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FULL-LENGTH ORIGINAL RESEARCH

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Treatment of psychogenic nonepileptic seizures (PNES) using video telehealth

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Abstract

Objective: Previous studies have shown the effectiveness of manual-based treatment for psychogenic nonepileptic seizures (PNES), but access to mental health care still remains a problem, especially for patients living in areas without medical professionals who treat conversion disorder. Thus, we evaluated patients treated with cognitive behavioral therapy–informed psychotherapy for seizures with clinical video telehealth (CVT). We evaluated neuropsychiatric and seizure treatment outcomes in veterans diagnosed with PNES seen remotely via telehealth. We hypothesized that seizures and comorbidities will improve with treatment.

Methods: This was a single-arm, prospective, observational, cohort, consecutive outpatient study. Patients with video-electroencephalography–confirmed PNES (n = 32) documented their seizure counts daily and comorbid symptoms prospectively over the course of treatment. Treatment was provided using a 12-session manual-based psychotherapy treatment given once per week, via CVT with a clinician at the Providence Veterans Affairs Medical Center.

Results: The primary outcome, seizure reduction, was 46% ($P = .0001$) per month over the course of treatment. Patients also showed significant improvements in global functioning (Global Assessment of Functioning, $P = < .0001$), quality of life (Quality of Life in Epilepsy Inventory–31, $P = .0088$), and health status scales (Short Form 36 Health Survey, $P < .05$), and reductions in both depression (Beck Depression Inventory–II, $P = .0028$) and anxiety (Beck Anxiety Inventory, $P = .0013$) scores.

Significance: Patients with PNES treated remotely with manual-based seizure therapy decreased seizure frequency and comorbid symptoms and improved functioning using telehealth. These results suggest that psychotherapy via telehealth for PNES is a viable option for patients across the nation, eliminating one of the many barriers of access to mental health care.

KEYWORDS

clinical video telehealth, psychogenic nonepileptic seizures, treatment, veterans

1 | INTRODUCTION

One-quarter to one-third of people admitted to seizure monitoring units are diagnosed with psychogenic nonepileptic seizures (PNES).[1] PNES have long been documented among civilians[2] and in veterans[3]; however, until recently treatment options have been limited.[4] Although evidence-based treatment for PNES exists,[5] many patients have trouble accessing it. There are a number of barriers to treatment in patients with seizures, including access to care, consequences of symptoms (eg, transportation restrictions), and insurance coverage. Likewise, access to mental health care from clinicians interested in addressing conversion (functional) disorder still remains a problem,[6] not only in urban areas, but also and especially for patients living in rural areas without available medical professionals.[7] Specialty care for neuropsychiatric aspects of epilepsy and seizures may be a great distance from the patient. In addition, PNES can directly hinder access to treatment due to limitations in driving ability.[8] Thus, clinical video telehealth (CVT) is being used increasingly as a comparable and cost-effective alternative to in-clinic treatment.[9]

The challenge in accessing mental health care for people with PNES reflects the broader public health challenge with the shortage of mental health professionals in the USA, particularly in rural areas[10] without specialty care. Therefore, an emerging literature has demonstrated the effectiveness in delivering mental health services through CVT to help address barriers to access.[11] A recent systematic review of the literature has shown no major differences between telepsychiatry and in-clinic treatment in many past studies, in terms of patient and clinician satisfaction, reliability, treatment outcome, and implementation in a variety of disorders, including depression, posttraumatic stress disorder (PTSD), and attention-deficit/hyperactivity disorder.[9]

Other studies have also shown similar treatment outcomes between telehealth and in-person treatment for mental disorders, for example, PTSD in veterans.[1218] Many reviews have assessed telehealth treatment for depression in veterans[1923] and epilepsy in civilians[24] as well. However, no current studies on the effectiveness of telehealth for PNES treatment exist.

Previously, we have demonstrated reduction in seizures and improvement in comorbidities in patients seen in person in pilot psychotherapy treatment[25] and multisite randomized clinical trials[26] using a manualized therapy for seizures,[27] which is based on a neurobehavioral therapy (NBT) for epilepsy.[28] Although CVT has been shown to be effective across behavioral health issues, PNES are particularly challenging, given the need to coordinate care between neurology and mental health, the diagnostic challenges, the barrier of travel with seizures limiting driving, and the visible and often frightening nature of the seizures. Therefore, the authors aimed to explore the effectiveness of an evidence-based therapy for PNES[25,26] using CVT.

