

## Feasibility and impact of virtual reality exposure therapy on epilepsy-specific anxiety: Phase 3 of the AnxEpiVR pilot clinical trial

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### ABSTRACT

People with epilepsy (PwE) commonly experience interictal anxiety related to their epilepsy and seizures. However, therapeutic interventions have received minimal investigation. This study was the third phase of the “AnxEpiVR” pilot that examined the feasibility and effectiveness of a novel virtual reality exposure therapy (VR-ET) program to treat epilepsy-specific (ES) interictal anxiety in PwE. Participants (N = 5) completed the Epilepsy Anxiety Survey Instrument (EASI), Perceived Stress Scale, Igroup Presence Questionnaire, System Usability Scale, and an adapted version of the diagnostic protocol that Hingray et al. (2019) proposed. They also participated in a semi-structured interview. Participants were assigned to a personally relevant VR-ET scenario (dinner party, shopping mall, or a subway station/train). Over 12 to 14 days within a 14-day period, participants engaged in the VR-ET intervention, progressing through an individualized hierarchy of exposures. Preliminary findings suggest promising feasibility of VR-ET and high tolerability, achieving a 100% completion rate. The EASI scores showed that two of the four participants who scored above the cut-off for a probable anxiety disorder before VR-ET (brief EASI  $\geq 7$ ) scored below the cut-off after VR-ET (brief EASI  $< 7$ ). Subjective reports of the VR-ET’s impact supported the intervention’s potential for reducing ES-interictal anxiety. This trial represents the inaugural use of VR-ET as a potential remote intervention for ES-interictal anxiety. Moreover, these findings support the feasibility of conducting larger clinical trials to further evaluate and to validate VR-ET as a therapeutic tool for managing interictal anxiety in PwE.

### 1. Introduction

Anxiety is one of the most common psychiatric comorbidities in people with epilepsy (PwE) but is often undertreated [1–4]. Anxiety may also be closely related to the seizure itself; for example, PwE may have peri-ictal anxiety or anxiety about others’ perceptions of a seizure [2,3,5]. Epilepsy-specific (ES-) interictal anxiety may involve the fear of having a seizure and is commonly related to the uncertain nature of epilepsy [2,3,5–7]. This form of anxiety has long been reported; for example, 80% of PwE in the 1992 National General Practice Study of

Epilepsy reported a “fear of having seizures” [[7], p.1416]. The fear and uncertainty related to epilepsy have previously been described as “the worst thing about having epilepsy”, significantly and negatively impacting quality of life [[6] p.39, [8,9]].

Evidence suggests that therapeutic interventions commonly used in anxiety treatment for people without epilepsy, such as cognitive behavioral therapy (CBT), could be effective in the epilepsy population [10–12]. However, there is minimal existing literature on the use of CBT, or other anxiety interventions, for ES-interictal anxiety.

This paper explores the use of a CBT technique called exposure

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therapy (ET) to treat ES-interictal anxiety [13]. Traditionally, ET is delivered through a graded approach [14]. Individuals may habituate to a situation that would typically cause a small amount of fear before being exposed to progressively more anxiety-provoking situations [13,14]. Previous research, mostly from pediatrics and case reports, has shown that ET on its own or intervention programs that include ET may help to decrease ES-interictal anxiety in PwE [10,12,15–17].

Exposure therapy is traditionally conducted in the real-world environment (in vivo), but this presents challenges with respect to feasibility, repeatability of the environmental conditions, and accessibility [18,19]. Imaginal ET may overcome some of these challenges but can be limited by the individual's ability or willingness to vividly visualize the scenario [18].

An alternative to both in vivo and imaginal ET is to deliver exposures through virtual reality (VR) (VR-ET) [18,19]. Using a head-mounted display (HMD) that stimulates both visual and auditory senses, VR places the user in an immersive and realistic computer-simulated environment such that they feel as though they are present in that environment [18–20]. VR offers a potentially cost-effective method to accessibly deliver customizable ET, as the initial hardware investment can be amortized over repeated use across patients and sessions, and clinicians could minimize their time spent off-site while still being present with their patient during exposures [18,19,21]. Moreover, VR-ET has been successfully used for treating post-traumatic stress disorder and numerous anxiety disorders in non-epilepsy populations, such as social anxiety disorder, panic disorder, and specific phobias [18,21–24].

