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Mindfulness-based intervention to promote psychological wellbeing in people with epilepsy: A randomized controlled trial

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ABSTRACT

Background: We investigated the efficacy of mindfulness-based intervention (MBI) in promoting psychological wellbeing in people with epilepsy (PWE) using an assessor-blinded randomized controlled design.
Methods: A total of 28 PWE were randomly assigned to either intervention (n = 14 cases) or control group (n = 14 controls). The intervention group received a six 2.5-hour weekly MBI, while the control group did not receive any intervention. They were assessed at three timepoints (T0: before intervention, T1: immediately after intervention, and T2: 6 weeks after intervention). Repeated measures of analyses of variance (RM-ANOVAs) were used for inter-group comparisons to determine intervention effect from baseline –to T1 and –to T2 for all outcome measures. The individual changes were calculated using the reliable change index (RCI). Key outcomes included depression (BDI-II), anxiety (BAI), epilepsy-related quality of life (QOLIE-31), satisfaction with life (SWLS), and level of mindfulness (MAAS).
Results: Participants who participated in the MBI showed significant reduction in BDI-II (p = 0.001), significant increases in MAAS (p = 0.027) and QOLIE-31 (p = 0.001) at T1 when compared with the control group. However, BAI and SWLS were not significant. The trend was similar at 6-week follow-up, all outcome measures of MBI remained significant (p < 0.05) except for BAI and SWLS. Beyond the 6-week intervention, RCI analysis showed a significant improvement in levels of mindfulness (45.45% vs. 21.43%, p = 0.009), depression (45.45% vs. 0.00%, p = 0.016), quality of life (45.45% vs. 14.29%, p = 0.017) with MBI, as compared to the no-intervention phase.
Conclusion: Mindfulness-based intervention is effective in reducing psychological distress and improving the quality of life in PWE.

1. Introduction

The burdens of having epilepsy are multifold. While medical therapies aim to modify the progression of epilepsy, psychological treatments for PWE aim at reducing psychiatric comorbidities, improve coping as well as quality of life [1]. Substantial evidence showed that psychological interventions (i.e., cognitive behavioral therapy and mindfulness-based therapies) were effective in improving psychological well-being and seizure control among PWE [1,2]. Among the range of psychological therapies, mindfulness-based interventions (MBIs) are increasingly used to alleviate physical and psychological suffering in people with neurological conditions like Parkinson's disease, stroke, and epilepsy [3,4]. As a major component in MBIs, "mindfulness" has been operationalized as a training of mental process including cultivation of self-awareness, non-judgmental observations, and acknowledgment of bodily states, emotions, thoughts, and other sensations in the present moment [5].

A recent systematic review concluded the effectiveness of MBIs in reducing anxiety and depressive symptoms, as well as improving the quality of life (QOL) in PWE [4]. However, only three articles were reviewed (n = 231), which limited the applicability of the findings [4]. These studies had a few limitations. Firstly, none of the studies include measures to assess the participants' level of mindfulness, which made it difficult to determine if the intervention produced the desired effect. Secondly, only Tang et al.'s [6] intervention was targeted toward drug-resistant epilepsy; whereas epilepsy characteristics in both Thompson et al.'s [7,8]

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studies were poorly reported. It was therefore unclear whether the same outcomes could be expected among those who are drug-responsive. Considering these limitations, more research focusing on MBIs for PWE is required to make comparisons on the beneficial effects of MBIs.

Based on a recent recommendation statement made by the Psychology Task Force of the International League Against Epilepsy (ILAE) regarding psychological intervention research designs [2,9,10], studies should consider GRADE recommendations based on clinically meaningful effects on (i) symptoms of the disorder being treated or (ii) on functional outcomes. Previous studies of MBIs for PWE were based on the means of each group, results based on '*statistical*' significance may overlook an individual's responsiveness to treatment effects and the clinical relevance of such findings could not be concluded. Jacobson and colleagues [11] introduced the concept of Reliable Change Index (RCI) that determines the proportion of patients who deteriorate, remain unchanged, and improve with treatment. RCI is particularly useful in small-sample studies, as a manipulation check and as a statistical measure of category membership.

The present study examined the effects of a mindfulness-based therapy on psychological well-being among PWE using a randomized case-control design. We utilized standardized criteria to evaluate the clinical relevance of symptom changes in PWE at post-intervention. Our primary objective was to evaluate the effect of mindfulness-based therapy on anxiety, depression, epilepsy-specific QOL, and life satisfaction in PWE, applying the concept of RCI. The secondary objective was to assess whether the results correlate with the level of mindfulness.

2. Method

2.1. Trial design

The present study was an assessor-blinded randomized controlled trial. There were three measurement time points for each group (T0: baseline before randomization, T1: immediately after intervention (i.e., 6 weeks), and T2: 6-week follow-up after completion of the intervention). The intervention group received the intervention after randomization, whereas the control group received treatment as usual (e.g., attending medical routine check-ups at the outpatient clinic). The control group, in this case is known as the wait-list controls (WLC).

2.2. Participants

A consecutive sampling method was adopted to recruit participants who were attending the clinical consultations at the University Malaya Medical Center (UMMC) neurology clinic, Kuala Lumpur, Malaysia. All patients (16 years or older) with a diagnosis of epilepsy by a neurologist, who was able to read and write English were recruited. Patients with any of the following criteria were excluded: 1) a diagnosis of severe learning disability or cognitive impairment that affects individuals who are unable to comply with study procedure, 2) substance dependence, 3) suicidality, and 4) limited language proficiency. If suicidality was identified, they were referred to the psychiatrist for specialty care.

2.3. Procedure

This study was approved by the UMMC Ethics Committee (MECID.NO: 20175295282), National Medical Research Register Center (NMRR. NO: 1818139703), and retrospectively registered at clinicaltrials.gov (Identifier NO: NCT04313686). The Consolidated Standards of Reporting Trials (CONSORT) guidelines for conducting randomized trials of nonpharmacological treatments were followed [12].

