Publications (in year wise descending order).

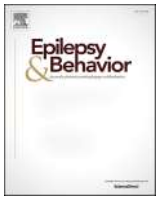
S.No.	Author(s)	Title	Name of Journal	Volume	Page	Year
1.	Neetu Choudhary, Ashok Kumar, Vaishali Sharma, Kirandeep Kaur, Parampreet Singh Kharbanda, Jitupam Baishya, Kamalesh Chakravarty	Effectiveness of CBT for reducing depression and anxiety in people with epilepsy: A systematic review and meta-analysis of randomized controlled trials	Epilepsy & Behavior	151	109608	2024
2.	Vaishali Sharma, Kamalesh Chakravarty, Sucharita Ray	Questionnaire-based Assessment of Sleep Abnormalities in Patients with Migraine: A Cross-Sectional Study with a Comparison Group	Annals of Indian Academy of Neurology	26S186		2023
3.	Vaishali Sharma, Kamalesh Chakravarty, Sucharita Ray	Questionnaire-based evaluation of sleep abnormality in patients with primary headache disorder: A cross-sectional study from tertiary care centre	Journal of the Neurological Sciences	455	212	2023
4.	Vaishali Sharma, Kamalesh Chakravarty, Vivek Lal, Parampreet Singh Kharbanda, Sucharita Ray, Aastha Takkar Kapila	Sleep and Headache Characteristics in Patients with Idiopathic Intracranial Hypertension (IIH) - An Observational Study	Annals of Indian Academy of Neurology	25	S296-297	2022
5.	Vaishali Sharma, Kamalesh Chakravarty, Sucharita Ray, Vivek Lal, Aastha Takkar, Parampreet Kharbanda	Evaluation of prevalence and severity of obstructive sleep apnea using overnight-polysomnography in patients with idiopathic intracranial hypertension	Journal of the Neurological Sciences	429	209	2021

Epilepsy & Behavior 151 (2024) 109608

Contents lists available at ScienceDirect

Epilepsy & Behavior

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



Effectiveness of CBT for reducing depression and anxiety in people with epilepsy: A systematic review and *meta*-analysis of randomized controlled trials

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ARTICLE INFO

Keywords:
Epilepsy
Cognitive Behavioral Therapy
CBT
Depression
Anxiety

ABSTRACT

Background: Patients with epilepsy suffer from depression and anxiety that reduces quality of life. Cognitive behavioral therapy (CBT) among various non pharmacological treatment recommended for depression and anxiety. Since there are several articles reporting CBT treatment for depression in patients with epilepsy, we conduct a *meta*-analysis to evaluate the effectiveness of CBT for adult patients with epilepsy.

Methods: Four electronic databases PubMed, Scopus, Embase, and the Cochrane library searched for relevant studies. A detailed "RISK of bias" assessment has been done for included studies. Funnel plot was used for assessing publication Bias. R Software- RStudio 2022 was used to calculate standard mean difference (SMD). The study has been registered in PROSPERO (CRD42023447655).

Results: Eventually, a Total 13 studies involving 1222 patients met the eligibility criteria. There was decline in the Patient Health Questionnaire (PHQ) [SMD = -0.42, 95 % CI = -0.63 to −0.22], Neurologic Disorder Depression Inventory-Epilepsy (NDDI-E) [SMD = -0.53, 95 % CI = -0.75 to −0.31], Beck depression Inventory (BDI) [SMD = -0.69, 95 % CI = -1.08 to −0.30], Hospital Anxiety and Depression Scale-Depression (HADS-D) [SMD = -0.73 , 95 % CI = -0.94 to -0.52] and Hospital Anxiety and Depression Scale Anxiety subscale (HADS-A) [SMD = -0.66, 95 % CI = -0.87 to −0.45] score of the CBT group than that of the control group at post-intervention. The results showed that the improvement in QOLIE-31 score of the CBT group than that of the control group [SMD = 0.67, 95 % CI = 1.33] at post-intervention.

Conclusion: The result of our study showed that Cognitive behavioral therapy is a superior therapy for treating anxiety and depression in epilepsy patients. CBT was effective in improving Quality of life in patients with epilepsy. However, the sample size varied across the trials, additional high-quality studies are needed in the future.

1. Introduction

Epilepsy is the most prevalent chronic neurological condition, affecting 65 million people globally [1]. Epileptic seizures have a detrimental effect on the patient's mental well-being and social life, which includes their education, interpersonal relationships, and career [2,3]. In addition to the increased prevalence of comorbid conditions such as insomnia, despair, mental problems, anxiety, and cognitive and behavioral impairment, cognitive and neurobiological implications are secondary effects [3–5]. Around one-third of the population suffering from epilepsy is more likely to experience depression, anxiety, and stigma [6]. In real-world clinical practice, higher levels of anxiety and depression are associated with a lower quality of life in patients with epilepsy [7]. Anti-epileptic medications used to treat epilepsy can also affect a patient's behavior and mood. People with epilepsy (PWE) experience a lower quality of life due to the unpredictable nature of seizures and the presence of co-occurring disorders. All of these indicators underscore the importance of identifying effective interventions

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https://doi.org/10.1016/j.yebeh.2023.109608
Received 18 September 2023; Received in revised form 18 November 2023; Accepted 21 December 2023
Available online 5 January 2024

for depression, anxiety, and quality of life in individuals with epilepsy. To address these psychiatric issues and improve their quality of life, various therapies are utilized, such as mindfulness-based treatment, cognitive behavioral therapy (CBT), yoga, and meditation [8–10]. CBT is mostly utilized to resolve these issues, which subsequently improves their quality of life. Cognitive Behavioral Therapy (CBT) was proposed many years ago, but it has not been widely adopted in regular settings. It is recommended as a very effective approach in reducing depression and anxiety in people with epilepsy [11]. A review has shown that cognitive-behavioral treatment does not significantly alleviate depression in the majority of epileptic patients [12].

The majority of previous reviews were limited to mixer of various types of psychological interventions, age groups (childhood, adult, and older adult), and different research designs (RCTs, case-control) [11,13]. To the best of our understanding, previous systematic reviews have included all age ranges in a comprehensive review, rather than focusing on specific age groups such as childhood, adulthood, or older adulthood. None of these reviews specifically compared cognitive behavioral therapy (CBT) with an identical control group that did not receive any intervention, such as pharmacotherapy or psychotherapy.

Therefore, to address these difficulties quantitatively, a systematic review and *meta*-analysis are currently required. This is the first systematic review focusing exclusively on the effects of CBT for depression and anxiety in adults with epilepsy as both are highly comorbid and coexists with each other.

The current review aims to investigate the effect of Cognitive behavioral therapy (CBT) in reducing depression and anxiety among people with epilepsy at post-intervention. Furthermore, it is important to note that depression and anxiety significantly affect an individual's overall well-being. Therefore, our study also seeks to investigate the enhancement of quality of life in these individuals following the administration of cognitive behavioral therapy.

2. Methods-

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards and Cochrane recommendations were followed for the systematic review. Prospero (CRD) was used to register the protocol (CRD42023447655).

2.1. Search strategy

The search was carried out using four electronic databases: PubMed, Scopus, Embase, and the Cochrane library. No language restriction filter was employed during the search. The last search was conducted in September 2022. The search term used "(Epilepsy or Seizure) AND (Cognitive behavioral therapy OR CBT) AND (Anxiety OR Depression)".

2.2. Eligibility criteria

The trials considered were all randomized controlled trials (RCTs) that matched the following criteria: [1] The intervention should incorporate cognitive-behavioral therapy [2] There should be no intervention in the control group (care as usual, waitlist control); [3] The study population should only comprise adult epilepsy patients; [4] There should be outcome measures of depression, anxiety, or both as an outcome, and The following were the exclusion criteria: [1] A psychogenic nonepileptic seizure (PNES) was included in the study; [2] There was a lack of among depression, anxiety, and quality of life as measuring outcomes. [3] Other than RCT studies.