To our knowledge, VR-ET for PwE has yet to be investigated, perhaps due to the relative novelty of VR technology and safety concerns that VR might provoke photosensitive seizures. However, researchers and clinicians are increasingly allowing and exploring the use of VR in PwE, and initial safety concerns remain unsubstantiated [25–30]. With the need for effective treatments for ES-interictal anxiety, we propose the use of VR-ET in a three-phase study, referred to in previous papers as the “AnxEpiVR” study [31–33].

The overall aim of the AnxEpiVR study was to design and implement a clinical trial piloting VR-ET for PwE who suffer from ES-interictal anxiety. The protocol for each phase is detailed in Gray et al. (2023) [31], and the results for Phases 1 and 2 are described in Tchao et al. (2023) [32] and Lewis-Fung et al. (2023) [33], respectively. In brief, Phase 1 of the AnxEpiVR trial involved gathering information on ES-interictal fears through an online questionnaire delivered to PwE or people affected by epilepsy (such as through a family member or a healthcare professional). The details about common ES fears identified in Phase 1 informed the settings and features of the 360-experiences that would be created in Phase 2. Three exposure scenarios were ultimately produced in Phase 2: a dinner party, a large Toronto shopping mall, and a Toronto subway station/train. Each scenario was associated with its own series of videos that varied in its difficulty level (i.e., causing more or less anxiety), based on the results from Phase 1. These videos were delivered in an HMD for PwE in the Phase 3 investigation, described herein.

### 1.1. Objectives and significance

This study describes the first use of VR-ET in PwE, contributing to the limited existing literature for under-treated ES-interictal anxiety. The objective for Phase 3 of AnxEpiVR was to evaluate the intervention's feasibility in terms of its usability, acceptability, willingness to adopt, and potential effectiveness for decreasing ES-interictal anxiety. The results of this study will be used to inform future larger-scale trials. We hypothesized that VR-ET would be feasible for PwE with ES-interictal anxiety, and that participants would habituate to their ES-interictal fears and ultimately experience decreased ES-interictal anxiety when exposed to the same scenes.

## 2. Methods

This study was designed as a mixed-methods interventional pilot that took place between February 2023 and August 2023. The study protocol was approved by the York University Human Participants Review Committee on March 21, 2022, with the final amendment approved on May 4, 2023 (certificate number: 2022–105). This study is listed on ClinicalTrials.gov (ID: NCT05296057). Participant rights were maintained in accordance with confidentiality and privacy procedures approved by the York University Human Participants Review Committee.

### 2.1. Participants

This pilot study had a target sample size of five PwE with no control group. Recruitment was achieved by emailing Phase 1 participants who indicated they would like to be contacted about Phase 3, and through advertisements with Epilepsy Toronto via their email listserv and social media accounts (Instagram, Meta (Facebook), Twitter (X)). All participants signed online informed consent forms.

Inclusion criteria were: self-reporting having diagnosed epilepsy; being 18 to 65 years old; living in Toronto; and identifying as having anxiety related to epilepsy/seizures. Exclusion criteria were: not speaking and understanding English; having a current diagnosis of photosensitive epilepsy or photoparoxysmal responses; suspecting, regardless of what a neurologist may have told them, that flashing or flickering lights were a current seizure trigger for them; having open wounds on their face; having cervical conditions or injuries that would make it unsafe for them to use the VR headset; having started an antidepressant, antianxiety drug, or medical marijuana in the last twelve weeks; having tonic-clonic seizures more than once a month; meeting criteria for a diagnosis of panic disorder within the past six months; or having psychogenic non-epileptic seizures. We removed stress-related seizures as an exclusion criterion initially published in the protocol [31]. Instead, we asked targeted questions about each individual's seizure triggers using the Background Questionnaire to help assess safety for study participation.