(STL) screened and assessed all participants for eligibility based on medical records. Confirmation of eligibility was performed by a neurologist (KSL). This was a single-center trial conducted in the UMMC neurology clinic, where all eligible participants were approached consecutively in the clinic by (STL). All participants were given a consent form and information sheet that detailed the study information. Those who consented completed the baseline measures and were assigned a unique identification number before randomization. A computer-based randomization software was used to allocate participants into the intervention or the WLC groups (SuppInfo, Fig. 1S).

All participants completed the questionnaire on the day of recruitment before randomization. The questionnaire was comprised of demographic information and five scales that assessed outcome measures. Outcome measures were collected at three time points: ($T_{0:}$ baseline before randomization; T_1: immediately after intervention (i.e., 6 weeks); T_2: 6-week follow-up)

2.4. Outcomes

The outcome measures included anxiety (BAI), depression (BDI-II), epilepsy-related quality of life (QOLIE-31), levels of mindfulness (MAAS), and satisfaction with life (SWLS).

2.4.1. Clinical and sociodemographic information

The questionnaire had a sociodemographic section including age, sex, education, employment, marital status, psychiatric comorbidity, and whether they had previously attended any mindfulness/meditation program. Clinical information of epilepsy was obtained from the clinical epilepsy database, namely age at seizure onset, disease duration, seizure types, number of antiepileptic drugs (AEDs), and seizure control. Drug responsiveness was operationally defined as seizure freedom for at least 1 year with AEDs.

2.4.2. Beck Anxiety Inventory (BAI)

The BAI is comprised of 21 items that measure cognitive, somatic, and affective symptoms of anxiety [13]. Each item is rated on a 4-point Likert scale for symptom severity experienced, ranging from 0 (not at all) to 3 (severely). The scores ranged between 0 and 63, with higher numbers suggesting greater degrees of anxiety. High internal consistency (Cronbach's $\alpha = 0.87$) has been reported in the local context [14] and was tested in the epilepsy community [6].

2.4.3. Beck Depression Inventory (BDI-II)

The BDI-II is a 21-item self-reported instrument intended to assess the presence and severity of depressive symptoms [15]. All items were scored on a 4-point Likert scale ranging from 0 to 3. Total scores ranged from 0 to 63, higher scores represent higher degrees of depressive symptoms. The BDI-II was proven to be a reliable tool (Cronbach's $\alpha = 0.88$) and it was tested in a Malaysian epilepsy sample [16].

2.4.4. The Mindful Attention Awareness Scale (MAAS)

The MAAS is designed to assess individual differences in the tendency to attend to and be aware of the present-moment experience [17]. A total of 15 items were each rated on a 6-point Likert scale ranging from 1 (almost always) to 6 (almost never). Scores ranged from 15 to 90, higher scores reflect higher levels of dispositional mindfulness. The scale has been applied in the Malaysian context [18], and it demonstrated good internal consistency (Cronbach's $\alpha = 0.92$).

2.4.5. Satisfaction with Life Scale (SWLS)

The SWLS comprised five items, each was rated on a 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree) [19]. Total score ranges from 5 to 35, with higher scores indicating greater life satisfaction. The SWLS has been validated and translated in our local context for participants above 18 years old [18]; it was reported across different populations with strong internal consistency (Cronbach's $\alpha = 0.83$) [19].

2.4.6. Quality of Life in Epilepsy Inventory (QOLIE-31)

The QOLIE-31 has been widely cited as a reliable instrument (Cronbach's $\alpha = 0.93$) to assess epilepsy-related QOL [20]. It is a 31-item self-administered questionnaire. It contains seven multi-item scales that assess the following health concepts: seizure worry, emotional well-being, energy/fatigue, cognitive functioning, medication effects, social functioning, and overall QOL. A QOLIE-31 overall score is obtained using weighted average of the multi-item scale scores [20]. Each subscale and the overall score range from 0 to 100, with higher scores indicating better wellbeing.

2.5. Randomization

Randomization was conducted using a computer software [21]. The computer-based randomizer allocated the participants into prespecified groups (1 = intervention group, 2 = wait-list control group) once the numbers recruited were sufficient to begin a group mindfulness course (i.e., 5-10-person per group). The computer-based randomizer ensured the researchers could not influence the order of allocation, preserving pre-randomization allocation concealment.

Due to the nature of the intervention, it was not feasible to blind the participants or mindfulness instructor to their treatment allocation. To limit study bias, participants were told that there were two start times for the mindfulness course, with randomization to either date. The group randomized to the later date was the WLC, who received treatments as usual before the intervention. Participants were blinded until the start of the treatment program. A neutral coordinator was appointed to coordinate appointments and arrangements of venue and blinded to the outcome assessments.

2.6. Interventions

2.6.1. Format

The mindfulness-based intervention was delivered by the first author, a PhD candidate who obtained a master's degree in health psychology (STL), under the supervision of a registered clinical psychologist and expert mindfulness practitioner (VT). Before conducting the study, STL completed a total of 70 hours of mindfulness training program which included mindfulness meditation practices, self-inquiries, mindful movement, an understanding of stress physiology and cognitive awareness in the Breathworks/Paradigm system of mindfulness-based approaches, as well as training in delivery of the mindfulness-based intervention.

Participants received intervention weekly for six weeks in group format. Each group was comprised of 5–10 participants and each session lasted for 2–3-hours; this design was based on our published data that reported needs assessment from patients' perspectives [22]. Participants signed a consent form acknowledging that they understood they were being video-recorded and that recordings would be destroyed after review. To ensure fidelity to the intervention protocol and the quality of delivery, all intervention sessions were video-recorded and made available to the study supervisors and a clinical psychologist for review. No violation to protocol was reported. As an additional precaution, emergency contact of participants was obtained in the event of emergency. None of these conditions developed in the study course.

