Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

"In adults with non-epileptic or dissociative seizures, what is the most effective treatment (psychological or medical, with particular focus on trauma focused treatment such as EMDR) in improving patient outcomes, such as a reduction in the frequency of seizures and improved quality of life."

Clarification of question using PICO structure (PICTRO for diagnostic questions)

Patients:	Adults with non-epileptic or dissociative seizures
Intervention:	Any intervention
Comparator:	Any other intervention
Outcome:	Any patient outcomes (including, reduction in the of frequency of seizures and improved quality of life)

Clinical and research implications

The authors of a systematic review (SR) reported that there is currently no sound evidence on which to base treatment decisions for people with non-epileptic attacks. Two randomised controlled trials (RCTs) presented some evidence to suggest that behavioural treatment may reduce the number of seizures, however, the trials had small sample sizes – and no definite clinical implications can be made from this evidence. The authors of one pilot RCT stated that they could neither substantiate nor refute the utility of a serotonin selective reuptake inhibitor treatment in patients with psychogenic non-epileptic seizures.

The need for further large, multi-centre, randomised controlled trials that evaluate a number of treatments was commonly reported in the included studies. The author of one RCT also suggested that future studies may benefit by stratifying groups on the presence of personality disorders.

What does the evidence say?

Number of included studies/reviews (number of participants)
We identified one SR (including 3 RCTs with a total of 119 participants) (Martlew et al. 2007), and three RCTs (n=122 participants) that met the inclusion criteria (Aamir et al. 2011; Goldstein et al. 2010; LaFrance et al. 2010). These latter two trials were described as pilot RCTs by the study authors.

Main Findings
The SR reported that there were no detailed reports of improved seizure frequency or quality of life outcomes in the included studies, and that the included trials provided no reliable evidence of a beneficial effect of behavioural interventions (i.e. hypnosis or paradoxical therapy) for non-epileptic attack disorder.

One RCT conducted in Pakistan compared 15 sessions of behavioural therapy with routine treatment (Aamir et al. 2011). The authors reported that those in the experimental group experienced on average, significantly fewer fits (6.4 ± 3.7 vs. 27.8 ± 9.2, $p < 0.0001$), a significantly lower score on the HADS Depression (1.8 ± 1.9 vs. 6 ± 2.4, $p < 0.0048$), and Anxiety subscales (2.8 ± 2.54 vs. 7 ± 3.33. $p=0.0198$) compared to the control group after 2.5 months of treatment. No other outcomes were reported.

The second RCT was conducted in the UK, and compared CBT with standardised medical care (Goldstein et al. 2010). The authors reported that after 4 months of treatment, there was a significantly lower mean seizure frequency in the intervention group compared to the control group (2.0 vs. 6.75, $p=0.002$). However, there were no significant differences between groups for any other outcome assessed.

The third RCT was conducted in the US, and compared sertraline with placebo (LaFrance et al. 2010). No significant differences between groups were observed for any of the outcomes assessed: seizure rates, depression, anxiety, impulsivity, somatic symptoms, QOL scores, and psychosocial functioning.

Authors Conclusions
The authors of the SR reported that there is no reliable evidence to support the used of any treatment including hypnosis or paradoxical injunction therapy in the treatment of non-epileptic attack disorder. Two of the RCTs generally concluded that behaviour therapy is more effective than

usual care for reducing seizure frequency. The authors of third RCT made conclusions based on within-treatment differences rather than between-treatment differences; they stated that PNES were reduced in patients treated with a serotonin selective reuptake inhibitor, whereas those treated with placebo slightly increased.

Reliability of conclusions/Strength of evidence

The systematic review was well conducted, although the authors stated that the included trials were of poor methodological quality. Nevertheless, the authors' cautions conclusions are likely to be reliable. One of the RCTs had an unclear (possibly high) risk of bias (Aamir et al. 2011), and the other two were well conducted. However, all of the RCTs had small sample sizes, which increases their risk of bias. Thus any conclusions made from these studies should be treated with caution.

What do guidelines say?

None available.

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Date searches conducted: 17/05/2012
Date answer completed: 25/05/2012

References

SRs

Martlew J, Baker GA, Goodfellow L, Bodde N, Aldenkamp A. Behavioural treatments for non-epileptic attack disorder. *Cochrane Database of Systematic Reviews* 2007, Issue 1. Art. No.: CD006370. DOI: 10.1002/14651858.CD006370.