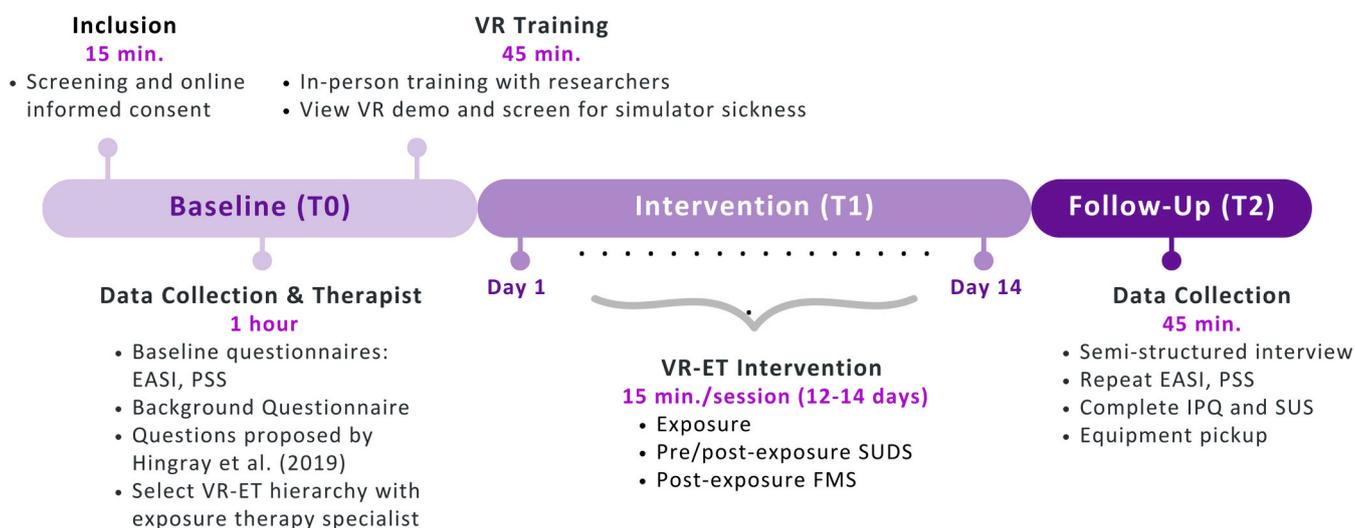
### 2.2. Protocol and interventions

Phase 3 involved three timepoints (Fig. 1). In brief, before beginning the program (T0), participants completed baseline questionnaires, received training on how to use VR, and participated in an interview to be assigned to one of the three ET scenarios (a dinner party, a large Toronto shopping mall, or a Toronto subway station/train) [33]. Then, participants performed the VR-ET intervention for 12 to 14 consecutive days (T1). Finally, participants completed post-intervention questionnaires and participated in an interview to provide feedback and additional reflections on the subjective impact of VR-ET (T2).

#### 2.2.1. Baseline (T0)

Participants completed the Epilepsy Anxiety Survey Instrument (EASI) and Perceived Stress Scale (PSS) over the Qualtrics online platform [34,35]. The baseline interview was conducted over a two-to-one video call using a secure Zoom account with two members of the research team (HGG – herein referred to as the Research Coordinator (RC), and GCG – a registered social worker who is an exposure therapy specialist (ETS)). During the interview, the Background Questionnaire was administered along with questions suggested by Hingray et al. (some of which were omitted when they were deemed to be redundant for our purposes) [2].

Next, the ETS read a brief overview of the available exposure scenarios (dinner party, shopping mall, or subway) and worked with the participant to select the scenario that most resonated with their anxiety. Then the ETS read a description for each associated video and created a hierarchy (i.e., the order in which the videos would be watched during



**Fig. 1.** Study Timeline. Abbreviations: EASI = Epilepsy Anxiety Survey Instrument; PSS = Perceived Stress Scale; VR = virtual reality; VR-ET = virtual reality exposure therapy; SUDS = Subjective Units of Distress Scale; FMS = Fast Motion Scale; IPQ = Igroup Presence Questionnaire; SUS = System Usability Scale.

the VR-ET program) with the participant and asked them to rate their anticipated anxiety using the Subjective Units of Distress Scale (SUDS) (using the figure by Wagner, 2013) [36]. The participant's hierarchy was developed based on these SUDS scores. Finally, the ETS briefly reviewed a set of anxiety coping mechanisms that participants were sent prior to the interview [31].

At participants' residences, two researchers (DT and SLF) provided in-person training for VR. Participants practiced using the equipment and were screened for cybersickness using the VR Induced Symptoms and Effects (VRISE) section of the Virtual Reality Neuroscience Questionnaire after watching a neutral video in VR (a 2-minute video of a nature scene) [31,37].

