by one of the study investigators from patients expressing interest in participating in the study. Patients who wished to complete the clinical study questionnaire at home were emailed a link to the electronic study database on our institutional secure RedCap® account. The rest could complete the questionnaire on the study tablet computer on first day of admission to the EMU.

All epilepsy characteristics including age at onset, duration, seizure frequency, seizure semiology, seizure, and epilepsy classification (focal [temporal or extratemporal lobe] or generalized), epilepsy etiology and medication history, were recorded in the study database.

Subjective sleep evaluation was conducted using the Pittsburgh Sleep quality index (PSQI), (Mollayeva et al., 2016) Epworth Sleepiness scale (ESS) (Johns, 1991) as well as a pre-structured sleep quality questionnaire for epilepsy patients (Zanzmera et al., 2012) all included in the study database.

2.1.1. Objective evaluation of sleep

All patients fulfilling inclusion criteria were admitted in our single or double room EMU following completion of the informed consent process. All measures to minimize sound and/or light-related or movement-related disturbance in the patient's environment, were taken by trained nursing staff and technologists. In addition to the prolonged video-EEG monitoring using the 10–20 International system for electrode placement, with additional placement of anterior temporal and sub-temporal electrodes for epilepsy and ECG recording; the neurophysiological evaluation included continuous electro-oculogram (EOG) and submental electromyogram (EMG); respiratory parameters (thermistor, nasal pressure transducer, thoracic and abdominal belts) and leg movement (tibialis anterior muscle surface electrode) recording on the first night of admission, using XLTEK® long term monitoring systems. Patients continued to take home doses of their anti-seizure medications during sleep evaluation.

Preliminary analysis of EEG and sleep data were carried out by a senior certified technologist (ZS). Detailed sleep scoring was conducted by a certified agency sleepwellpsg.com, following secure transfer of deidentified and anonymized data in European Data Format (EDF) format.

Cannabis use assessment was carried out by collecting information on duration, frequency, and route of administration (consumption). Other details regarding use such as total daily amount and composition of product being used were collected wherever possible.

Mood and Behavior assessment was carried out using the Beck Depression Inventory (BDI), (Richter et al., 1998) Beck Anxiety Inventory (BAI), (Oh et al., 2018) and Neuropsychiatry Inventory (NPI) (Cummings, 2020) respectively.

2.2. Statistical analysis

All demographic details and epilepsy characteristics were analysed using descriptive statistics. The following outcome measures were analysed:

Subjective sleep – (PSQI scores, self-reported sleep quality)

Objective sleep (sleep onset latency, % with WASO >30 min, sleep efficiency, REM%, SWS%).

Mood and behavior - scores on the BDI and BAI questionnaires

Enrolled patients were divided into two groups: CAN group – cannabis users, and non-CAN group –cannabis non-users. Distribution of data were checked, and normally distributed variables are shown as means and standard deviation. If data were skewed/not normal, medians and interquartile range (IQR) were presented. For categorical data, frequencies and percentage were presented. Tests of significance comparing the two groups (CAN and non-CAN) were chosen according to the type of variables (Chi Square, Fisher's Exact, analysis of variance and Kruskal-Wallis tests) and correlation analysis was conducted by clinical epidemiologist AJ and team.

Further analysis was conducted to assess for correlations between cannabis use and mood (BAI and BDI scores) using Pearson correlation coefficients. Correlation between cannabis use and seizure control was assessed by categorizing included participants into those with poor seizure control (>1 seizure / 1–2 months) and good control, using the Chi Square test.

Linear regression analysis was conducted to assess important predictors (cannabis use, depression severity [BDI scores] and anxiety severity [BAI scores]) of sleep efficiency (on PSG), PSQI scores and ESS scores.

3. Results

Among 54 consenting patients, a total of 51 (21 males) underwent PSG and hence, could be enrolled during the study period. Further, 25 patients (13 females) reported cannabis use, hence were classified under group 1 and the remaining 26 (18 females) under group 2.

3.1. Demographic and epilepsy characteristics

A majority among enrolled patients (47/51) had focal onset epilepsy and a little more than 50 % had poorly controlled epilepsy.

Patients who used cannabis were significantly younger (p=0.01) with shorter epilepsy duration (p=0.01) compared to non-users. All other epilepsy characteristics were similar in both groups. (Tables 1A and 1B)

3.2. Cannabis use

All the patients reporting cannabis use, were daily or once per 2 days users and all had been using for >10 years. The route was both inhalational and oral, but mostly the former. None of these patients reported prescription use of cannabinoid, although all patients justified use by stating it would help their either sleep, lower anxiety, relieve pain or combinations of these indications.