Key Points

- Thirty-two patients treated for PNES via CVT had significant seizure reduction and improvement in depression, anxiety, QoL, and global functioning
- Manual-based psychotherapy for seizures via CVT is a viable option for remote treatment for patients with PNES
- We evaluated treatment outcomes of CVT psychotherapy for patients with PNES

In a separate prior study, we conducted a cross-sectional cohort study within the Veterans Health Administration comparing baseline characteristics of patients seen locally at the Providence Veterans Affairs Medical Center (PVAMC) and those seen remotely through CVT at other Veterans Affairs (VA) locations throughout the nation via the VA National TeleMental Health Center (NTMHC) Tele-Seizures clinic. We compared sociodemographic characteristics, clinical and social history, symptoms, and comorbidities and provided information on the eye-to-eye (in clinic) versus face-to-face (CVT) settings, showing no significant differences between milieu.[29] The aim of the current study includes determining effects of treatment using a seizure psychotherapy via CVT on outcomes including seizures, comorbidities, functioning, and quality of life (QoL). We hypothesized that seizures and comorbidities would reduce in those treated remotely with CVT.

2 | MATERIALS AND METHODS

The study was approved by the PVAMC Institutional Review Board. Veterans diagnosed with PNES were evaluated and treated by one of the authors (W.C.L.) at the PVAMC Neuropsychiatry Clinic via CVT NTMHC Tele-Seizures clinic. For this study, we assessed a prospectively followed observational cohort over the course of treatment. The clinical evaluation methods, social and symptomatic description, and sample are extensively described in LaFrance et al.[29]

2.1 | Sample

After an initial screening of 56 consecutively evaluated veterans seen via CVT by a single clinician at the PVAMC Neuropsychiatry Clinic from November 2012 to April 2018, 32 met all enrollment criteria for this treatment study. Inclusion criteria for the sample were male and female veterans between 18 to 89 years of age and diagnosed with

video-electroencephalography (EEG)-confirmed PNES, according to the International League Against Epilepsy PNES standards.[30] Video-EEG was conducted through the VA Epilepsy Centers of Excellence and affiliate sites.[31] Those with a history of epilepsy and current PNES were included in the study (n = 2). Exclusion criteria were a diagnosis of lone epilepsy or equivocal video-EEG findings in discerning between epileptic seizures and PNES; suicidality with current intent to harm self; serious medical or neurological illness that precludes treatment; and current substance or alcohol use or dependence that could interfere with participation (based on clinician examination with the patient, as clinically indicated). All patients had been previously told they had a diagnosis of PNES by the referring clinicians. Of the 56 patients who underwent consultative evaluation for seizures, none met exclusion criteria, 19 (33.9%) elected not to receive treatment, and five were scheduled to begin but had not yet initiated treatment. The 19 who did not enroll and the five who had not yet initiated treatment were not included in this treatment analysis study.

2.2 | Measures

A complete neuropsychiatric evaluation was obtained before the patient's first treatment session and completed within two consultation visits as described in the baseline evaluation paper.[29] Sociodemographic information was recorded, including age, biological sex, race, age at PNES onset, number of years of education, employment, disability, and marital and driving status. Developmental history included direct questioning of physical, verbal, emotional, and sexual trauma or abuse as a child or adult; history of psychotherapy and types; and current and past medications, including antiepileptic drugs and psychotropics. Current and past substance use and abuse and traumatic brain injury (TBI) history (defined by Diagnostic and Statistical Manual of Mental Disorders, 5th edition [DSM-5] TBI classification) were obtained via consultation interviewing and medical record reviews.

Neuropsychiatric cognitive tests, mental status, and neurological examinations were administered before treatment began or obtained from previous records (in the case of remote neurological examination). DSM-5 criteria psychiatric diagnoses were obtained by systematic symptom evaluation, including all mood, anxiety/PTSD, somatic symptom, psychotic, substance use, and personality disorders. Laboratory workup reviewed included brain magnetic resonance imaging, video EEG, routine EEG, and ambulatory EEG records. Seizure semiology, from symptom reports and video-EEG review, was also recorded at baseline.

As done in the seizure treatment clinical trials,[25,26] the primary outcome of the cognitive behavioral therapy–informed psychotherapy (CBT-ip) for seizure treatment was seizure frequency, where patients prospectively kept a daily seizure log on a 1-week diary sheet, to record details of each seizure, triggers, and daily frequency, throughout treatment, which was reviewed at each weekly session.

Secondary outcomes included baseline demographics and psychosocial symptom scales used to measure comorbidities and symptoms prospectively at three intervals: baseline (pretreatment), midpoint (session 6), and endpoint (session 11). The baseline measures were collected at the initial evaluation. Psychosocial measures included Beck Depression Inventory–II (BDI),[32] Beck Anxiety Inventory (BAI),[33] Family Assessment Device (FAD),[34] Quality of Life in Epilepsy Inventory–31 (QOLIE-31),[35] Short Form 36 Health Survey (SF-36),[36] Symptom Checklist–90,[37] CAGE (alcohol),[38] PTSD Checklist-Specific,[39] and Health Locus of Control.[40] A clinician-scored measure included Global Assessment of Functioning (GAF)[41] at each visit. Seizure freedom at the end of treatment was also analyzed.