### 2.2.2. VR-ET intervention (T1)

For 12 to 14 days within a 14-day period, participants completed a 5-minute VR-ET exposure in the HMD with the RC present on Zoom. All VR experiences were delivered on a Meta Quest 2 HMD (refresh rate 72 Hz; capable of up to 90 Hz). The intervention used passive 360° videos with no flashing lights, strobing, rapid luminance changes, or rapid scene cuts; visual transitions were smooth and continuous, and the luminance profile was largely stable throughout the videos. Literature, although limited, does not present a particular heightened risk for seizures if specific visual triggers are avoided [27,30]. Content should avoid light flashes that are at least 20 candelas/m<sup>2</sup>, alternate color flashes (especially red-blue), or stripes (static or oscillating) or a zig-zag pattern of approximately one to eight cycles per visual degree [27,30]. All these stimuli should be avoided in the 3–60 Hz range, especially if they are 10–20 Hz (10–20 Hz according to [30], 15–20 Hz according to [27]), and if they make up more than approximately 25% of the visual field of both eyes for longer than approximately 0.5 seconds [27,30]. For additional visual stimuli that should be avoided, see Fisher et al. (2022) [27] and Fisher et al. (2025) [30]. For additional information regarding the structure and content of the VR-ET hierarchies, see Lewis-Fung et al. (2023) [33].

At the beginning of each session, the RC typically provided a brief description of the day's video and participants provided a pre-SUDS score (SUDS-1) to indicate their anticipatory anxiety level [33]. Next, participants selected the video from a customized private playlist on YouTube, watched it in the HMD, and immediately after removing the HMD, provided a second SUDS score (SUDS-2). The RC and participant then stayed on the Zoom call for 10 minutes while the RC turned her video and microphone off (with the exception of Participant 1 for the first four days; further details are provided in Table S1). Participants

were told that they could do anything during the 10-minute period as long as they stayed in front of the camera or were around a trusted person as a safety precaution. They were instructed that if they needed anything to call the RC's name. After 10 minutes, participants provided a final SUDS score (SUDS-3) and described any motion sickness they may have experienced using the Fast Motion Scale (FMS) [38].

A participant's daily SUDS scores were used to guide progression through their exposure hierarchy. When a participant's SUDS-2 was low (defined by the authors as  $\leq 3$ ) for any particular scene, they typically progressed to the next level in the hierarchy the following day. Levels were repeated as necessary to facilitate habituation to the exposure. When a participant reported a SUDS-3 score  $\geq 5$  (a score that is suggestive of mild to moderate distress), the RC stayed on the video call with the participant for another 15 to 20 minutes until their anxiety subsided as a safety precaution [39]. When participants reported any simulator sickness, the RC stayed on the call with the participant until it subsided.

### 2.2.3. Post-intervention (T2)

A two-to-one post-intervention interview was conducted in the participant's residence or over Zoom (with SLF and DT) [31]. Participants also completed the EASI (and simultaneously, the brief EASI (brEASI)), PSS, Igroup Presence Questionnaire (IPQ), and System Usability Scale (SUS) [40,41].

## 2.3. Analyses

Due to the small sample size, inferential statistical analyses could not be conducted. Descriptive statistics (mean, median, frequencies) were used as applicable.

### 2.3.1. Feasibility

We assessed the feasibility of VR-ET based on the applicable criteria described by Misawa et al. [42], which were developed based on prior research and CONSORT guidelines: (1) usability, (2) acceptability, (3) willingness to adopt the intervention, and (4) effectiveness. We evaluated usability of the intervention based on SUS scores and participant feedback from the T2 interviews. A median SUS score  $\geq 68$  was defined as the acceptable benchmark for system usability [43]. We also assessed acceptability based on feedback from the T2 interviews and on the completion rates (i.e., how many participants attended the VR-ET sessions on Zoom for at least 12 days within a 14-day period). Consistent with Misawa et al. [42], this feasibility criterion would be satisfied by a

completion rate of  $\geq 80\%$ . We evaluated willingness to adopt the intervention based on feedback from the T2 interviews. Finally, we assessed effectiveness based on pre/post-intervention changes in epilepsy-related anxiety using the brEASI scores, PSS scores, and changes in anxiety that participants reported in the T2 interview. We also assessed the effectiveness of VR by using IPQ scores for the sense of presence in VR and T2 interview feedback for the realism of the VR-ET scenarios [44].

### 2.3.2. Qualitative analysis

The ETS and RC recorded notes during the baseline interviews (T0) and then compared them for any discrepancies or missing details. Two researchers (the RC and DT) separately summarized participants' responses to the questions that Hingray et al. [2] proposed, and the research team then met to determine the similarities and frequencies of responses across participants through discussion.

Exit interviews (T2) were audio-recorded, digitally transcribed and compared with hand-written notes taken during the interviews (SLF). We conducted a thematic analysis on the T2 interviews using a deductive coding framework related to the aspects of feasibility outlined in Section 2.3.1. Two authors (the RC and SLF) independently coded each participant's responses and categorized their responses or attitudes based on several metrics. The coders met to discuss their findings and resolved any disagreements through discussion.