RCTs

Aamir S, Hamayon S, Sultan S. Behavior Therapy in Dissociative Convulsion Disorder. (2011). Behavior Therapy in Dissociative Convulsion Disorder. *J Depress Anxiety* 1:103. doi:10.4172/jda.1000103

Goldstein L H, Chalder T, Chigwedere C, Khondoker M R, Moriarty J, Toone B K, Mellers J D C. Cognitive-behavioral therapy for psychogenic nonepileptic seizures: A pilot RCT. *Neurology*, 2010;74:1986–1994.

LaFrance W C Jr, Keitner G I, Papandonatos G D, Blum A S, Machan J T, Ryan C E, Miller I W. Pilot pharmacologic randomized controlled trial for psychogenic nonepileptic seizures. *Neurology*, 2010;75:1166–1173.

Results

Systematic Reviews

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Martlew et al. (2007)	July 2005	Randomised or quasi-randomised studies were included that assessed one or more types of psychological or non-psychological interventions for the treatment of non-epileptic seizures (NES) in adults.	3 RCTs (n=119 patients)	Two trials assessed hypnosis vs. waiting list (Moene 2003) or talking sessions (Moene 2002), and the other assessed paradoxical therapy vs. diazepam (Ataogulu 2003). There were no detailed reports of improved seizure frequency or quality of life outcomes, and these trials provide no reliable evidence of a beneficial effect of these interventions.	Low

RCTs

Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
Aamir et al. (2011)	*Participants:* patients 18-50 years diagnosed with conversion disorder (having pseudo seizures only) as per ICD 10 criteria with no co morbid psychiatric or physical illness and whose total duration of illness was not more than 6 months. *Intervention:* Behaviour therapy (15	18 (9 in each arm)	At follow-up (2.5 months), the experimental group experienced on average, significantly fewer fits compared to the control group (6.4 ± 3.7 vs. 27.8 ± 9.2, $p < 0.0001$), a significantly lower score on the HADS Depression subscale (1.8 ± 1.9 vs. 6 ± 2.4, $p < 0.0048$), and a significantly lower score on the HADS Anxiety subscale (2.8 ± 2.54 vs. 7 ± 3.33. $p=0.0198$). Dropout rate in experimental group was 9-1=8 (11.1%) and	Unclear (likely high)

	sessions). *Comparison:* Routine treatment as usual (pharmacotherapy). *Outcomes:* Outcome measures were reduction in the number of fits, decline in the level of anxiety and depression and adherence to the treatment and follow up sessions by the patients.		control group was 9-3=6 (33.3%).	
Goldstein et al. (2010)	*Participants:* aged 18–70 years with a clinical diagnosis of PNES, and no coexistent diagnosis (past or current) of epilepsy. *Intervention:* Cognitive-behavioural therapy (up to 12 weekly/fortnightly hour-long outpatient sessions) *Comparison:* Standard medical care *Outcomes:* Primary outcome measure was monthly seizure frequency. Secondary outcomes included 1) seizure freedom; 2) Work and Social Adjustment Scale (WASAS) scores; 3) Hospital Anxiety and Depression Scale (HADS) scores; and 4) a modified Client Service Receipt Inventory.	66 (33 in each arm)	After 4 months treatment, there was a significantly lower mean seizure frequency in the intervention group compared to the control group (2.0 vs. 6.75, p=0.002). There were no significant differences between groups for any other outcome assessed: Work and Social Adjustment Scale, HADS anxiety, HADS depression, number of hospital emergency dept visits, no of emergency hospital visits by ambulance, number of general practitioner consultations, number of prescribed medications, and number of antiepileptic drugs. The authors reported that one patient in the CBT group, with a diagnosis of emotionally unstable personality disorder, committed suicide in the follow-up period. This was considered to be unrelated to her seizure disorder.	Some risk of bias: well-reported but small sample size; pilot RCT
LaFrance et al. (2010)	*Participants:* aged 18-65 years diagnosed with video-EEG–confirmed PNES. Patients had to have experienced at least 1 event in the month before enrolling. Patients with mixed epileptic seizures and PNES	38 (19 in each arm)	There were no significant differences between groups for any outcome assessed: seizure rates, depression, anxiety, impulsivity, somatic symptoms, QOL scores, and psychosocial functioning. The authors also reported that patients in the sertraline	Some risk of bias: well-reported but small sample size; pilot