2.6.2. Intervention content

The content of the manual was adapted from the Breathworks' Mindfulness program developed by Vidyamala Burch [23]. Breathworks' Mindfulness utilizes many of the core concepts of mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT), such as a class structure that includes psychoeducation, formal meditation and movement practices, teacher-led discussion and inquiry, and daily home practices and exercises [24,25]. The main distinction between Breathworks and other programs was the inclusion of loving-kindness exercises, aimed to strengthen the connection of shared humanity [25].

In terms of session content, there were few modifications compared to a prototypical Breathworks' program. The main differences between our program and Breathworks were the shorter duration of our sessions and the duration of the retreat. Shorter sessions were provided to minimize the perceived barriers to intervention participation [22]. Modifications to our program session content included the following: (1) reduced duration of in-session meditation practices, with typical durations of meditation practices in our sessions ranging from 15 to 30 min, whereas 30 to 40 minutes are the usual practices in Breathworks; (2) addition of a 2.5-hour home meditation retreat due to traveling time constraints; and (3) in the first session, brief psychoeducation was provided about the interconnection among psychology and physiology of lifestyle, stress, and seizure. Participants were encouraged throughout the program to reflect on how mindfulness relates to daily life challenges as well as aspects related to the experience of having seizure/epilepsy.

The content of the coursebook was developed with an experienced mindfulness practitioner who has implemented mindfulness for PWE [6]. The program included daily home practice based on audio CDs with instruction and a daily record keeping of mindfulness exercises. Formal mindfulness exercises included body scan, sitting meditation with awareness of breath, and mindful movement (Appendix; Table 1S).

2.6.3. Participation adherence

Adherence was assessed based on the attendance to the MBI sessions. To maximize the retention of participants, a small monetary incentive (USD12) was given for each session attended. Based on the number of attendances, the sum would only be provided after the 6-week session ended. Participants were also added in an online social group using WhatsApp to discuss barriers faced while practicing mindfulness, and received instructions on their homework assignments.

2.7. Sample size

A priori power analysis was conducted using a sample size calculator software (i.e., G*Power3) to test the difference between two repeated independent group means using a two-tailed test, an effect size of ($d = .25$), and an alpha of 0.05. Result showed that a total sample of 24 participants with two equal-sized groups of ($n = 12$) was required to achieve a power of 0.80.

2.8. Statistical methods

Data were analyzed using the Statistical Package for Social Sciences version 19 (SPSS 19.0). Normality testing using the Kolmogorov–Smirnov (K-S) test showed a non-significant result ($p>0.05$) for all outcome measures in both groups. Levene's test showed a non-significant homogeneity of variance ($p>0.05$). These

normality checks fulfilled the assumptions required for parametric testing.

Demographic data were reported using descriptive statistics. Correlations between the demographic characteristics and key outcomes for continuous variables were performed using Pearson Correlation analysis.

The effect of mindfulness-based intervention on change in the dependent variables was examined with the analysis of variance (ANOVA) repeated measures. Questionnaire outcomes were analyzed using change from baseline to postintervention via analysis of covariance (ANCOVA), where analyses included common confounders including age, sex, and drug responsiveness. For further comparisons of groups, post hoc analysis was carried out for significant variables. Partial η^2 was used to determine effect sizes, with values of 0.01–0.06 indicating small, 0.07–0.14 medium, and >0.14 large.

The clinical significance of the treatment was determined by Jacobson's Reliable Change Index (RCI) [11]. The RCI was calculated for each primary and secondary outcome measure using individual patient data (IPD). The RCI identifies the threshold beyond which symptoms must change on an outcome measure for it to be considered reliable. An RCI greater than ±1.96 was required for the change to qualify as statistically reliable at $p<0.05$.

The chi-square test was performed to compare the number of patients who had clinically important change in main outcome measures from baseline to postintervention and in the follow-up assessment between the intervention and WLC groups. Phi coefficient (φ) was used to determine the effect size, with values of, 0.20, 0.20–0.60, and 0.60 representing small, medium, and large effect sizes, respectively.

3. Results

A total of 988 patients were screened consecutively for eligibility, 186 met the inclusion criteria, a total of 28 were successfully recruited and randomized into either the intervention ($n = 14$) or the WLC ($n = 14$) groups (Fig. 1).

3.1. Socio-demographic and clinical characteristics

The participants were primarily women (60.7%) with a mean age of 35 years, mostly Chinese (50.0%), single (67.9%), currently employed (57.1%), and having at least secondary education (71.4%). Most participants had focal epilepsy (67.9%), with a mean age of seizure onset at 16 years old (SD = 12.2), were drug resistant (57.1%), and on antiepileptic drug treatment (80.0%). None of them had prior experience in mindfulness or meditation practices. There were no significant differences in demographic or clinical variables between the intervention and WLC groups (Table 1).

3.2. Immediate effects of the mindfulness-based intervention (T_1-T_0)

Immediately after MBI (T_1), the mean score of BDI-II ($p = .001$, partial $\eta^2 = .358$) was significantly reduced in the intervention group as compared to the WLC group. Following mindfulness-based intervention, the mean score of MAAS ($p = .027$, partial $\eta^2 = .175$), and QOLIE-31 ($p = .0001$, partial $\eta^2 = .404$) in the intervention group had significantly improved as compared to the WLC group (Fig. 2). Sub-analysis on the subscales of QOLIE-31 showed statistically significant improvements in seizure worry ($p = .036$, partial $\eta^2 = .158$), emotional well-being ($p = .003$, partial $\eta^2 = .284$) and cognitive functioning ($p = .001$, partial $\eta^2 = .398$) (Table 2).

3.3. Sustained effects of the mindfulness-based intervention at 6-week follow up (T_2-T_0)

At the 6-week follow-up after the completion of MBI training, the intervention group reported a significant reduction in the mean score of BDI-II ($p = .010$, partial $\eta^2 = .254$) as compared to the WLC group. The intervention group also reported significant improvement in the mean score of MAAS ($p = .006$, partial $\eta^2 = .282$) and QOLIE-31 ($p = .002$, partial $\eta^2 = .348$). Improvement was also found in the QOL subscales for seizure worry ($p = .005$, partial $\eta^2 = .299$), emotional well-being ($p = .002$, partial $\eta^2 = .346$) and cognitive functioning ($p = .012$, partial $\eta^2 = .244$) (Table 3).