## 3. Results

Five PwE enrolled in the study (Fig. 2); the sample demographics and clinical factors are presented in Table 1.

### 3.1. Application of the Hingray et al. (2019) diagnostic protocol

The responses to the questions about interictal anxiety symptoms from Hingray et al. (2019)'s proposed diagnostic interview [2] are summarized as follows:

All participants reported being "afraid of having an epileptic seizure" and three participants reported feeling "persistently preoccupied or concerned about [their] seizures and their possible consequences", although one of these participants said that this fear was only persistent when they were in a public place. The mean overall rating for "fear of having a seizure on a scale of 0–10" with 10 being the highest was 5.8.

**Table 1**  
Sample demographic and clinical information.

Age (median, range)	47 years (18–62 years)
Sex, N	
Male	4
Female	1
Duration of epilepsy (i.e., time since date of epilepsy diagnosis) (median, range)	34 years (1.5–39 years)
Frequency of auras, N	
All of the time	1
Almost all of the time	1
Sometimes	2
Never	1 (nocturnal seizures only)
Known types of seizures, N	
History of tonic-clonic seizures	3 (one of these participants only had nocturnal seizures)
Focal seizures with impaired consciousness <sup>a</sup>	3
Seizure(s) within the past year, N	3
Currently taking $\geq 2$ anti-seizure medications <sup>a</sup> , N	5*
Currently taking antidepressants, N	3
Previous experience with virtual reality, N	2
Undergoing therapy at T0, N	2

T0 = Baseline. \*One participant reported that they were on one anti-seizure medication for seizure control and on Clonazepam for anxiety (prescribed decades prior to the study). <sup>a</sup>According to the current classification of seizures [45].

Note that this mean was calculated using six scores. Specifically, P1 volunteered two examples of scenarios and gave them different ratings: a rating of 1–2 (taken as 1.5) when at their house or local grocery store and a rating of 5–6 (5.5) when downtown or in a busy or loud environment. Other participants' scores were: 8, 3, 8, and 9. Levels of reported strictness in avoiding any potential rise in seizure risk such as avoiding alcohol and monitoring sleep duration varied among participants. All participants reported that it was "frightening to imagine having a seizure in front of others" (for more details, see the Supplementary Text).

Regarding avoidance behaviors, participants reported no or minimal avoidance of places where they previously had a seizure, in some cases because it was not applicable such as when most of their seizures happened at home. Only one participant reported avoiding public transit, but another reported that out of necessity, they could not avoid it. No participants avoided the household or personal activities that Hingray et al. [2] posed. Most participants (four) reported being less anxious in some environments if they were with someone. Also, three participants reported that they "tend[ed] to avoid situations" where others might witness their potential seizure.

Finally, four participants reported experiencing symptoms associated with overwhelming anxiety/panic attacks as defined by Hingray et al. [2]; one of these participants experienced these symptoms as a part of an aura only.

### 3.2. Feasibility

Table 2 summarizes qualitative feedback from the T2 exit interviews related to usability, acceptability, willingness to adopt, and efficacy. Table S1 provides a complete summary of feedback provided in the interviews.

**Usability.** The median SUS was 92.5 (range: 65 to 100), which surpassed the acceptable benchmark for system usability (SUS score of 68) (Table 2) [43]. Simulator sickness did not impact participation: no participants were withdrawn due to their VRISE score and FMS scores were consistently 0 except for one participant, who scored an average of FMS = 1.79 (range = 0 to 6, out of a possible total of 20) over the course of the VR-ET program.

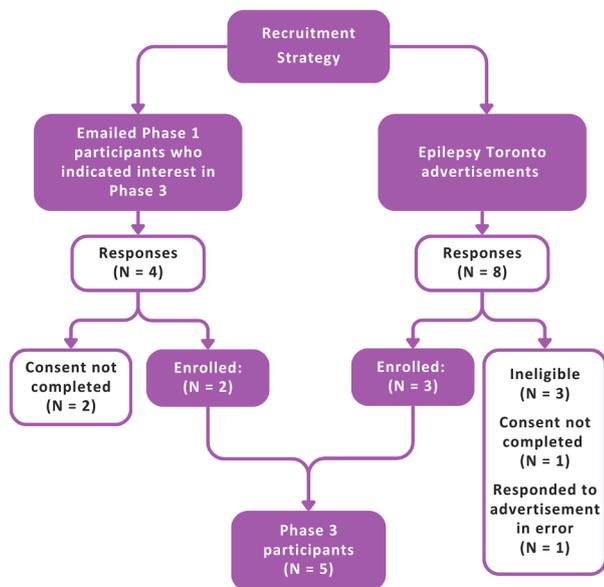


Fig. 2. Recruitment flow diagram.