2.3. Data extraction

Data were retrieved by two independent reviewers (NC, AK), who included screening titles and abstracts. A complete test screening was also performed. If these two reviewers couldn't agree, a third reviewer (VS) was asked for a discussion. The authors were contacted for more information and to clear up any inaccuracies. The data were extracted from the selected articles e.g., authors, year, country, design, population, intervention, comparator, sample size, outcomes, measurements, and other characteristics of chosen RCTs included type of Intervention, Mode of Intervention, number of sessions, duration (weeks), Therapy provider and follow-up etc. Demographic details, pre-treatment to post-treatment measures of depression, anxiety and QoL were extracted. Depression and anxiety were the primary focus of the study, measured by using various assessment scales. Depression scales used in these RCTs were- Neurologic Disorder Depression Inventory-Epilepsy (NDDI-E), Geriatric Depression Scale (GDS), Center for Epidemiologic Studies Depression Scale (CES-D), Patient Health Questionnaire–9 items (PHQ-9), Depression, Anxiety and Stress Ssscale (DASS), Beck Depression Inventory (BDI), Hospital Anxiety and Depression Scale-Depression (HADS-D), Hamilton Rating Scale for Depression (HAMD). Hopkins Symptom Checklist-20 (HSCL-20), and Quick Inventory of Depressive Symptomatology (QIDS). Anxiety scales used in these RCTs were- Hospital Anxiety and Depression Scale (HADS)-Anxiety subscale, Generalized Anxiety Disorder-7 and Self-Rating Anxiety Scale (SAS). Quality of life evaluated by world health organization's quality of life (WHOQOL), the Behavioral Risk Factor Surveillance System (BRFSS), the quality of life in epilepsy-10-P items (QOLIE-10-P), and the quality of life in epilepsy-31 items (QOLIE-31).

2.4. Statistical analysis

Data were analyzed using the R Software RStudio 2022. We calculated standard mean difference (SMD) and its 95 % CI using (Hedges' g) method to estimate effect of a treatment. The efficacy of CBT was assessed using the mean and standard deviation of the difference between pre-treatment and post-treatment depression, anxiety, and QoL measures to calculate effect sizes. Considering the issue of heterogeneity, we used a random effects model for the calculation. Heterogeneity was assessed with the I^2 statistics for each analysis. The findings of I^2 were categorized as mild (25 %), moderate (50 %), and high (75 %) in their interpretation.

Mainly $I^2 > 50$ % and $p < 0.10$ was considered as heterogeneity among studies. To assess publication bias we used funnel plot in QoL studies as it includes 7 studies. We also used Egger's test to detect publication symmetry.

2.4.1. Meta-analysis

Out of 13 studies included in this review, few studies gave the data in the form of means ± SE (Standard error) So we changed the Standard error into standard deviation by the following formula:

$SD = SE \times \sqrt{n}$.

A missing outcome data is the standard deviations of the mean changes from baseline. SD change was calculated by the following formula for each study:

$$SDchange = \sqrt{SD^2\,baseline + SD^2\,final - (2 \times r \times SD\,baseline \times SD\,final)}$$

Where SD baseline is the Standard deviation at baseline (before intervention), SD final is the standard deviation at post intervention and r is the correlation coefficient that talks about the correlation between the baseline and post intervention measurements. The r value was not mentioned by any of these studies. Corresponding authors were contacted to share their data but none of them share the valued. Later Sd change was calculated by putting value of $r = 0.7$ [14,15], to provide a conservative estimate, in the formula as undertaken by previous systematic reviews [16–18]. This recommended correlation coefficient value of 0.7 was proposed by Rosenthal et al. in 1993 [15].

3. Results

3.1. Study selection

The selection process for articles from four electronic databases is illustrated in Fig. 1. From the initial search, which yielded a total of 2338 articles, 829 duplicate records were removed. Subsequently, 1509 records were screened, and 760 records were removed based on the irrelevance of the abstracts and titles. The full texts of the subsequent 50 articles were accessed for eligibility based on the selection criteria. On the basis of the reasons outlined in Fig. 1, a total of 37 articles were excluded. Finally, 13 articles were included in this review.

3.2. Study characteristics

A table summary of the selected 13 RCTs including authors, year, country, design, population, intervention, comparator, sample size and outcomes measurements are shown in Table 1. Items for the description of the intervention included type of Intervention, Mode of Intervention, number of sessions, duration (weeks), Therapy provider and follow-up (Table 2). The mean, standard deviation, and number of participants for continuous measures such as depression, anxiety, and quality of life at the end of the intervention were obtained. A total of 623 participants in the CBT group and 599 participants in the control group were included in our systematic review and *meta*-analysis.

3.3. Risk of biases

A detailed "RISK of bias" assessment has been done for each included study according to the COCHRANE COLLABORATION bias risk tool, which was used to assess the risk of bias in randomized trials from five areas (selection, performance, attrition, detection and reporting bias). A graphical representation of both the overall and the single-domain risk of bias for the included studies is provided in Fig. 8. A low overall risk of bias was identified in 46.15 % of the included studies (6/13), with six studies having some concerns (46.15 %) and one study having a high risk of bias (7.69 %) Figs. 8 and 9.