3.4. Reliability and direction of change on depression, mindfulness, and quality of life immediately after intervention (T_1) and at the 6-week follow-up (T_2)

With mindfulness-based intervention (T_1), there was a significant improvement in quality of life (6/14; 42.9% vs. 1/14; 7.1%, $p<0.01$). Although not statistically significant, the intervention group had a clinically reliable improvement in the level of mindfulness (5/14; 35.7% vs. 3/14; 21.4%), anxiety (5/14; 35.7% vs. 2/14; 14.3%), depressive score (5/14; 35.7% vs. 1/14; 7.1%), and life satisfaction (6/14; 42.9% vs. 1/14; 7.1%) when compared to the WLC group (Table 4).

At 6-week follow-up (T_2), RCI analysis showed statistical reliable improvement in levels of mindfulness [(5/11; 45.5% vs. 3/14; 21.4%, $p = 0.009$], depressive score [(5/11; 45.5% vs. 0/14; 0.0%, $p = 0.016$], and quality of life [5/11; 45.5% vs. 2/11; 14.3%, $p = 0.017$]. More in intervention group experienced improvement in anxiety score at T_2 (36.4%), when compared to the WLC group (7.1%), but not statistically significant (Table 4).

3.5. Correlation between the level of mindfulness and the clinical-psychological characteristics

Sub-group analyses were performed only in the intervention group to examine whether the true effect of mindfulness (i.e., changes in mindfulness scores) is correlated with other outcome measures (SuppInfo; Table 5S). Our findings showed that the change in the level of mindfulness (MAAS) with intervention was correlated negatively with BDI-II scores ($r = -0.669$, $p = 0.009$), and positively with the overall quality of life ($r = .608$, $p = 0.021$). Applying the change of mindfulness level (MASS) as a covariate, the effect of MBI on depression (BDI-II), anxiety (BAI), life satisfaction (SWLS), and QOLIE-31 became non-significant. This indicated that the improvements in these psychological variables with MBI are likely mediated by an increase in mindfulness level.

The mean score for adherence toward attending the mindfulness class was 5.32 (SD, 1.83). There were no significant differences between the intervention group (Mean, 5.57; SD, 1.34) and WLC group (Mean, 5.07; SD, 2.24) in levels of adherence ($t(26) = 0.718$, $p = 0.064$).

4. Discussion

In this RCT design, a 6-week MBI was shown to be effective in reducing psychological distress, increasing levels of mindfulness and enriching quality and satisfaction in life among adult PWE. More than 40% of PWE demonstrated clinical improvement in depression compared to individuals in the WLC group. At the 6-week follow-up, the beneficial effects of MBI (i.e. mindfulness, depression, and QOL) persisted.

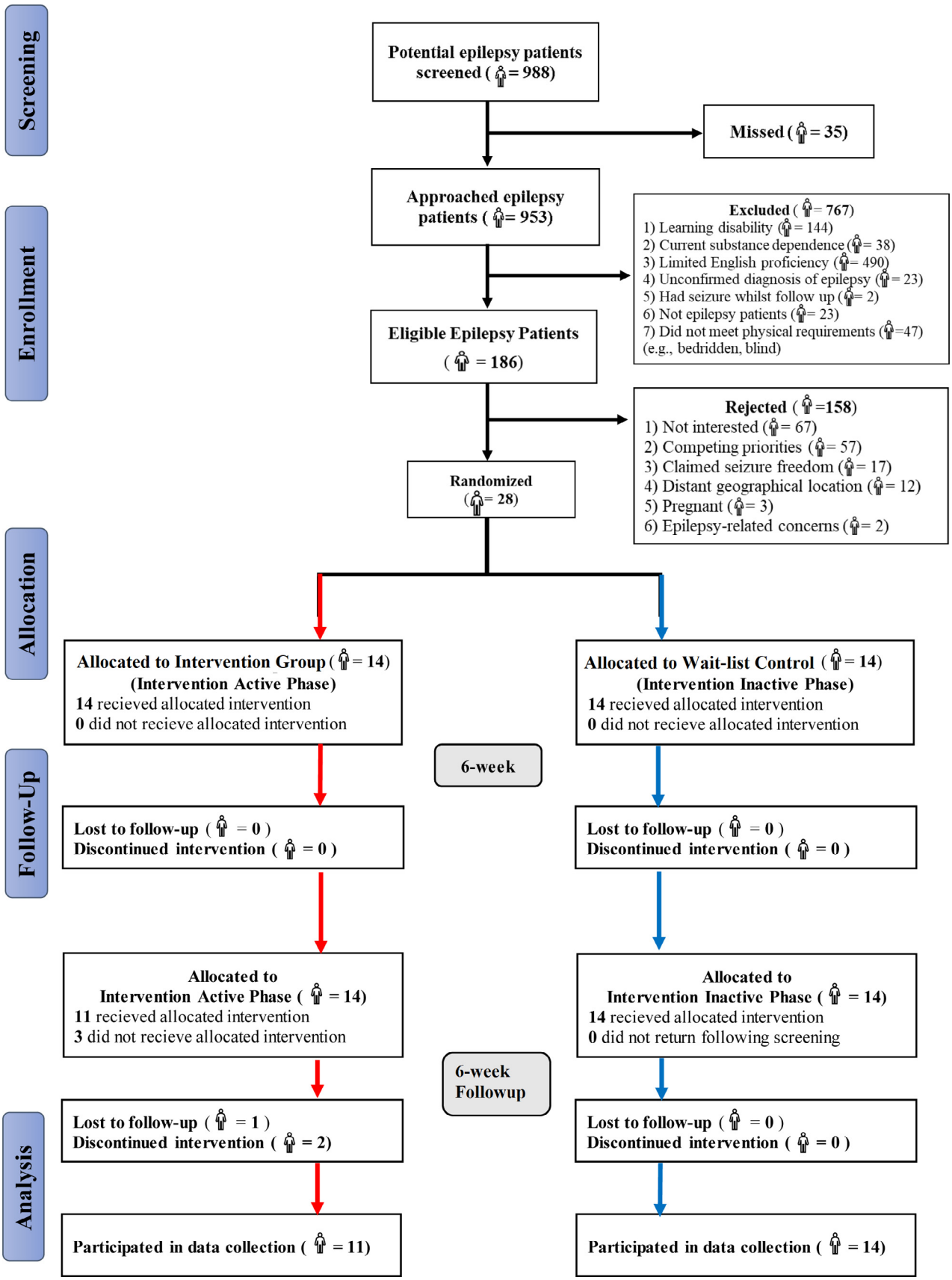

Fig. 1. Flowchart of study participants.