**Table 2**  
Responses to the post-intervention (T2) interview.

	P1	P2	P3	P4	P5
<b>Usability</b>					
System Usability Scale score	100	65	85	95	92.5
Ease of using the VR (1–10, 10 = easiest)	10	8	8	9	10
VR HMD and training experience	+	–	+	+	+
<b>Acceptability: Intervention Format</b>					
Format (i.e., at home on Zoom)	+	+	+	+	+
Video length (5 min)	+	<	+	+	+
Session frequency (daily)	+	<	+ or >	+	+
Program length (12–14 days)	+ or >	N/A <sub>0</sub>	+ or >	+	>
Presence of the RC	+	+	/	+	+
<b>Willingness to Adopt</b>					
Recommend to a friend	+	–	+	+	+
Overall sentiment towards VR-ET <sup>a</sup>	+	–	+	+	+ or /
<b>Effectiveness</b>					
Change in fear of scenario they were exposed to	<	=	<	N/A	N/A
Change in ES-interictal anxiety	<	=	<	<	=
Realistic simulation of real-world anxiety (1–10, 10 = most realistic)	10	2	7–8*	8	6–7

+ Positive.

– Negative.

/ Neutral.

> Increased/more/longer.

< Decreased/less/shorter.

= No change.

N/A: Not applicable – participants reported being unable to tell as they had not yet been in the real-life situation by the time of the T2 interview.

N/A<sub>0</sub>: Missing response.

<sup>a</sup>Based on a summary of Table S1.

\*Participant specified a score of 7–8 when watching the scene for the first time but that the realism decreased with repetition of the video.

**Acceptability.** Participants attended 98.6% of the scheduled sessions with the RC, with only 1/70 sessions missed. All five participants completed 12 to 14 days of the VR-ET, participated in the T2 interview, and completed the self-report measures (except for one question missing on the EASI for P1). Therefore, there was a 100% completion rate and there were no participant drop-outs.

Participants progressed through varying numbers of exposure scenes in one or two scenarios, with consultation from the ETS as appropriate. For example, on Day 8 of the dinner party scenario, P4, who reported having diagnosed social anxiety, watched a scene that caused heightened anxiety and they reported having an aura at the end of the video. P4 immediately removed the HMD and used anxiety coping mechanisms, as they were instructed to do at the beginning of the call if they felt too overwhelmed (SUDS-1 was high, at a score of 8). P4 reported that the aura “went away” after they did deep breathing and a grounding exercise. The following day, the RC discussed with P4 the option of switching from the party to the mall scenario. The mall scenario was still compatible with the fears that P4 reported during the T0 interview but included fewer social components than the party scenario. With P4’s permission, the ETS joined the beginning of the call on Day 9 to further discuss switching exposure scenes, and together the ETS and the participant developed a new hierarchy for the mall scenario.

Four participants described the presence of the RC during the exposure sessions as helpful either because they felt more comfortable or safer having another person present during the intervention, or for accountability. The remaining feedback about the format of the intervention is summarized in Table 2.

**Willingness to Adopt.** Four of five participants indicated that they would recommend the VR-ET program to a friend with ES-anxiety. Participants who recommended the intervention stated that they found it personally helpful or that it could help others. P3 mentioned having told their local epilepsy agency about the intervention. P4 also mentioned “[i]t’s so much fun but it’s also anxiety provoking” (Table S1). P5 said they would “specifically [recommend the program to a friend] if they had strong social anxiety mixed with epilepsy”. The participant who did not recommend the study (P2) did not find it

helpful.

**Efficacy.** All participants reported having less anxiety at T2 than T0 on the EASI and brEASI (Table 3). The median change in EASI scores was –9 (range: –26 to –5) and the median change in brEASI scores was –3 (range: –10 to –1). At T0, four participants scored  $\geq 7$  on the brEASI, the cut-off for a probable anxiety disorder [34]. At T2, only two participants still scored  $\geq 7$ . The median change in PSS scores was 0 (range: –5 to 6; Table 3).