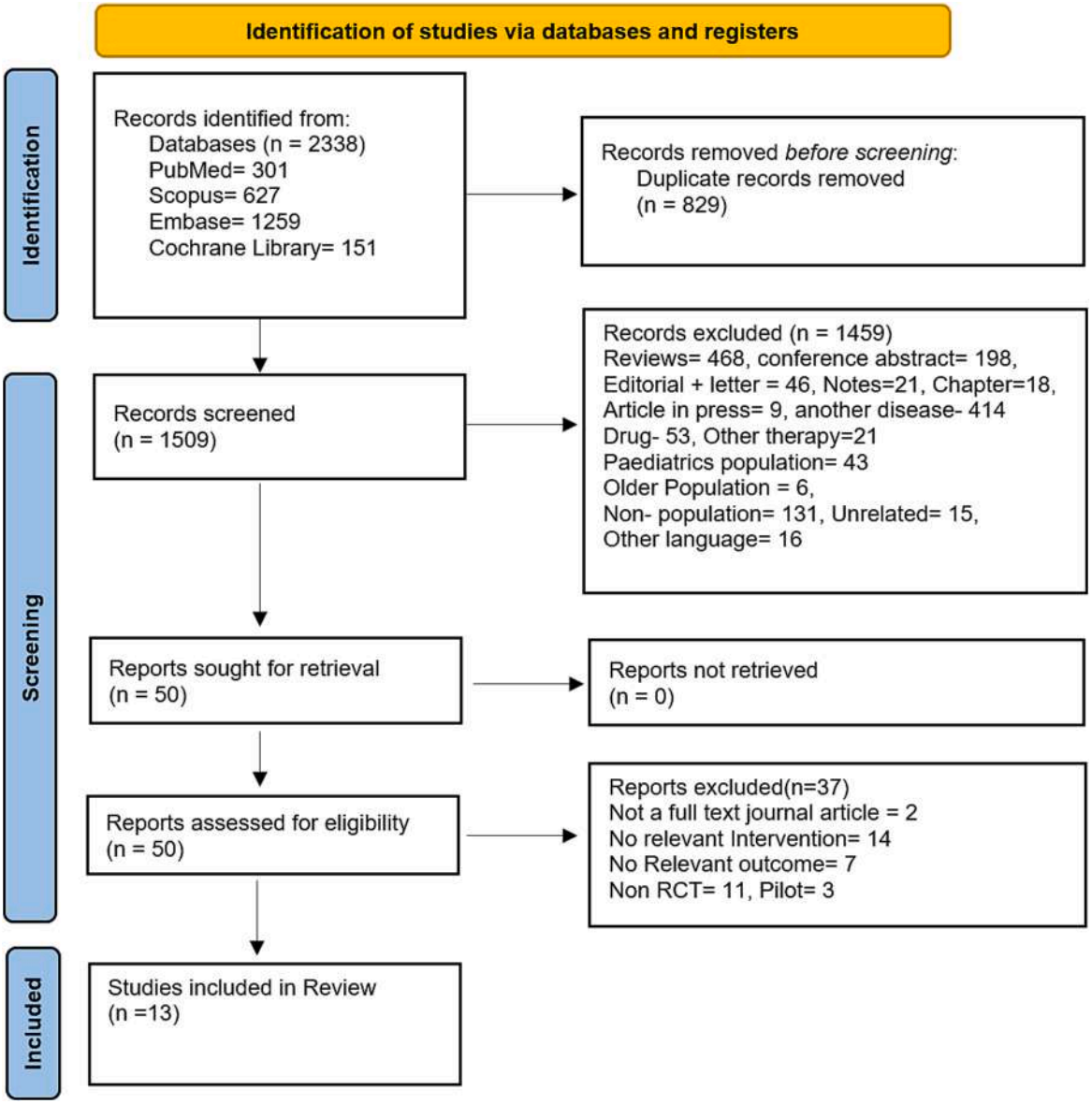

Fig. 1. PRISMA flow diagram.

Table 1
Characteristics of selected 13 randomized controlled trials.

Sr. no	Author Name	Place	Population	Study Design	Sample Size, n (CBT/ Control)	Demographic(Age Mean (SD)) (CBT/Control)	Outcome Measures Depression Scale	Anxiety Scale	Quality o f life scale	Follow up
1	Martinović et al., 2006 [19]	Serbia	Newly diagnosed epilepsy patient	CBT vs TAU	15/15	17.2(2.5)/17.6(2.2)	BDI CES-D HAMD	—	QOLIE-31	9 months
2	Thompson et al., 2010 [20]	USA	People with epilepsy	CBT vs. WLC	26/27	36.4(34.0)/35.4 (31.0)	BDI	—	BRFSS	—
3	Ciechanowski et al., 2010 [21]	USA	People with epilepsy	CBT vs. UC	40/40	44.4(11.1)/43.4 (11.0)	HSCL-20	—	QOLIE-31	12 months
4	Gandy et al., 2014 [22]	Australia	People with epilepsy (PWE)	CBT vs. WLC	20/25	41(12)/38(13)	HADS-D NDDI-E	HADS-A	QOLIE-31	3 months
5	Schr€oder et al., 2014 [23]	Germany	People with epilepsy (PWE)	CBT vs. WLC	38/40	40.03(11.85)/35.03 (9.99)	BDI	—	QOLIE-31	—
6	Thompson et al.,2015 [24]	USA	Adults with epilepsy and mild/moderate depressive symptoms.	CBT vs. TAU	62/56	41.2 (Combined Mean for both groups/SD-NM)	BDI PHQ NDDI-E	—	BRFSS	—
7	Caller et al., 2016 [25]	US	Adult patients with epilepsy with or without uncontrolled seizures	CBT vs. WLC	29/20	49.3(9.2)/41.4 (11.2)	PHQ-9 NDDI-E	—	QOLIE-31	—
8	M. Hum et al., 2019 [26]	Canada	Adult patients with epilepsy	CBT vs EpINFO vs WLC	20/11	36.90(12.96)/29.36 (7.62)	QIDS NDDI-E	—	WHOQOL	—
9	Meyer et al., 2019 [27]	Germany	Participants with epilepsy	CBT vs. CAU	100/100	40.53(12.90)/40.07 (13.40)	PHQ-9 NDDI-E	GAD	QOLIE-10	—
10	Ahorsu et al., 2020 [28]	Hong Kong	People with epilepsy	CBT-I vs. PE	160/160	38.37(13.45)/37.99 (9.88)	HADS-D	HADS-A	QOLIE-31	—
11	M. Spruill et al., 2021 [29]	USA	Hispanic patients with elevated depressive symptoms	CBT vs. CAU	36/36	47.0(11.4)/39.6 (10.0)	PHQ-9	—	—	12 months
12	Moncrief et al., 2021 [30]	US	Adults with epilepsy	CBT vs. CAU	31/20	49.16(9.13)/41.45 (11.20)	PHQ-9	—	—	—
13	Feng et al., 2022 [31]	China	Patient with Epilepsy	CBT vs CONTROL	46/49	30.56(5.57)/31.16 (6.32)	HDMA	SAS	QOLIE-31	—

SD- Standard Deviation, CBT- Cognitive Behavioral Therapy, TAU- Treatment as usual, WLC- Wait-list Control, UC- Usual Care, PE- Patient education, The Neurologic Disorder Depression Inventory-Epilepsy (NDDI-E), Geriatric Depression Scale (GDS), Center for Epidemiologic Studies Depression Scale. (CES-D), Patient Health Questionnaire–9 items (PHQ-9), Depression, Anxiety and Stress Scale (DASS), Beck Depression Inventory (BDI), Hospital Anxiety and Depression Scale-Depression (HADS-D), Hamilton Rating Scale for Depression (HAMD). Hopkins Symptom Checklist-20 (HSCL-20), and Quick Inventory of Depressive Symptomatology (QIDS), Hospital Anxiety and Depression Scale (HADS)-Anxiety subscale, Generalized Anxiety Disorder-7 and Self-Rating Anxiety Scale (SAS), the world health organization's quality of life (WHOQOL), the Behavioral Risk Factor Surveillance System (BRFSS), the quality of life in epilepsy-10-P items (QOLIE-10-P), and the quality of life in epilepsy-31 items (QOLIE-31).

3.4. Effect of CBT on depressive symptoms at post-intervention

Total 10 scales used in all 13 RCTs to measure depression. Out of 10 scales, 4 scales used in *meta*-analysis. The remaining six scales were not included in the *meta*-analysis because of limited evidence available (single study for each scale). Depression was assessed by The Neurologic Disorder Depression Inventory-Epilepsy (NDDIE), Geriatric Depression Scale (GDS), Center for Epidemiologic Studies Depression Scale. (CES-D), Patient Health Questionnaire–9 items (PHQ-9), Depression, Anxiety and Stress Scale (DASS), Beck Depression Inventory (BDI), Hospital Anxiety and Depression Scale-Depression (HADS-D), Hamilton Rating Scale for Depression (HAMD). Hopkins Symptom Checklist-20 (HSCL-20), and Quick Inventory of Depressive Symptomatology (QIDS). The negative values of SMDs on the depression scale indicated a reduction in symptoms of depression in patients.

3.4.1. Effect of CBT on PHQ score

Four studies used PHQ scale to measure depression [25,27,29,30]. There was moderate heterogeneity among the four studies ($I^2 = 48$ %, P = 0.12). The results showed the decline in the PHQ score of the CBT group than that of the control group (SMD = -0.42, 95 % CI = -0.63 to −0.22) at post-intervention. A forest plot representing the effect sizes of the studies included in this *meta*-analysis is shown in Fig. 2.

3.4.2. Effect of CBT on NDDI-E score-

Four studies used NDDI-E scores to measure depression in patients with Epilepsy [22,25–27]. There was no heterogeneity among the Four studies [$I^2 = 0$ % (P = 0.82)]. The results showed the decline in the NDDI-E score of the CBT group compared to the control group (SMD = -0.53, 95 % CI = -0.75 to −0.31) at post-intervention. A forest plot for the same in Fig. 3.