2.3 | Treatment

Patients were given CBT-ip for seizures, a psychotherapy that consists of 12 manual-based sessions, in individual weekly appointments, delivered to this cohort through telehealth. Treatment corresponded to a therapy manual focused on gaining control of seizures that was used in prior treatment trials.[25,26] The evidence-based treatment is fully described in the treatment trial papers and in text chapters.[42]

Veterans seen remotely used CVT at their local VA medical center or community-based outpatient clinic (CBOC), which was facilitated by mental health or neurology clinic staff at the site, where VA staff (telehealth clinician technicians) checked in the patient, set up the video conference equipment, forwarded the weekly seizure logs, and completed treatment manual materials for review, and were available via instant messaging if any clinical issues arose during the appointment. CVT was conducted using high-definition, encrypted video connecting clinician to patient site for all appointments, providing high-quality audio/video fidelity. Any acute psychiatric issues or in-session seizures were dealt with according to acute telehealth standards[43] and seizure safety protocol.[44] Due to occasional missed appointments, cancellation, and rescheduling, treatment period often lasted >12 weeks for some patients. Completers were defined as those who attended 12 sessions.

2.4 | Statistical analysis

All analyses were conducted using SAS Software (SAS Institute). Patient seizures were modeled over time using generalized linear mixed modeling (GLMM) assuming a negative binomial distribution with classic sandwich estimation, where

each patient (including noncompleters) had their own slope and intercept, with the GLIMMIX procedure. GLMM was used to model time as a random effect (time varies between patients) so that the results better generalize to clinical settings where patients miss and complete sessions at varied times.[45]

Secondary outcomes were examined using generalized mixed modeling assuming a binomial distribution with sandwich estimation, where time was evaluated at three timepoints (baseline [at evaluation], midpoint [session 6], endpoint [session 10]), with observations nested within patient. Multiple comparisons were conducted using Tukey-Kramer adjustments. Alpha was established a priori at the .05 level, and all interval estimates were calculated for 95% confidence.

3 | RESULTS

A total of 32 patients met all criteria for inclusion in the treatment study. Five of the patients dropped from treatment (Table 1). All 32 subjects were included in analyses. Veterans evaluated were patients at VA Medical Centers across the nation, ranging from San Francisco to Houston to Boston. The five veterans who dropped out did so before session 5. Reasons for dropping out included symptom improvement (n = 3) and because of reported personal and family issues. The 19 who elected not to receive treatment reported reasons, including prioritizing other diagnoses treatment (eg, PTSD), distance to the VA or CBOC where they would log into VA telehealth units, and not being sure of the given PNES diagnosis.

Mean age was 49.1 years at baseline evaluation and 38.4 years at PNES onset. Treatment for PNES occurred an average of 119.1 months (approximately 10 years) after PNES onset. A majority of the veterans were male (84%), white (91%), and unemployed (66%) at initial evaluation. In addition, many were diagnosed with multiple comorbid disorders before enrollment. Thirty of 32 who enrolled in treatment had one or more anxiety disorders, and 26 of 32 veterans had one or more mood disorders. The prevalence of anxiety disorders and mood disorders was also exceptionally high, with 60% diagnosed with PTSD, 94% with anxiety disorders, and 81% with mood disorders among the 32 patients. Regarding ictal semiology, 47% of the patients had auras and 47% had major-motor manifestations. The demographics, medical history, and diagnoses are summarized in Tables 1 and 2.

TABLE 1 Demographics and clinical factors, obtained by interview and record review at baseline (n = 32)

Demographics	Frequency	Mean
Completed, n (%)	27 (84)	
Race		
White, n (%)	29 (90.63)	
Ethnicity		
Hispanic/Latino, n (%)	2 (6.25)	
Sex		
Female, n (%)	5 (15.63)	
Patient age, y [95% CI]		49.1 [44.3-54]
Education, y [95% CI]		13.9 [13.3-14.6]
Employment status		
Unemployed, n (%)	21 (65.63)	
Disability status		
Receiving disability, n (%)	25 (78.13)	
Currently driving, n (%)	13 (40.63)	
Marital status		
Married, n (%)	21 (65.63)	
Age at onset of PNES, y [95% CI]		38.4 [33.1-43.8]
Onset to PNES treatment, mean y [95% CI]		9.91 [6.23-13.6]
PNES diagnosis to treatment initiation, mean y [95% CI]		1.9 [0.36-3.44]
Current alcohol use, n (%)	8 (25.00)	
Current illicit drug use, n (%)	3 (9.38)	
History of trauma/abuse, n (%)		
Physical	14 (43.75)	
Verbal	13 (40.63)	
Emotional	14 (43.75)	
Sexual	17 (53.13)	
Currently on AED(s), n (%)	24 (77.42)	
Currently on psychotropic medications, n (%)	28 (87.50)	
History of psychotherapy, n (%)	25 (78.13)	
History of TBI, n (%)	26 (81.25)	

Abbreviations: AED, antiepileptic drug; CI, confidence interval; PNES, psychogenic nonepileptic seizures; TBI, traumatic brain injury; y, years.

