Neglected Patients, Few Treatments, and Minimal Evidence: The Updated Cochrane Review on Psychological and Behavioral Treatments for Nonepileptic Seizures

Psychological and Behavioural Treatments for Adults With Nonepileptic Attack Disorder.

BACKGROUND: Psychogenic non-epileptic seizures, also known as non-epileptic attack disorder (NEAD), have the outward appearance of epilepsy in the absence of physiological or electroencephalographic correlates. Non-epileptic seizures can occur in isolation or in combination with epileptic seizures. The development and maintenance of non-epileptic seizures has been well documented and there is a growing literature on the treatment of non-epileptic seizures which includes non-psychological (including anti-anxiety and antidepressant pharmacological treatment) and psychological therapies (including cognitive behavioural therapy (CBT), hypnotherapy and paradoxical therapy). Various treatment methodologies have been tried with variable success. The purpose of this Cochrane review was to establish the evidence base for the treatment of non-epileptic seizures with behavioural and psychological therapies only.

OBJECTIVES: To assess whether behavioural or psychological treatments for non-epileptic seizures or NEAD result in a reduction in the frequency of seizures or improvement in quality of life, or both, and whether any treatment is significantly more effective than others.

SEARCH METHODS: We searched the Cochrane Epilepsy Group's Specialised Register (4 February 2013), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2013, Issue 1) (January 2013), MEDLINE (1946 to 4 February 2013), PsycINFO (4 February 2013) and SCOPUS (4 February 2013). No language restrictions were imposed. We checked the reference lists of retrieved studies for additional reports of relevant studies.

SELECTION CRITERIA: Randomised controlled trials (RCTs) and before and after controlled and non-controlled studies were eligible for inclusion. Studies were required to assess one or more types of behavioural or psychological interventions, or both, for the treatment of non-epileptic seizures. Studies of childhood non-epileptic seizures were excluded from our review.

DATA COLLECTION AND ANALYSIS: Two review authors (JM, JP) independently assessed the trials for inclusion and extracted data. Outcomes included reduction in seizure frequency and improvements in quality of life.

MAIN RESULTS: Twelve studies, with a total of 343 participants, met our inclusion criteria (four RCTs and eight before and after non-controlled studies). Of the four RCTs, one examined patients with non-epileptic seizures and three had a mixed diagnosis (pseudoseizures, conversion disorder and somatisation disorder). Most of the non-randomised studies used non-epileptic seizure patients exclusively. Overall, five studies examined the effectiveness of psychotherapy, three examined CBT, two investigated hypnosis, one that assessed paradoxical intention and one had a mixed intervention design. We classified two included studies as low risk of bias, one as unclear and nine as high risk of bias. Meta-analysis could not be undertaken due to the heterogeneity of design and interventions. Most included studies reported improved outcomes for the intervention under investigation. One RCT investigating the effectiveness of CBT in this patient group found a significant reduction in seizure frequency compared to controls (P < 0.001).

AUTHORS’ CONCLUSIONS: There is little reliable evidence to support the use of any treatment, including CBT, in the treatment of non-epileptic seizures. Further randomised controlled trials of CBT and other interventions are needed.

Commentary
Psychogenic nonepileptic seizures (PNES) represent the most common functional neurologic symptom disorder (FNSD) and the new terminology in DSM 5 for conversion disorder.

While the terminology has varied over the years, the majority of the research on PNES has centered around risk factors and diagnosis, especially differentiating the disorder from epilepsy. There have been relatively few studies that mention management or treatment for this disorder, although a growing interest began in 2010 with the first pilot randomized control trials (RCT). Differentiating PNES from epilepsy is of critical importance and is commonly investigated at epilepsy centers.
It is striking, however, that evidence for effective treatments lags way behind. Despite descriptions of PNES as far back as the 18th century, there is still an enormous vacuum in the quality and quantity of data available regarding management and treatment of this disorder. Over the past 20 years, there has been recognition of a need to find treatments, and a variety of small uncontrolled, unblinded, nonrandomized, or retrospective studies were conducted. In 1998, Devinsky called for “better trials for treatment for this neglected group of patients” (1). In the March/April 2014 issue of Epilepsy Currents, Smith called for more research for this “borderland diagnosis” to overcome the wasteland” when it comes to randomized controlled trials (2). Why is it that there has been so little published in the area of treatment in all these years? Is it lack of interest in this group of patients who neurologists believe should be cared for by psychiatrists, and who psychiatrists refer back to neurologists for not believing the video-EEG results (3)—thus truly “caught in the borderland” between two disciplines?