All participants except P2 reported various benefits of the VR-ET during the T2 interview, including decreased feelings of anxiety, feeling more prepared to face their feared scenarios in real life, and developing a greater understanding of their ES fears. For example, P3 reported that “just talking about it [i.e., their anxiety] a little bit everyday with [the RC] and going through the experience everyday gave me the chance to reflect on what I thought was the root cause of the anxiety and better define what it was”. They identified that their fear was “not so much just public spaces”, but of being seen in a vulnerable state by acquaintances. They also reported appreciating “the reminder that people are generally kind and helpful...we need that nudge that it’s not so bad, people will be helpful and won’t judge you.” However, three participants (P3-5) reported that they were not able to tell or were uncertain about exactly how much their ES-anxiety had changed since ending the VR-ET program because they had not yet been in their real-life feared scenario (for example, a mall). Additional comments on perceived benefits of the intervention and comparison to previous therapies that they tried can be found in Table S1.

Most participants reported high levels of presence on the IPQ (Table 4) [44]. However, scores for spatial presence, involvement, and experienced realism were varying, with P2 reporting most of the lowest scores. Comments on subjective feelings of realism, including reports from participants that the seizure stimulation videos were realistic, are included in Table S1.

Participants commented during the program and during the T2 interview that rewatching the same exact video when they repeated a level was less anxiety-provoking due to the nature of knowing what to expect. P3 specified that this happened after watching a scene twice and

**Table 3**  
Scores on the assessments for anxiety at baseline and post-intervention.

ID	Scenario(s)	# Levels	EASI			brEASI			PSS
			T0	T2	Delta	T0	T2	Delta	Delta
1	Subway	6; 1	6 <sup>+</sup>	0	-6	4	0	-4	-3
2	Party; Subway	7; 4	25	8	-17	9*	3	-6	0
3	Mall	5	27	18	-9	11*	8*	-3	-5
4	Party; Mall	3; 3	37	11	-26	13*	3	-10	1
5	Party	6	28	23	-5	11*	10*	-1	6

Differences (Delta) in anxiety levels post VR-ET intervention (T2) compared to baseline (T0) on the complete and brief versions of the Epilepsy Anxiety Survey Instrument (EASI and brEASI), and the Perceived Stress Scale (PSS). \*Represents a score on the brEASI  $\geq 7$ , which is the cut-off for a probable anxiety disorder [34]. <sup>+</sup>The participant did not answer one of the questions. The brEASI does not include this question [34].

**Table 4**  
Igroup Presence Questionnaire scores.

ID	Presence	Spatial Presence	Involvement	Experienced Realism
1	5	5.4	4.75	4
2	0	2.4	2.5	1.75
3	4	4.8	3.5	2.75
4	5	4.8	2	3.75
5	5	4	4	3
<b>Mean (SD)</b>	<b>3.8 (2.17)</b>	<b>4.28 (1.16)</b>	<b>3.35 (1.11)</b>	<b>3.05 (0.89)</b>

P4 specified that it was “always easier the second time”. P5 reported that the video was “having less and less impact because there’s some familiarity to it”. With regard to designing future exposures, participants described that the level of familiarity with the actors in the video, the ability to interact with the actors, and an individual’s unique fears and seizure symptoms are potential considerations. Additional comments on subjective feelings of realism and suggestions for designing additional scenarios are included in Table S1.

#### 4. Discussion

Overall, there were three main findings from Phase 3. First, this investigation supported the findings of earlier phases of the AnxEpiVR study in that at least one of the scenarios, created in Phase 2 based on the fears identified in Phase 1, resonated with each participant. Second, we showed that this VR-ET intervention has promising feasibility on numerous fronts and that VR was well-tolerated. Third, we showed that VR-ET has the potential to reduce ES-interictal anxiety.

As expected, changes in ES-interictal anxiety based on brEASI and EASI scores generally corresponded with T2 reports. An exception was P2, who did not find the intervention helpful despite showing a decrease in brEASI and EASI scores of 6 and 17 points respectively (Table 3). One possible explanation for this inconsistency is that the changes to P2’s anxiety were not substantial enough to impact how they perceived their overall anxiety. Alternatively, P2 may have found the intervention unhelpful potentially because they experienced a low sense of presence and feelings of realism (Table 4). Previous research has reported mixed findings on the role of presence in the efficacy of VR-ET [46–49]; here, we offer an example where a lack of presence may have hindered VR-ET’s success. Greater feelings of presence lead to increased feelings of anxiety, which is important for the success of ET and theoretically increases its likeness to in vivo ET, the gold standard [46,50]. Additionally, response bias may have been present.