3.1 | Primary outcome: Seizure frequency

An analysis of the daily prospectively collected, weekly seizure logs showed a statistically significant reduction in seizure frequency. On average, seizures were reduced by 45.7% per month of treatment (0.543, 95% confidence interval = 0.41-0.72, $P = .0001$), with seizures approaching 0 by month 6 (see Figure 1). Time to complete the 12 sessions ranged from 12 to 24 weeks.

3.2 | Secondary outcomes: Comorbidities, QoL, and functioning

Changes in secondary outcomes at the three interval timepoints (baseline, midpoint, and endpoint) were examined,

TABLE 2 Psychiatric diagnoses, obtained by interview and record review at baseline (n = 32)

Current diagnosis	Frequency
Axis I diagnosis, cumulative frequency, n	
Anxiety disorders	61
Mood disorders	33
Somatoform disorders	34
Substance-related disorders	24
Psychotic disorders	5
Other cognitive disorders	29
Other disorders	6
Axis II diagnosis, cumulative frequency, n	
Obsessive-compulsive personality disorder	18
Avoidant personality disorders	3
Borderline personality disorder	1
Dependent personality disorder	2
Personality disorder NOS	3
Cluster B personality traits	13
Cluster C personality traits	10
PTSD, n (%)	19 (59.38)
Anxiety disorder, n (%)	30 (93.75)
Mood disorder, n (%)	26 (81.25)
Somatoform disorder, n (%)	31 (96.88)
Learning disorder, n (%)	8 (25.00)
Substance abuse disorder, n (%)	17 (53.13)
Cognitive disorder NOS, n (%)	29 (90.63)

Note: Cumulative frequencies show the number of times a certain disorder was diagnosed.

Abbreviations: NOS, not otherwise specified; PTSD, posttraumatic stress disorder.

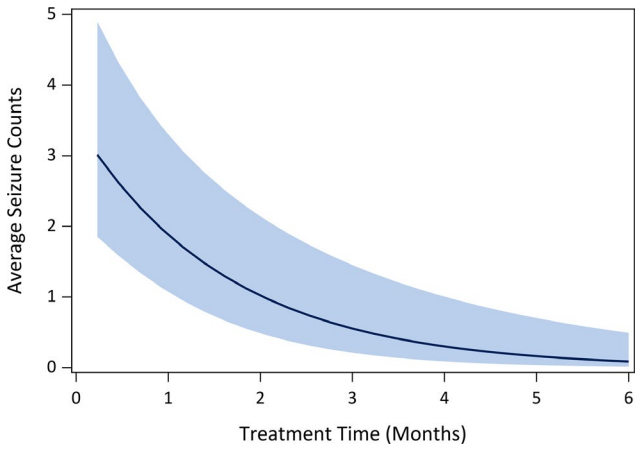

FIGURE 1 Seizure reduction per month of treatment (n = 32). Line indicates function of the seizure count over time (shaded area, 95% confidence interval) during cognitive behavioral therapy-informed psychotherapy, $P = .0001$. Median time in treatment was 20 weeks

which included depression, anxiety, somatic symptoms, QoL, and psychosocial functioning (see Table 3).

As shown in Table 3, a statistically significant decrease in depression and anxiety symptoms was observed, as indicated by depression and anxiety scores, respectively. There was also a statistically significant increase in psychosocial functioning and QoL. The decrease in PTSD symptoms and locus of control scores failed to be statistically significant.

Table 4 shows the subscale scores for SF-36, which showed a significant increase (improvement) from baseline to endpoint in all of the subscales (see Table 4). Although not statistically significant, all FAD subscales decreased from baseline to endpoint (lower FAD scores indicate improved functioning). Symptom scores documented at three intervals over time are shown in Figure 2. Most patients receiving telehealth showed high levels of satisfaction on surveys assessing care delivery method.

3.3 | Tertiary analysis: Enrolled versus nonenrolled

To assess for potential differences between those who enrolled and the nonenrolled, we analyzed baseline symptoms and demographics. Those who did not enroll reported a mildly higher mean BDI (33.2 vs 26.6 in enrolled, $P < .0001$) and mildly higher mean BAI (31.6 vs 26.1 in enrolled, $P < .0007$). Other measures, for example, NES at baseline, PTSD symptoms, GAF, age, sex, education, and employment, did not significantly differ.

4 | DISCUSSION

Patients with PNES receiving a manualized CBT-ip for seizures (referred to as NBT) had significant improvements in seizures and comorbid symptoms relative to baseline treated remotely using CVT, as evidenced by significant reduction in seizure frequency, improvement in comorbid symptoms, such as depression and anxiety, and improvements in psychosocial functioning and QoL.

