A preliminary efficacy study of eye movement desensitisation and reprocessing therapy in reducing epilepsy-related anxiety

Broekman-Labinac, K.; Aben, L.; Thijs, R.D.; Smeding, H.M.M.; Jongh, A. de; Hiele, K. van der

Epilepsy & Behavior 171 (2025) 110493

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

A preliminary efficacy study of eye movement desensitisation and reprocessing therapy in reducing epilepsy-related anxiety

K. Broekman-Labinac [a], L. Aben [b], R.D. Thijs [a,c,*], H.M.M. Smeding [a], A. de Jongh [d,e,f,g], K. van der Hiele [h]

[a] Stichting Epilepsie Instellingen Nederland (SEIN), Department of Psychology and Neurology, Heemstede, Netherlands
[b] Amsterdam University Medical Centre, Department of Psychiatry, Amsterdam, Netherlands
[c] Leiden University Medical Centre (LUMC), Department of Neurology, Leiden, Netherlands
[d] Research Department, PSYTREC, Bilthoven, Netherlands
[e] Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and VU University Amsterdam, Netherlands
[f] School of Psychology, Queen's University, Belfast, Northern Ireland, United Kingdom
[g] Institute of Health and Society, University of Worcester, United Kingdom
[h] Leiden University, Department of Psychology, Health, Medical and Neuropsychology Unit, Leiden, Netherlands

ARTICLE INFO

Keywords:
Epilepsy
Anxiety
EMDR
Health-related quality of life
Subjective cognitive functioning

ABSTRACT

Objective: To determine whether eye movement desensitisation and reprocessing (EMDR) therapy reduces anxiety in people with epilepsy-related anxiety. Secondary outcomes included health-related quality of life (HRQOL), subjective cognitive functioning and seizure frequency.

Methods: Prospective uncontrolled study with a pre-post follow-up design, including measurements before, immediately after, and three months after EMDR therapy, focused on the individuals' fear of future seizures (i.e. flashforwards). We recruited participants with epilepsy-related anxiety from a Dutch tertiary epilepsy centre. Questionnaires were used to monitor general and epilepsy-related anxiety, HRQOL, subjective cognitive functioning and seizure frequency. Repeated-measures ANOVA was used.

Results: Eleven participants were included. We observed a significant reduction in general and epilepsy-related anxiety from before to immediately after EMDR treatment, and three months hereafter ($p \leq 0.001$, $\eta^2 = 0.698$ and $p \leq 0.001$, $\eta^2 = 0.641$, respectively). This coincided with an improvement in HRQOL ($p \leq 0.001$, $\eta^2 = 0.550$). Despite a main treatment effect for subjective cognitive functioning ($p = 0.023$, $\eta^2 = 0.415$), no significant post hoc effects were observed. No effects were found for informant-reported cognitive functioning ($p = 0.261$, $\eta^2 = 0.236$) and seizure frequency ($p = 0.495$, $\eta^2 = 0.075$).

Conclusion: This study provides preliminary evidence that EMDR therapy reduces anxiety in people with epilepsy-related anxiety. This effect sustained over three months and coincided with an improved HRQOL. Subjective cognitive functioning and seizure frequency did not change over time. Our findings suggest that EMDR therapy is a potentially safe treatment for epilepsy-related anxiety.

1. Introduction

Epilepsy is one of the most common chronic neurological conditions, affecting 70 million people worldwide [1,2]. The impact is not limited to seizures alone, as epilepsy has marked neurobiological, cognitive, behavioural, emotional, and social consequences [3]. Severe mental health comorbidities often occur in people with epilepsy, almost half of people with epilepsy have mental health disorders [4–6]. Despite the recognition of different mental health comorbidities in epilepsy, most studies have focused on depressive disorders. Anxiety disorders have been described as a 'forgotten' mental health comorbidity in epilepsy [7–10]; the incidence is up to a third of people with epilepsy [5], in contrast to an incidence of up to 9 % in the general population [11].

The experience of epilepsy-related anxiety is based on anxiety symptoms that occur during the interictal period. These symptoms can manifest as anticipatory anxiety for seizures, seizure phobia, social

* Corresponding author at: Stichting Epilepsie Instellingen Nederland (SEIN), Department of Psychology and Neurology Achterweg 3, 2103 SW Heemstede, Netherlands.
E-mail address: rthijs@sein.nl (R.D. Thijs).

https://doi.org/10.1016/j.yebeh.2025.110493
Received 30 January 2025; Received in revised form 12 May 2025; Accepted 13 May 2025
Available online 24 May 2025

anxiety related to epilepsy, and episodes of panic associated with epilepsy [12]. A common feature of epilepsy-related anxiety is fear of future seizures [13]. This type of anticipatory anxiety is described as daily persistent fear, dread, or excessive worry about experiencing a seizure, similar to anticipatory anxiety reported in general panic attacks [14]. Clark's vicious circle [15], a model for panic disorder, may help explain the development of anxiety in epilepsy. In this model, people with epilepsy interpret external stimuli (e.g. the place of the last seizure) or internal stimuli (e.g. body sensations, such as palpitations or dizziness) as evidence of impending danger (e.g. a new seizure), leading to mild apprehension accompanied by bodily sensations. When these sensations are interpreted catastrophically, apprehension increases, resulting in a further increase in bodily sensations in a vicious cycle.

Evidence suggests a bidirectional association between anxiety and susceptibility to seizures in persons with epilepsy [16], indicating that they may influence each other. Stress, fear, anxiety, and agitation are frequently reported to coincide with seizures and are described as potential seizure-related factors [17]. High levels of anxiety can increase seizure susceptibility via stress-related neurophysiological and hormonal changes that affect neuronal excitability [18]. Treating anxiety in individuals with epilepsy may therefore not only decrease anxiety levels, but also indirectly decrease seizure frequency by eliminating a critical seizure trigger.

Reducing anxiety may have a positive effect on other concepts of well-being, including health-related quality of life (HRQOL), which is lower in people with epilepsy than in those with other chronic diseases [19]. It has been found that comorbid anxiety disorders have an even more profound adverse impact on the HRQOL than seizures [20]. Recent evidence highlights the association between mood, quality of life, and objective cognitive status in people with epilepsy [21]. Symptoms of anxiety and depression are linked to both cognitive impairment and lower quality of life in this population [22]. Additionally, people with epilepsy report a wide range of subjective cognitive complaints, which may not always align with objectively measured cognitive impairment. Worse subjective cognitive functioning has been associated with anxiety and a more negative perception of one's functioning, even in the absence of significant objective cognitive deficits [23–28].

The importance of identifying and alleviating epilepsy-related anxiety has been recognised in literature [29]. A review of 36 randomised controlled trials of psychological epilepsy treatments showed that psychological therapies, either skills-based or educational interventions, improved quality of life and emotional well-being in adults with epilepsy [30], but none of the interventions were explicitly aimed at treating anxiety. Interventions focusing primarily on anxiety in epilepsy are urgently needed.

Eye movement desensitisation reprocessing (EMDR) therapy is an evidence-based treatment that has been successfully used for anxiety disorders in the general population [31],to break the panic circle in people with panic disorder [32], and for post-traumatic stress disorder (PTSD) [33,34]. During EMDR therapy, traumatic memories are processed, negative beliefs reformulated, and physiological arousal is reduced. In EMDR therapy, the individual is exposed to two elements simultaneously: (1) focusing on the most emotionally charged image with associated physical sensations; (2) at the same time, a dual attention task that taxes the individual's working memory – typically this task is rapid lateral eye movements guided by the therapist's hand. EMDR therapy is a highly protocol-driven procedure as the treatment is delivered in the same way across the Netherlands, increasing the ability to disseminate treatment and test its effectiveness through research [34]. This applies to face-to-face and remote therapy, which are equally effective [35]. EMDR therapy has not been previously assessed as a treatment for epilepsy-related anxiety in adults. The application of EMDR therapy in epilepsy is sometimes hindered by the concern that EMDR therapy might trigger a seizure. A case series of five children with epilepsy and seizure-related anxiety found EMDR therapy to be a potentially successful, quick, and safe psychological treatment for relieving epilepsy-related anxiety [36]. EMDR therapy may be decisive in breaking the vicious circle of epilepsy and anxiety by alleviating feelings of apprehension and body sensations associated with a disaster image of a seizure or its consequences. Therefore, we hypothesised that EMDR may ameliorate epilepsy-related anxiety and potentially reduce the occurrence of seizures.

