



Self and informant report ratings of psychopathology in genetic generalized epilepsy



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ARTICLE INFO

Article history:

Received 6 July 2016

Revised 23 September 2016

Accepted 7 November 2016

Available online xxxx

Keywords:

Genetic generalized epilepsy

Psychopathology

Comorbidity

ABSTRACT

The psychological sequelae of genetic generalized epilepsies (GGE) is of growing research interest, with up to a third of all adults with GGE experiencing significant psychiatric comorbidity according to a recent systematic review. A number of unexplored questions remain. Firstly, there is insufficient evidence to determine relative prevalence of psychopathology between GGE syndromes. Secondly, the degree to which self-report and informant-report questionnaires accord in adults with epilepsy is unknown. Finally, while epilepsy severity is one likely predictor of worse psychopathology in GGE, evidence regarding other possible contributing factors such as epilepsy duration and antiepileptic drugs (AEDs) has been equivocal. The potential impact of subclinical epileptiform discharges remains unexplored.

Self-report psychopathology symptoms across six DSM-Oriented Subscales were prospectively measured in 60 adults with GGE, with informant-report provided for a subset of 47. We assessed the burden of symptoms from both self- and informant-report, and the relationship between clinical epilepsy variables and self-reported symptoms.

Results showed elevated symptoms in almost half of the sample overall. Depression and anxiety were the most commonly reported types of symptoms. There was a trend towards greater symptoms endorsement by self-report, and relatively modest interrater agreement. Symptoms of ADHD were significantly positively associated with number of AEDs currently prescribed. Other psychopathology symptoms were not significantly predicted by epilepsy duration, seizure-free duration or total duration of epileptiform discharges over a 24-hour period.

The high prevalence of psychological needs suggests that routine screening of psychopathology and provision of psychoeducation may be essential to improving patient care and outcomes. Further investigation is required to better understand predictive and causal factors for psychopathology in GGE.

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1. Introduction

The cognitive, psychological, and psychosocial sequelae of the genetic generalized epilepsies (GGE) is a topic of recent research interest, with accumulating evidence suggesting that GGE is not the benign condition as once thought [1,2]. A recent systematic review found that clinically significant psychiatric comorbidity may occur in up to half of all children and a third of all adults with the condition [3]. As is the case with psychiatric symptoms in the general population, the most common comorbidities in adults with GGE were depression and anxiety, followed by conditions such as addiction, impulse control, and psychotic

disorders [3,4]. It is unclear whether this survey encompasses the full burden of undiagnosed and untreated dimensional psychopathological symptoms or is limited to patients with existing diagnoses, since many studies did not prospectively measure symptoms.

The significance of these outcomes for quality of life in epilepsy is well-recognized, and improving these patient outcomes has become an important clinical goal [5,6]. Indeed, several authors have posited that psychological and behavioral comorbidities such as mood disorders are intimately related to the epilepsy, and that the relationship is best understood as bidirectional; i.e. epilepsy is a risk factor for mood disorder and mood disorder is a risk factor for epilepsy [7,8]. While a neurobiological underpinning to psychopathology is considered likely, specific causal relationships are rarely identified, which may be due - at least in part - to the heterogeneity of epilepsy as a condition and that studies have mostly focused on epilepsy-related risk factors [9]. Epilepsy severity has been identified as one likely predictor of poor

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psychosocial outcomes in adults with GGE, with findings of other factors such as longer epilepsy duration and antiepileptic drug (AED) treatment proving equivocal - both negative and null associations with psychopathological outcome have been reported [3]. Finally, while subclinical epileptiform discharges (ED) are known to disrupt cognitive functioning in epilepsy and bear a relationship to depression in epilepsy [10, 11], their potential role in mood and psychosocial functioning in GGE and other epilepsies remains unexplored.

In a large, prospectively recruited sample of adults with GGE, we aimed to a) assess the burden of psychopathology across different symptom types on the basis of both categorical and dimensional outcomes; b) consider a self- and informant-report version of a comprehensive symptom severity questionnaire; c) examine the relationship between ED and other clinical variables and psychopathological symptom ratings. On the basis of previous research, we anticipated that the questionnaire would identify a 30% prevalence of people with GGE vulnerable to psychopathological comorbidity.

2. Methods

2.1. Participants and procedure

As part of a larger study regarding the prognosis and EEG characteristics of GGE [12], adults with EEG-confirmed GGE completed the Adult Self-Report form of the Achenbach System of Empirically Based Assessment. We established the diagnosis of GGE and classified patients into childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), and generalized epilepsy with generalized tonic-clonic seizures (GTCS) only (GTCSO) according to ILAE criteria [13,14]. Patients who did not fulfill the criteria of the four major syndromes were classified as “GGE unspecified”. All medical records including EEG and neuroimaging were reviewed independently by two epilepsy specialists (authors WD & US) with any discordance on diagnosis resolved by consensus based on ILAE criteria. The Achenbach System comprises screening questionnaires that produce DSM-Oriented Subscales that are designed to be consistent with DSM-IV diagnostic criteria for depression, anxiety, somatization, avoidant personality, attention deficit, and antisocial personality [15]. The Achenbach System is intended to screen for these domains of functioning, not to provide psychiatric diagnosis such as that resulting from a structured clinical interview. Participating patients were asked to provide the Adult Behavior Checklist, the informant version of the same form, to a partner or close friend to complete. Frequencies of elevated symptoms in the GGE sample were contrasted with 7% prevalence in the normative sample of the Achenbach measure. Cognitive functioning data were collected using the Woodcock Johnson III Tests of Ability [16] and compared to Australian age-based norms provided by the test software.