The primary outcome of PNES frequency reported in all seizure trials is the symptom often leading to unemployment and reduced functioning. Patients treated with the intervention demonstrated significant reduction of seizures. Seizure count was reduced by 46% per month of treatment. Although it is possible that seizures would have reduced without treatment, the majority of participants (75%) had already received prior psychotherapy, yet they were referred because they continued to experience seizures and comorbidities at the time of treatment enrollment. Given the high comorbidities known to occur in PNES, it is expected that some form of psychotherapy had been offered in the past,

TABLE 3 Secondary outcomes scores at baseline, midpoint, and endpoint

	Baseline		Midpoint		Endpoint		
	Mean	95% CI	Mean	95% CI	Mean	95% CI	*P*[a]
BDI	25.6	20.1-31.4	20.4	15.6-25.8	15.0	10.9-20.1	.0024[b]
BAI	25.5	21.3-29.9	20.6	16.1-25.8	16.7	13.0-21.1	.0034[b]
GAF	50.8	49.0-52.5	55.9	54.1-57.7	60.3	58.4-62.3	<.0001[b]
QOLIE	36.7	32.9-40.5	41.7	37.5-45.9	46.8	42.6-51.1	<.0001[b]
PCL-S	53.2	45.5-58.8	49.7	41.9-55.8	46.0	37.6-53.0	.2430
HLOC	54.1	51.4-56.8	54.3	50.8-57.8	52.2	48.9-55.5	.8795

Note: Higher score indicates worse condition, except for GAF and QOLIE.

Abbreviations: BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory–II; CI, confidence interval; GAF, Global Assessment of Functioning; HLOC, Health Locus of Control; PCL-S, PTSD Checklist-Specific; QOLIE, Quality of Life in Epilepsy−31.

[b]Statistically significant.

[a]*P* values refer to change between baseline and endpoint, using Tukey corrections.

as was the case. Although those treatments separately and individually may not reduce PNES, the seizure therapy is comprised of elements from multiple modalities from other psychotherapies to target known pathologies in the PNES population, and their synergistic combination may impact seizures and comorbidities.

The above is written with a caveat that, although the NBT treatment components are drawn from other conventional psychotherapy modalities, the application of this treatment may differ. What may be unique to effective PNES/functional neurological (conversion) disorder treatments where symptom reduction is observed is that the clinicians teaching patients the tools have to understand the patient and this syndrome. Without this knowledge of the disorder and the patients' pathologies, many clinicians may fail to help these patients, as they do not sense the nuances of this patient population and condition. For example, some patients with PNES report they are not depressed, yet with being equipped with tools in the therapy, after they are "connected" to their underlying emotional state (eg, addressing alexithymia, avoidance, etc), patients "become depressed" (or rather gain insight into what they were already experiencing). Both in-clinic and in clinical trials, we often observe that "symptoms increase before they decrease." While the psychotherapy components are derived from other treatments, knowledge of the core syndrome of PNES (or other conversion disorder presentation) allows the effective therapist/therapeutic program to persist in the face of symptom increase, patient ambivalence, diagnostic doubts, or therapy-interfering behaviors, and to use the tools to target the common and known psychopathological features of the syndrome itself. Throughout the course of treatment, there are many critical points where simply understanding the condition, with the whole-person narrative framed in the biopsychosociospiritual integrative model, and abiding with the patient to hold up a mirror in a nonjudgmental fashion to reveal "blind spots," may empower these "common techniques" to synergistically be more effectively employed in this population.

Other studies of PNES treatment have described high dropout rates. Of the 32 who enrolled in treatment, adherence was >80% for this treatment. (Treatment adherence does not include those who elected not to seek treatment, who are discussed below.) Interestingly, those who did not complete treatment dropped out early on, and all dropped out before the midpoint of treatment. Most noncompleters dropped out at either session 4 or session 2, and one patient terminated treatment at session 5. These sessions deal with getting support and identifying negative emotions.

Because seizure frequency is one of the many outcomes of interest, other measures were included to document treatment progress. Secondary outcomes included comorbidities, functioning, and QoL. QoL measures used addressed QoL as it relates to seizures (QOLIE-31) and physical and mental health QoL (SF-36), which improved over the course of treatment. Results showed a significant reduction of depression and anxiety symptoms and an improvement of psychosocial functioning and QoL by the end of treatment.

Other measures studied included PTSD symptoms, family functioning, and locus of control, which did not show statistically significant changes. All FAD subscale scores were at or below the healthy threshold score at baseline, except for Affective Involvement, and all scores nonsignificantly decreased by the endpoint, indicating healthy family functioning in all of the subcategories by the end of treatment. Symptom substitution can occur in conversion disorders; we did not quantitatively track the emergence of other symptoms. However, qualitatively, patients did not report an increase in somatic symptoms over the course of treatment. In this study, we focused on the demonstration of primary and secondary outcomes of seizure and symptom reduction, not on possible mediators and moderators of variables such as trauma subtypes, which could be addressed in future studies.