The purpose of this exploratory, uncontrolled study with a three-month follow-up was to determine the efficacy of EMDR therapy in reducing anxiety in people with epilepsy-related anxiety. To ensure rigorous assessment, we employed a twofold approach using both the Hospital Anxiety and Depression Scale (HADS), a widely used general anxiety measure with established cut-off points for individuals with epilepsy, and the Epilepsy Anxiety Survey Instrument (EASI), an epilepsy-specific anxiety measure. This combination allowed for both broad comparability with existing research and a more targeted evaluation of epilepsy-related anxiety. Secondary outcomes included quality of life, subjective cognitive functioning and seizure frequency.

2. Materials and methods

2.1. Design

This was an uncontrolled study with a pre-post follow-up design, including measurements before, immediately after, and three months after EMDR treatment.

2.2. Participants and procedure

Participants were recruited from patients referred to the psychology department of Stichting Epilepsie Instellingen Nederland (SEIN), a tertiary epilepsy referral centre in the Netherlands. Considering the specialized care, the population at SEIN predominantly consists of patients with a long-standing history of epilepsy. Patients are referred for various reasons, including cognitive and socio-emotional symptoms. Those who reported epilepsy-related anxiety upon referral received an information letter explaining the study procedure. The initial setup included 20 participants with epilepsy-related anxiety symptoms. At the first appointment in the psychology department, a healthcare psychologist with experience in assessing epilepsy-related anxiety conducted a thorough evaluation of the potential participant's anxiety symptoms. This included a detailed interview to ensure that the anxiety symptoms were specifically related to the person's epilepsy, for example, anxiety related to a (future) experience of a seizure, fear of falling during a seizure or fear of a particular place related to a seizure. Additionally, the healthcare psychologist inquired about negative future targets, asking participants to verbally describe any mental disaster scenarios related to their epilepsy-related anxiety. For inclusion, at least one negative future target related to epilepsy, according to the EMDR flashforward protocol [37], had to be present. The HADS was completed three times, approximately every two weeks (at referral to the psychology department, during the interview at the department, and just before the start of the treatment). Eligible participants required all HADS scores to show anxiety (anxiety subscale score $\geq$ 8) [38]. In sum, participants had to meet all of the following criteria: diagnosis of definite epilepsy, HADS anxiety sub score >=8 at all three time points, epilepsy-related anxiety symptoms as determined by an interview and operationalized as having a seizure-related disaster target. We used the following exclusion criteria: age < 18 years, estimated IQ < 80, inability to read, write, and communicate in Dutch, the presence of suicidal intent or acute psychosis, currently receiving another form of psychological treatment, presence of psychogenic non-epileptic seizures, diagnosis of a neurodegenerative disorder, epilepsy surgery within the last year, and the use of benzodiazepines, unless prescribed as antiseizure medications. A series of baseline measurements were taken before treatment, and then immediately and three months after treatment (Fig. 1). Subjective cognitive functioning was assessed not only from the perspective of the

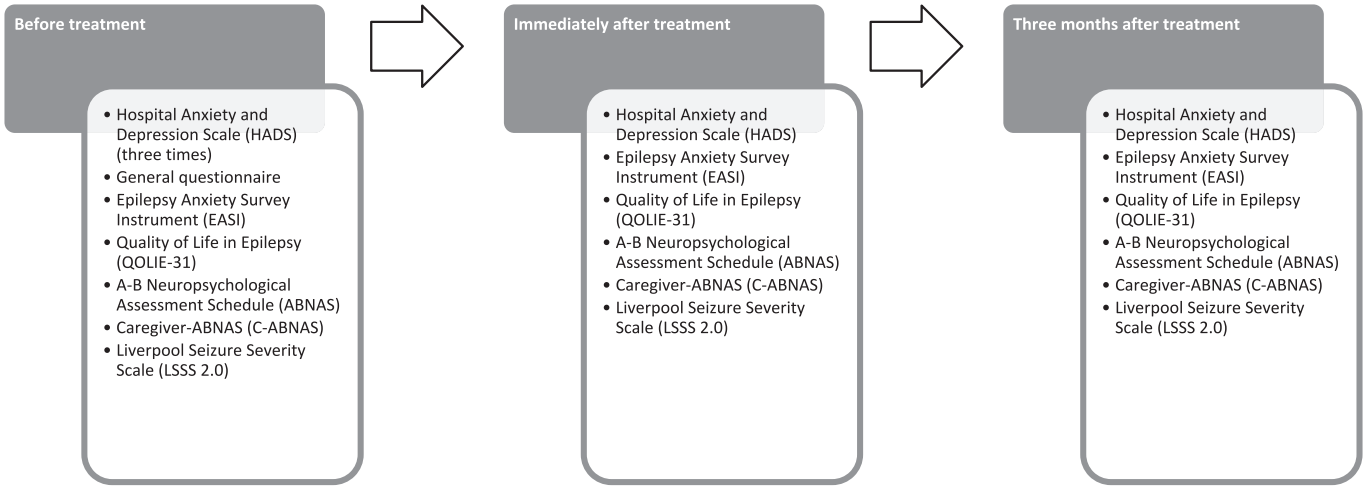

Fig. 1. Study procedure and measurements.

person with epilepsy but also from the perceived impression of an informant, such as a life partner or a family member. A general questionnaire concerning demographic and disease characteristics was completed before treatment. The questionnaires were offered as hard copies at the location or sent to the participants' homes.

This study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee Leiden The Hague Delft, recognized by the Dutch Central Committee on Research Involving Human Subjects (NL80250.058.22).

2.3. Treatment

EMDR therapy was delivered according to the protocol in weekly sessions, each lasting a maximum of 90 min, either face-to-face or online. The total number of sessions was not pre-established, and there was no minimum or maximum. Following the standardised EMDR protocol, the most disturbing negative future targets (so-called "flashforwards") related to seizures were targeted [37]. During each session, the level of distress associated with the flashforward was repeatedly measured using the Subjective Units of Distress (SUD) scale, in which participants were asked to indicate their level of disturbance, ranging from 0 ('no disturbance at all') to 10 ('as disturbing as possible'). Certified healthcare psychologists delivered the EMDR therapy. They were certified and experienced with EMDR therapy in epilepsy. A. de Jongh[5], an accredited supervisor of the Dutch EMDR Association (Vereniging EMDR Netherlands) provided supervision to standardise the EMDR therapy as much as possible. The leading researcher did not administer EMDR therapy.

2.4. Measures

2.4.1. General questionnaire

A general questionnaire, with questions about demographics and disease characteristics, was completed before treatment.

2.4.2. Hospital anxiety and depression scale (HADS)

The HADS is a self-reported 14-item scale with subscales for depression and anxiety. The participants were asked to indicate on a four-point scale the extent to which a statement was applicable during the previous week. Scores range from 0 to 21 per subscale, with higher scores indicating higher levels of anxiety and depression. The HADS provides valid markers for major depression and generalised anxiety disorder [39,40]. It not only provides clinically meaningful results as a psychological screening tool but is also sensitive to changes in response to psychotherapeutic intervention [41]. The HADS has acceptable internal consistency and sufficient construct validity in epilepsy [38,42]. The HADS was completed five times: three times before treatment, once immediately after, and once three months after treatment.

2.4.3. Epilepsy anxiety survey instrument (EASI)

The EASI [43] is a self-reported 18-item scale which assesses anxiety in epilepsy, providing clinicians with in-depth insight into the nature and severity of an individual's anxiety. Participants used a four-point scale to describe the extent to which they experienced anxiety symptoms. Scores range from 0 to 54, with higher scores indicating higher levels of anxiety. Responses to the EASI may help clinicians understand whether peoples anxiety symptoms reflect a problematic adjustment to living with epilepsy (e.g. exaggerated fear of the social or physical consequences of having a seizure, excessive worry about seizures), or whether anxiety symptoms are independent of epilepsy. Validity and reliability are considered excellent. We translated the questionnaire into Dutch, using multiple forward and backward procedures. The process began with two independent forward translators who translated the original questionnaire into Dutch. Their translations were then synthesized into a single version through discussion and consensus. Next, an independent native English-speaking translator who was blinded to the original version performed a back-translation. Finally, a review committee consisting of experts in epilepsy, psychology, and translation carefully examined all versions, comparing them to the original questionnaire to ensure conceptual accuracy and cultural appropriateness.

