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FULL-LENGTH ORIGINAL RESEARCH

Impulsivity and seizure frequency, but not cognitive deficits, impact social adjustment in patients with juvenile myoclonic epilepsy

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Summary

Purpose: Despite growing evidence on the occurrence of poor psychosocial adjustment, to the moment there is no formal assessment of social adjustment (SA) using a validated instrument developed and standardized for this purpose in patients with juvenile myoclonic epilepsy (JME). We aimed to: (1) verify social adjustment in patients with JME with an objective scale and; (2) identify whether clinical variables, impulsiveness, and neuropsychological profile are associated with worse social adjustment.

Methods: We prospectively evaluated 42 patients with an unequivocal diagnosis of JME and 42 controls. The inclusion criteria for patients and controls included age range from 16 to 40 years and an estimated intelligence quotient (IQ) ranging from 85 to 110. One trained neuropsychologist administered the scales and tests in a standard sequence. Social Adjustment was evaluated by The Self-Report Social Adjustment Scale (Weissman & Bothwell, 1976), a 42-item scale, measuring performance in seven major areas: work; social and leisure activities; relationship with extended family; marital role as a spouse; parental role; membership in the family unit; and economic adequacy. Impulsivity was assessed by using the Temperament and Character Inventory (Cloninger, 2000). Patients with JME and control subjects were evaluated with a comprehensive battery of neuropsychological tests evaluating executive and memory functions. We evaluated the age at onset; time from onset to seizure control with antiepileptic drugs (duration of epilepsy); seizure control; frequency of myoclonic seizures; frequency of generalized tonic–clonic GTC seizures; frequency of absence seizures; family history of epilepsy; family history of psychiatric disorders; and personal history of psychiatric disorders.

Key Findings: The score on Global Social Adjustment was worse than controls ($p = 0.001$), especially on the factors: Work ($p = 0.032$); Extended Family ($p = 0.005$). Higher Novelty Seeking (NS) scores were significantly correlated with worse on Global ($p = 0.002$); Work ($p = 0.001$) and Leisure ($p = 0.003$). There was no correlation between cognitive performance and Social Adjustment Scale (SAS) factors. Higher seizure frequency—myoclonic ($p = 0.005$) and GTC ($p = 0.035$)—were correlated with higher scores on factor Work of SAS.

Significance: Our findings suggest that patients with JME have worse social adjustment in two relevant aspects of their lives—work and familiar relationship. In this series of patients with JME, higher seizure frequency and impulsive traits, but not cognitive performance, were correlated with worse social adjustment.

KEY WORDS: Juvenile myoclonic epilepsy, Neuropsychologic tests, Impulse control, Social adjustment, Quality of life.

In the current context of *treating beyond seizures*, psychosocial aspects of epilepsy are particularly relevant. People with epilepsy face social issues such as family problems, reduced social interactions, decreased job opportunities, low self-esteem, and high levels of anxiety and depression (Jacoby et al., 1996; Gaitatzis et al., 2004a,b), even with controlled seizures (Specht, 2001).

Quality of life (QOL) is defined as "an individual's perception of their position in life in the context of the culture and value system in which they live and in relation to their goals, expectations, standards, and concerns." (World Health Organization, 1990). Therefore, measures of QOL evaluate the patient's personal and subjective perceptions.

On the other hand, social adjustment is defined as the interaction between the individual and his social environment (Gorenstein et al., 2002). Social adjustment is

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evaluated with an objective and quantitative scale, and patients are compared to matched controls, which is not allowed by QOL questionnaires. Therefore, patients who perceive their lives as satisfactory may present low scores in an objective instrument of social adjustment.

Despite evidence of poor psychosocial adjustment (Janz & Christian, 1957; Lund et al., 1976; review in Hommet et al., 2006), to date there is no formal assessment of social adjustment using a validated instrument developed and standardized for this purpose in patients with juvenile myoclonic epilepsy (JME).

We postulate that social adjustment scales can provide relevant and detailed information on patients' social interaction with their environment. Therefore, in this study, our first endpoint was to verify social adjustment in patients with JME with an objective scale. Our second endpoint was to identify whether clinical variables, impulsiveness and neuropsychological profile are associated with worse social adjustment.

Methods

Study population

Patients

We prospectively evaluated 42 consecutive patients with an unequivocal diagnosis of JME, according to the International League Against Epilepsy (ILAE – Commission on Classification & Terminology of the International League Against Epilepsy, 1989) proposal for syndrome classification.

Only patients with classic JME were included, since different electroclinical subtypes of JME, such as childhood absence epilepsy persisting and evolving into JME, JME with adolescent onset pyknoleptic absence, and JME with astatic seizures were excluded.

Controls

A control group of 42 healthy volunteers were matched to the patients as to age, gender, schooling, and socioeconomic status. A neurologist and a psychiatrist ruled out individuals with psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (American Psychiatric Association, 2000) using Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and with previous or current history of neurologic disorders.

