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Cognitive behavioral therapy for patients with psychogenic non-epileptic seizures

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ABSTRACT A critical appraisal and clinical application of Goldstein L, Chalder T, Chigwedere C, et al. Cognitive-behavioral therapy for psychogenic nonepileptic seizures: A pilot RCT. *Neurology.* 2010;74(24):1986-1994. doi: 10.1212/WNL.0b013e3181e39658.

Keywords: *PNES, pseudoseizures, cognitive-behavioral therapy, CBT, psychogenic, non-epileptic*

Clinical Context

A 30-year-old Caucasian male with history of bipolar disorder and traumatic brain injury (TBI) presented to the hospital with a chief complaint of loss of consciousness and an episode of "shaking" described by witnesses. His labs showed elevated creatine kinase of 5000. Multiple video electroencephalogram (vEEG) showed abnormal patterns, consistent with TBI, but no epileptiform activity. He was admitted to the floor from observation for management of rhabdomyolysis and further seizure work up, suspicious for psychogenic non-epileptic seizures (PNES). Prior to discharge, follow-up recommendations were considered. A 2014 Cochrane Review found no reliable evidence supporting the use of any specific treatment in non-epileptic seizures.[1] The current mainstay of treatment in PNES involves tapering anti-epileptic medications, communication of the diagnosis, and referral to psychiatry for treatment.[2] The team investigated whether cognitive behavioral therapy would be effective in reducing seizure frequency for this patient with PNES.

Clinical Question

Is cognitive behavioral therapy (CBT) effective in reducing seizure frequency in patients with psychogenic non-epileptic seizures (PNES)?

Research Article

Goldstein L, Chalder T, Chigwedere C, et al. Cognitive-behavioral therapy for psychogenic nonepileptic seizures: A pilot RCT. *Neurology.* 2010;74(24):1986-1994. doi: 10.1212/WNL.0b013e3181e39658.

Related Literature

Articles used to assess this question were found on PubMed using the keywords “psychogenic nonepileptic seizures treatment” and further filtered into a set that included clinical trials, randomized controlled trials (RCTs), meta-analyses, clinical, and comparative studies. This search yielded 47 articles. The chosen article published the first results of a pilot RCT using directed psychotherapy techniques in the form of CBT. It is the most recent RCT that used a head-to-head comparison of standard, supportive, medical

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treatment with supervised withdrawal of anti-epileptic drugs compared to weekly CBT sessions in addition to traditional medication withdrawal.[3] Prior to this study, LaFrance et al. published a report on the use of CBT in PNES; however, their research focused on psychiatric symptomatology.[2]

Critical Appraisal

As a pilot, the study is inherently limited in measuring effect size. The lack of blinding within the study is a potential source of bias that may overestimate seizure frequency reduction. Further, due to small sample sizes found within pilot studies, generalization of the results of the study are restricted to patients who meet the inclusion and exclusion criteria.

The patient population consisted of 192 participants referred to the service from NHS neurologists. Of these, 89 were excluded for failing to meet inclusion criteria: age 18-70, PNES confirmed by vEEG or clinical consensus; and exclusion criteria: coexistent epilepsy, <2 seizures per month, drug or alcohol use, more than 10mg of diazepam per day, or an IQ below 70. These exclusion criteria are reasonable and were likely chosen because of the confounding effects on possible seizure activity and therapy participation. From the 103 potential participants, 37 declined to participate. Of the 66 remaining, 33 participants were randomized into each treatment regimen, slightly less than the study's goal of 35 per treatment protocol. 88% of participants in the study were Caucasian; 75% were female.

Patients were appropriately assigned using an independent random number generator and allocation to either standard medical care or CBT plus standard medical care. The randomization process was appropriate for the context of the study as there was no significant difference in the demographic data between the two groups. There were a greater number of divorcees (n = 5) in the CBT arm of the study, with none included in the standard medical care arm (n = 0). All clinically relevant demographic data was reported in this study.

Confounding variables were appropriately controlled and reported in this study by analyzing the possible confounders of individual therapist interaction, length of treatment, and follow-up on seizure frequency. Their analysis showed no effect from these variables using an appropriate Wald Chi-Square analysis and Z-score interpretation, giving confidence in the interpretation that the reduction in seizure frequency can be attributed to the psychotherapy techniques. Protocol deviations with participant crossover and differences in therapy session frequency were accounted for but introduce a source of bias that may overestimate CBT's effect due to the small sample size. One participant was accidentally included in the experimental group instead of the assigned control group. Another patient received 1 extra CBT session due to perceived need by the medical staff. There was also crossover of 2 patients from the control group to the CBT group due to perceived need. Additionally, 3 participants in the control group received more sessions than the rest of the group in the follow-up period.

Appropriate analysis was used within this study, with an intention-to-treat analysis that is most similar to clinical applications. This technique also provides adequate protection against bias in analysis of the results. All the participants in the study were accounted for in the results, including 1 removed from data analysis due to death of the patient and 6 being lost to follow up. Using a last observation carried forward technique in the event of a patient death or follow up loss, the study was able to include participant data for all but two participants. The primary outcome of interest in the study, seizure frequency, showed a significant median monthly reduction of 12.0 to 2.0 seizures for the CBT arm. Median monthly seizures were reduced from 8.0 to 6.75 in the control arm. Additionally, the authors calculated a number needed to treat of 5.1 to achieve seizure freedom, however the raw data is not available to confirm their calculations. No differences in results were found when accounting for subgroup data.

Overall, this study was the best available evidence regarding the efficacy of CBT in the reduction of seizure frequency in patients suffering from PNES. Limitations of the study, including sample size, heterogeneous psychiatric comorbidities, lack of blinding, short follow-up, and selection bias from referrals, contribute to potential sources of error. Some of these limitations are similar to ones that patients with PNES face clinically, such as referral bias, however the others possibly contribute to an overestimation of the effect of CBT. The study's homogeneous population and sample size reduce generalizability of the results. The results do suggest though that CBT may be effective in the treatment of PNES in Caucasian patients.

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Clinical Application

Although male, our patient fit within the criteria of the study, as he was Caucasian with no epileptiform activity across multiple vEEG with seizure activity. Based on the findings of Goldstein et al., initial treatment should include finalizing a diagnosis of PNES via epilepsy monitoring unit observation with provocation and no medications. If ictal vEEG fails to show epileptiform activity, a diagnosis of PNES can be made. He was discharged from the hospital after resolution of his rhabdomyolysis with follow-up with neurology for confirmation of the diagnosis; if proven, I would recommend the use of CBT based on the results of this study.

Take-home points:

1. CBT may be effective as treatment for PNES as patients experienced significant reduction in seizure frequency compared to standard medical treatment.
2. Pilot studies, although limited in their generalizability, have potential to change management and treatment of patients who meet the inclusion/exclusion criteria.
3. Future studies investigating the role of psychotherapy should focus on investigations of other targeted therapy techniques in the reduction of seizure frequency.

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