2.4.4. Quality of life in Epilepsy-31 (QOLIE-31)

The QOLIE-31 [44,45] is a reliable and valid measure of HRQOL in epilepsy. The survey was cross-culturally translated into Dutch. The inventory contains seven scales (emotional well-being, social functioning, energy/fatigue, cognitive functioning, seizure worry, medication effects, and overall quality of life). Scores range from to 0–100, with higher scores indicating better quality of life.

2.4.5. A-B Neuropsychological Assessment Schedule (ABNAS)

The ABNAS [46] is an epilepsy-specific instrument that measures subjective cognitive functioning. The ABNAS comprises 24 statements across five cognitive domains: fatigue, slowing, memory, concentration, and motor coordination and language, with an overall score ranging from 0 (no symptoms) to 72 (severe symptoms). It has significant clinical sensitivity, excellent reliability, and excellent validity. Internal consistency reliability is excellent.

2.4.6. Caregiver-ABNAS (C-ABNAS)

The C-ABNAS [25] is a modified version of the ABNAS, involving the

replacement of the first-person statements on the original ABNAS with third-person statements (e.g., "He/she has difficulties remembering names of people"). It can be completed by caregivers, friends, or other relatives. The response options and scoring are identical to those of the original ABNAS.

2.4.7. Liverpool seizure severity scale 2.0 (LSSS 2.0)

The LSSS 2.0 [47,48] provides a patient-reported seizure severity index, focusing on the most severe seizure experienced during the last four weeks. Ictal and postictal characteristics are examined, with answers on a 4-point scale. The scale yields a severity score ranging from 0 (no seizures) to 100 (most severe possible seizures). The scores were found to be reliable, have construct validity (known-groups validity), and are responsive to changes in the persons' epilepsy, as noted by their physicians. The first question about the number of seizures experienced by an individual during the last four weeks was used to determine the seizure frequency. The seizure severity score was used descriptively.

2.5. Statistical analyses

2.5.1. Power analysis

The primary aim of this study was to examine the efficacy of EMDR therapy in reducing anxiety from before to after treatment. Anxiety measures are rarely used as outcome measures in interventions for epilepsy; therefore, the power analysis was based on two studies that used EMDR therapy as a treatment for other people with anxiety. Wallis and de Vries (2020) [49] examined the flashforward EMDR procedure as a treatment option in people with multiple sclerosis, which, like epilepsy, has paroxysmal attacks. This study used the HADS anxiety subscale as an outcome measure. Treatment measures were included in the power analysis: mean sample pre-treatment: 11.3 (SD: 2.4), mean sample follow-up treatment after three months: 7.71 (SD: 3.9). A power analysis based on a two-tailed paired sample *t*-test with an effect size (Cohen's *d*) of 1.06, found that 14 individuals should be included (Using G*power 3.1.9.7) [50]. Szpringer and colleagues (2018) [51] examined the effectiveness of EMDR therapy for anxiety in people with glioblastoma multiforme. Treatment measures on the HADS for anxiety were included in the power analysis; the mean sample before treatment was 17.50 (SD: 2.36), and the mean sample post-treatment was 9.89 (SD: 3.79). A power analysis with an effect size (Cohen's *d*) of 2.11 suggested the inclusion of six participants. Considering the possible dropouts and the lower effect size of secondary measures, we aimed to include 20 participants.

2.5.2. Analyses

Descriptive statistics were used to report demographic characteristics (age, educational level, socioeconomic status, and employment status) and disease characteristics (type of epilepsy, medication, and medication side effects). Repeated-measures analysis of variance (ANOVA) was used to assess changes in HADS anxiety scores over time. Repeated-measures ANOVA was also used to determine the change over time in the secondary outcomes: anxiety as measured with the EASI, quality of life, subjective cognitive functioning and seizure frequency. The effect size Partial Eta Squared was calculated for all the measures. The strength of the effect was labelled as small: $\eta^2 = 0.01$, medium: $\eta^2 = 0.06$ and large: $\eta^2 > 0.14$. Participants with missing scores were excluded from the statistical analyses. This led to the exclusion of nine cases. Non-replies resulted in missing data from the questionnaires. To provide a more in-depth view of treatment effects in individuals, the reliable change index (RCI) was calculated according to the Jacobson-Truax formula [52] to determine whether anxiety (that is, HADS scores) changed significantly from before treatment to immediately after treatment and from before treatment to three months after treatment. The RCI was computed as the difference in scores divided by the standard error of difference, with a threshold of $\pm$ 1.96 to indicate statistically reliable change. Test-retest reliability coefficients and standard deviations were extracted from a validation study [38]. RCI distinguishes actual changes from random variability at the individual level, making it particularly useful in clinical settings. This complements the effect sizes by adding a layer of analysis that is essential for practical applications and rigorous scientific research. A *p*-value below 0.05 was considered statistically significant and confidence intervals were 95 %. All analyses were performed using IBM SPSS Statistics for Windows, version 29.

3. Results

3.1. Participants

The study was conducted between October 2022 and April 2024. The inclusion process is illustrated in Fig. 2. We assessed 11 participants fulfilling the inclusion criteria, with complete measurements of the HADS from pre- to post-treatment. No significant differences were found between participants with complete and incomplete measurements for age ($p = 0.648$), sex ($p = 0.665$), educational level ($p = 0.774$), or epilepsy type ($p = 0.054$).

3.2. Descriptive data

The demographic and clinical characteristics of participants are shown in Table 1. Six females and five males had a mean age of 36.6 years. Eight reported side effects of antiseizure medications; tiredness (n = 4), dizziness (n = 4), headache (n = 2), decreased appetite (n = 2), and concentration problems (n = 1). Therapists conducted EMDR therapy for an average of five sessions (SD = 3; median = 4; range 2–13), with an average of four flashforwards (SD = 1.7; median = 4; range 2–6), all SUD scores reaching a minimum of 0.

3.3. Treatment outcome

3.3.1. HADS anxiety

Repeated measures ANOVA with Greenhouse-Geisser correction showed that HADS anxiety scores differed significantly between time points ($F(2.29, 22.85) = 23.07$, $p \leq 0.001$, $\eta^2 = 0.698$). The strength of this effect was large. Bonferroni post hoc tests showed that HADS anxiety scores immediately after treatment were significantly lower than those before treatment ($p = 0.002$, $p \leq 0.001$, $p = 0.003$) and three months after treatment ($p = 0.002$, $p = 0.002$, $p = 0.003$), indicating a decrease in anxiety over time. No difference was found between the scores immediately after and three months after treatment ($p = 1.000$) (Fig. 3).

At the individual level, the RCI showed that 9 participants (82 %) had a clinically meaningful decline in HADS anxiety scores immediately after treatment, whereas 2 participants showed no reliable change. Three months after treatment, the results were comparable; 8 participants (73 %) showed a consistent improvement immediately and three months after treatment, 1 participant consistently showed no reliable change, 1 participant initially showed no reliable change yet improved three months after treatment, and 1 participant improved immediately after treatment and showed no change three months after treatment.

3.3.2. EASI

Repeated measures ANOVA showed that the EASI total scores differed significantly between time points ($F(2, 16) = 14.29$, $p \leq 0.001$, $\eta^2 = 0.641$). Bonferroni post-hoc tests showed that the EASI total scores before treatment were significantly higher than the EASI total scores immediately after treatment ($p = 0.002$) and three months after treatment ($p = 0.011$), showing decreased epilepsy-specific anxiety over time. No difference was found between the scores immediately and three months after treatment ($p = 1.000$). The results are shown in Fig. 4.