The results from this study align with results from other studies that examined the effect of NBT for PNES in civilians. Previous studies using the Beckian-based CBT-ip similarly have shown seizure reduction and improvement in depression and anxiety symptoms for civilians with PNES.[25,26] The current study also reports reduced seizure frequency, depression, and anxiety in veterans. The psychotherapy used in these studies aims to reattribute symptoms by identifying precursors and triggers and applying techniques to gain control over their seizures. The tools and approaches used for the seizures are also used for the many psychiatric comorbidities found in this population, and result in decreased psychiatric symptoms. That PTSD symptom scores did not significantly improve may reflect a difference in psychopathology between PTSD and depression and anxiety disorders. Given the consistency of results and similarity of treatment outcomes between local and remote groups, the telehealth platform does not seem to be a barrier between the patient and clinician for the delivery of this therapy. In addition, many past studies have examined the quality of telehealth and have shown its effectiveness in mental health care delivery. Rather than a feared hindrance, telehealth has an added benefit with its ability to overcome travel and distance barriers, as demonstrated by years of extensive research.[46]

In our study comparing baseline characteristics of veterans seen locally (eye-to-eye) versus remotely (face-to-face), via CVT, the samples failed to show evidence for differences between the local and remote groups.[29] The sample mostly consisted of white male veterans, and a majority of the sample were unemployed and receiving disability benefits. Many reported a history of substance abuse and remote trauma (more than one-half had a history of sexual abuse) and were diagnosed with more than one comorbid condition. These characteristics are similar to other veteran samples in other diagnostic studies.[47]

Psychiatric comorbidities are the rule in PNES. Anxiety, mood, and personality disorders are the most common comorbidities among the sample. The majority of veterans also had a history of one or more TBI. The lack of evidence of a significant difference between the local and remote groups at baseline[29] may suggest that known population biases between veterans in Providence, Rhode Island and other veterans across the nation are minimal, allowing an equal comparison of outcomes between in-person and CVT therapy. Of note, a cohort of local patients at PVAMC (N = 8) were treated using the same NBT intervention, showing similar reductions in seizures and comorbidities, but the local sample was too small for statistical comparison between local and remote groups for this study.

The main limitation of this study is the unblinded treatment, observational design without a control arm. That weekly seizures counts were unmasked is another limitation. A randomized controlled trial with an untreated comparison group followed prospectively would allow for treatment effect inference to be made that is compared to standard of care; however, patients with PNES are aware that treatments exist and are less likely not to be treated with targeted therapy, knowing that treatments exist. A comparison group of untreated patients with PNES followed longitudinally could be an appropriate control, but because patients who are not seen in the clinic are not followed, this was not an option. Thus, a standard comparison group for noninferiority assessment was not available.

It is also possible that the improvements we observed in this study may be due to time or attention, rather than the psychotherapy. However, it is unlikely that the improvements were merely due to time; many of the veterans had their symptoms for a significant amount of time (an average of almost 10 years) since PNES onset, and they persisted over time and did not go away on their own (even with accurate diagnosis an average of 1.9 years before the seizure

TABLE 4 Short Form 36 Health Survey subscale scores at baseline, midpoint, and endpoint

Subscale	Baseline, mean	Midpoint, 95% CI	Endpoint, mean	95% CI	Mean	95% CI	*P*[a]
Physical Functioning	36.7	23.9-51.6	47.6	32.9-62.6	48.2	33.5-63.2	<.0001[b]
Role Limitations Due to Physical Health	2.3	0.5-9.3	4.3	1.0-16.7	7.8	1.9-27.2	<.0001[b]
Bodily Pain	37.8	30.0-46.2	36.6	28.9-45.1	38.1	30.2-46.7	.9771
General Health	37.6	31.9-43.7	40.4	34.3-46.7	42.6	36.4-49.0	.0157
Vitality	27.5	20.3-36.1	24.3	17.7-32.5	32.4	24.2-41.7	.0109
Social Functioning	40.2	30.7-50.5	41.4	31.6-51.9	49.2	38.8-59.7	<.0001[b]
Role Limitation Due to Emotional Problems	10.3	3.7-25.2	19.0	7.4-40.9	20.1	7.9-42.6	<.0001[b]
Mental Health	44.4	35.6-53.6	53.2	43.9-62.3	57.6	48.4-66.4	<.0001[b]

[b]Statistically significant.

Abbreviation: CI, confidence interval.

[a]*P* values refer to change between baseline and endpoint, using Tukey corrections.