Table 1
Demographic, epilepsy related, sleep and mood characteristics of PWE using cannabis versus those not using cannabis.

Table 1A

Characteristics	CAN group (n=25) Cannabis users		Non-CAN group (n=26) Cannabis non-users		p-value
	Mean	SD	Mean	SD	
Age (years)	36.3	14.8	48.3	15.0	**0.01**
Epilepsy duration (years)	10.4	7.3	19.0	14.3	**0.01**
PSQI score	7.2	2.9	10.2	5.2	**0.02**
ESS score	14.0	4.1	15.3	5.9	0.37
BDI score	38.9	10.0	45.6	13.3	0.06
N3 %	18.4	9.1	21.3	15.6	0.44
REM%	17.4	8.5	18.4	6.8	0.70
WASO number	20.1	13.5	25.0	14.5	0.25
	Median	IQR	Median	IQR	
BAI score	23.0	0.0	23.0	0.0	0.19
Sleep onset latency (min)	1.9	9.5	3.4	5.5	0.51
Sleep efficiency (%)	89.8	22.0	87.9	19.1	0.71
RDI (#/hr)	6.2	13.1	7.2	17.1	0.87
PLMI (#/hr)	0.5	7.4	3.0	18.6	0.19
Spontaneous arousal index (#/hr)	2.6	7.4	1.4	4.5	0.14
WASO duration (min)	36.5	76.5	50.0	78.8	0.87

Table 1B

Characteristics	Group 1 (n=25) Cannabis users		Group 2 (n=26) Cannabis non-users		p-value
	Frequency	%	Frequency	%	
Sex					0.28
Male	12.0	48	9.0	33	
Female	13.0	52	18.0	66	
# of ASM					0.83
1	7	28	6	22	
2	11	44	12	44	
3	4	16	5	18	
4	1	4	3	11	
Epilepsy Type					0.66
Focal	22	91	24	92	
Generalized	2	8	2	7.7	
Epilepsy Control					0.49
Poor	11	44	14	53	
Good	14	56	12	46	
Excessive daytime sleepiness					0.17
No (ESS <10)	2	8	5	22	
Yes (ESS >/=10)	22	92	17	77	
SE					0.97
Normal (SE>85 %)	14	56	14	54	
Not Normal (SE<85 %)	11	44	12	46	
BAI					0.10
Low Anxiety	0	0	3	13	
Moderate Anxiety	24	100	19	86	
Severe Anxiety	0	0	0	0	
BDI					0.07
Normal	0	0	0	0	
Mild	0	0	0	0	
Borderline	0	0	0	0	
Moderate	6	25	4	18	
Severe	8	33	2	9	
Extreme	10	41	16	72	

PWE=people with epilepsy; PSQI=Pittsburgh sleep quality index; ESS=Epworth sleepiness scale; BDI= Beck's depression inventory; N3 %= percentage of slow wave sleep; REM%= percentage rapid eye movement sleep; WASO=wake after sleep onset; BAI=Beck's Anxiety inventory; RDI= Respiratory disturbance index; PLMI= periodic limb movement index
ASM=antiseizure medication; BAI=Beck's Anxiety inventory; BDI= Beck's depression inventory; ESS = Epworth sleepiness scale; SE = Sleep efficiency

3.3. Sleep characteristics

Self-reported sleep quality assessed by the PSQI was significantly better (p=0.02) among cannabis users (mean score 7.2 ±2.9,) compared

to cannabis non-users (mean score 10.2 ±5.2). ESS scores were similar in both groups and the number of patients with ESS score >10 (excessively sleepy) was also similar (Table 1A).

In terms of PSG, there were no significant differences observed between the two groups on all parameters studied (Fig. 1 and Table 1). Median *sleep efficiency* was normal (>85 %) in both groups, however, almost half of the patients in both groups had sleep efficiency out of the normal range (<85 %) (Pacek et al., 2017; Boulos et al., 2019), with a total of 9 cannabis users and 7 cannabis non-users having low sleep efficiency (<80 %) and 6 cannabis users and 4 non-users demonstrating high sleep efficiency (>95 %). Median *sleep onset latency* was observed to be very low in both groups, indicative of possible overall excessive sleepiness, which was observed on subjective assessment through the ESS in majority patients enrolled in both groups. Twelve cannabis users (48 %) fulfilled PSG criteria for diagnosis of obstructive sleep apnea, compared to 7 non-users (27 %). Two cannabis users and one -cannabis non-user had significant periodic limb movement activity. (Tables 1A and 1B)

3.4. Mood disturbances

All cannabis users (100 %) and 19 cannabis non-users (86 %) reported moderate anxiety, as assessed through the BAI. Importantly, all patients in both groups reported significant depressive symptoms, the majority scoring in the severe or extreme range on the BDI. No significant difference was observed between the two groups.