3.3.3. QOLIE-31

QOLIE-31 total scores differed significantly between time points

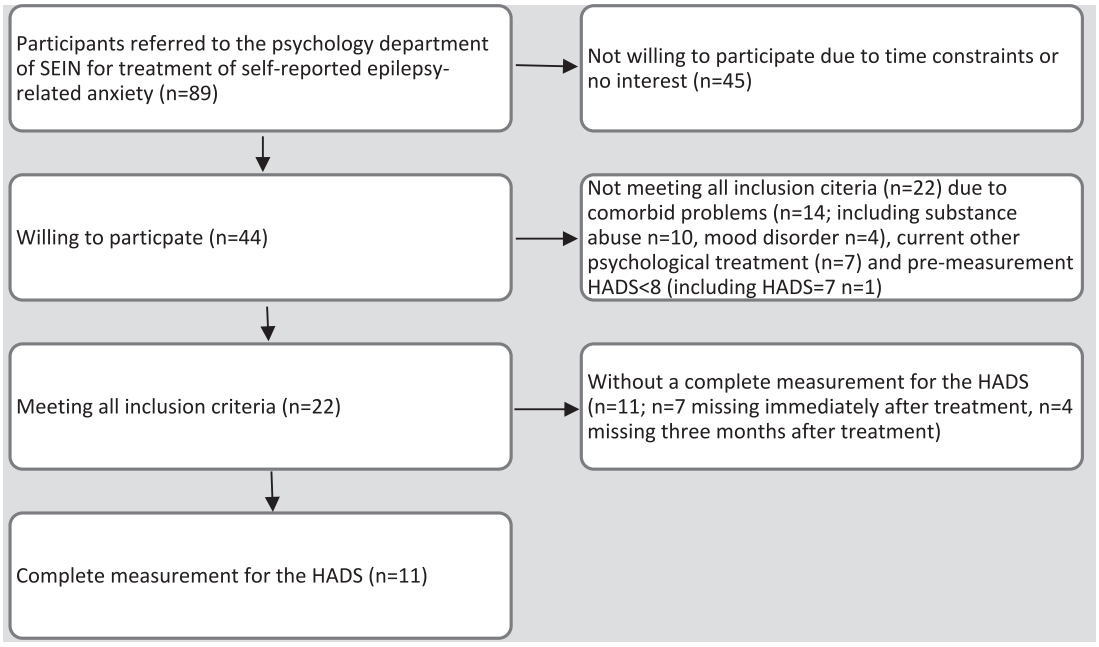

Fig. 2. Participants inclusion flow diagram.

Table 1
Demographic and clinical characteristics of the study population.

	participants with epilepsy (n = 11)
Age (years; mean (SD) (range))	36.6 (13.1) (20–66)
Sex (N (%))	
Female	6 (54 %)
Educational level (n (%))	
Lower vocational education	1 (9 %)
Secondary vocational education	5 (45.5 %)
Higher vocational or scientific education	5 (45.5 %)
Employment status (n (%))	
Paid work > 10 h/week	7 (64 %)
Unemployed, not looking for work	1 (9 %)
Unemployed, completely incapacitated	1 (9 %)
Student	1 (9 %)
Retired	1 (9 %)
Epilepsy type (n (%))	
Focal	7 (64 %)
Generalised	4 (36 %)
Antiseizure medications (n (%))	
Monotherapy	7 (64 %)
Polytherapy	4 (36 %)
Side effects of antiseizure medications (n (%))	
Yes	8 (72 %)

(repeated-measures ANOVA; $F(2, 20) = 12{,}22$, $p \leq 0.001$, $\eta^2 = 0.550$). Bonferroni post hoc tests showed that the QOLIE-31 total score before treatment was significantly lower than the QOLIE-31 total scores immediately after treatment ($p = 0.008$) and three months after treatment ($p = 0.008$), suggesting an increase in HRQOL over time. No difference was found between the scores immediately and three months after treatment ($p = 1.000$) (Fig. 5).

3.3.4. ABNAS

Repeated measures ANOVA showed that ABNAS scores, based on n = 8 due to missing questionnaires, differed significantly between time points ($F(2, 14) = 4.97$, $p = 0.023$, $\eta^2 = 0.415$). Bonferroni post-hoc tests showed that the ABNAS pre-treatment scores did not differ significantly from the ABNAS scores immediately after treatment ($p = 0.653$) or three months after treatment ($p = 0.05$). From immediately after treatment to three months after treatment no significant difference could be detected ($p = 0.287$), indicating that there was no further improvement or relapse after treatment. The results are shown in Fig. 6.

3.3.5. C-ABNAS

Repeated measures ANOVA showed that C-ABNAS scores, based on N = 6 due to missing questionnaires, did not differ significantly between the time points ($F(2, 10) = 1.54$, $p < 0.261$, $\eta^2 = 0.236$). Bonferroni post-hoc tests showed that the C-ABNAS pretreatment scores did not differ significantly from the C-ABNAS scores immediately after treatment ($p = 0.881$) or three months after treatment ($p = 0.676$). From immediately to three months after treatment, there was also no significant difference ($p = 1.000$). The results are shown in Fig. 7.

3.3.7. Seizure frequency

The frequency of seizures measured with LSSS 2.0, based on N = 8 due to missing questionnaires, did not differ significantly between time points (repeated measures ANOVA with Greenhouse-Geisser correction $F(1.14, 7.98) = 0.57$, $p = 0.495$, $\eta^2 = 0.075$). Bonferroni post-hoc tests showed no significant differences between time points (Fig. 8).

4. Discussion

In this uncontrolled study with a small sample of participants with epilepsy, we investigated whether EMDR therapy reduced anxiety in participants with epilepsy-related anxiety. Even in this small sample, we found significant reductions in anxiety from before to immediately after treatment, with a large effect size. The effects were sustained for up to three months after treatment. Furthermore, effects were found for the HADS, a general anxiety scale, and the EASI, which measures specific epilepsy-related anxiety. These findings suggest that EMDR therapy is associated with a reductions in anxiety levels and the maintenance of these reductions over a period of three months. The majority of participants (73 %) showed a clinically meaningful decline (RCI > 1.96) in general anxiety immediately after treatment and at the three-month follow-up.

The results of the present study suggest that EMDR therapy may be effective in reducing epilepsy-related anxiety. While the mean HADS anxiety score at follow-up was lower than pre-treatment levels, it remained relatively high, just below the most validated cut-off point of 8

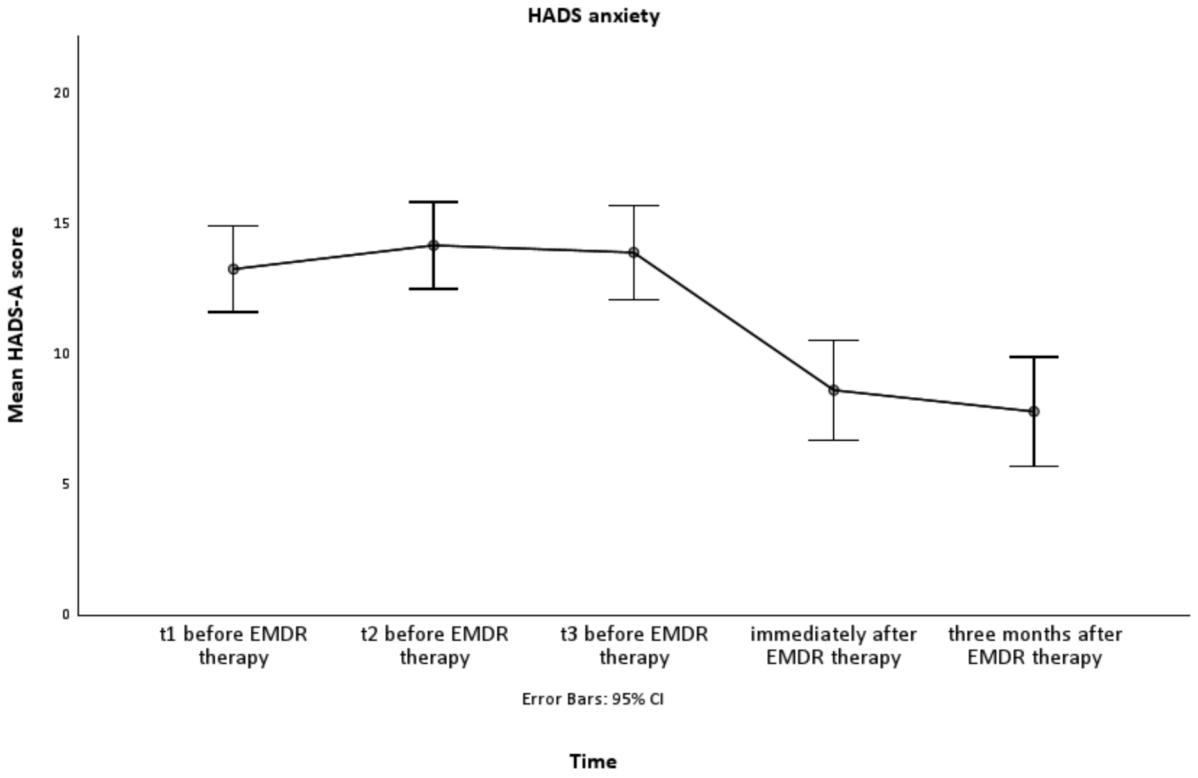

Fig. 3. Anxiety scores measured with HADS (expressed as mean with 95 % confidence intervals) before (t1, t2, t3), immediately after, and three months after eye movement desensitisation and reprocessing (EMDR) therapy in 11 participants with epilepsy-related anxiety. HADS: Hospital Anxiety and Depression Scale (n = 11).