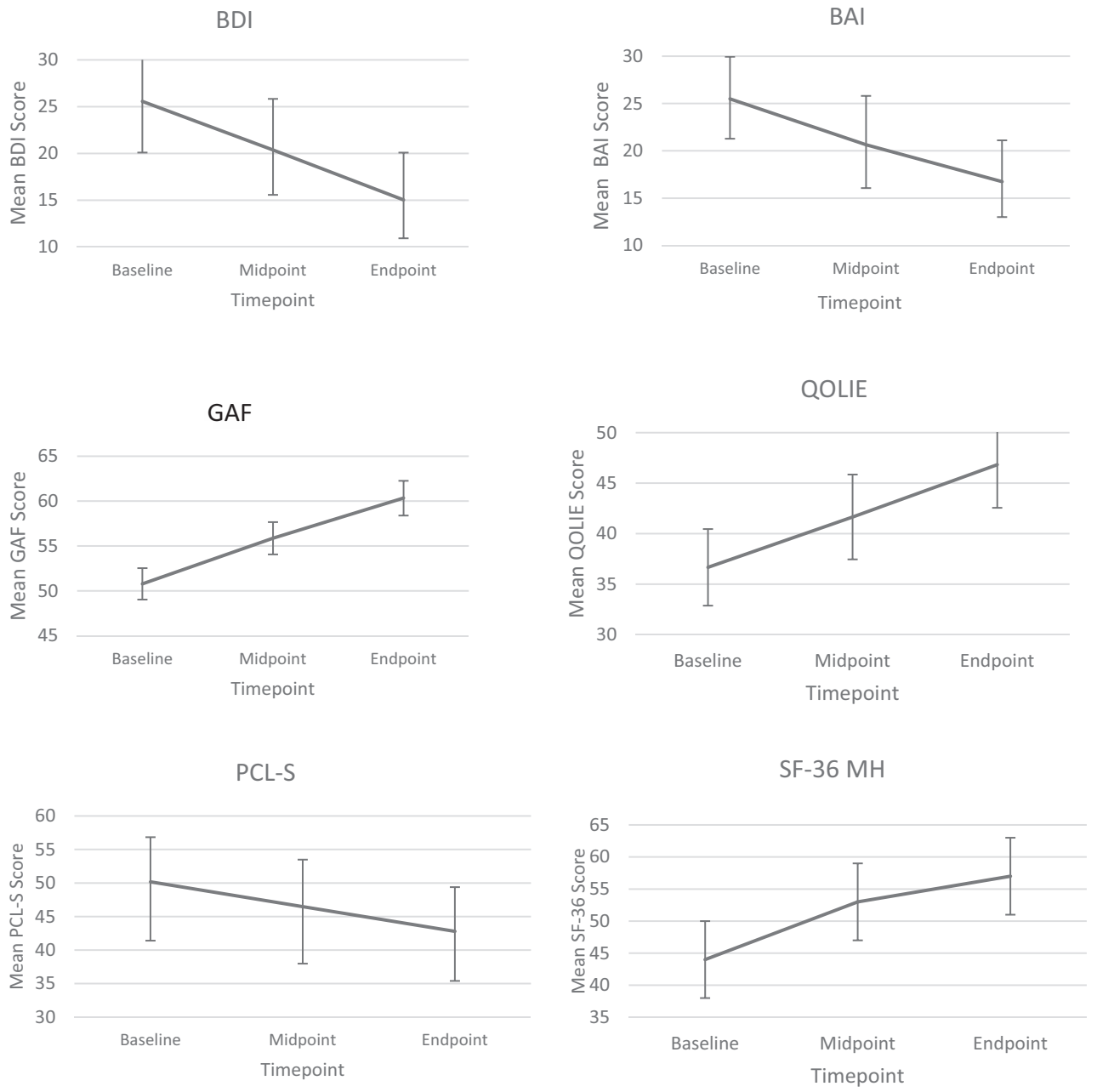

FIGURE 2 Mean plots of secondary outcomes over baseline, midpoint, and endpoint. Means are shown with 95% confidence interval limits. Higher score indicates worse condition, except for GAF, QOLIE, and SF-36. All scales showed significant difference ($P < .005$) except for PCL-S. BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory–II; GAF, Global Assessment of Functioning; PCL-S, PTSD Checklist-Specific; QOLIE, Quality of Life in Epilepsy–31; SF-36 MH, Short Form 36 Health Survey–Mental Health subscale

treatment was initiated). Moreover, despite having received attention in other psychotherapies for their comorbidities (eg, depression, PTSD, insomnia) over time, prior to enrollment, patients did not have seizure reduction and were referred because of persistent seizures. In other treatment studies, the same seizure and symptom reductions were observed in the 2009 single group[25] and in the two 2014 randomized clinical trial (RCT) CBT-ip arms, and although time and attention in a clinical trial can influence outcomes (ie, Hawthorne effect), the standard medical care group in the four-arm RCT did not show significant improvement in seizure frequency or secondary outcomes.[26] Although we cannot exclude potential impact of time and attention on outcomes, we have now observed in multiple studies of chronically symptomatic patients that reductions in seizures and comorbid symptoms began to reduce significantly since they started this seizure treatment and not with time and attention given in their prior psychotherapies.