	who could clearly distinguish between their events were included (n = 2). *Intervention:* Sertraline (SSRI) - flexible-dose up to a maximum dose of 200 mg. *Comparison:* Placebo. *Outcomes:* Primary outcome measure was frequency of psychogenic non-epileptic seizures (PNES). Secondary outcome measures are: subjective and objective depression symptoms; anxiety/PTSD symptoms; dissociative symptoms; impulsivity; family functioning; somatic symptoms; patient symptoms and social functioning; disability; psychosocial functioning; coping techniques; Quality of Life.		arm manifested a significant 45% decline in biweekly seizure rates vs control subjects, who experienced a non-significant 8% increase, suggesting that subjects assigned to the sertraline arm received some benefit relative to placebo.	RCT

Risk of Bias:

SRs

Author (year)	Risk of Bias				
	Inclusion criteria	Searches	Review Process	Quality assessment	Synthesis
Martlew et al. (2007)	☺	☺	☺	☺	☺

RCTs

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Aamir et al. (2011)	?	?	NA	☺	☹	?
Goldstein et al. (2010)	☺	☺	NA	☺	☺	☺
LaFrance et al. (2010)	☺	☺	☺	☺	☺	☺

☺Low Risk ☹High Risk ? Unclear Risk

Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
SRs and Guidelines			
NICE	(non adj2 epileptic) OR psychogenic OR NEAD OR ((pseudo OR hysterical OR functional) adj2 seizure) OR somataform OR ((dissociative OR conversion) adj2 disorder)	32	0
DARE	1 MeSH DESCRIPTOR Seizures EXPLODE ALL TREES 39 2 seizure* 366 3 epilep* 361 4 non-epileptic attack* 0 5 non-epileptic seizure* 0 6 (psychogenic and attack*) 1 7 (psychogenic AND seizure*) 3 8 pseudoseizure* 0 9 functional seizure* 0 10 NEAD 0 11 non-epileptic attack disorder 1 12 hysterical seizure* 0 13 somatoform disorder* 31 14 MeSH DESCRIPTOR Somatoform Disorders EXPLODE ALL TREES 29 15 psychophysiologic* disorder* 13 16 MeSH DESCRIPTOR Psychophysiologic Disorders EXPLODE ALL TREES 12	421	1

	17 dissociative disorder* 1 18 MeSH DESCRIPTOR Dissociative Disorders EXPLODE ALL TREES 0 19 MeSH DESCRIPTOR Conversion Disorder EXPLODE ALL TREES 1 20 conversion disorder*3 21 (somatisation OR somatization) 15 22 non adj epilep* 15 23 #1 OR #2 OR #6 OR #7 OR #11 OR #13 OR #14 OR #15 OR #16 OR #17 OR #19 OR #20 OR #21 OR #22 421		
Primary Studies			
CENTRAL	#1 (nonepileptic):ti,ab,kw or (non-epileptic):ti,ab,kw or ("non epileptic"):ti,ab,kw or (dissociative):ti,ab,kw or (psychogenic):ti,ab,kw 607 edit delete #2 (seizures):ti,ab,kw or (fits):ti,ab,kw or (attacks):ti,ab,kw 12184 edit delete #3 (pseudoseizure*):ti,ab,kw or (PNES):ti,ab,kw or (NES):ti,ab,kw 45 edit delete #4 (#1 AND #2) 29 edit delete #5 (#3 OR #4) 68 edit delete #6 (#5), from 2005 to 2012 31 edit delete	28	3
MEDLINE	99. MEDLINE; (nonepileptic adj3 seizure*).ti,ab; 415 results. 100. MEDLINE; ("non epileptic" adj3 seizure*).ti,ab; 275 results.	130	

	101. MEDLINE; ("non-epileptic" adj3 seizure*).ti,ab; 275 results. 102. MEDLINE; ("psychogenic" adj3 seizure*).ti,ab; 525 results. 103. MEDLINE; ("dissociative" adj3 seizure*).ti,ab; 19 results. 104. MEDLINE; 99 OR 100 OR 101 OR 102 OR 103; 853 results. 105. MEDLINE; pseudoseizure.ti,ab; 65 results. 106. MEDLINE; 104 OR 105; 910 results. 109. MEDLINE; "randomized controlled trial".pt; 327424 results. 110. MEDLINE; "controlled clinical trial".pt; 84102 results. 111. MEDLINE; randomi?ed.ab; 290776 results. 112. MEDLINE; placebo.ab; 135952 results. 113. MEDLINE; "drug therapy".fs; 1530686 results. 114. MEDLINE; randomly.ab; 178278 results. 115. MEDLINE; trial.ab; 251477 results. 116. MEDLINE; groups.ab; 1164070 results. 117. MEDLINE; 109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115 OR 116;		