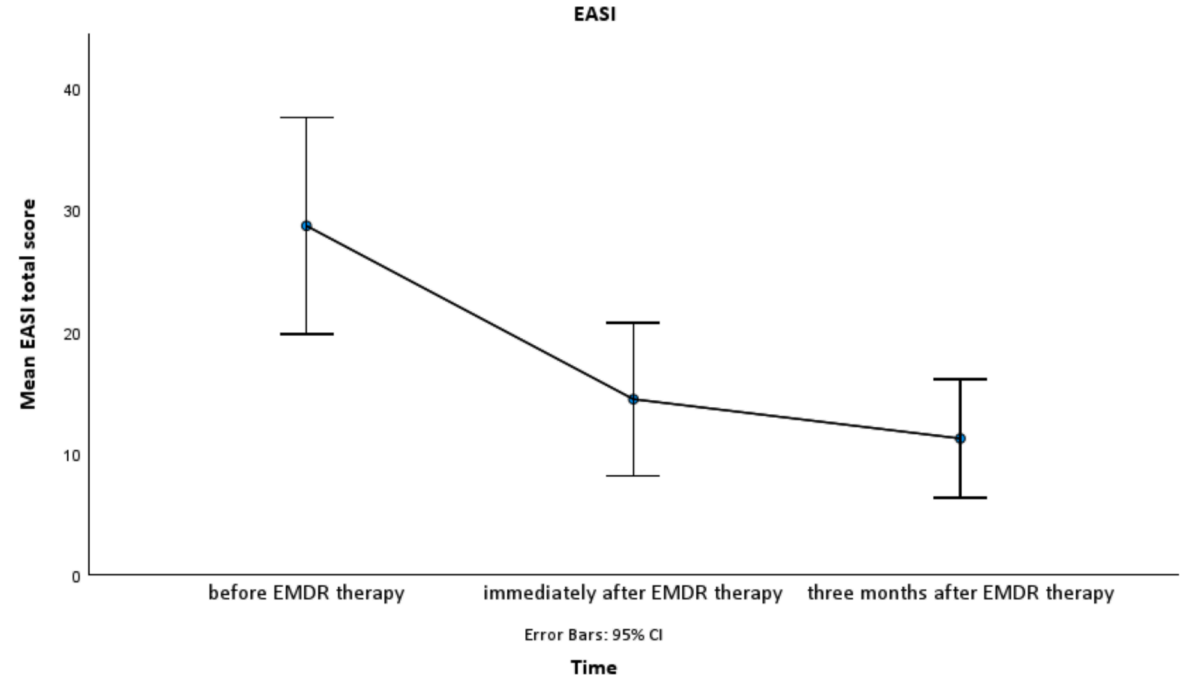

Fig. 4. Epilepsy anxiety total scores measured with EASI (expressed as mean with 95 % confidence intervals) before, immediately after and three months after eye movement desensitisation and reprocessing (EMDR) therapy in 11 participants with epilepsy-related anxiety. EASI: Epilepsy Anxiety Survey Instrument (n = 11).

[53]. This suggests that although EMDR therapy significantly alleviated anxiety levels, it may not have completely addressed all anxiety symptoms in this study sample. This could be related to the specificity of epilepsy-related anxiety, for which we added the EASI score. Although a cut-off point is not available for addressing clinical levels of anxiety for this instrument, our results show a significant decrease in anxiety on the EASI. Another issue regarding residual anxiety might be the chronic nature of epilepsy and its associated psychosocial stressors, which continue to affect people even after therapy. Epilepsy-related anxiety is multifaceted and influenced by factors such as fear of seizures, social stigma, and medication side effects. These persistent and pervasive factors may require ongoing or additional therapeutic interventions

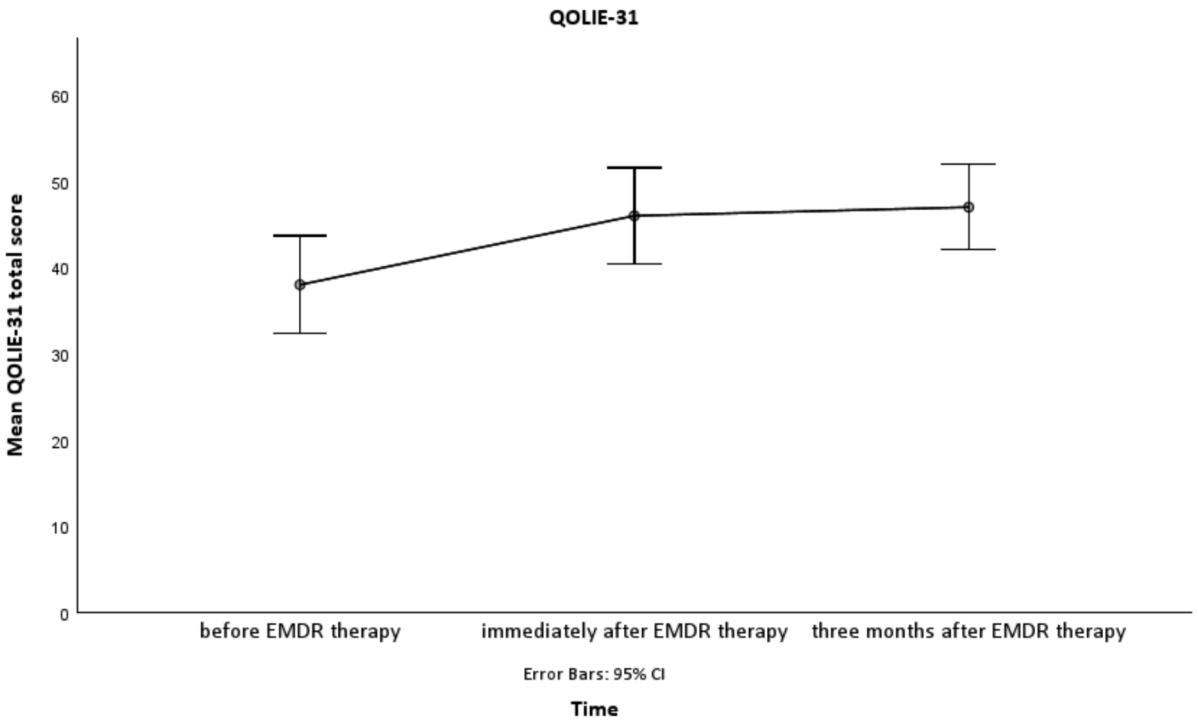

Fig. 5. Quality of life total scores measured with QOLIE-31 (expressed as mean with 95 % confidence intervals) before, immediately after and three months after eye movement desensitisation and reprocessing (EMDR) therapy in 11 participants with epilepsy-related anxiety. QOLIE-31: Quality of Life in Epilepsy – 31 (n = 11).