3.5. Correlation and linear regression analysis

Cannabis use was not found to be significantly correlated with age, sex, sleep quality (PSQI scores and sleep efficiency) or severity of daytime sleepiness (ESS scores).

There was a significant linear correlation between depression severity (BDI scores) and subjective sleep quality (PSQI scores) as well as excessive daytime sleepiness (ESS scores), but not with objectively assessed sleep efficiency (Table 2).

Table 2
Correlation analysis of sleep quality with cannabis use and mood among PWE.

Parameters	Parameter estimate	Standard error	T Value	P	95 % confidence limits
Objectively assessed sleep quality (Sleep efficiency)					
Cannabis use	−4.34	5.7	−0.76	0.44	−15.8–7.2
Anxiety scores (BAI)	1.2	1.07	1.16	0.25	−0.9 – 3.4
Depression scores (BDI)	0.2	0.25	0.83	0.41	−0.3 – 0.7
Subjective sleep quality (PSQI scores)					
Cannabis use	−1.53	1.2	−1.28	0.2	−3.9 – 0.8
Anxiety scores (BAI)	−0.14	0.2	−0.61	0.54	−0.6 – 0.3
Depression scores (BDI)	0.17	0.04	3.53	0.001	0.07 – 0.3
Excessive daytime sleepiness (ESS scores)					
Cannabis use	0.9	1.3	0.72	0.5	−1.6 – 3.6
Anxiety scores (BAI)	−0.46	0.25	−1.84	0.07	−0.9–0.05
Depression scores (BDI)	0.25	0.05	4.76	<0.0001	0.1 – 0.3

PWE=people with epilepsy; BAI=Beck's Anxiety inventory; BDI= Beck's depression inventory; ESS = Epworth sleepiness scale; PSQI=Pittsburgh sleep quality index

4. Discussion

This prospective study compared sleep quality and sleep architecture as well as mood among PWE who were cannabis users versus non-users who were admitted to a Canadian tertiary epilepsy care referral center. While cannabis users reported significantly better sleep quality than non-users, surprisingly, no objective differences in polysomnography were observed. Cannabis users were younger, with a significantly shorter epilepsy duration compared to the non-users. Importantly, excessive daytime sleepiness and depressive symptomatology was found to be highly prevalent in both groups, without any significant difference between groups.

To our knowledge, this is the first study prospectively examining sleep quality on both subjective and objective (PSG) measures among

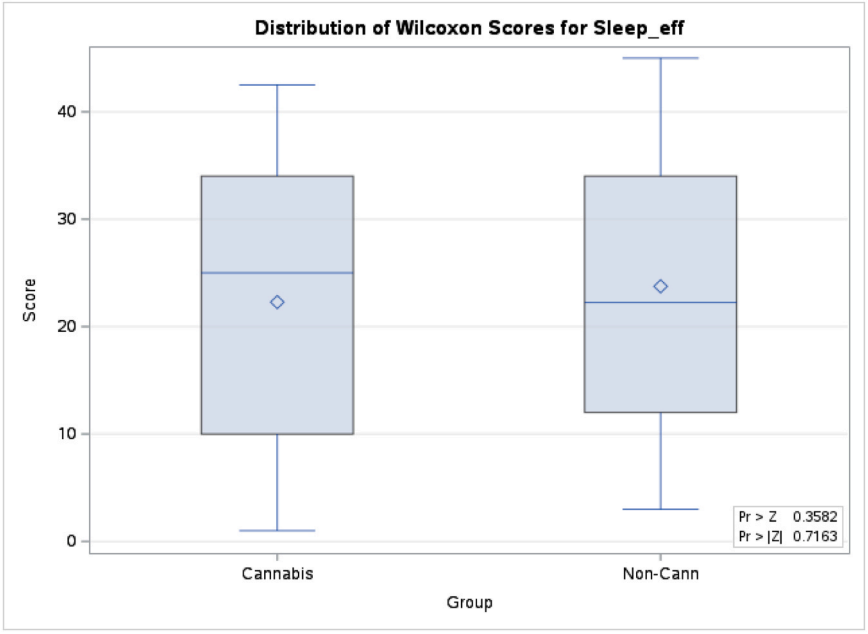

Fig. 1. No significant relationship between sleep efficiency (Sleep_eff) and cannabis use, (Cannabis=Cannabis users and Non_Cann=Cannabis non-users) with $p<0.05$ significance level, using the Wilcoxon sign rank sum test. Y-axis demonstrates the Wilcoxon scores.