	2938382 results. 118. MEDLINE; 106 AND 117; 263 results. 119. MEDLINE; 118 [Limit to: Publication Year 2005-2012]; 130 results.		
EMBASE	29. EMBASE; random*.tw; 722076 results. 30. EMBASE; factorial*.tw; 18697 results. 31. EMBASE; placebo*.tw; 173569 results. 32. EMBASE; (crossover* OR cross-over*).tw; 60681 results. 33. EMBASE; (doubl* adj3 blind*).tw; 127267 results. 34. EMBASE; (singl* adj3 blind*).tw; 13948 results. 35. EMBASE; assign*.tw; 201557 results. 36. EMBASE; allocat*.tw; 67476 results. 37. EMBASE; volunteer*.tw; 155036 results. 38. EMBASE; CROSSOVER PROCEDURE/; 33755 results. 39. EMBASE; DOUBLE-BLIND PROCEDURE/; 108636 results. 40. EMBASE; SINGLE-BLIND PROCEDURE/; 15834 results.	74	

	41. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 321249 results. 42. EMBASE; 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41; 1192918 results. 43. EMBASE; 28 AND 42; 116 results. 44. EMBASE; 43 [Limit to: Publication Year 2005-2012]; 83 results. 45. EMBASE; (nonepileptic adj3 seizure*).ti,ab; 584 results. 46. EMBASE; ("non epileptic" adj3 seizure*).ti,ab; 443 results. 47. EMBASE; ("non-epileptic" adj3 seizure*).ti,ab; 443 results. 48. EMBASE; ("psychogenic" adj3 seizure*).ti,ab; 759 results. 49. EMBASE; ("dissociative" adj3 seizure*).ti,ab; 47 results. 50. EMBASE; 45 OR 46 OR 47 OR 48 OR 49; 1248 results. 51. EMBASE; pseudoseizure.ti,ab; 84 results. 52. EMBASE; 50 OR 51; 1323 results. 53. EMBASE; 42 AND 52; 106 results. 54. EMBASE; 53 [Limit to: Publication Year 2005-2012]; 74 results.		
PsychINFO	1. PsycINFO; non-epileptic.ti,ab; 331 results. 2. PsycINFO; nonepileptic.ti,ab; 636 results.	40	

	3. PsycINFO; "non epileptic".ti,ab; 331 results. 4. PsycINFO; psychogenic.ti,ab; 4387 results. 5. PsycINFO; dissociative.ti,ab; 4918 results. 6. PsycINFO; 1 OR 2 OR 3 OR 4 OR 5; 9738 results. 7. PsycINFO; (6 adj3 seizure*).ti,ab; 187 results. 8. PsycINFO; CLINICAL TRIALS/; 6016 results. 9. PsycINFO; random*.ti,ab; 108705 results. 10. PsycINFO; groups*.ti,ab; 323490 results. 11. PsycINFO; (doubl* adj3 blind*).ti,ab; 16279 results. 12. PsycINFO; (singl* adj3 blind*).ti,ab; 1339 results. 13. PsycINFO; EXPERIMENTAL DESIGN/; 8214 results. 14. PsycINFO; controlled.ti,ab; 67972 results. 15. PsycINFO; (clinical adj3 study).ti,ab; 6773 results. 16. PsycINFO; trial.ti,ab; 57237 results. 17. PsycINFO; "treatment outcome clinical trial".md; 21794 results. 18. PsycINFO; 8 OR 9 OR 10 OR 11 OR		

	12 OR 13 OR 14 OR 15 OR 16 OR 17; 496443 results. 19. PsycINFO; 7 AND 18; 53 results. 20. PsycINFO; 7 [Limit to: Publication Year 2005-2012]; 117 results. 21. PsycINFO; 19 [Limit to: Publication Year 2005-2012]; 40 results.		
Summary	**NA**	**NA**	

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