Adherence with psychotherapy and treatment outcomes for psychogenic nonepileptic seizures

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Neurology® 2019;92:e675-e679. doi:10.1212/WNL.0000000000006848

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Abstract

Objective

We conducted a prospective cohort study of patients with psychogenic nonepileptic seizures (PNES) to examine the association between adherence with psychotherapy and outcomes, including significant ($\geq 50\%$) reduction in PNES frequency, PNES freedom, improvement in quality of life, and reduction in emergency department (ED) utilization.

Methods

A total of 105 participants were referred to receive psychotherapy either at Brigham and Women's Hospital or with a local therapist. We called participants at 12–24 months follow-up and obtained detailed follow-up data from 93 participants (89%). Participants were considered adherent with psychotherapy if they attended at least 8 sessions within a 16-week period starting at the time of referral.

Results

Adherence with psychotherapy was associated with reduction in seizure frequency (84% in adherent group vs 61% in nonadherent, $p = 0.021$), improvement in quality of life ($p = 0.044$), and reduction in ED utilization ($p = 0.040$), with medium effect sizes; there was no difference in PNES freedom. The association between adherence and $\geq 50\%$ reduction in PNES frequency persisted when controlling for potential confounders in a multivariate model. Psychotherapy nonadherence was associated with baseline characteristics of self-identified minority status (odds ratio 7.47, $p = 0.019$) and history of childhood abuse (odds ratio 3.30, $p = 0.023$).

Conclusions

Our study is limited in that it cannot establish a causal relationship between adherence with psychotherapy and outcomes, and the results may not generalize beyond the single quaternary care center study site. Among participants with documented PNES, adherence with psychotherapy was associated with reduction in PNES frequency, improvement in quality of life, and decrease in ED visits.

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Go to [Neurology.org/N](https://www.neurology.org/N) for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Glossary

BWH = Brigham and Women's Hospital; ED = emergency department; EMU = epilepsy monitoring unit; OR = odds ratio; PNES = psychogenic nonepileptic seizures; QOLIE-10 = Quality of Life in Epilepsy-10.

Psychogenic nonepileptic seizures (PNES) are paroxysmal events involving involuntary movements or alterations of consciousness caused by psychological factors. PNES are highly disabling¹ and commonly encountered, with approximately one-third of patients admitted to epilepsy monitoring units (EMUs) diagnosed with PNES.²

Psychotherapy, and particularly cognitive-behavioral therapy, is effective in treating PNES.^{3,4} Yet 86% of patients drop out of behavioral health treatments within 17 months.⁵ Clinical experience suggests that PNES patients' nonadherence with psychotherapeutic treatment may be associated with worse outcomes, but this association has never been studied. We therefore conducted a prospective cohort study examining the association between adherence with psychotherapy and treatment outcomes. We hypothesized that adherence with psychotherapy would be associated with a higher responder rate, or proportion of participants with a $\geq 50\%$ reduction in PNES frequency.

Methods

From March 2013 to January 2016, we prospectively recruited consecutive patients, aged 18 and older, diagnosed with documented PNES by board-certified epileptologists via video-EEG capture of typical events. This corresponds to the highest degree of clinical certainty in the diagnosis of PNES, as per International League Against Epilepsy criteria.⁶ Patients with comorbid epileptic seizures were eligible so long as they could consistently distinguish their epileptic and psychogenic seizures as demonstrated on video-EEG. Our exclusion criteria included estimated IQ < 70 , active alcohol and drug use disorders, pregnancy, or severe medical illness expected to prevent regular participation in psychotherapy. A neuropsychiatrist, certified by the American Board of Psychiatry and Neurology and the United Council for Neurologic Subspecialties, prospectively collected baseline demographic, medical, and psychiatric data, including PNES frequency, quality of life (as assessed by the Quality of Life in Epilepsy-10 [QOLIE-10] instrument), and emergency department (ED) utilization in a semi-structured psychiatric interview. A separate semi-structured interview classified work prior to PNES by the Hollingshead⁷ occupation scale, as well as self-identified race and ethnicity by National Institute of Neurological Disease and Stroke common data elements.

All participants were referred for psychotherapy, either with a licensed social worker therapist at Brigham and Women's Hospital (BWH) or with a local therapist if the participant

already had an existing therapeutic relationship or lived > 1 –2 hours from BWH. Treatment at BWH consisted of a manualized regimen of 12 weekly hour-long mindfulness-based psychotherapy sessions.⁸ For all participants treated outside of BWH, the neuropsychiatrist called the local therapists to review the diagnosis and principles of treatment. All participants were also scheduled for 4 additional appointments with the neuropsychiatrist at BWH.