Table 1
Demographic characteristics of participants.

Demographics	Recruited[b] (*n* = 28)	Intervention (*n* = 14)	WLC (*n* = 14)	*p*-value
Clinical characteristics				
Age at seizure onset (years)[a]	16.6 (12.2, 13.5)	17.6 (14.9, 14.5)	15.6 (9.2, 12.5)	.673
Duration of disease (years)[a]	18.6 (13.4, 16.0)	16.4 (13.8, 14.0)	20.9 (13.2, 18.0)	.392
Seizure types				.240
Focal	19 (67.9%)	9 (64.3%)	10 (71.4%)	
Generalized	4 (14.3%)	1 (7.1%)	3 (21.4%)	
Undetermined	5 (17.9%)	4 (28.6)	1 (7.1%)	
Seizure control				1.000
Drug responsive	12 (42.9%)	6 (42.9%)	6 (42.9%)	
Drug resistant	16 (57.1%)	8 (57.1%)	8 (57.1%)	
Seizure frequency, last 6 weeks				
Reported having seizures	12 (40.7%)	6 (42.9%)	6 (42.9%)	
Average seizure [a]	2.5 (4.5)	2.2 (4.1)	2.7 (4.9)	
Antiepileptic drug (AED) treatment				.389
Monotherapy	11 (39.3%)	4 (28.6%)	7 (50.0%)	
Two AEDs	9 (32.1%)	5 (35.7%)	4 (44.4%)	
Three AEDs	5 (17.9%)	2 (14.3%)	3 (21.4%)	
Four or more AEDs	2 (7.1%)	2 (14.3%)	0 (0.0%)	
Not on AED	1 (3.6%)	1 (7.1%)	0 (0.0%)	
Most commonly used AEDs				
Lamotrigine (LTG)	10 (35.7%)	3 (21.4%)	7 (50.0%)	.115
Levetiracetam (LVT)	10 (35.7%)	6 (42.9%)	4 (28.6%)	.430
Carbamazepine (CBZ)	8 (28.6%)	6 (42.9%)	2 (14.3%)	.094
Valproate (VPA)	8 (28.6%)	4 (28.6%)	4 (28.6%)	1.000
Clonazepam (CLZ)	5 (17.9%)	3 (21.4%)	2 (14.3%)	.622
Zonisamide (ZNS)	4 (14.3%)	1 (7.1%)	3 (21.4%)	.280
Socio-demographic				
Age (years)[a]	35.3 (13.5, 30.5)	34.1 (14.3, 28.50)	36.5 (13.1, 34.5)	.643
Gender				
Male	11 (39.3%)	4 (28.6%)	7 (50.0%)	.246
Female	17 (60.7%)	10 (71.4%)	7 (50.0%)	
Ethnicity				.710
Malay	4 (14.3%)	2 (14.3%)	2 (14.3%)	
Chinese	14 (50.0%)	6 (42.9%)	8 (57.1%)	
Indian	10 (35.7%)	6 (42.9%)	4 (28.6%)	
Marital status				
Single	19 (67.9%)	11 (78.6%)	8 (57.1%)	.225
Married	9 (32.1%)	3 (21.4%)	6 (42.9%)	
Education levels				
Primary	1 (3.6%)	0 (0.0%)	1 (7.1%)	.149
Secondary	7 (25.0%)	5 (35.7%)	2 (14.3%)	
Diploma/Pre-University	6 (21.4%)	2 (14.3%)	4 (28.6%)	
Undergraduate	11 (39.3%)	4 (28.6%)	7 (50.0%)	
Postgraduate	3 (10.7%)	3 (21.4%)	0 (0.0%)	
Employment status				
No	12 (42.9%)	7 (50.0%)	5 (35.7%)	.445
Yes	16 (57.1%)	7 (50.0%)	9 (64.3%)	
Income range				
Less than RM 1000	1 (6.3%)	1 (14.3%)	0 (0.0%)	.617
RM 1000 to RM 2000	3 (18.8%)	1 (14.3%)	2 (22.2%)	
RM 2000 to RM 3000	5 (31.3%)	2 (28.6%)	3 (33.3%)	
RM 3000 to RM 4000	3 (18.8%)	2 (28.6%)	1 (11.1%)	
More than RM 4000	4 (25.0%)	1 (14.3%)	3 (33.3%)	
History of psychiatric treatment				
No	25 (89.3%)	13 (92.9%)	12 (85.7%)	.541
Yes	3 (10.7%)	1 (7.1%)	2 (14.3%)	
History of mindfulness or meditation practices				N/A
No	28 (100.0%)	14 (100.0%)	14 (100.00%)	

Note. [a]Values are means (standard deviation, median). N/A, No statistics are computed because this variable is a constant value. [b]Group comparing intervention (*n* = 14) and wait-list controls (WLC) (*n* = 14).