3.4.3. Effect of CBT on BDI score

Two studies used BDI to measure depression in patients with Epilepsy [19,23]. There was no heterogeneity among the two studies [$I^2 =$ 25 %, (P = 0.25)]. The results showed the decline in the BDI score of the CBT group than that of the control group (SMD = -0.69, 95 % CI = -1.08 to −0.30) at post-intervention. A forest plot representing for the same shown in Fig. 4.

3.4.4. Effect of CBT on HADS-D score

Two studies used HADS-D scores to measure depression in patients with Epilepsy [22,28]. The results showed the decline in the score of the CBT group than that of the control group (SMD = -0.73 , 95 % CI = -0.94 to -0.52) at post-intervention. There was moderate heterogeneity between two studies ($I^2 = 46$ %, P = 0.17). A forest plot for the same shown in Fig. 5.

Table 2
Details of CBT in 13 randomized controlled trials.

Sr. no	Author Name	Name of CBT Intervention	Format of Intervention (Individual/ Group)	Mode of Intervention (Online/Offline)	No of Session/ Duration of Session	Therapy Provider	Home based practice after sessions (Yes/NO)
1	Martinović et al., 2006 [19]	————	Individual	Offline	8 x 1 h sessions over 2 months	Not reported	Not Reported
2	Thompson et al., 2010 [20]	UPLIFT	Group	Online (net or phone)	8 weekly x 1 h sessions = 8 h	Clinical Psychologist	Yes
3	Ciechanowski et al., 2010 [21]	PEARLS	Individual	Offline (Home based)	8 x 1 h session among 19 weeks	master level social workers	Not Reported
4	Gandy et al., 2014 [22]	————	Individual	Offline	9 weeks	Postgraduate Doctorate level intern psychologists	Yes
5	Schr€oder et al., 2014 [23]	DEPREXIS	Individual	Online (Internet)	9 weeks	Depretis	Not Reported
6	Thompson et al., 2015 [24]	UPLIFT	Group	Online (web/ telephone)	8 weekly x 1 h session = 8 h	Graduate student	Yes
7	Caller et al., 2016 [25]	HOBSCOTCH	Group	Both (Offline and Online)	8 weekly x 45–60 min	Memory coaches	Yes
8	M. Hum et al., 2019 [26]	UPLIFT	Group	Online (Internet or telephone)	8 weekly x 1 h session = 8 h	Licensed mental health professional	Yes
9	Meyer et al., 2019 [27]	EMYNA	Group	Online (Internet)	180 days	Fully automatic Internet Intervention	Accessed over 180 days
10	Ahorsu et al., 2020 [28]	————	Group	Online (mobile app)	6 weeks	Mobile app	Not Reported
11	M. Spruill et al., 2021 [29]	UPLIFT	Group	Telephone	8 weekly x 1 h session = 8 h	Professional	Not Reported
12	Moncrief et al., 2021 [30]	HOBSCOTCH	Group	Offline (Home based)	8 weekly x 45–60 min	Trained HOBSCOTCH coach	Not Reported
13	Feng et al., 2022[31]	————	Group	Both (Offline and Online)	8 weekly x 1 h session = 8 h	Psychotherapist	Not Reported

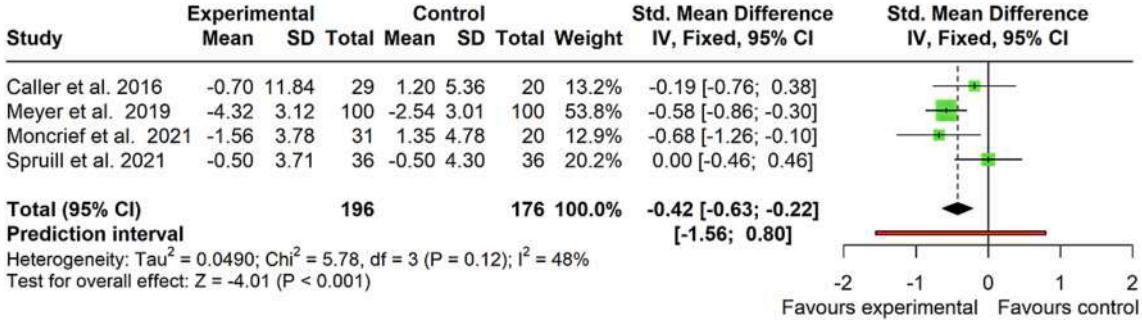

Fig. 2. Forest plot showing the SMD with 95% confidence interval on PHQ scale for depression between CBT group and control group.

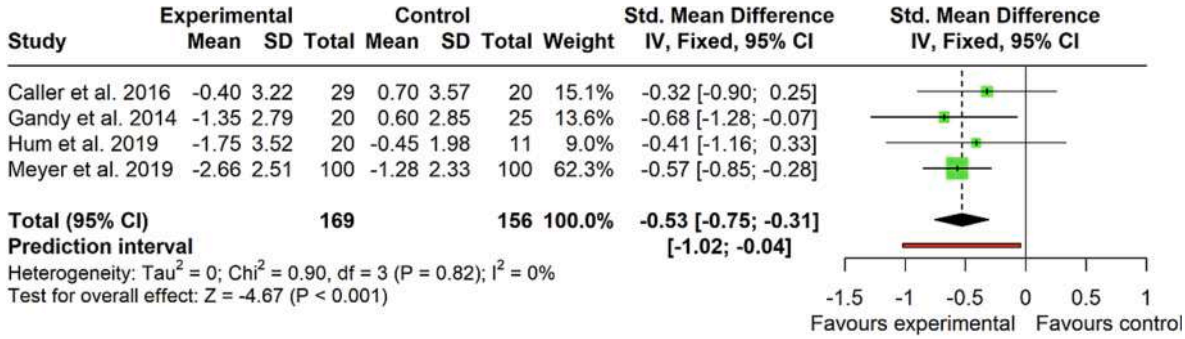

Fig. 3. Forest plot showing the SMD with 95% confidence interval on NDDI-E scale for depression between CBT group and control group.

3.5. Effect of CBT on anxiety symptoms at post-intervention

Anxiety can be assessed by Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A), Generalized Anxiety Disorder-7 and Self-Rating Anxiety Scale (SAS). Amongst them, only one Scale was used in *meta*-analysis.

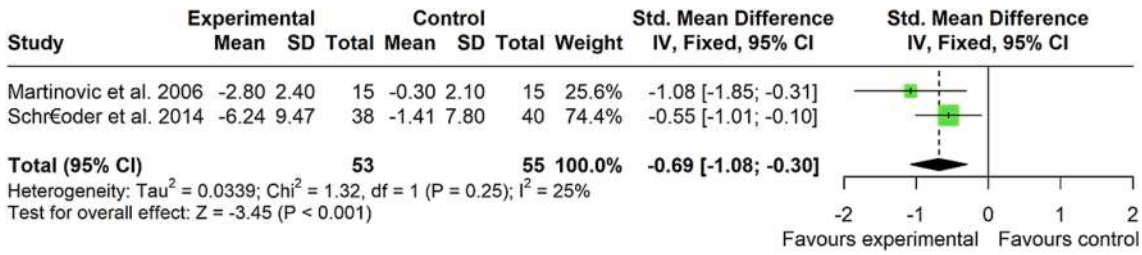

Fig. 4. Forest plot showing the SMD with 95% confidence interval on BDI scale for depression between CBT group and control group.