Benbadis, discussing this same issue on lack of information and research for psychogenic or somatoform disorders, states that there seems to be a severe disconnect between the frequency of the problem and the amount of attention devoted to it, as well as lack of psychiatrists’ interest in recognizing this as a psychiatric disease (4). Focusing on this dualistic approach has never worked for patients, which may be one reason for the treatment problem for PNES, as neurologists have referred patients “into limbo” to treaters who do not acknowledge the condition as psychiatric in origin or are not knowledgeable or comfortable with this population (2). In addition, there are biases against these patients. One study provided interesting data that emergency and neuroscience ward staff believe that patients with PNES are not acknowledged as psychiatric in origin, and are not knowledgeable or comfortable with this population. In addition, there are biases against these patients. One study provided interesting data that emergency and neuroscience ward staff believe that patients with PNES are not acknowledged as psychiatric in origin, and are not knowledgeable or comfortable with this population.

In addition, many epilepsy centers do not include psychiatric consultation in their EMU evaluation. There may also be inertia or even ignorance around engagement of PNES patients into the right treatments, removing treatments for epilepsy that are not working, and reducing the stigma that will help to steer us out of the incredible fog. In addition to these provider factors, patient factors also interfere with treatment. Patients with PNES are difficult to engage in treatment, including participation in clinical trials. The underlying mechanisms of PNES include avoidance and denial of emotional factors in their symptoms, and having an external locus of control, making it less likely for these patients to readily engage with psychiatrists (6).

The emergence of the field of neuropsychiatry and the growing number of dually trained specialists in neurology and psychiatry provide hope that we are at the dawn of really creating seamless care for these patients. LaFrance, Goldstein, Reuber, and colleagues (5, 7, 8) have begun the critical work of enhancing interest in management and treatment, as well as designing appropriate randomized controlled trials with video-EEG-proven PNES and defined psychiatric comorbidities, detailed to provide the evidence necessary to move this research forward.

The current paper is a Cochrane review. Cochrane reviews emerged in 1993 and consist of a large group of volunteers who review health care interventions that carry the highest evidence. It is a not-for-profit collaborative, tasked with trying to minimize the extensive bias that exists in research. In 2007, there was a Cochrane review performed in the area of treatment for PNES, which concluded that there was little to no evidence available (9). Martlew, Pulman, and Marson (10) performed an updated Cochrane review that has systematically evaluated the current evidence for effective nonpharmacologic treatments for PNES in adults in reducing frequency of episodes as well as improving quality of life. They were unable to perform a meta-analysis because of the heterogeneous nature of the studies. Out of 649 studies included, 46 were eligible, but the researchers eliminated another 34, leaving 12 studies meeting their stringent criteria: 4 RCTs, only 1 focused on lone PNES (the other 3 were mixed disorders). Then, there were eight before-and-after studies; nine of them, however, revealed high risk of bias. Two had low risk of bias, and one was unclear. Only one study emerged as having low chance of bias, testing 33 patients with PNES using CBT versus 33 receiving standard medical treatment (9). The descriptive narrative provided for all other studies concluded that the evidence remains slim. Since the studies are not comparable to one another, it has been impossible to show effectiveness for one therapy over another. Still, CBT is the treatment that continues to be mentioned with the best evidence, including a very recent RCT (8) at three centers that utilized a within-group analysis of four interventions with a small number of subjects in each group. Unfortunately, this form of psychotherapy is probably not appropriate treatment for all patients with PNES.

Even if there were effective evidence-based treatments for PNES, there are other issues that should be investigated, including getting patients to engage in treatment both acutely and more chronically, getting providers interested and trained in delivering the treatments, and stopping them from reintroducing the possibility of epilepsy, which leads to repeat expensive diagnostic testing. The heterogeneous nature of this population makes generalizations about treatment difficult and applicability of the specific interventions tested in RCTs problematic. These are some of the next major hurdles to overcome that future research in this important area should address.

by Barbara A. Dworetzky, MD

References


American Epilepsy Society

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Disclosure of Potential Conflicts of Interest

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1. Today's Date: 4/28/2014

2. First Name Barbara  Last Name Dworetzky  Degree MD

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If no, enter your name as co-author:

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