The inclusion criteria for patients and controls included an age range from 16 to 40 years and an estimated IQ ranging from 85 to 110. The criteria for exclusion were clinical signs of drug intoxication or any condition leading to cognitive impairment; diagnosis of a psychiatric disorder; alcohol or drug abuse; and any brain-related surgical intervention.

Instruments

All patients signed an informed consent form approved by the local ethics committee.

Social adjustment scale

The Self-Report Social Adjustment Scale – SAS (Weissman & Bothwell, 1976; Gorenstein et al., 2002) is a 42-item scale, measuring performance over the preceding 2 weeks in seven areas: work (as a worker, housewife or student); social and leisure activities; relationship with extended family; marital role as a spouse; parental role; membership in the family unit; and economic adequacy. The overall score is obtained by summing up the scores of all items assessed and dividing that sum by the total number of items. Each item is scored on a five-point scale, the higher scores being indicative of greater impairment (1, normal; 5, severe maladjustment).

Impulsivity evaluation

Impulsivity was assessed by using the Temperament and Character Inventory- TCI (Cloninger et al., 1993; Cloninger, 2000). We use the factor of temperament Novelty Seeking (NS) to assess Impulsivity (Moschetta et al., 2011). A trained psychiatrist evaluated patients and controls using a structured psychiatric interview.

Neuropsychological evaluation

Patients with JME and controls were evaluated with a comprehensive battery of neuropsychological tests, selected from those included in collections of neuropsychological tests (Spreen & Strauss, 1991; Lezak, 2005), studies of generalized epilepsies and JME (Hommet et al., 2006), and studies correlating neuropsychological test with frontal lobe functions (Weinberger et al., 1992) (Fig. S1).

The IQ of each subject was estimated with the Matrix Reasoning and Vocabulary subtests of the Wechsler Abbreviated Intelligence Scale (Wechsler, 1999).

Clinical variables

We evaluated the age at onset; time from onset to seizure control with antiepileptic drugs (duration of epilepsy); seizure control; frequency of myoclonic seizures; frequency of generalized tonic–clonic (GTC) seizures; frequency of absence seizures, family history of epilepsy and; family history of psychiatric disorders.

Statistical analysis

The descriptive statistics included means and standard deviations, calculated for each variable. Demographic variables were compared using the chi-square test in order to verify that the two groups were matched. The differences between the two groups in terms of the estimated IQ were analyzed using independent *t*-tests for continuous variables. We compared performance on the SAS scores

using analysis of covariance in which the estimated IQ was the covariate. The level of significance was set at $p \leq 0.05$.

The correlation between SAS scale and impulsivity measures, neuropsychological tests and clinical variables were compared using Pearson's correlation coefficient. The level of significance was set at $p \leq 0.05$. For the statistical analysis, we used the Statistical Package for the Social Sciences, version 11.0 for Windows (SPSS Inc., Chicago, IL, U.S.A.).

Results

Twenty patients (47.6%) were male with mean age of 26.6 (standard deviation [SD] 8.4; ranging from 16 to 40 years); 10.1 (SD 1.8) years of education and estimated IQ of 91.5 (SD 9.9). Nineteen patients (45.2%) were seizure–free and 15 (35.7%) had myoclonic seizures. Eight (19%) patients had sporadic GTC seizures. Mean age of onset was 14 years (SD 4.4). The epilepsy duration considering epilepsy onset and treatment was 17.8 years. All patients received sodium valproate/divalproate.

A control group of 42 healthy volunteers (45.2% male; mean age of 27 years [SD 8.5]) were matched to the patients as to gender (chi-square test: $p = 0.827$), age (Student's *t*-est: $p = 0.959$), years of education (Student's *t*-est: $p = 0.653$), and socioeconomic status.

Social adjustment

The score on Global Social Adjustment was worse than for controls ($p = 0.001$). There were significant differences on the factors: Work ($p = 0.032$) and; Extended Family ($p = 0.005$) (Table 1). No significant differences were found on other factors.

Impulsivity and psychiatric evaluation

Higher NS scores were significantly correlated with global ($p = 0.010$), work ($p = 0.044$), and social/leisure ($p = 0.024$); but not with extended family ($p = 0.155$), marital relationship ($p = 0.220$), parental relationship ($p = 0.195$), family unit ($p = 0.100$), and economic condition ($p = 0.115$).

Presence of personality disorder related to impulse control, diagnosed by psychiatric evaluation, was correlated with higher scores on Marital Relationship ($p = 0.031$) and Global Measures of SAS ($p = 0.042$).

Table 1. Comparison of SAS scores between JME and controls

	JME (n = 42) μ ± SD	Controls (n = 42) μ ± SD	p-Value (*t*-test)
Global	2.06 ± 0.51	1.65 ± 0.39	**0.001**[b]
Work	2.14 ± 0.72	1.42 ± 0.35	**0.032**[b]
Social and leisure	1.87 ± 0.42	1.80 ± 0.54	0.228[a]
Extended family	1.89 ± 0.47	1.64 ± 0.49	**0.005**[a]
Marital	1.85 ± 0.71	1.69 ± 0.47	0.670[a]
Parental	1.62 ± 0.53	1.43 ± 0.50	0.409[a]
Family unit	1.76 ± 0.42	1.88 ± 0.55	0.565[a]
Economic condition	2.45 ± 1.37	1.76 ± 0.95	0.059[b]

Bold entries indicate $p \leq 0.05$.