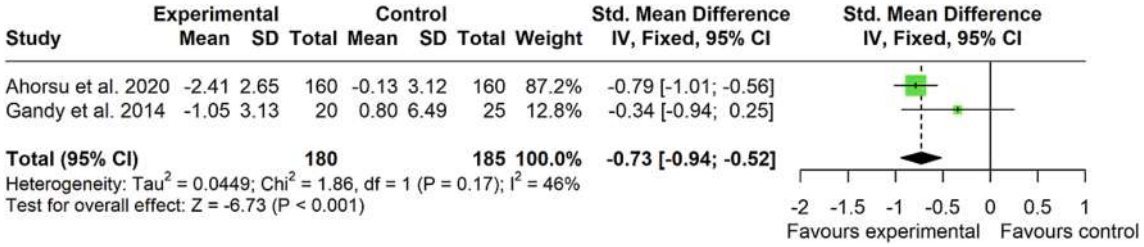

Fig. 5. Forest plot showing the SMD with 95% confidence interval on HADS-D scale for depression between CBT group and control group.

3.5.1. *Effect of CBT on HADS-A score*

Out of 13 trials, only 4 trials measure the anxiety symptoms [22,27,28,31]. These trials showed that CBT was effective in treating anxiety. Only two studies included in this *meta*-analysis, used HADS-A scale to measure anxiety in patients with Epilepsy [22,28]. The remaining two scales (SAS, GAD) were not included in the *meta*-analysis because of limited evidence available (single study for each scale). There was mild heterogeneity among the two studies ($I^2 = 34$ %, $P = 0.22$). The results showed the decline in the score of the CBT group than that of the control group (SMD = -0.66, 95 % CI = -0.87 to −0.45) at post-intervention. The negative values of SMDs on the anxiety scale indicated a reduction in symptoms of anxiety in patients. A forest plot representing for the same shown in Fig. 6.

3.6. *Effect of CBT on quality of life at post-intervention*

The world health organization's quality of life (WHOQOL), the Behavioural Risk Factor Surveillance System (BRFSS), the quality of life in epilepsy-10-P items (QOLIE-10-P), and the quality of life in epilepsy-31 items (QOLIE-31) are all useful tools to assess an individual's quality of life. Only one scale (QOLIE-31) scoring used in *meta*-analysis. The remaining four scales were not included in the *meta*-analysis because of limited evidence available (single study for each scale).

3.6.1. *Effect of CBT on QOLIE-31 scores*

Seven studies used QOLIE-31 scale to measure Quality of life [19,25,28,31,21–23]. There was considerable heterogeneity among the studies ($I^2 = 85$ %, $P < 0.01$) might be due to small sample size (Martinović et al., 2006, n = 16) which was analyzed using a Fixed effects model. The results showed the improvement in QOLIE-31 score of the CBT group than that of the control group (SMD = 0.67, 95 % CI = 1.33) at post-intervention. The positive values of SMDs on the QOLIE-31 scale indicate an improvement in quality of life. A forest plot representing the overall effect of the studies included in this *meta*-analysis is shown in Fig. 7.

3.7. *Publication bias-*

We draw funnel plot for assessing publication Bias for QOLIE-31, and the figure showed that the shape was asymmetric. The P value of the Egger test was 0.284, which indicated significant publication bias existed in this *meta*-analysis (Fig. 10).

4. Discussion

4.1. *Outline of the principal conclusions*

Epilepsy, depression, and anxiety are interconnected through common neurobiological pathways, involving changes in neurotransmitter systems (e.g., serotonin, dopamine, and GABA), inflammatory processes, and alterations in neural circuitry [32,33]. These shared mechanisms contribute to the bidirectional relationship between epilepsy and mental health disorders [34]. The management of depression and anxiety in individuals with epilepsy necessitates an integrated approach, encompassing psychotherapy, cognitive-behavioral therapy (CBT), and pharmacotherapy as prevalent treatment modalities [11,22]. However, caution should be exercised in selecting the appropriate treatment, taking into account potential interactions between antiepileptic drugs

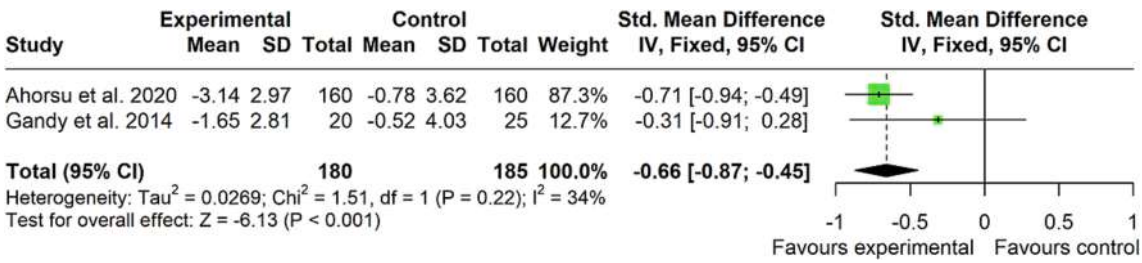

Fig. 6. Forest plot showing the SMD with 95% confidence interval on HADS-A scale for anxiety between CBT group and control group.

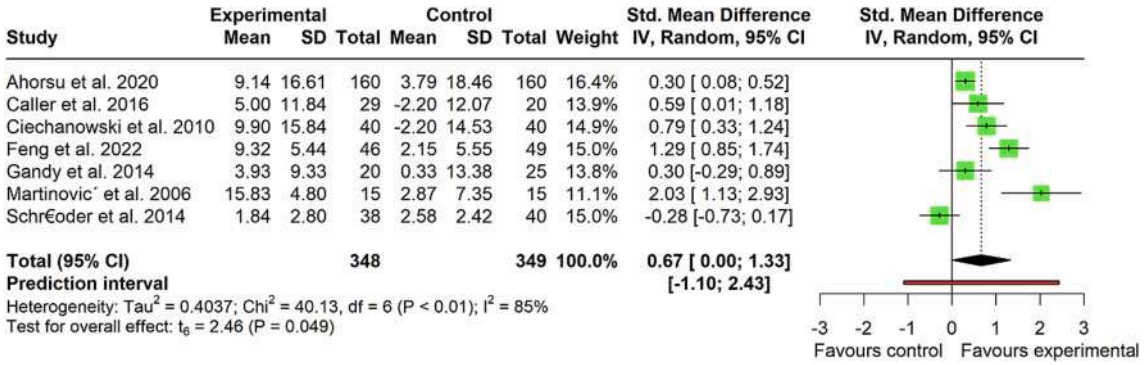

Fig. 7. Forest plot showing the SMD with 95% confidence interval on QOLIE-31 scale for quality of life between CBT group and control group.

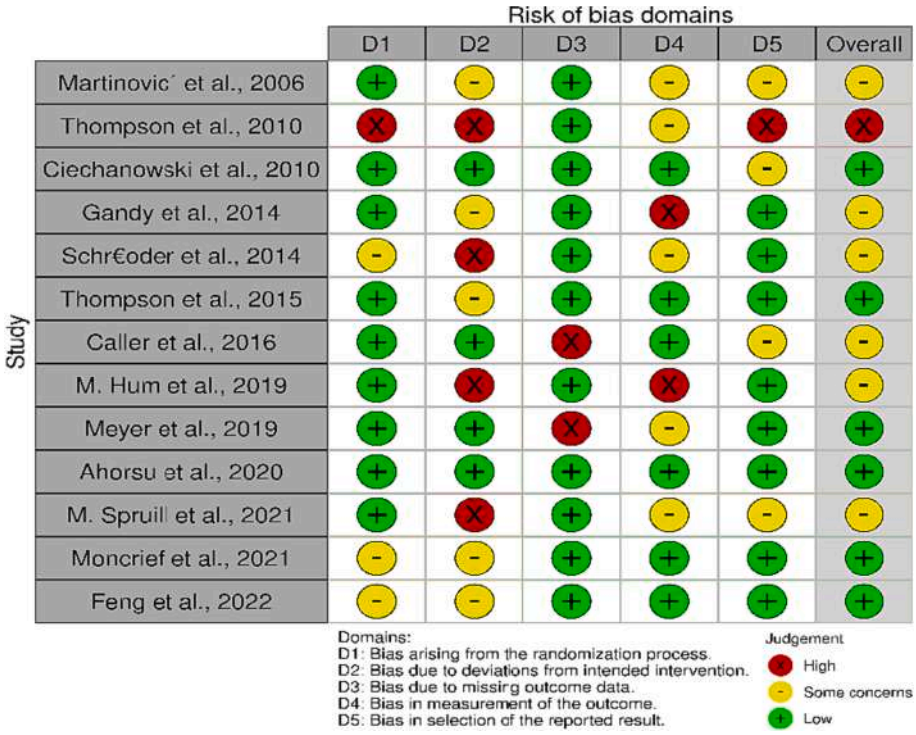

Fig. 8. Risk of bias summary of each included study.