Based on review of prior studies,³ participants were contacted once between 12 and 24 months following the delivery of the diagnosis and assessed for adherence with psychotherapy, PNES frequency, quality of life (as measured by the QOLIE-10), and ED utilization. Participants who could not be contacted after 7 phone calls and a mailed letter were excluded from the analysis. Psychotherapy adherence was confirmed with therapists for 87 participants (94%). Participants were considered adherent with psychotherapy if they attended at least 8 sessions over 16 weeks, starting at the time of referral. The decision to dichotomize adherence and the specific cutoff of 8 sessions was based on review of preliminary data and prior studies showing maximal rate of change in symptom severity through psychotherapy session 8.^{3,9}

The primary outcome was responder rate: the proportion of participants with a $\geq 50\%$ reduction in weekly PNES frequency, measured over the prior week at baseline and follow-up. Power analysis suggested at least 42 participants each in adherent and nonadherent groups to detect an anticipated difference in proportions of 0.60 in the adherent group vs 0.30 in the nonadherent group with power 0.80 and α 0.05. Secondary outcomes included 3-month PNES freedom, change in quality of life, and change in number of monthly ED visits. Outcomes were assessed for differences between adherent and nonadherent participants using the Fisher exact test and Student *t* test. We examined the possibility that association between the primary outcome ($\geq 50\%$ reduction in PNES frequency) and adherence was confounded by performing multivariate logistic regression.

Finally, we conducted multivariate logistic regression to evaluate baseline covariates (table 1) as potential predictors of nonadherence with psychotherapy. All statistical analyses were performed using Stata IC v14.1 (StataCorp, College Station, TX).

Standard protocol approvals, registrations, and patient consents

The BWH institutional review board approved the study. All participants provided written informed consent.

Table 1 Demographics and baseline characteristics

Demographics	Values (n = 105)
Female, n (%)	89 (85)
Age, y, mean (SD; range)	39.1 (14.3; 18–82)
Race/ethnicity, n (%)	
White, non-Hispanic	79 (75)
Hispanic	13 (12)
African American	12 (11)
Other	2 (2)
Marital status, n (%)	
Single	41 (39)
Married	40 (38)
Separated/divorced	15 (14)
Live-in partner	7 (7)
Widowed	2 (2)
Employment, n (%)	
Unemployed, collecting disability	43 (41)
Unemployed, not on disability	22 (21)
Employed part-time	19 (18)
Employed full-time	11 (10)
Student	8 (8)
Retired	2 (2)
Occupational status prior to PNES (Hollingshead occupational scale, n = 84), median (IQR; range)	5 (2–7; 1–9)
Household income (n = 58), median (IQR; range)	\$42,500 (\$20–\$90,000; \$5,900–\$400,000)
Psychiatric history	
Quality of life (QOLIE-10), mean (SD; range)	28.2 (8.4; 12–47)
Beck Depression Inventory II (n = 78), mean (SD; range)	16.6 (11.5; 0–48)
Referred to psychotherapy at Brigham and Women's Hospital, n (%)	46 (44)
Weekly PNES frequency, median (IQR; range)	2 (0.6–10; 0–350)
Delay to diagnosis, mo, median (IQR; range)	12 (2.75–60; 0–612)
History of suicide attempt, n (%)	22 (21)
Prior psychiatric hospitalization, n (%)	37 (35)
Current substance use, n (%)	13 (12)
Cognitive symptoms, n (%)	77 (73)
In psychotherapy at diagnosis, n (%)	24 (23)
Psychiatric/seizure comorbidities, n (%)	

Table 1 Demographics and baseline characteristics
(continued)

Depression	80 (76)
Anxiety disorder	63 (60)
PTSD	55 (52)
Panic disorder	45 (43)
Personality disorder	36 (34)
Borderline personality disorder	15 (14)
Psychotic disorder	16 (15)
Any psychiatric comorbidity	99 (94)
Comorbid epilepsy	14 (13)
Abuse history, n (%)	
Emotional abuse	53 (50)
Physical abuse	45 (43)
Sexual abuse	44 (42)
Childhood abuse	50 (48)
Any abuse	72 (69)

Abbreviations: IQR = interquartile range; OCD = obsessive-compulsive disorder; PNES = psychogenic nonepileptic seizure; PTSD = posttraumatic stress disorder; QOLIE-10 = Quality of Life in Epilepsy 10-item inventory.

