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BRIEF COMMUNICATION

Aggressive behavior and epilepsy: A multicenter study

***Ada Piazzini, †‡Francesca Bravi, †Valeria Edefonti, *Katherine Turner, *Aglaia Vignoli, †Monica Ferraroni, and *Maria Paola Canevini**

***Epilepsy Center, Neurology II, St. Paolo Hospital, Milan, Italy; †Section of Medical Statistics and Biometry G.A. Maccaro, Department of Clinical Sciences and Community Health L. Devoto, University of Milan, Milan, Italy; and ‡Department of Epidemiology, Mario Negri Institute for Pharmacological Research, Milan, Italy**

Summary

The aim of this study is to describe aggressiveness in the epilepsy population and to identify possible relationships between this type of behavior and clinical and sociodemographic variables. Aggressive responses were measured by the Aggression Questionnaire (AQ), a standardized and validated instrument, which was administered to 503 patients from nine Italian centers for the care of epilepsy. Aggressive behavior in patients with epilepsy was different from that in the normal Italian population. After adjustment for age and sex, when appropriate, the following variables significantly affected aggressiveness: presence of compromised intellectual functioning, psychiatric disturbances, disability status, number of medications, geographic distribution, education, chronologic age, and disease duration. Our study offers a starting point for further investigations aimed at better understanding the mechanisms connecting aggression and epilepsy.

KEY WORDS: Aggressiveness, Epilepsy, Adults, Italian standardized questionnaire.

The relationship between aggressiveness and epilepsy is complex and controversial, and the literature has not reached definitive conclusions so far, also considering that incidence and prevalence of aggressive behavior have not yet been quantified (Alpher et al., 2002).

Some studies have analyzed this issue in the past (Delgado-Escueta et al., 1981), but the number of investigations on this topic has decreased over the last decades; however, a new interest has emerged in recent years.

Therefore, we decided to initiate a new multicenter project on aggressive behavior and epilepsy to provide more detailed information on this topic.

The aim of this study is to describe aggressiveness during the interictal phase, as measured by the Aggression Questionnaire (AQ), already validated in Italy, in patients with epilepsy living in different Italian regions, and to assess potential sociodemographic and clinical determinants of aggressiveness.

Materials and Methods

Patients

All patients provided written informed consent before the psychological session. Nine secondary and tertiary Italian centers for the care of epilepsy participated in the study.

The selection criteria adopted by each center were the following: consecutive patients admitted to different centers, aged 18 or older, with a diagnosis of epilepsy (at least two unprovoked seizures 24 h apart), with the presence of idiopathic, cryptogenetic, or symptomatic epilepsy according to the International League Against Epilepsy (ILAE) syndromic scheme (Commission on Classification and Terminology, 1989; Commission on Epidemiology and Prognosis, 1993), with good compliance with treatment and study participation. Each center was asked to enroll at least 50 patients. A total number of 503 adults with epilepsy were recruited.

Demographic and clinical variables were recorded for each eligible patient during a separate interview preceding the AQ. Table 1 summarizes the demographic and clinical characteristics of our study population.

Measures

The AQ is a validated Italian instrument assessing aggression (Fossati et al., 2003; Maffei, 2008). This questionnaire consists of 29 items belonging to a four-factor structure: Physical Aggression (nine items), Verbal Aggression (five items), Anger (seven items), and Hostility (eight items). Each item is expressed on a 5-point Likert scale format ranging from "never" (1) to "always" (5); single-domain scores can be added together to obtain a total score. The higher the results, the higher the measure of aggressiveness for both the overall and the single-domain scores.

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Address correspondence to Ada Piazzini, Epilepsy Center, Neurology II, St Paolo Hospital, Via A. Di Rudini 8, 20142, Milan, Italy. E-mail: ada.piazzini1@gmail.com

Table 1. Demographic and clinical characteristics of the study population (n = 503)

Characteristic	N (%)
Geographic distribution	
Northern Italy	114 (22.66)
Central Italy	90 (17.89)
Southern Italy	299 (59.44)
Age (years)	
Mean ± SD	39.55 ± 14.18
Gender	
Male	239 (47.51)
Female	264 (52.49)
Education	
0–8 years	225 (44.73)
9–13 years	214 (42.54)
>13 years	64 (12.72)
Marital status	
Single	247 (50.00)
Nonsingle	247 (50.00)
Occupational status	
Retired	40 (8.05)
Housewife	93 (18.71)
Other	40 (8.05)
Student	33 (6.64)
Unemployed	93 (18.71)
White collar	145 (29.18)
Blue collar	53 (10.66)
Epilepsy syndrome	
Focal epilepsy	401 (80.68)
Generalized epilepsy	96 (19.32)
Seizure type	
Partial	236 (47.01)
Generalized	239 (47.61)
Mixed	27 (5.38)
Seizure frequency in previous 12 months	
0	230 (46.00)
1–24	189 (37.80)
≥25	81 (16.20)
Etiology	
Idiopathic	90 (18.00)
Symptomatic	169 (33.80)
Cryptogenic	241 (48.20)
Disease duration (years)	
Mean ± SD	19.21 ± 14.11
Age at onset of seizures (years)	
Mean ± SD	20.65 ± 16.01
Concurrent diseases	
No	381 (75.75)
Yes	122 (24.25)
Number of medications	
Monotherapy	247 (50.20)
Polytherapy	245 (49.80)
Adverse treatment events	
Yes	44 (8.75)
No	459 (91.25)
Intellectual function	
Normal	412 (82.24)
Mildly or severely compromised	89 (17.76)
Psychiatric disturbances	
Yes	88 (17.50)
No	415 (82.50)
Disability status	
Yes	175 (34.93)
No	326 (65.07)