4.1. Effect of mindfulness on psychopathology and quality of life

Mindfulness-based interventions primarily aim to increase intentional self-regulation of attention and facilitate the practice of non-judgmental present-moment awareness [5]. Thoughts, emotions, and sensations are all treated as events that can come and go, detached observation, recognition, and acceptance are cultivated, which aim at eventually allowing the presence of any sensations, including negative ones, rather than resisting negative emotions. Based on the theory of mindfulness, this process lessens distress [26]. In mood disorders, suppression of intrusive or unwanted thoughts may reflect vulnerability to psychopathology [27]. In our mindfulness therapy, participants were taught to recognize negative feelings associated with seizures (e.g. fear of breakthrough seizures, physical discomfort) with an attitude of recognition and acceptance. Jon Kabat-Zinn described mindful acceptance as not passively accepting one's fate, it is to embrace with a deep understanding of how things are – "*it is a pause, a period of allowing, of letting be, of clear seeing*" [5]. The cultivation of mindful acceptance is likely to enhance positive coping strategies with seizures, thereby improving overall QOL, including improvement in mood, seizure worries, cognitive and medication effects.

Table 2
Comparisons of the effects of mindfulness-based interventions between the intervention (n = 14) and WLC (n = 14) groups at completion of the 6-week training.

Measures[a]	T_0 [b,c]		T_1 [b,c]				
	INT Mean (SD)	WLC	INT	WLC	F-Statistic F [df (1, 26)]	Effect Size ηp^2	p-value
BDI-II	16.43 (8.64)	12.14 (8.24)	8.57 (6.15)	14.14 (9.91)	14.475	.358	0.001**
BAI	17.07 (9.52)	14.79 (12.22)	11.00 (7.39)	15.79 (11.48)	2.337	.082	0.138
MAAS	52.79 (15.99)	56.29 (11.67)	65.43 (10.23)	54.00 (10.79)	5.509	.175	0.027*
SWLS	19.07 (4.10)	17.50 (6.56)	21.36 (3.84)	16.64 (6.54)	2.268	.080	0.144
QOLIE-31 total	53.28 (14.28)	59.14 (14.03)	65.42 (14.17)	49.33 (18.39)	17.593	.404	0.001**
Seizure worry	38.77 (22.87)	51.07 (29.56)	51.74 (26.66)	40.53 (32.10)	4.870	.158	0.036*
Overall Quality of life	56.43 (16.14)	67.68 (15.36)	65.89 (13.89)	55.71 (21.11)	7.726	.229	0.010*
Emotional well-being	61.14 (12.50)	65.14 (17.07)	68.57 (16.81)	55.71 (19.69)	10.329	.284	0.003**
Cognitive functioning	50.18 (26.09)	57.50 (14.76)	68.94 (16.15)	42.26 (21.87)	17.217	.398	0.001**
Medication effects	53.76 (30.11)	52.98 (30.61)	62.51 (27.27)	34.93 (37.03)	2.860	.099	0.103
Social functioning	58.71 (22.72)	69.07 (23.23)	69.07 (23.23)	54.64 (23.20)	2.066	.074	0.163
Energy/fatigue	46.79 (20.44)	52.86 (21.46)	56.43 (16.69)	50.00 (21.12)	2.914	.0101	0.100

Note. ** p < .01; *p < .05.
[a] Measures used to test the dependent variables and were denoted as follows: BDI, Beck Depression Inventory-II; BAI, Beck Anxiety Inventory; MAAS, Mindful Attention Awareness Scale; SWLS, Satisfaction with Life Scale; QOLIE-31, Quality of Life in Epilepsy Inventory.
[b] Pretest, Baseline before intervention; Posttest, immediately after 6 weeks of pretest.
[c] Group comparing intervention (INT; n = 14) and wait-list controls (WLC; n = 14).