The sample was limited to video-EEG–confirmed diagnosis of PNES within the veteran population referred to the PVAMC Neuropsychiatry Clinic seen in the VA NTMHC Tele-Seizures clinic. Because the study was limited to veterans treated by a single clinician at the PVAMC Neuropsychiatry Clinic, the sample may not be indicative of the entire veteran population across the USA. However, because the remotely treated veterans were referred through the VA Epilepsy Centers of Excellence, the remote cohort was likely to be representative of a national veteran sample.[48] Being such, the study sample itself consisted largely of males, who are older (as would be expected of veterans) and have many comorbidities, past treatments, and long delay to PNES treatment, which may be less generalizable to the civilian population with PNES. The choice to enroll only video-EEG–confirmed diagnoses provided the gold standard of diagnosis for PNES.[30]

At this VA seizure clinic, there was no specific number of cancellations or missed appointments that would necessitate discharge from clinic. If patients had to reschedule appointments, or took two appointments to master a tool, they were given this flexibility. Cancelled or missed appointments were brought up in discussion as a therapeutic topic. This flexibility ultimately may increase completion over time but may not be practical in all community practices.

The use of a single therapist could limit the generalizability of the treatment results, as the effect of the therapist could drive outcomes, rather than the therapy itself. Future studies, similar to the pilot multisite civilian RCT,[26] where different clinicians provided the same interventions, could assess potential for bias due to the clinician.

Another limitation is that one-third of those who underwent consultative evaluation did not engage in therapy and were not followed longitudinally because they did not remain in the Tele-Seizures clinic. This enrollment percentage from clinical referrals is comparable to other studies of PNES treatment, illustrating that some patients with PNES have challenges in engaging in treatment.[49,50] Differences between those who refused and those who enrolled in treatment are noted in the results, and they included mildly higher levels of depression and anxiety, which may have influenced their decision on enrollment. Those who elected to receive treatment could benefit most, related to motivation, expectations, or acceptance of the diagnosis. Likewise, conversely, it is possible that those who refused treatment may be least likely to benefit from the treatment.

A final limitation of the study design is that PNES frequency and symptoms were not assessed after treatment completion. Once patients complete (or drop from) the adjunctive treatment, they are discharged from the clinic. To examine whether a sustained benefit exists, future studies can incorporate longitudinal follow-up.

In conclusion, in this first-of-its-kind study assessing treatment of veterans with PNES, we found that patients with PNES receiving telehealth treatment experienced significant seizure reduction. CVT can be a promising alternative to patients who may not have access to mental health professionals for specific disorders at their local VA care center or to trained seizure counselors who use psychotherapies for seizure disorders. Prior to the COVID-19 global pandemic, patients had to travel to a facility with telehealth capabilities. Now that insurance and regulatory restrictions have been revised, home-based telehealth is also being made available and could continue postpandemic, benefitting urban and rural patients. The effectiveness of both NBT for PNES and the VA's telehealth system infrastructure can make evaluation and treatment more readily available to veterans across the nation and could be a model for telehealth in civilian hospitals and epilepsy centers, nationally and internationally.

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ETHICAL APPROVAL

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.

CONFLICT OF INTEREST

W.C.L. has served on the editorial boards of *Epilepsia*, *Epilepsy & Behavior*, *Journal of Neurology, Neurosurgery, and Psychiatry*, and *Journal of Neuropsychiatry and Clinical Neurosciences*; receives editor's royalties from the publication of *Gates and Rowan's Nonepileptic Seizures*, 3rd ed (Cambridge University Press, 2010) and 4th ed (2018); receives author's royalties for *Taking Control of Your Seizures: Workbook* and *Therapist Guide* (Oxford University Press, 2015); has received research support from the Department of Defense (W81XWH-17-0169), National Institutes of Health (National Institute of Neurological Disorders and Stroke 5K23NS45902 [principal investigator]), PVAMC, Center for Neurorestoration and Neurotechnology, Rhode Island Hospital, American Epilepsy Society, Epilepsy Foundation, Brown University, and Siravo Foundation; serves on the Epilepsy Foundation New England Professional Advisory Board, the Functional Neurological Disorder Society Board of Directors, and the American Neuropsychiatric Association

Advisory Council; has received honoraria for the American Academy of Neurology Annual Meeting Annual Course; has served as a clinic development consultant at University of Colorado Denver, Cleveland Clinic, Spectrum Health, Emory University, and Oregon Health Sciences University; and has provided medicolegal expert testimony.

None of the other authors has any conflict of interest to disclose.

DISCLAIMERS

This material is the result of work supported with resources and the use of facilities at the Providence Veterans Affairs Medical Center, Providence, Rhode Island. The contents do not represent the views of the US Department of Veterans Affairs or the US Government.

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