History of psychiatric diagnosis and prescription of psychotropic medication information was collected from the medical record. Epilepsy history was collected according to the research protocol and included seizure type, frequency, epilepsy age of onset, and AED currently used. In addition, patients underwent 24-hour ambulatory EEG following standard protocol as previously described [12]. An experienced EEG reader (author US) reviewed all recordings with ProFusion 4 software (Compumedics Ltd., Melbourne, Australia). Ten-second pages were reviewed page-by-page on longitudinal bipolar montage with 0.5 to 70 Hz bandwidth. When an epileptiform abnormality was detected, detailed analysis of the waveform was undertaken on common average referential montage [17]. A measuring tool incorporated in the software was used to manually measure amplitude and duration of discharges.

Participants were excluded if they had another significant neurological condition, or structural abnormalities apparent on brain MRI. This research was approved by the Human Ethics Research Committees of participating sites. Participants provided written informed consent as per the Declaration of Helsinki.

2.2. Statistical analysis

To maximize the representativeness of the final dataset, data were retained from all participants, even if they were unable to provide an informant report questionnaire. The equivalence of the demographic characteristics of the group with both self- and informant-report available (the paired data group) and the total sample was evaluated using *t*-tests and chi-squared tests as appropriate. One sample *t*-tests with Bonferroni corrections were used to compare GGE scores with those of the Achenbach measure normative sample. Multivariate analysis of variance (MANOVA) tests on the paired data group were used to examine the concordance of self- and informant-report T-scores across the six DSM-Oriented Subscales and appropriately control for the family-wise error rate. Kappa statistics were calculated for comparison of interrater classifications of normal, borderline-clinical, and clinical range classifications. Finally, associations between epilepsy variables and psychopathology symptom endorsement were assessed using Spearman correlation coefficients and multiple linear regression. We used an alpha level of 0.05 for all statistical tests.

3. Results

3.1. Patient characteristics

Prospective recruitment yielded 60 people with EEG-confirmed GGE (18 males; mean age: 31.6, SD: 11.0). For a subset of 47, a family member or close friend also completed the corresponding Adult Behavior Checklist. The majority of informant-report questionnaires were completed by spouses/partners (43%), and parents or adult children (36%). Smaller proportions were completed by friends (8%), siblings (4%) or were not reported (9%). The group with both self- and informant-report data available (the paired data group) was compared to those with only self-report data available. A higher proportion of males was in the self-report only group than in the paired data group ($\chi^2(1) = 5.41, p = 0.02$). No other significant differences were found on any demographic or epilepsy variables to suggest that these groups differed systematically (see Supplementary Table 1 for these analyses). For this reason, subsequent analyses were conducted on the entire sample ($n = 60$).

Aside from a slight bias against CAE due to our predominantly adult sample, GGE syndromes were distributed approximately evenly within the sample (Table 1a). The majority of patients were prescribed AED treatment (95.2%), and 50% had a history of absence seizures (Table 1b). Seizure-free duration ranged from 1 to 9855 days (median: 129, interquartile range: 660 days). Detailed clinical data were unavailable from a small minority of patients (available n marked in Table 1b). A summary with one-sample *t*-tests comparing patient scores to age-

Table 1a
Demographic characteristics.

Variables	Total sample ($n = 60$)	Paired data ($n = 47$)	Unpaired self-report only data ($n = 13$)	Sig. (2-tailed)*
Age (years)				
Range	18–58	18–58	18–57	–
Mean (standard deviation)	31.62 (10.95)	31.11 (10.80)	33.46 (11.73)	NS
Gender (n)				
M	18 (30%)	18 (38.3%)	13 (100%)	$p = 0.02$
F	42 (70%)	29 (61.7%)	0 (0%)	
Syndrome (n)				
CAE	6 (10%)	6 (12.8%)	0 (0%)	NS
JAE	17 (28.3%)	13 (40.4%)	4 (30.8%)	
JME	16 (26.7%)	12 (25.5%)	4 (30.8%)	
GTCSO	20 (33.3%)	16 (34.0%)	4 (30.8%)	
Other	1 (1.7%)	0 (0%)	1 (0.8%)	

* These tests compare paired data group ($n = 47$) with self-report only group ($n = 13$) to establish equivalence of these.

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