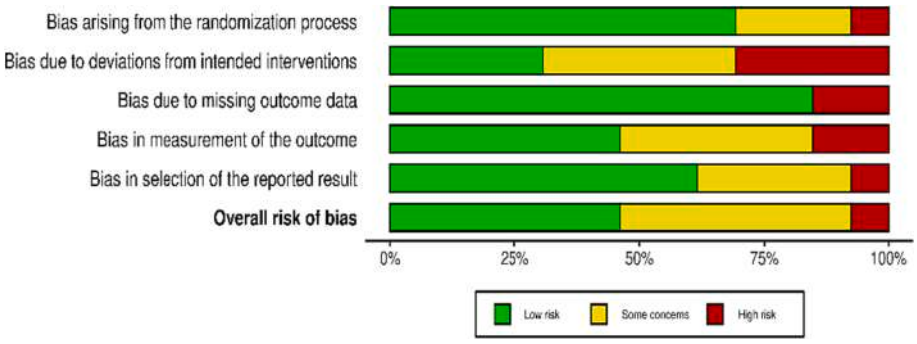

Fig. 9. Proportion of studies with low (green), high (red), or unclear (yellow) risk of bias. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

and antidepressant or anxiolytic medications. Generally, CBT interventions have shown to offer a higher likelihood of improvement in individuals with epilepsy. Based on the trials, majority of PWE who underwent the treatments showed significant improvement in their depressive symptoms and Quality of life. To extent of our knowledge, this is the first *meta*-analysis to calculate the effect of CBT on both depression and anxiety in PWE. Previous systematic reviews were either limited by a therapeutic mix or failed to calculate the effect on anxiety

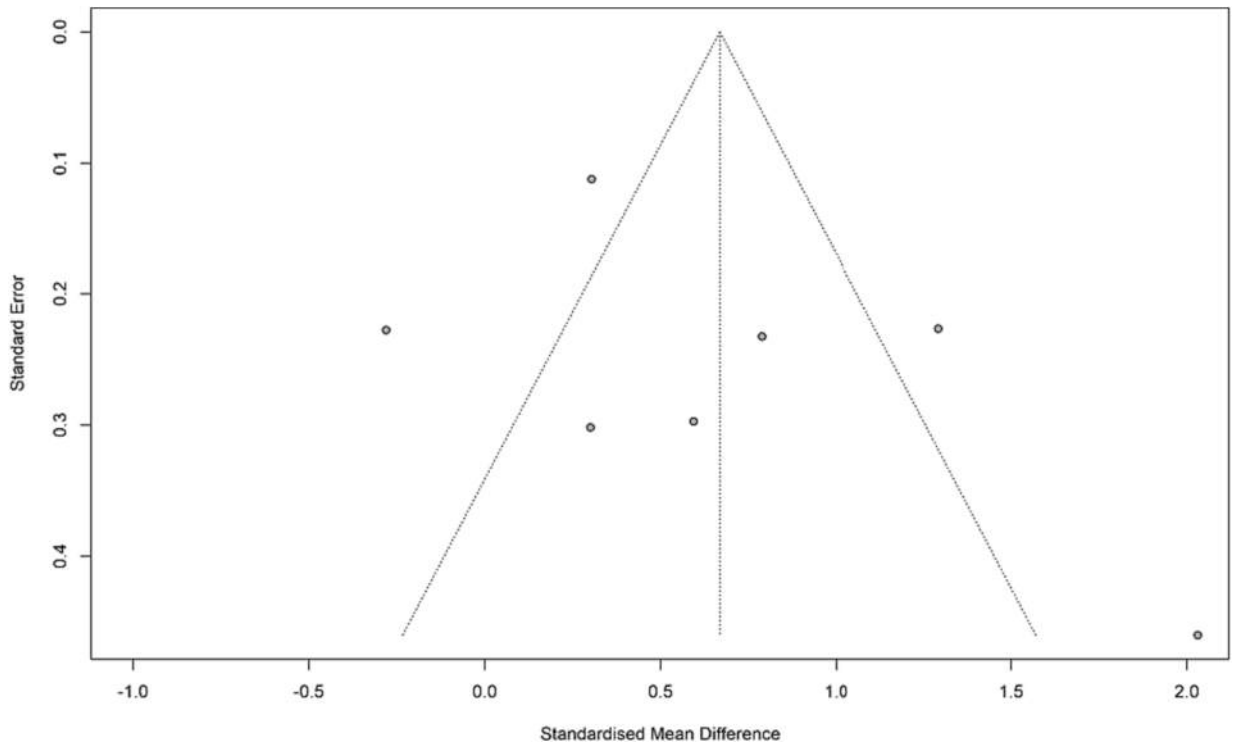

Fig. 10. Funnel plot of publication bias.

[11,13]. Our systematic review and *meta*-analysis included 623 participants in the experimental group and 599 participants in the control group among 13 RCTs. The results of the *meta*-analysis showed that CBT is an effective treatment/ intervention in reducing depression and anxiety in patients with epilepsy.

4.2. Agreement and disagreement with other studies

Among the 13 RCTs included in this analysis, blinding of patients and therapy provider in training was difficult; therefore, the evaluator was single blinded. All studies compared the baseline data of patients' age, sex, pathological grade and stage, treatment plan, and so on. Although many reviews have explored the effectiveness of CBT in PWE [12,13] but no related *meta*-analysis of this topic has been published which include both depression and anxiety together. Previous study has suggested that current CBT treatments have limited effectiveness in reducing depressive symptoms in PWE [12]. Another study showed that CBT is effective in reducing depression [13]. While short-term response rates are higher compared to usual care, most patients do not show significant improvement at long term. It is still unclear whether these treatments have long-term benefits for depression and anxiety. A study by Michaelis et al., 2018 assessed the impact of a CBT intervention on depression and anxiety in epilepsy patients [35]. The study found that CBT led to significant reductions in both depression and anxiety scores, indicating its potential as a therapeutic approach. A study by Macrodimitris et al., 2011 examined the outcomes of CBT in a subset of epilepsy patients with depression and anxiety [36]. The results indicated that while CBT helped reduce depression and anxiety to some extent, its effectiveness was limited in patients with more severe and treatment-resistant forms of both epilepsy and depression.

4.3. Implication for clinical practice

CBT, when utilized alongside conventional treatment methods, has demonstrated efficacy in augmenting the management of anxiety and depression, resulting in a comprehensive enhancement of an individual's overall quality of life. CBT may indirectly reduce seizure frequency in some individuals with epilepsy by addressing stress, anxiety, and medication adherence. Only 2 RCTs focuses on seizure frequency which indicating no significant difference in the effect of CBT on seizure control [21,23].