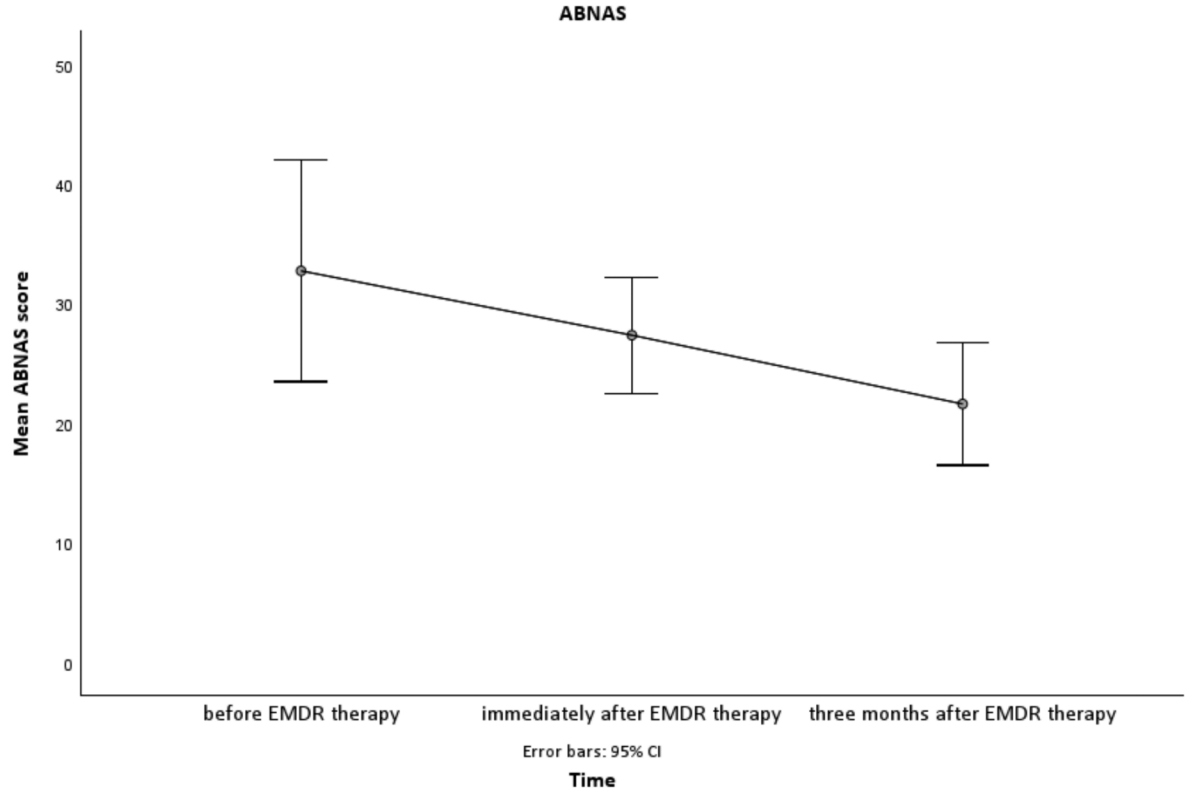

Fig. 6. Subjective cognitive functioning scores measured with ABNAS (expressed as mean with 95 % confidence intervals) before, immediately after and three months after eye movement desensitisation and reprocessing (EMDR) therapy in eight participants with epilepsy-related anxiety. ABNAS: A-B Neuropsychological Assessment Schedule (n = 8).

beyond the initial EMDR therapy to achieve a further reduction in anxiety. Future studies should consider extended follow-up periods to assess the long-term efficacy of EMDR therapy and durability of its effects on anxiety. Understanding how anxiety levels evolve can help design more effective maintenance strategies. Moreover, significant improvements in quality of life were found immediately after treatment

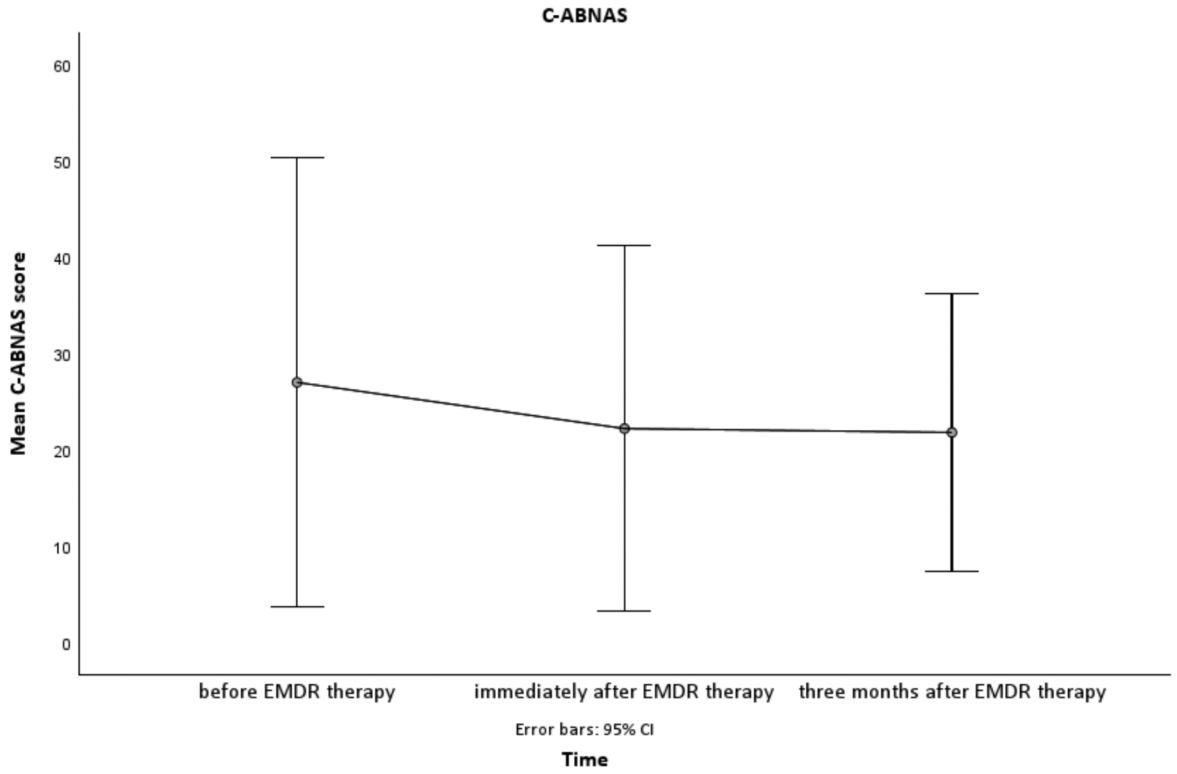

Fig. 7. Caregiver subjective cognitive functioning scores measured with C-ABNAS (expressed as mean with 95 % confidence intervals) before, immediately after and three months after eye movement desensitisation and reprocessing (EMDR) therapy in six participants with epilepsy-related anxiety. C-ABNAS: Caregiver A-B Neuropsychological Assessment Schedule (n = 6).

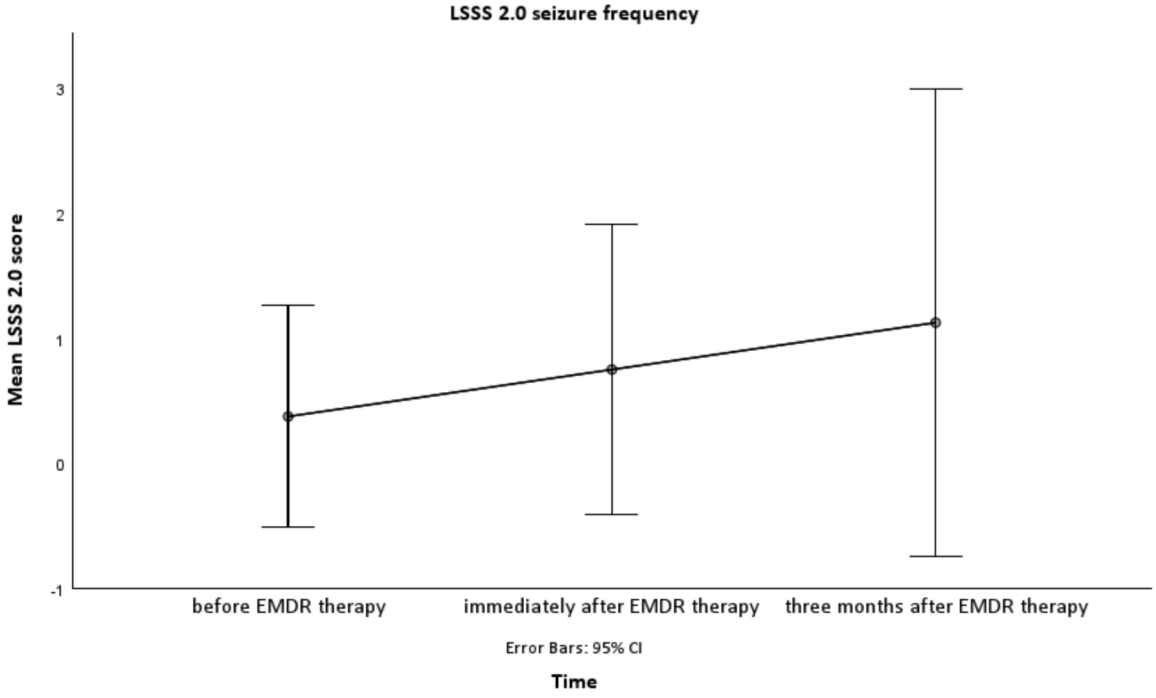

Fig. 8. Seizure frequency scores measured with LSSS 2.0 (expressed as mean with 95 % confidence intervals) before, immediately after, and three months after eye movement desensitisation and reprocessing (EMDR) therapy in eight participants with epilepsy-related anxiety. LSSS 2.0: Liverpool Seizure Severity Scale 2.0 (n = 8).

and at the three-month follow-up, supporting previous findings that anxiety reduction can positively impact overall well-being, including health-related quality of life in people with epilepsy.