Neuropsychological evaluation

There was no correlation between cognitive tests that evaluated executive, attention and memory functions, and SAS factors (Table S1).

Clinical variables

Higher seizure frequency—myoclonic ($p = 0.005$) and GTC ($p = 0.035$)—were correlated with higher scores on factor Work of SAS (Table S2).

Discussion

This is the first study addressing social functioning of patients with JME using the Social Adjustment Scale. This approach provides a unique opportunity to compare patients and healthy controls. Furthermore, this standardized instrument makes use of objective questions on the subject's life in many ways.

This was a prospective, controlled, and transverse study with matched controls. In addition, our sample of patients was homogeneous, since restrictive inclusion criteria (e.g., age range from 18 to 40 years and IQ from 85 to 110), and only patients with classic JME were included. Patients with different electroclinical subtypes of JME, which might influence prognosis, were excluded.

Some limitations of the current study must be considered. The presence of restrictive criteria of inclusion may create a bias, and these patients may not represent those with non-classical forms of JME or higher IQ. In addition, this study comprised a small sample size of patients referred to a tertiary center that may not represent patients of unselected population (Cornaggia et al., 2007).

Patients with JME had worse performance than controls, considering overall social adjustment, work, and family relationship.

One similarity between patients with JME and those with TLE, previously described by our group (Gois et al., 2011), is the work-related question. It is reasonable to state that work seems to be affected in patients with different types of epilepsy, including "benign" forms, such as JME. Work seems to be a major concern in different studies on epilepsy. The work-related problems are associated with activity limitations, fear of losing their jobs, and expectations of a different type of work (Salgado & Souza, 2002).

Patients with JME and higher seizure frequency had worse performance in factor work. Higher frequency of

seizures can result in absences, sick leaves, and stigma. Among the factors related to unemployment are comorbidity with psychiatric disorders, intellectual impairment, and the limitations caused by seizures (Facure et al., 1992). Presence of seizures in social circumstances reduces social interaction and compromises the quality of interpersonal relationships (Woodward, 1982).

In our work with temporal lobe epilepsy (TLE) (Gois et al., 2011), seizure frequency was not related to work; however, in this group all patients had refractory epilepsy. Most patients with JME were controlled with monotherapy.

Beyond work, family relationship was impaired in patients with JME. Epilepsy can generate negative reactions in family members (Facure et al., 1992). Individuals with epilepsy often feel stigmatized, marry less, and have more relationship difficulties (Levin et al., 1988; Cramer, 1994; Baker et al., 1998).

Presence of psychiatric disorders and cognitive deficits have been identified as predictors of poorer QOL in patients with epilepsy, especially those with refractory epilepsy (Perrini et al., 1995; Choi-Kwon et al., 2003; Boylan et al., 2004; Loring et al., 2004; Kwan et al., 2009).

In patients with JME, cognitive performance was not related to social adjustment scores. This represents a major difference between this work with JME and our previous work with TLE. In TLE (Gois et al., 2011), attention and verbal memory dysfunction were correlated with social adjustment. Cognitive deficits in TLE are very relevant and therefore its impact is recognized (Giovagnoli & Avanzini, 2000). It seems reasonable to postulate that although cognitive deficits are well-described in JME (Swartz et al., 1996; Sonmez et al., 2004; Pascalicchio et al., 2007; Piazzini et al., 2008; Moschetta & Valente, 2012), they are more subtle than in TLE, especially memory, and are not independent predictors of impaired social functioning.

On the other hand, psychiatry disorders and impulsive traits had a relevant impact on SA, regarding different aspects such as leisure, marital, work, and overall social adjustment.

Personality traits and personality disorders are described in JME (Gélisse et al., 2001; de Araújo Filho et al., 2007; Moschetta et al., 2011). Social adaptation issues have been identified in JME (Janz & Christian, 1957; review in Hommet et al., 2006).

Poor impulse control leads to maladaptive behaviors and predicts greater difficulty in solving social problems and acquiring social skills (Green, 1996). Corroborating these data, we found that better impulse control was significantly associated with higher social functioning in patients with JME.

In conclusion, we observed that patients with JME have worse SA in two relevant aspects of their lives—work and relationship with family. Although this study comprises a small sample of patients with JME, higher seizure frequency and impulsive traits, but not cognitive performance, were correlated with worse social adjustment.

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Disclosure

None of the authors report has any conflict of interest to disclosure. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Tests and functions of neuropsychological evaluation.

Table S1. Pearson correlation between neuropsychological tests and SAS scores of patients with JME.

Table S2. Influence of clinical variables on the overall scores in the SAS of patients with JME.