4.4. Strength

This is the first *meta*-analysis demonstrating the effectiveness of Cognitive Behavioral Therapy intervention for both depression and anxiety and also checked effectiveness on different scales. The criteria for including and excluding literature were rigorous, and the assessment of literature quality revealed that the studies included were of a relatively high standard, thus reinforcing the credibility of the findings This study contributes to the literature on the effectiveness of cognitive behavioral therapy in improving depression, anxiety and quality of life. Furthermore, this *meta*-analysis proved that both individual and group format of delivery are equally effective in improving depression, anxiety and quality of life.

4.5. Limitation

The following are some of this study's limitations: 1) The sample size varied across the trials, with some having fewer than 40 patients and other ranging between 200 and 320. 2) There may have been publication bias because of the few original studies included and the small sample size, which may have affected the aggregated results' correctness, reliability, and scientific validity. 3) Lack of on-going treatment details for epilepsy patients in included studies. 4) The trials included were mostly from high-income countries such as the USA, Australia, Canada, China, and Germany, as different countries might have different standards and approaches to healthcare5). Several Scale used for each outcome measures in these RCTs but we included only limited number of scales 6). Clinical parameters were missing.

4.6. Implications for Future research-

Future research needs to be done to include those studies include anxiety. Further trials with high methodological quality, low-bias risk, and larger sample size are needed to construct a comprehensive literature base, which would facilitate a more thorough cognitive rehabilitation for patients with Epilepsy. Nonetheless, further RCTs are required to establish the effectiveness of CBT in treating anxiety specifically in individuals with epilepsy.

5. Conclusion

Through *meta*-analysis, we have come to the conclusion that CBT is a superior therapy for treating anxiety and depression in epilepsy patients. However, the majority of patients who received the treatments did exhibit significant improvement for depression and anxiety. In general, the findings suggest that there is significant potential for enhancing psychological treatments for distress in PWE. Future research on the management of epilepsy that coexists with depression and anxiety will benefit from this.

CRediT authorship contribution statement

Neetu Choudhary: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing. **Ashok Kumar:** Data curation, Formal analysis, Methodology. **Vaishali Sharma:** Data curation, Resources, Visualization, Writing – original draft. **Kirandeep Kaur:** Data curation, Project administration, Resources, Visualization, Writing – original draft. **Parampreet Singh Kharbanda:** Conceptualization, Methodology, Project administration, Supervision, Validation, Writing – review & editing. **Jitupam Baishya:** Conceptualization, Methodology, Project administration, Supervision, Validation, Writing – review & editing. **Devender Kumar:** Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing. **Akhilesh Sharma:** Conceptualization, Methodology, Project administration, Validation, Writing – review & editing. **Kamalesh Chakravarty:** Conceptualization, Methodology, Project administration, Supervision, Validation, Writing – review & editing, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] Milligan TA. Epilepsy: A Clinical Overview. Am J Med 2021 Jul;134(7):840–7.
[2] Kerr MP. The impact of epilepsy on patients' lives. Acta Neurol Scand Suppl 2012; 194:1–9.
[3] Novak A, Vizjak K, Rakusa M. Cognitive Impairment in People with Epilepsy. J Clin Med 2022 Jan 5;11(1):267.
[4] Macêdo PJOM, Oliveira PS de, Foldvary-Schaefer N, Gomes M da M. Insomnia in people with epilepsy: A review of insomnia prevalence, risk factors and associations with epilepsy-related factors. Epilepsy Res. 2017 Sep; 135:158–67.
[5] Hermann BP, Struck AF, Busch RM, Reyes A, Kaestner E, McDonald CR. Neurobehavioural comorbidities of epilepsy: towards a network-based precision taxonomy. Nat Rev Neurol 2021 Dec;17(12):731–46.
[6] Ridsdale L, Wojewodka G, Robinson E, Landau S, Noble A, Taylor S, et al. Characteristics associated with quality of life among people with drug-resistant epilepsy. J Neurol 2017 Jun 1;264(6):1174–84.
[7] Gonzalez-Martinez A, Planchuelo-Gómez Á, Vieira Campos A, Martínez-Dubarbie F, Vivancos J, De Toledo-Heras M. Perceived quality of life (QOLIE-31-P), depression (NDDI-E), anxiety (GAD-7), and insomnia in patients with epilepsy attended at a refractory epilepsy unit in real-life clinical practice. Neurol Sci 2022 Mar 1;43(3):1955–64.
[8] Hofmann SG, Gómez AF. Mindfulness-Based Interventions for Anxiety and Depression. Psychiatr Clin North Am 2017 Dec;40(4):739–49.
[9] Nakao M, Shirotsuki K, Sugaya N. Cognitive–behavioral therapy for management of mental health and stress-related disorders: Recent advances in techniques and technologies. Biopsychosoc Med 2021 Oct;3(15):16.
[10] Panebianco M, Sridharan K, Ramaratnam S. Yoga for epilepsy. Cochrane Database Syst Rev 2017. Oct 5;2017(10):CD001524.
[11] Maguire MJ, Marson AG, Nevitt SJ. Antidepressants for people with epilepsy and depression. Cochrane Database Syst Rev 2021. Apr 16;4(4):CD010682.
[12] Noble AJ, Reilly J, Temple J, Fisher PL. Cognitive-behavioural therapy does not meaningfully reduce depression in most people with epilepsy: a systematic review of clinically reliable improvement. J Neurol Neurosurg Psychiatry 2018 Nov;89 (11):1129–37.
[13] Li D, Song Y, Zhang S, Qiu J, Zhang R, Wu J, et al. Cognitive behavior therapy for depression in people with epilepsy: A systematic review and meta-analysis. Epilepsy Behav EB 2023 Jan;138:109056.
[14] Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane Handbook for Systematic Reviews of Interventions. 2nd Edition. Chichester (UK): John Wiley & Sons; 2019.
[15] Rosenthal R. Meta-Analytic Procedures for Social Research; Sage Publications: Newbury Park. USA: CA; 1993.
[16] Yagiz G, Esedullah A, Kubis HP, Owen J. The Effects of Resistance Training on Architecture and Volume of the Upper Extremity Muscles: A Systematic Review of Randomised Controlled Trials and Meta-Analyses. Appl Sci 2022. Feb 2.
[17] Kallapiran K, Koo S, Kirubakaran R, Hancock K. Review: Effectiveness of mindfulness in improving mental health symptoms of children and adolescents: a meta-analysis. Child Adolesc Ment Health 2015;20(4):182–94.
[18] Papadopoulos VP, Apergis N, Filippou DK. Nocturia in CPAP-Treated Obstructive Sleep Apnea Patients: a Systematic Review and Meta-Analysis. SN Compr Clin Med 2020 Dec 1;2(12):2799–807.
[19] Martinović Z, Simonović P, Djokić R. Preventing depression in adolescents with epilepsy. Epilepsy Behav EB 2006 Dec;9(4):619–24.
[20] Thompson NJ, Walker ER, Obolensky N, Winning A, Barmon C, Diiorio C, et al. Distance delivery of mindfulness-based cognitive therapy for depression: project UPLIFT. Epilepsy Behav EB 2010 Nov;19(3):247–54.
[21] Ciechanowski P, Chaytor N, Miller J, Fraser R, Russo J, Unutzer J, et al. PEARLS depression treatment for individuals with epilepsy: A randomized controlled trial. Epilepsy Behav 2010 Nov 1;19(3):225–31.
[22] Gandy M, Sharpe L, Nicholson Perry K, Thayer Z, Miller L, Boserio J, et al. Cognitive behaviour therapy to improve mood in people with epilepsy: a randomised controlled trial. Cogn Behav Ther 2014;43(2):153–66.
[23] Schröder J, Brückner K, Fischer A, Lindenau M, Köther U, Vettorazzi E, et al. Efficacy of a psychological online intervention for depression in people with epilepsy: a randomized controlled trial. Epilepsia 2014 Dec;55(12):2069–76.
[24] Thompson NJ, Patel AH, Selwa LM, Stoll SC, Begley CE, Johnson EK, et al. Expanding the efficacy of Project UPLIFT: Distance delivery of mindfulness-based depression prevention to people with epilepsy. J Consult Clin Psychol 2015 Apr;83 (2):304–13.
[25] Caller TA, Ferguson RJ, Roth RM, Secore KL, Alexandre FP, Zhao W, et al. A cognitive behavioral intervention (HOBSCOTCH) improves quality of life and attention in epilepsy. Epilepsy Behav EB 2016 Apr;57(Pt A):111–7.
[26] Hum KM, Chan CJ, Gane J, Conway L, McAndrews MP, Smith ML. Do distance-delivery group interventions improve depression in people with epilepsy? Epilepsy Behav EB 2019 Sep;98(Pt A):153–60.
[27] Meyer B, Weiss M, Holtkamp M, Arnold S, Brückner K, Schröder J, et al. Effects of an epilepsy-specific Internet intervention (Emyna) on depression: Results of the ENCODE randomized controlled trial. Epilepsia 2019 Apr;60(4):656–68.
[28] Ahorsu DK, Lin CY, Imani V, Carlbring P, Nygårdh A, Broström A, et al. Testing an app-based intervention to improve insomnia in patients with epilepsy: A randomized controlled trial. Epilepsy Behav EB 2020 Nov;112:107371.
[29] Spruill TM, Friedman D, Diaz L, Butler MJ, Goldfeld KS, O'Kula S, et al. Telephone-based depression self-management in Hispanic adults with epilepsy: a pilot randomized controlled trial. Transl Behav Med 2021 Jul 29;11(7):1451–60.
[30] Moncrief GG, Aita SL, Tyson BT, Abecassis M, Roth RM, Caller TA, et al. Self-rated executive dysfunction in adults with epilepsy and effects of a cognitive-behavioral intervention (HOBSCOTCH). Epilepsy Behav EB 2021 Aug;121(Pt A):108042.
[31] Feng HX, Wang MX, Zhao HM, Hou XX, Xu B, Gui Q, et al. Effect of cognitive behavioral intervention on anxiety, depression, and quality of life in patients with epilepsy. Am J Transl Res 2022;14(7):5077–87.
[32] Akyuz E, Polat AK, Eroglu E, Kullu I, Angelopoulou E, Paudel YN. Revisiting the role of neurotransmitters in epilepsy: An updated review. Life Sci 2021 Jan;15 (265):118826.
[33] Krishnan V. Depression and Anxiety in the Epilepsies: from Bench to Bedside. Curr Neurol Neurosci Rep 2020 Jul 14;20(9):41.
[34] Mula M. Epilepsy: Bidirectional link between epilepsy and psychiatric disorders. Nat Rev Neurol 2012 Apr 17;8(5):252–3.
[35] Michaelis R, Tang V, Wagner JL, Modi AC, LaFrance WC, Goldstein LH, et al. Cochrane systematic review and meta-analysis of the impact of psychological treatments for people with epilepsy on health-related quality of life. Epilepsia 2018 Feb;59(2):315–32.
[36] Macrodimitris S, Wershler J, Hatfield M, Hamilton K, Backs-Dermott B, Mothersill K, et al. Group cognitive-behavioral therapy for patients with epilepsy and comorbid depression and anxiety. Epilepsy Behav EB 2011 Jan;20(1):83–8.