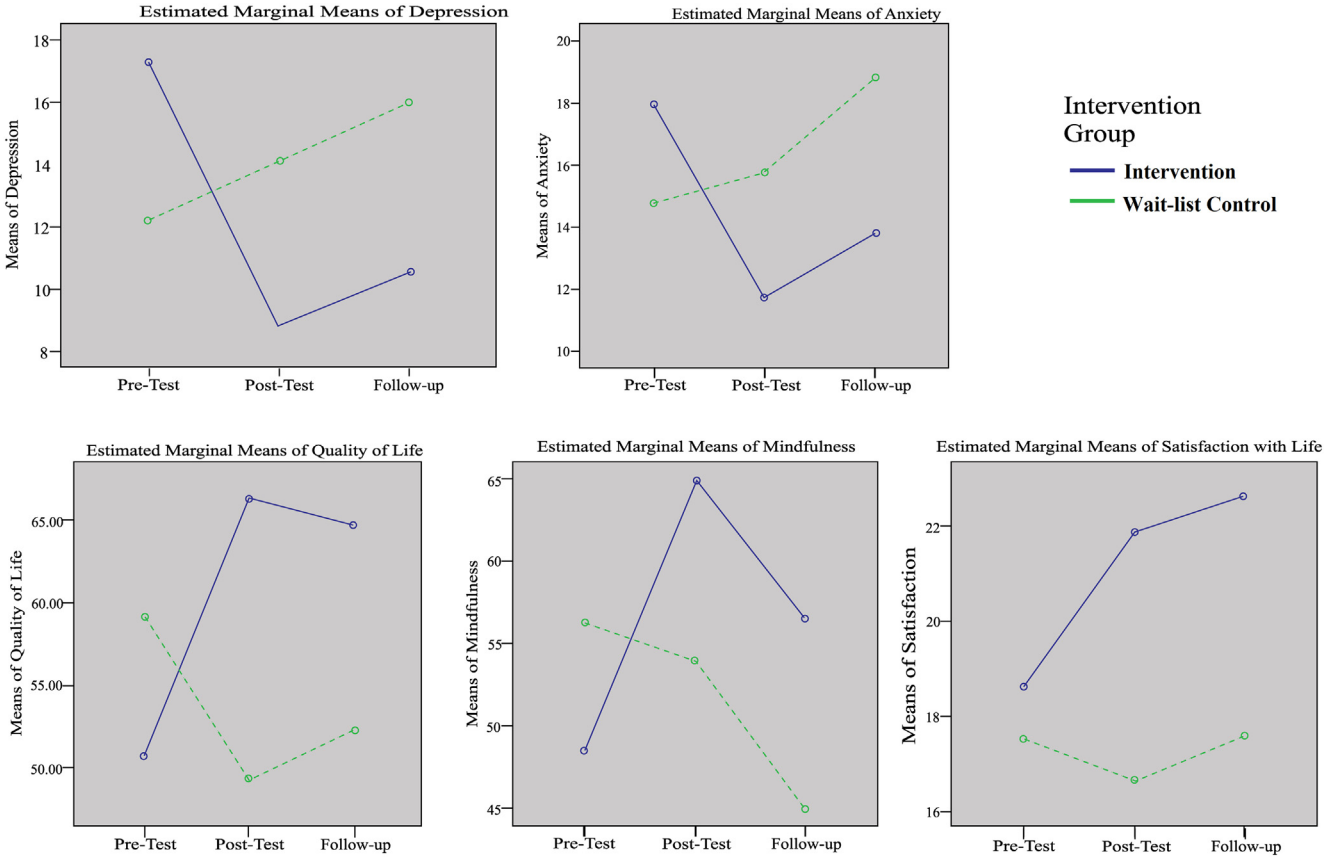

Fig. 2. Immediate effects of the mindfulness-based intervention (T_1-T_0).

In line with previous studies, participants in our study reported a significant reduction in levels of depression at post-intervention [6–8] and the improvement persisted for 6 weeks beyond the intervention. Those who were in the MBI had decreased in psychological distress and increased mindfulness scores, more than those in the control group. Changes in levels of depression and mindfulness were not significantly associated with the number of sessions attended. This finding echoed the study by Thompson et al [8], that the number of sessions attended probably does not accurately reflect the utilization of program materials. In our study, MBI participants were given accessibility to the session materials and meditation home exercises. This could account for the motivation to use the materials on their own beyond mere session attendance. It may be useful for future research to examine the dose-relationship between the number of sessions attended and changes in psychopathological symptoms.

Table 3
Comparison of the effects of mindfulness-based intervention in the intervention (n = 11) and WLC (n = 14) groups at the 6-week follow-up after MBI training

Measures[a]	T_0 [b,c]		T_2 [b,c]				
	INT Mean (SD)	WLC	INT	WLC	F-Statistic F [df (1, 23)]	Effect Size ηp^2	p-value
BDI-II	17.36 (9.30)	12.14 (8.24)	10.55 (12.33)	16.00 (9.84)	7.825	.254	0.010*
BAI	18.00 (9.30)	14.79 (12.22)	13.82 (11.95)	18.86 (12.79)	3.429	.130	0.077
MAAS	48.55 (14.68)	56.29 (11.67)	56.55 (15.09)	45.00 (11.67)	9.019	.282	0.006**
SWLS	18.64 (4.57)	17.50 (6.56)	22.64 (6.34)	17.57 (5.80)	1.990	.080	0.172
QOLIE-31 total	50.67 (14.74)	59.14 (14.03)	64.80 (17.82)	52.24 (18.14)	12.279	.348	0.002**
Seizure worry	35.45 (17.92)	51.07 (29.56)	65.93 (25.18)	42.20 (28.67)	9.832	.299	0.005**
Overall Quality of life	53.64 (16.52)	67.68 (15.36)	71.82 (17.75)	54.11 (17.56)	15.001	.395	0.001**
Emotional well-being	59.27 (12.50)	65.14 (17.07)	73.09 (11.18)	55.43 (18.82)	12.194	.346	0.002**
Cognitive functioning	50.20 (29.39)	57.50 (14.76)	61.20 (25.98)	47.12 (22.94)	7.418	.244	0.012*
Medication effects	47.21 (29.74)	52.98 (30.61)	71.22 (32.16)	47.02 (31.04)	2.999	.115	0.097
Social functioning	53.18 (22.21)	58.79 (25.09)	64.64 (26.50)	60.93 (25.58)	0.547	.023	0.467
Energy/fatigue	44.09 (22.00)	52.86 (21.46)	52.27 (26.02)	50.34 (21.88)	1.171	.048	0.290

Note. ** p < .01; *p < .05.
[a] Measures used were denoted as follows: BDI, Beck Depression Inventory-II; BAI, Beck Anxiety Inventory; MAAS, Mindful Attention Awareness Scale; SWLS, Satisfaction with Life Scale; QOLIE-31, Quality of Life in Epilepsy Inventory.
[b] Pretest, Baseline before intervention; Posttest, immediately after 6 weeks of pretest; Follow-up, immediately after 6 weeks from posttest.
[c] Group comparing intervention (INT; n = 11) and wait-list controls (WLC; n = 14).

Table 4
Classification of change (RCI) in psychological distress in individual trials between T_0 and T_1, and T_0 and T_2 assessment

Outcome Measures	Group comparison[a]	S_1	r_{xx}*	S_E	S_{diff}	(RC-)	(RC0)	(RC+)	Percentage[b] (%)	p [c]
T_0 and T_1										
Depression (BDI-II)	Intervention	8.644	0.88	2.995	4.235	1	8	5	35.71%	0.176
	WLC	8.236	0.88	2.853	4.035	2	11	1	7.14%	
Anxiety (BAI)	Intervention	9.515	0.87	3.431	4.852	1	8	5	35.71%	0.214
	WLC	12.217	0.87	4.405	6.230	4	8	2	14.29%	
Quality of Life (QOILIE-31)	Intervention	14.277	0.93	3.777	5.342	0	8	6	42.86%	0.004**
	WLC	14.026	0.93	3.711	5.248	7	6	1	7.14%	
Mindfulness (MAAS)	Intervention	15.986	0.92	4.522	6.395	0	9	5	35.71%	0.093
	WLC	11.665	0.92	3.299	4.666	4	7	3	21.43%	
Life Satisfaction (SWLS)	Intervention	4.104	0.83	1.692	2.393	2	6	6	42.86%	0.092
	WLC	6.560	0.83	2.705	3.825	3	10	1	7.14%	
T_0 and T_2										
Depression (BDI-II)	Intervention	8.644	0.88	3.150	4.455	1	5	5	45.45%	0.016*
	WLC	8.236	0.88	2.853	4.035	4	10	0	0.00%	
Anxiety (BAI)	Intervention	9.515	0.87	3.431	4.852	1	6	4	36.36%	0.175
	WLC	12.217	0.87	4.405	6.230	3	10	1	7.14%	
Quality of Life (QOILIE-31)	Intervention	14.277	0.93	3.777	5.342	0	6	5	45.45%	0.017*
	WLC	14.026	0.93	3.711	5.248	7	5	2	14.29%	
Mindfulness (MAAS)	Intervention	15.986	0.92	4.522	6.395	0	6	5	45.45%	0.009**
	WLC	11.665	0.92	3.299	4.666	8	3	3	21.43%	
Life Satisfaction (SWLS)	Intervention	4.104	0.83	1.692	2.393	1	5	5	45.45%	0.395
	WLC	6.560	0.83	2.705	3.825	3	8	3	21.43%	