Although EMDR therapy was associated with reductions in anxiety, we found no evidence of a direct impact on seizure frequency. The low seizure frequency (mean 0–3) may have contributed to the lack of significant changes over time. Additionally, the LSSS 2.0, which provides a retrospective report of the number of seizures over the previous four

weeks, may be subject to recall bias. Continuous measurements of seizure frequency, supported by close informants, could help to obtain more thorough information. It is also important to measure the effect of the first seizure occurring after EMDR treatment on anxiety levels. This factor is vital for understanding the specific benefits of EMDR therapy in a population in which chronicity of the condition and (re-)occurrence of seizures are present. Seizure frequency may be low, but the impact of seizures on psychological factors, such as anxiety and overall quality of life, may be substantial. Even isolated seizures occurring over an extended period can significantly affect the well-being of individuals with epilepsy [11]. Moreover, other seizure characteristics, such as focal versus generalized seizures, may be differently associated with anxiety and should be explored in future research.

Furthermore, the results presented a nuanced picture of subjective cognitive improvement associated with EMDR therapy. Patient-reported outcomes indicated a trend toward improvement in subjective cognitive functioning, which was not observed in informant-reported outcomes for subjective cognitive functioning. The subject-reported outcomes for the overall improvement of subjective cognitive functioning might suggest the interconnectedness of cognitive and emotional symptoms in people with epilepsy and their anxiety. Anxiety may cause symptoms of cognitive dysfunction or cognitive dysfunction as experienced by individuals can cause symptoms of anxiety [21]. This association suggests that improvements in one domain may be reflected in another. The relationship between anxiety and subjective cognitive symptoms may also be mediated by other factors, such as personality traits and coping [54,55], as well as antiseizure medications (ASM) and seizure frequency [23,27,56]. This finding may have been relevant to our population with refractory epilepsy of up to half using ASM polytherapy. Future, larger studies are needed to examine how these factors are related to one another.

Our study had some limitations. The most important factor is the small sample size. We received 89 referrals for epilepsy-related anxiety during the study period. Fourty-four cases expressed their willingness to participate but only 22 met the full inclusion criteria, primarily due to comorbid conditions. Ultimately, only eleven participants completed the study due to incomplete questionnaires which turned out too challenging for this target group. A digital format with automated reminders can improve compliance, especially for people with epilepsy who often experience cognitive difficulties. Future research should consider digital administration to enhance accessibility and response rates. The small sample size and high attrition rate limit the generalisability of our findings and may have introduced bias. However, it is important to emphasize that the study did not have dropouts. All participants completed EMDR therapy, defined according to the EMDR protocol by the desensitisation of all identified targets (i.e., flashforward) to a SUD level of 0, with number of sessions ranging from 2 to 12. Given the absence of a control group or sham intervention, we cannot conclusively attribute the observed improvements to the EMDR intervention itself. Alternative explanations include the natural evolution of the condition or the establishment of a therapeutic bond rather than a specific EMDR related effect. The key strengths of this study include the focus on a relatively underexplored topic, epilepsy-related anxiety and the attempt to address a critical gap in the treatment of mental health comorbidities in epilepsy. The inclusion of a three-month follow-up adds valuable insights into the sustained effects of the EMDR intervention beyond the immediate post-treatment period.

A primary concern of some therapists regarding the use of EMDR therapy in epilepsy is the potential risk of triggering seizures, mainly due to the use of saccadic eye movements or light tube stimuli. In this study, various distractors were used during the EMDR therapy sessions. These distractors include visual, tactile, and auditory stimuli, allowing for a flexible approach tailored to maximise working memory loading. Notably, no single seizure was reported during the administration of EMDR therapy in all participants. Stress is recognised as a common trigger for seizures in persons with epilepsy [17]. This presents a unique challenge in treating anxiety in epilepsy, as many effective psychological treatments, including EMDR therapy, inherently involve some degree of stress owing to their exposure components. The successful and safe application of EMDR therapy in our study underscores the importance of a comprehensive and individualised approach that thoroughly assesses seizure triggers, active patient involvement and real-time monitoring during therapy sessions. These safety precautions, along with a solid collaborative therapeutic relationship, ensure that EMDR therapy can be effectively and safely administered to people with epilepsy, thereby providing a valuable tool for managing epilepsy-related anxiety.

In conclusion, EMDR therapy shows promise for improving epilepsy-related anxiety and quality of life in people with epilepsy. Further larger scale and controlled studies are needed to confirm these findings and to optimise therapeutic strategies for emotional and cognitive rehabilitation in people with epilepsy.

CRediT authorship contribution statement

K. Broekman-Labinac: Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **L. Aben:** Writing – review & editing, Supervision, Methodology, Conceptualization. **R.D. Thijs:** Writing – review & editing. **H.M.M. Smeding:** Writing – review & editing, Conceptualization. **A. de Jongh:** Writing – review & editing, Supervision, Conceptualization. **K. van der Hiele:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Funding

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: R. D. Thijs has received personal compensation for serving on the Advisory Boards or Speaker's Bureau for Xenon, Livassured, Theravance, Novartis, Esai, Angelini Pharma and UCB Pharma and research support from New Life Wearables Netherlands. A. de Jongh receives income from published books on EMDR therapy and the training of postdoctoral professionals in this method. The other 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.

Acknowledgements

We thank all people for their willingness to participate in this clinical trial. We also thank all staff at SEIN involved in this study, among which special thanks to the health psychologists performing the EMDR therapy. We also thank R. Rijnders, in her role as psychology student, for data acquisition.

Data availability

Data will be made available on request.

References

[1] Milligan TA. *Epilepsy: a clinical overview*. Am J Med 2021;134(7):840–7.
[2] Thijs RD, et al. *Epilepsy in adults*. Lancet 2019;393(10172):689–701.
[3] Mula M, Sander JW. *Psychosocial aspects of epilepsy: a wider approach*. BJPsych Open 2016;2(4):270–4.
[4] Mula M, et al. *Psychiatric comorbidities in people with epilepsy*. Neurol Clin Pract 2021;11(2):e112–20.