Month 3, indicating the positive and sustained impact of fremanezumab on the QoL of patients with migraine.

doi:10.1016/j.jns.2023.121662

121663

Questionnaire-based evaluation of sleep abnormality in patients with primary headache disorder: A cross-sectional study from tertiary care centre

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Background and aims

Background: Patients with headache frequently have co-existent sleep-related abnormalities. This underlying sleep abnormality might be a contributing factor to increased disease burden. Aims: To evaluate sleep abnormalities in patients diagnosed with primary headache using validated questionnaires and compare that within subgroups of primary headache.

Methods

80 patients were enrolled. Baseline characteristics were noted and patients were divided into three groups: Migraine with or without aura (Group-1), Tension type headache (Group-2), and Chronic migraine (Group-3). Headache assessment done using MIDAS questionnaire. Sleep assessment done using Pittsburg sleep quality index (PSQI), Epworth Sleepiness Scale (ESS), Restless Leg Syndrome Scale (RLS) and Berlin questionnaire.

Results

Mean age was 36.21 (10.17). Male-female ratio was 17:63. Severity of headache (VAS) mean was 7.74 (1.04). Mean MIDAS Score was 15.78 (26.23). Both VAS and MIDAS score were found highest in Group-3. PSQI mean score was 6.35 (4.61). Out of 80 patients, 53.75% had PSQI score > 5, indicating poor sleep quality and among them, it was found highest in Group-3. Mean ESS score was 7.03 (4.83), excessive daytime sleepiness (ESS > 10) was found in 26.25% patients and was highest in Group-1. RLS was present in 30% patients being highest in Group-3. High risk of OSA (Berlin questionnaire) was found in 7.5% patients.

Conclusions

Patients with primary headache tend to have a poor sleep quality and have co-existent disease like RLS that might be contributing to headache burden. Among the three subgroups, Chronic migraine patients tend to have more sleep abnormalities followed by Migraine with or without aura and Tension type headache.

doi:10.1016/j.jns.2023.121663

121664

To demonstrate safety and efficacy of administration of greater occipital nerve block and botulinum toxin A in patients with chronic migraine

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Background and aims

Aim: To demonstrate safety and efficacy of administration of greater occipital nerve block and botulinum toxin A in patients with chronic migraine. Migraine is a common primary headache disorder that can result in significant disability, particularly in those with chronic migraine. In this study, the safety and efficacy of greater occipital nerve block (GONB) and botulinum toxin A were investigated in patients with chronic migraine.

Methods

A non-randomized prospective observational study was conducted on 20 adult patients with chronic migraine who were offered either GONB or botulinum toxin A after discussing all available treatment options. Patients were followed for 28 days, and a headache diary was used to evaluate the frequency and intensity of headaches.

Results

The results showed that both treatments led to a reduction in the number of monthly headache days and decreased headache severity, according to the Visual Analog Scale.

Table 1. Baseline demographics

	Botox group	GONB group
N	4	16
Age (y), mean (SD)	42.25	42.13
Female	4	13
Headache duration (years), mean (SD)	13.00	13.44
Headache location		
Left hemicranial	2	4
Right hemicranial	1	4
Holocranial	1	7
Occipital	0	1
Triggers		
None	0	2
Fasting	0	1
Sleep deprivation	0	1
Weather change	0	1
Travelling	0	1
Sleep deprivation, fasting	1	2
Stress, sleep deprivation, weather change	0	1
Travelling, fasting	0	1
Travelling, sleep deprivation	1	3
Travelling, sleep deprivation, fasting, stress	1	1
Travelling, sleep deprivation, stress	1	1
Travelling, sleep deprivation, weather change	0	1
Headache days (last 4 weeks)	26.00	22.63

Comparison of Headache days prior and after procedure

	Patient	Mean	SD	Minimum	Maximum	Median	IQR
BOTOX							
Headache days prior to injection	4	26.00	4.000	20	28	28.00	22–28
Headache days after injection	4	12.25	5.123	5	17	13.50	7–16.25
GONB							
Headache days prior to injection	16	22.63	5.188	15	28	20.00	20–28
Headache days after injection	16	10.81	6.327	2	23	10.00	6.25–14.75