Data availability

For any data not published within this article, anonymized data will be shared by request from any qualified investigator.

Results

A total of 105 participants were enrolled (table 1) with 93 (89%) providing 12–24 months (mean 18.6 ± 1.9 months) follow-up data. There were no statistically significant differences in baseline characteristics between participants who completed follow-up and those who did not. There was no difference in follow-up time between adherent (18.5 ± 1.9 months) and nonadherent (18.8 ± 2.0 months) participants ($p = 0.467$). Of 93 participants providing follow-up, 72 (77%) attended at least one session of psychotherapy and 37 (40%) met criteria for adherence. Adherence was similar among those treated at BWH (17 participants, 39%) and by outside therapists (20 participants, 41%, $p = 1.000$).

When analyzed by adherence with psychotherapy, the responder rate—the proportion of participants with $\geq 50\%$ reduction in PNES frequency—was 61% (34 participants) among those who were nonadherent with psychotherapy, vs 84% (31 participants) among those who were adherent ($p = 0.021$).

In a univariate screen of 43 baseline characteristics (including all covariates listed in table 1), $\geq 50\%$ reduction in PNES frequency was associated with adherence with psychotherapy,

Table 2 Predictors of significant ($\geq 50\%$) decrease in psychogenic nonepileptic seizure (PNES) frequency at 12–24 months follow-up

	Univariate odds ratio (95% CI)	<i>p</i> Value	Multivariate odds ratio (95% CI)	<i>p</i> Value
Age	1.00 (0.96–1.03)	0.803	0.99 (0.95–1.03)	0.701
Female	0.34 (0.07–1.63)	0.177	0.59 (0.11–3.25)	0.548
Adherent	3.34 (1.20–9.32)	0.021	3.46 (1.07–11.18)	0.038 ^a
Weekly frequency	1.14 (1.01–1.29)	0.038	1.12 (1.001–1.26)	0.047 ^a
Borderline personality disorder	0.34 (0.13–0.87)	0.024	0.38 (0.12–1.17)	0.093
Minority	0.23 (0.07–0.68)	0.008	0.40 (0.10–1.52)	0.176

Abbreviation: CI = confidence interval.

Univariate screen includes 43 baseline characteristics, including all covariates listed in table 1. Multivariate model includes age, female sex, plus covariates found to be associated with $\geq 50\%$ decrease in PNES frequency in the univariate screen with $p < 0.05$.

^a Significant, with $p < 0.05$.

lack of self-identified minority status, weekly PNES frequency, and absence of borderline personality disorder (table 2). Self-identified minority status included Hispanic ethnicity, black race, and other race/ethnicity, excluding white, non-Hispanic. When these 4 covariates were included in a multivariate model with sex and age as potential confounders, only 2 covariates demonstrated a significant association with responder rate: adherence with psychotherapy (odds ratio [OR] 3.46, $p = 0.038$) and weekly seizure frequency (OR 1.12, $p = 0.047$) (table 2).

Regarding secondary outcomes, 57% of nonadherent patients were PNES-free for at least 3 months at follow-up, vs 70% of adherent patients ($p = 0.269$). For change in quality of life, as assessed by change in QOLIE-10 score, nonadherent participants had a mean 2.8 ± 9.0 point improvement on the 10–50 point scale, while adherent participants had a 7.2 ± 8.6 point improvement ($p = 0.044$, Cohen d 0.50). In terms of change in monthly ED visits, nonadherent participants had a mean increase of 0.4 ± 2.2 ED visits, whereas adherent participants had a mean decrease of 0.5 ± 1.3 ED visits per month ($p = 0.040$, Cohen d 0.44).

We next performed multivariate logistic regression to identify predictors of nonadherence with psychotherapy. In the univariate screen of 43 baseline characteristics, nonadherence was associated with being on disability at the time of diagnosis, lower occupational status (Hollingshead occupational scale), self-identified minority status, and a history of childhood abuse (table 3). When added to a multivariate model with age and sex as potential confounders, only self-identified minority status (OR 7.47, $p = 0.019$) and a history of childhood abuse (OR 3.30, $p = 0.023$) remained as independent predictors of nonadherence.