Our findings include several practical recommendations that may inform the design of VR-ET for PwE as well as future trials. To proceed through the hierarchy at a safe rate and still gain adequate exposure to higher intensity fears, individuals may need more than 12 to 14 exposure sessions. Additionally, we were unable to meaningfully measure the impact of the intervention on participants’ behaviors post-intervention (such as their avoidance behaviors) because of the study’s short

timeframe. Future studies should include a longer follow-up period to provide participants with adequate opportunities to visit their feared scenarios in real life. Future work should also investigate the impact of VR-ET for PwE with anxiety disorders but without ES-specific fears.

We offer one of the first instances in research to demonstrate that VR-ET can be used by PwE. In our study, five PwE used VR a total of 74 times (training + intervention) and it was well-tolerated. There was one instance where a participant experienced an aura that resolved after removing the HMD and using anxiety coping mechanisms. Nevertheless, our study supports growing evidence that VR can be safely used by PwE. Research should continue to investigate VR in the epilepsy population so that PwE are not unnecessarily excluded from the benefits of this technology. We recommend incorporating individualized safety protocols, as we did in our study.

#### 4.1. Limitations

The results of this study must be taken with caution given the small sample size and that there was no control group. Potential limitations may also lie within the videos to which the participants were exposed. For example, some members of the research team (not the RC or ETS) were actors in the VR videos, which may have led to response bias in the T2 interview with those same people. Moreover, the participants’ familiarity with the videos and knowing what to expect when repeating the video for a given level may have contributed to their decreased anxiety, rather than a genuine habituation to the real-life anxiety-evoking situation portrayed; however, previous research has suggested that habituation may not be required for the success of ET [13]. The results of the PSS for all participants should also be interpreted with caution. The scale asks about perceived stress levels over the previous two weeks. When participants repeated the PSS at T2, one of the weeks under consideration was actually the second week of the intervention.

#### 5. Conclusion

This is one of the first studies to trial the use of VR in PwE. Further, we demonstrated the promising feasibility and efficacy of a low-cost and remote intervention for ES-interictal anxiety. The chronic undertreatment of anxiety in PwE, often due to a lack of resources, makes the development of an accessible intervention essential. These findings pave the way for PwE to experience the benefits of this technology. Our report of a high tolerability of VR for PwE suggests that next steps should include further evaluation of VR-ET with a larger sample in a randomized trial. As such, the intervention has been implemented in a randomized controlled trial (ClinicalTrials.gov ID: NCT06028945; “AnxEMU”) in an Epilepsy Monitoring Unit in Toronto, Canada.

#### 6. Disclosure of conflicts of interest

None of the authors have any conflict of interest to disclose. The VR intervention used an off-the-shelf Meta Quest 2 headset, selected due to its affordability, accessibility, and prior use in clinical research. All 360°

video content was developed by the research team solely for this study, and displayed using the embedded YouTube App. The authors have no financial or commercial relationships with Meta or YouTube.

### Ethical statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines. The study was conducted in accordance with the ethical standards of the institution. Written informed consent was obtained from all participants. All efforts were made to protect patient confidentiality and anonymity.

### CRediT authorship contribution statement

**Hannah Gabrielle Gray:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Danielle Tchao:** Writing – review & editing, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Samantha Lewis-Fung:** Writing – review & editing, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Glenda Carman-Gray:** Writing – review & editing, Methodology, Investigation. **Susanna Pardini:** Writing – review & editing, Methodology. **Laurence R. Harris:** Writing – review & editing, Methodology. **Lora Appel:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition, Data curation, Conceptualization.

### Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Lora Appel reports financial support was provided by Beneva. 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.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ebr.2025.100845>.

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## Glossary

- Epilepsy-specific interictal anxiety (ES-interictal anxiety)*: Anxiety that occurs in the interictal period related to the fear of the seizures themselves [2].
- Cognitive behavior therapy (CBT)*: A treatment modality that aims to understand thought patterns and the relationships between thoughts, feelings, and behaviors.
- Exposure therapy (ET)*: A treatment modality under the umbrella of CBT that involves exposing an individual to their anxiety-provoking situations, often in a hierarchical manner, so that they can confront their fears [13,14].
- Virtual reality (VR)*: A simulated experience of the real world provided through multi-sensory stimuli (typically audio-visual) such that the person feels that they are actually present in the virtual environment.
- Head-mounted display (HMD)*: A device worn over the eyes that presents virtual reality environments.
- 360° video*: A video captured in every direction at the same time.
- Simulator sickness*: A type of motion sickness that can be experienced when interacting with simulated environments such as virtual reality and video games.