PWE. Median age of cannabis users among participants is similar to that in other recent reports on PWE, (Esmonde-White et al., 2023; Roberts-West and Baxendale, 2023) and while the non-users in our study were older. Our findings are in line with larger population-based age differences between cannabis users and non-users (Parekh et al., 2020).

4.1. Sleep quality and cannabis use - Subjective

In a cross-sectional and longitudinal study by Strickland et al., (Strickland et al., 2021) sleep scores (assessed using the PSQI) were reported better for CBD users (n=280) compared to non-users (n=138); findings similar to ours. Pesantez-Rios et al (Pesantez-Rios et al., 2017). found 50 % of 15 drug resistant PWE to report significant improvement in sleep (subjectively) along with other neurocognitive improvements at one year of cannabidiol use. In a questionnaire-based study on PWE admitted to an EMU, 216 of 292 had confirmed diagnosis of epilepsy. While only 10 % of these reported using cannabis products for sleep induction, sleep improvement was reported by 77.3 % (Massot-Tarrus and McLachlan, 2016). Esmonde-White et al (Esmonde-White et al., 2023). found 42.2 % of 395 participants (PWE and/or functional neurologic disorder admitted to EMU) reporting marijuana use for sleep disturbances, and majority experiencing a 'positive impact' on their sleep. The only other studies reporting sleep-related parameters are from PWE with epileptic encephalopathies (mostly Dravet's and Lennox Gastaut syndrome), which indicate cannabidiol use to not have any significant effect on subjective sleep quality or daytime sleepiness (Devinsky et al., 2017, 2018). More recently, these authors found no benefit for sleep duration among 29 drug resistant PWE. In a 2018 systematic review on safety and efficacy of cannabidiol in epilepsy, no change from baseline to end of cannabidiol treatment was observed in sleep disruption and ESS scores (Lattanzi et al., 2018). This is the only study among those using a validated sleep quality assessment tool (PSQI) to quantify subjective sleep quality in PWE. Moreover, there are no previous reports on PWE with comparative sleep assessment data for cannabis-users and cannabis non-users. Among non-epilepsy populations, Fisk and Montgomery have demonstrated no significant difference in ESS scores, sleep quality, average total sleep time and other sleep parameters comparing cannabis-users to substance-naïve participants (Fisk and Montgomery, 2009). These findings indicate fairly high perception of subjective sleep improvement with cannabis use among PWE, but not among otherwise healthy adults.

4.2. Sleep quality and cannabis use - PSG

We found many patients to have either very high (>95 %) (2 among cannabis users, 4 among non-users) or very low sleep efficiency (<80 %) (9 patients among cannabis users and 7 among non-users). Importantly, most patients in both groups had very short sleep onset latencies. These findings were in line with the very high percentage of patients reporting excessive daytime sleepiness (ESS scores >10).

There are no previous studies among PWE reporting polysomnographic findings among currently available in literature. However, in a non-epilepsy population, Pacek et al., reported portable polysomnographic assessment of a cannabis users (n=87). More than half (55 %) had average sleep efficiency of <85 % and 31 % had prolonged (>30 min) sleep onset latency (Pacek et al., 2017). The latter finding of prolonged sleep onset latencies (compared to very short latencies in our study) suggests differences between epilepsy and non-epilepsy populations.

Overall prevalence of sleep disordered breathing was high with 37 % patients fulfilling PSG criteria for sleep apnea diagnosis without any significant differences between cannabis users and non-users. Findings are largely similar from other studies on epilepsy patients (Phabphal et al., 2022; Sivathamboo et al., 2019).

While PWE who were cannabis users had significantly better self-reported sleep quality, no difference was observed on PSG, when compared to PWE not using cannabis, as stated earlier. One possible factor that could explain the discrepancy between the self-reported sleep quality and the PSG scores could be the psychoactive effects of cannabis. Therefore, cannabis may have been a key player in altering the perception of sleep without having a significant effect over the objective sleep parameters. For example, THC has great euphoric and sedative effects and these effects can make the users feel that their sleep quality might be better even if the physiological markers measured by the PSG remain unchanged.

4.3. Cannabis use, mood disturbances and sleep - interrelationships

We did not observe any correlation between cannabis use and mood disturbances (assessed with BDI and BAI). Wahby et al., (Wahby et al., 2019) on the other hand found cannabis use to be independently associated with depression and with lower Quality of Life (QoL), worse epilepsy-related disability, and lower satisfaction with anti-seizure medication.