Discussion

This study examines associations between psychotherapy adherence and outcomes among patients with PNES. Nonadherence rates (60%) were worse than reported short-term (13%) or long-term (42%) nonadherence rates among depressed patients undergoing psychotherapy.¹⁰ Our findings showed an association between adherence with psychotherapy

Table 3 Predictors of nonadherence

Covariate	Univariate screen		Multivariate model	
	Odds ratio (95% CI)	<i>p</i> Value	Odds ratio (95% CI)	<i>p</i> Value
Age	1.04 (1.003–1.07)	0.035 ^a	1.02 (0.99–1.07)	0.200
Female	1.16 (0.37–3.67)	0.799	1.07 (0.30–3.87)	0.909
On disability	3.38 (1.32–8.66)	0.011 ^a	1.33 (0.38–4.66)	0.653
Occupational status prior to PNES	0.83 (0.69–0.98)	0.031 ^a	0.81 (0.65–1.02)	0.070
Self-identified minority	6.73 (1.44–31.53)	0.016 ^a	7.47 (1.39–40.13)	0.019 ^a
Childhood abuse	3.08 (1.30–7.31)	0.011 ^a	3.30 (1.14–7.65)	0.023 ^a

Abbreviations: CI = confidence interval; PNES = psychogenic nonepileptic seizures.

Univariate screen includes 43 baseline characteristics, including all covariates listed in table 1. Multivariate model includes age, female sex, plus covariates found to be associated with nonadherence in the univariate screen with $p < 0.05$.

^a Significant, with $p < 0.05$.

and $\geq 50\%$ reduction in PNES frequency at 12–24 months of follow-up. This association persisted even when controlling for potential confounders in a multivariate model. The OR in the multivariate analysis remained at 3.81, which is considered a medium effect size.¹¹ Similarly, our study showed that adherence was associated with secondary outcomes of improvement in quality of life and reduction in monthly ED utilization. In both cases, the Cohen *d* was consistent with a medium effect size. There was no significant association between adherence and achieving 3-month PNES freedom. Improvements among nonadherent participants may be due to reversion to the mean (patients with PNES tend to present to medical attention in crisis and improve with time) and partial treatment (nonadherent patients attended a median of 2.5 psychotherapy sessions).

In addition to the association between treatment adherence and outcomes, our study demonstrated that baseline characteristics of self-identified minority status and a history of childhood abuse predicted nonadherence with psychotherapy. Therefore, minority patients and patients with a history of childhood abuse may particularly benefit from interventions to enhance adherence with psychotherapy. Disability and lower occupational status were associated with nonadherence in the univariate analysis, but not in the multivariate analysis, which might suggest that these are markers of minority status or childhood abuse rather than independent predictors of nonadherence.

Our study is limited in that it does not establish a causal relationship between adherence with psychotherapy and improved outcomes, only an association. Randomized controlled trials of interventions to improve psychotherapy adherence will be necessary to establish a clear causal link between treatment adherence and outcomes. In addition, our study was performed in a single quaternary care center with a special interest in PNES. This center utilizes treatment resources that may not be available in other settings, which may limit the findings' generalizability. Our results should ideally be replicated in a multicenter study spanning different treatment environments. Internal validity of the study is also limited by heterogeneous psychotherapy, variable follow-up time, and subjective measurements of PNES frequency, which allows recall bias. Our study is further limited by a lack of data on the types of therapy performed by outpatient therapists, and the use of psychotropic and anti-seizure medications during the course of psychotherapy.

Nonetheless, our results showed that among patients with PNES, adherence with psychotherapy was associated with reduction in PNES frequency, improvement in quality of life, and decrease in ED visits. Self-identified minority status and a history of childhood abuse were independent risk factors for nonadherence. Neurologists and behavioral

health care providers should collaborate to develop and test new interventions to improve PNES patients' adherence to efficacious psychotherapies.

Author contributions

B. Tolchin: drafting the manuscript, study concept and design, analysis and interpretation of data, acquisition of data, statistical analysis, obtaining funding. B.A. Dworetzky: revising the manuscript for content, study concept and design, analysis and interpretation of data, study supervision and coordination, obtaining funding. S. Martino: revising the manuscript for content, analysis and interpretation of data. H. Blumenfeld: revising the manuscript for content, analysis and interpretation of data. L.J. Hirsch: revising the manuscript for content, analysis and interpretation of data. G. Baslet: revising the manuscript for content, study concept and design, analysis and interpretation of data, study supervision and coordination, acquisition of data, obtaining funding.

Study funding

This study was supported by the American Academy of Neurology/American Brain Foundation, Practice Research Scholarship.

Disclosure

B. Tolchin received salary support through the American Academy of Neurology/American Brain Foundation, Practice Research Scholarship. B. Dworetzky, S. Martino, H. Blumenfeld, L. Hirsch, and G. Baslet report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication history

Received by *Neurology* January 10, 2018. Accepted in final form October 11, 2018.

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