Note. S_1, standard deviation at pretreatment; S_E, standard error of measurement; S_{diff}, standard error of difference; RC-, reliable deterioration; RC0, reliable indeterminate change; RC+, reliable improvement; r_{xx}, reliability of the scale. [a] Group comparing intervention and wait-list controls (WLC); [b] Efficacy of intervention in improving outcome measures; [c] Assessing group differences in RCI index; ** p < .01; *p < .05.

4.2. Effect of mindfulness on individual self-reported changes

We evaluated the clinical relevance of mindfulness therapy using IPD via Jacobson's RCI formulae. Overall speaking, 40% of PWE became more mindful after receiving MBI compared with the WLC condition. Upon receiving about 12 hours of mindfulness therapy, around 40% of PWE showed a reliable reduction in depressive symptoms as well as an improvement in QOL. A 6-week follow-up revealed that the proportion of patients who received the intervention showed significant clinically reliable improvement in depression and QOL compared to those in the WLC condition.

Surprisingly, findings showed no group differences in the RCI index for anxiety symptoms. Aside from the psychometric scales discussed, we contend that there are overlapping and distinctive features between anxiety and depression in reaping the benefits of mindfulness therapy. Eysenck raised the notion that if anxiety is associated with a future orientation, anxious individuals may exhibit an attentional bias (selective attention to threat-related stimuli) [28]. In contrast, if depression is associated with a past orientation, we might expect depression to be correlated with memory bias (disproportionate retrieval of negative information) [28]. As 60% of PWE in our study reported infrequent seizures (e.g. one seizure per year), the cultivation of a non-judgmental stance in mindfulness practice may trend toward reconstructing the negative cognitions and emotions associated to the demoralizing effects of being diagnosed with epilepsy. The assumption that the differing negative thoughts of anxious and depressed individuals reflect differences in their underlying cognitive schemas is very plausible, therefore future study is required.

In reviewing the clinical utility of mindfulness, the RCI method can assess individuals in their functional, real-world, lives in which clinically significant change is operationalized. We used the percentage of improvement (PI) to dictate the proportion of patients who responded to treatment. This indicator further allowed us to

differentiate the proportion of patients who failed to respond (i.e., reliable indeterminate change) or seem to be unable to improve into the normal range of functioning (i.e., reliable deterioration). Future research is required to discuss practical concerns of treatment responses, for example, should treatment be terminated if the cutoff is achieved, or other psychotherapeutic techniques be implemented if the response does not occur within a defined period.

4.3. Challenges in practice facilitation

Although it was indicated in previous study that PWE showed a strong willingness to participate in psychological intervention if available [22], only 15% of eligible PWE agreed to participate in this trial. This low response rate echoed the challenges reported in the implementation of evidence-based care within primary care setting [29]. The current study approached eligible participants via flyers and electronic mails. In retrospect, this approach may lack the personal touch to motivate and raise the intention to participate. The overall low response rate in this trial could be attributed to this passive recruitment strategy.

A systematic review on the efficacy of implementing clinical guideline using various strategies recommended that a multifaced approach, which includes interactive educational outreach, clinical reminders, decision support system, and the evaluation of such provision of services, should be advocated as the "best practices", and were found to increase successful recruitment and compliance to study trials [30]. The majority (n = 124, 78%) who declined in our study reported that they were either not interested or had competing priorities. The therapeutic needs of those who declined may unveil potential barriers to change within specific clinical setting. Further work is required to build consensus methods to increase compliance or ownership of patient-preference-based treatment.

5. Limitations

This study has several limitations. First, the outcome measures were based on self-reports only, thus, the conclusions drawn might be influenced by social desirability and cultural biases in the responses. Objective measures (e.g. physiological measures and brain imaging data) are likely valuable in future studies to rule out these influences and to examine the mechanism underlying the effects of mindfulness training. Second, we did not evaluate the amount of time or effort spent on individuals' mindfulness home practice. Given that the intervention aims to impart its essence of nonjudgmental attitude, tracking personal log entries may impose a negative attitude (e.g. peer pressure) toward home practice. Future studies could evaluate qualitatively and experimentally the relationship of home practice to mindfulness program outcomes. Although our findings indicated that a sample of 24 had a ~80% chance of detecting a difference with an alpha of 0.05, our study was still underpowered to detect the difference in mindfulness level using RCI analysis.

6. Conclusion

Mindfulness therapy improves the quality of life and reduces symptoms of depression in adult individuals with epilepsy, in a group as well as individual, and certain effects sustain beyond the 6-week mindfulness therapy. Future research may extend the study duration to evaluate the sustainability of therapeutic properties and include objective measures of symptomatic changes to assess the clinical utility of mindfulness therapy.

Author contributions

ST designed the project, wrote the protocol, obtained the data, performed the statistical analysis, interpreted the data, and drafted the manuscript. KS designed the study, reviewed the study protocol, supervised the execution, and coordinated the data analysis plan. VT reviewed the study protocol, supervised the execution, and interpreted the data. WY reviewed the study, research conceptualization, and supervised the execution. All authors reviewed, revised, and approved the manuscript.

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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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2021.107916.

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