We found high prevalence of mood disturbances with almost all PWE among cannabis users as well as non-users reporting depressive symptoms. Additionally, a majority among these also had high ESS scores suggestive of excessive daytime sleepiness, without any significant inter-group differences. A significant linear correlation of depression severity with excessive daytime sleepiness (ESS scores) was also observed, but not with cannabis use or any PSG sleep parameter. A recent multicenter study from Turkey on epilepsy patients, found excessive daytime sleepiness in 9.6 % with ESS>10, 46.5 % with poor sleep quality (on PSQI) and 26.1 % with BDI>16 (Athira et al., 2024). A Korean study on 235 patients who had obstructive sleep apnea and epilepsy found ESS>10 among only 24.7 % patients (Jo et al., 2022). Another study from Spain reported ESS>10 among 14 % and depression diagnosed through the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) scale score of greater than 13 in 33.3 % of 48 patients recruited from their epilepsy monitoring unit (Gonzalez-Martinez et al., 2022). Differences in prevalence of excessive daytime sleepiness and depression in these studies from our observations could be attributable to socio-cultural differences and the potential differences in patients' responses on tools which were originally standardised in the English language. Additionally, our patient population was older and with poorly controlled chronic epilepsy, recruited from the epilepsy monitoring unit.

In a case controlled study on 43 epilepsy patients, BDI scores were found to be the major determinant of sleep quality determined by PSQI scores, similar to observations in the current study (Karapinar et al., 2020). Similar findings were also reported in another study on patients with partial (focal onset) epilepsy (Moser et al., 2015). The complex interrelationship between depression and sleep quality has been well recognized (Asarnow and Manber, 2019) with clear effect of poor sleep quality on depressive symptoms (Joo et al., 2022), and the high prevalence of sleep problems among patients with depressive disorder (67–84 % of adults and 57 % of children and adolescents report difficulties initiating or maintaining sleep) (Ford and Kamerow, 1989; Emslie et al., 2012). These effects are likely reflected in the findings in the current study, although the association of BDI scores and ESS scores is much diverse among the studies cited above, compared to the strong correlation in the current study. This has been discussed above and could be due to an older patient population and the majority suffering from poorly controlled epilepsy.

4.4. Strengths and limitations

The major strength of this study is its prospective detailed structured subjective assessment as well as objective PSG assessment of sleep quality and structured mood assessment in PWE who are cannabis users versus non-users. This adds valuable information confirming the limited role of cannabis to affect sleep or mood, which are common reasons for

which PWE report using cannabis products.

One limitation of this study is its small sample size and lack of healthy control comparison groups. Although the study is sufficiently powered to address the research questions, especially for a difficult-to-treat epilepsy population which has high prevalence of sleep and mood related comorbidities, a larger sample size would have allowed us to better capture variability in the populations of interest. Nonetheless, this study does provide preliminary evidence to aid future multicenter studies on larger epilepsy populations.

Another limitation of our study is the focus on whole cannabis rather than specific cannabinoids like CBD or THC. This approach was more practical for our study as well as more representative of real-life associations between cannabis use and sleep among PWE, yet, it is important to understand that whole cannabis contains compounds like terpenes that may alter outcomes, making it difficult to isolate the effects of cannabinoids alone.

5. Conclusions

Self-reported sleep quality is better among PWE who report regular cannabis use. However, no significant difference on objective PSG assessment of sleep quality is observed between PWE who are cannabis users versus non-users. Additionally, severity of depressive symptoms is a significant predictor of sleep quality and of excessive daytime sleepiness among PWE.

Ethical conduct of research

The research project was initiated following approval of the proposal by Queen's University Health Sciences Research Ethics Board, TRAQ#6027926

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CRediT authorship contribution statement

Helen Driver: Writing – review & editing, Project administration, Methodology, Formal analysis. **Ana Johnson:** Writing – review & editing, Formal analysis. **Lysa Boissé Lomax:** Writing – review & editing, Project administration, Methodology. **Gavin P Winston:** Writing – review & editing, Validation. **Stuart Fogel:** Writing – review & editing, Methodology, Formal analysis. **Zaitoon Shivji:** Project administration, Methodology, Data curation. **Rishabh Sablok:** Writing – review & editing, Writing – original draft. **GARIMA SHUKLA:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Funding acquisition, Conceptualization.

Declaration of Competing Interest

None of the authors report any conflict of interest relevant to this manuscript.

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