[5] Gurgu RS, et al. *Psychiatric comorbidities in adult patients with epilepsy (A systematic review)*. Exp Ther Med 2021;22(2):909.
[6] Lu E, et al. *Systematic literature review of psychiatric comorbidities in adults with epilepsy*. J Clin Neurol 2021;17(2):176–86.
[7] Kanner AM. *Anxiety disorders in epilepsy: the forgotten psychiatric comorbidity*. Epilepsy Curr 2011;11(3):90–1.
[8] Scott AJ, et al. *Anxiety and depressive disorders in people with epilepsy: A meta-analysis*. Epilepsia 2017;58(6):973–82.
[9] Gandy M, et al. *Rates of DSM-IV mood, anxiety disorders, and suicidality in Australian adult epilepsy outpatients: a comparison of well-controlled versus refractory epilepsy*. Epilepsy Behav 2013;26(1):29–35.
[10] Jansen C, et al. *Interictal psychiatric comorbidities of drug-resistant focal epilepsy: Prevalence and influence of the localization of the epilepsy*. Epilepsy Behav 2019;94:288–96.
[11] Beyenburg S, et al. *Anxiety in patients with epilepsy: systematic review and suggestions for clinical management*. Epilepsy Behav 2005;7(2):161–71.
[12] Hingray C, et al. *The Relationship Between Epilepsy and Anxiety Disorders*. Curr Psychiatry Rep 2019;21(6):40.
[13] Krishnamoorthy ES, Trimble MR, Blumer D. *The classification of neuropsychiatric disorders in epilepsy: a proposal by the ILAE Commission on Psychobiology of Epilepsy*. Epilepsy Behav 2007;10(3):349–53.
[14] Ertan D, et al. *Anticipatory anxiety of epileptic seizures: An overlooked dimension linked to trauma history*. Seizure 2021;85:64–9.
[15] Clark DA, Beck AT. *Cognitive theory and therapy of anxiety and depression: convergence with neurobiological findings*. Trends Cogn Sci 2010;14(9):418–24.
[16] Mula M. *Epilepsy: Bidirectional link between epilepsy and psychiatric disorders*. Nat Rev Neurol 2012;8(5):252–3.
[17] Michaelis R, Schonfeld W, Elsas SM. *Trigger self-control and seizure arrest in the Andrews/Reiter behavioral approach to epilepsy: a retrospective analysis of seizure frequency*. Epilepsy Behav 2012;23(3):266–71.
[18] Kotwas I, et al. *Self-control of epileptic seizures by nonpharmacological strategies*. Epilepsy Behav 2016;55:157–64.
[19] Wang J, et al. *A comparison of quality of life in adolescents with epilepsy or asthma using the Short-Form Health Survey (SF-36)*. Epilepsy Res 2012;101(1–2):157–65.
[20] Johnson EK, et al. *The relative impact of anxiety, depression, and clinical seizure features on health-related quality of life in epilepsy*. Epilepsia 2004;45(5):544–50.
[21] Jarcuskova D, et al. *Which clinical and neuropsychological factors are responsible for cognitive impairment in patients with epilepsy?* Int J Public Health 2020;65(6):947–56.
[22] Tang V, Kwan P, Poon WS. *Neurocognitive and psychological profiles of adult patients with epilepsy in Hong Kong*. Epilepsy Behav 2013;29(2):337–43.
[23] Elixhauser A, et al. *The relationship between memory performance, perceived cognitive function, and mood in patients with epilepsy*. Epilepsy Res 1999;37(1):13–24.
[24] Fargo JD, et al. *Accuracy of self-reported neuropsychological functioning in individuals with epileptic or psychogenic nonepileptic seizures*. Epilepsy Behav 2004;5(2):143–50.
[25] Samarasekera SR, Helmstaedter C, Reuber M. *Cognitive impairment in adults with epilepsy: The relationship between subjective and objective assessments of cognition*. Epilepsy Behav 2015;52(Pt A):9–13.
[26] Salas-Puig J, et al. *Self-reported memory problems in everyday activities in patients with epilepsy treated with antiepileptic drugs*. Epilepsy Behav 2009;14(4):622–7.
[27] Marino SE, et al. *Subjective perception of cognition is related to mood and not performance*. Epilepsy Behav 2009;14(3):459–64.
[28] Feldman L, et al. *Evaluating subjective cognitive impairment in the adult epilepsy clinic: Effects of depression, number of antiepileptic medications, and seizure frequency*. Epilepsy Behav 2018;81:18–24.
[29] Bandelow B, et al. *World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for treatment of anxiety, obsessive-compulsive and posttraumatic stress disorders - Version 3. Part I: Anxiety disorders*. World J Biol Psychiatry 2023;24(2):79–117.
[30] Michaelis R, et al. *Psychological treatments for people with epilepsy*. Cochrane Database Syst Rev 2020;8(8). p. CD012081.
[31] Scelles C, Bulnes LC. *EMDR as Treatment Option for Conditions Other Than PTSD: A Systematic Review*. Front Psychol 2021;12:644369.
[32] Horst F, et al. *Cognitive Behavioral Therapy vs. Eye Movement Desensitization and Reprocessing for Treating Panic Disorder: A Randomized Controlled Trial*. Front Psychol 2017;8:1409.
[33] Shapiro F. *Eye Movement Desensitization and Reprocessing (EMDR) and the anxiety disorders: clinical and research implications of an integrated psychotherapy treatment*. J Anxiety Disord 1999;13(1–2):35–67.
[34] de Jongh A, de Roos C, El-Leithy S. *State of the science: Eye movement desensitization and reprocessing (EMDR) therapy*. J Trauma Stress 2024;37(2):205–16.
[35] Kaptan SK, Kaya ZM, Akan A. *Addressing mental health need after COVID-19: a systematic review of remote EMDR therapy studies as an emerging option*. Front Psychiatry 2023;14:1336569.
[36] Dautovic E, et al. *Pediatric seizure-related posttraumatic stress and anxiety symptoms treated with EMDR: a case series*. Eur J Psychotraumatol 2016;7:30123.
[37] De Jongh A, Ten Broeke E. *Handboek EMDR: een geprotocolleerde behandelmethode voor de gevolgen van psychotrauma*. 7 ed. Amsterdam: Pearson Benelux B.V; 2018.
[38] McCartney L, et al. *Psychometric properties of the Hospital Anxiety and Depression Scale in an inpatient video-monitoring epilepsy cohort*. Epilepsy Behav 2020;103(Pt A):106631.
[39] Spinhoven P, et al. *A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects*. Psychol Med 1997;27(2):363–70.
[40] Zigmond AS, Snaith RP. *The hospital anxiety and depression scale*. Acta Psychiatr Scand 1983;67(6):361–70.
[41] Herrmann C. International experiences with the Hospital Anxiety and Depression Scale–a review of validation data and clinical results. J Psychosom Res 1997;42(1):17–41.
[42] Zingano BL, et al. *Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A) and The State-Trait Anxiety Inventory (STAI) accuracy for anxiety disorders detection in drug-resistant mesial temporal lobe epilepsy patients*. J Affect Disord 2019;246:452–7.
[43] Scott AJ, et al. *Design and validation of two measures to detect anxiety disorders in epilepsy: The Epilepsy Anxiety Survey Instrument and its brief counterpart*. Epilepsia 2019;60(10):2068–77.
[44] Devinsky O, et al. *Development of the quality of life in epilepsy inventory*. Epilepsia 1995;36(11):1089–104.
[45] Cramer JA, et al. *Development and cross-cultural translations of a 31-item quality of life in epilepsy inventory*. Epilepsia 1998;39(1):81–8.
[46] Brooks J, Baker GA, Aldenkamp AP. *The A-B neuropsychological assessment schedule (ABNAS): the further refinement of a patient-based scale of patient-perceived cognitive functioning*. Epilepsy Res 2001;43(3):227–37.
[47] Baker GA, et al. *The development of a seizure severity scale as an outcome measure in epilepsy*. Epilepsy Res 1991;8(3):245–51.
[48] Scott-Lennox J, et al. *Reliability, validity and responsiveness of a revised scoring system for the Liverpool Seizure Severity Scale*. Epilepsy Res 2001;44(1):53–63.
[49] Wallis OC, de Vries J. *EMDR treatment for anxiety in MS patients: A pilot study*. Mult Scler J Exp Transl Clin 2020;6(4):2055217320974388.
[50] Faul F, et al. *G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences*. Behav Res Methods 2007;39(2):175–91.
[51] Szpringer M, Oledzka M, Amann BL. *A Non-randomized Controlled Trial of EMDR on Affective Symptoms in Patients With Glioblastoma Multiforme*. Front Psychol 2018;9:785.
[52] Jacobson NS, Truax P. *Clinical significance: a statistical approach to defining meaningful change in psychotherapy research*. J Consult Clin Psychol 1991;59(1):12–9.
[53] Wang Z, et al. *Anxiety screening tools in people with epilepsy: A systematic review of validated tools*. Epilepsy Behav 2019;99:106392.
[54] Dong J, et al. *Anxious Personality Traits: Perspectives from Basic Emotions and Neurotransmitters*. Brain Sci 2022;12(9).
[55] Nijsse B, et al. *Psychological factors are associated with subjective cognitive complaints 2 months post-stroke*. Neuropsychol Rehabil 2017;27(1):99–115.
[56] Meador KJ. *Cognitive outcomes and predictive factors in epilepsy*. Neurology 2002;58(8 Suppl 5):S21–6.