SD, standard deviation.

Statistics

To investigate sociodemographic, clinical, and age-related characteristics that potentially affected the overall AQ and its single-domain scores, we carried out a series of one-way and multivariate analysis of variance (ANOVA) models, with multivariate models providing adjustment for age (in categories) and sex, when appropriate.

In all the analyses, normal scores from the ranks of the dependent variable were used instead of the original dependent variable, to account for the presence of asymmetry and bimodality. When heterogeneity of variances was detected, we used the Welch's ANOVA to test for equal group means while adjusting for unequal group variances. Calculations were performed using SAS Statistical Software (SAS 9.1) (SAS Institute, Cary, NC, U.S.A.).

Results

The mean level of aggressiveness of our sample is statistically different compared to that of the general Italian population (Maffei, 2008). This happens for the overall AQ (p-value < 0.001) and for three single-domain scores (p-value < 0.001 for each of the domains), with the exception of the Anger domain (p-value < 0.001). However, patients with epilepsy showed lower mean values for the overall AQ score (68.23 for epilepsy patients vs. 74.34 for normal subjects) and for the Physical Aggression (17.18 vs. 20.44), Verbal Aggression (14.64 vs. 15.31), and Hostility (20.08 vs. 22.90) domains. For the Anger domain, the mean score of patients with epilepsy was slightly higher than that of the normal population (16.34 vs. 15.91).

Table 2 shows the overall AQ and single-domain scores organized by clinical characteristics of the study population. Multivariate ANOVA models highlighted that the overall AQ score was significantly affected by the presence of compromised intellectual function, psychiatric disturbances, and disability status, with consistent significant effects emerging also for the corresponding Physical Aggression, Anger, and Hostility domains.

Finally, the number of medications was statistically significant for the overall AQ and the Hostility domain scores, with patients in polytherapy showing a higher mean Hostility score.

Table 3 illustrates the overall AQ and single-domain scores by sociodemographic characteristics. Multivariate ANOVA models showed that the overall AQ score was significantly affected by geographic distribution and education, with a consistent significant effect of the Hostility domain for geographic distribution, and of Physical Aggression and Hostility for education.

Table 4 reports the overall AQ and single-domain scores organized by age-related characteristics of the study population. Multivariate ANOVA models showed that age

Table 2. Overall AQ and single-domain scores by clinical characteristics (n = 503)

	Overall functioning	Physical aggression	Verbal aggression	Anger	Hostility
Epilepsy syndrome					
Focal epilepsy	67.9 (17.98)	16.96 (6.51)	14.53 (3.96)	16.35 (5.74)	20.06 (6.69)
Generalized epilepsy	69.63 (17.06)	18.17 (7.04)	15.04 (3.07)	16.44 (5.60)	19.98 (6.58)
p-Value one-way[a]	0.3460	0.0977	0.2179	0.8301	0.9764
p-Value adjusted for age and gender[b]	0.9419	0.2516	0.7667	0.6414	0.5737
Seizure type					
Partial	68.42 (17.90)	17.17 (6.53)	14.47 (3.95)	16.58 (5.77)	20.19 (6.72)
Generalized	68.11 (17.81)	17.31 (6.85)	14.83 (3.66)	16.09 (5.64)	19.88 (6.62)
Mixed	67.78 (16.89)	16.19 (5.55)	14.44 (3.81)	16.44 (5.71)	20.70 (6.59)
p-Value one-way[a]	0.7740	0.9193	0.2837	0.3400	0.6728
p-Value adjusted for age and gender[b]	0.5432	0.6508	0.3987	0.2315	0.5706
Seizure frequency in previous 12 months					
0	67.7 (16.87)	17.18 (6.59)	14.53 (3.44)	16.33 (5.66)	19.66 (6.7)
1–24	67.7 (18.02)	17 (6.53)	14.44 (3.9)	16.09 (5.58)	20.16 (6.53)
≥25	71.11 (19.58)	17.59 (7.1)	15.43 (4.47)	16.91 (6.02)	21.17 (6.74)
p-Value one-way[a]	0.2213	0.8242	0.0675	0.4127	0.1219
p-Value adjusted for age and gender[b]	0.1350	0.6149	0.0275	0.4063	0.1000
Etiology					
Idiopathic	68.79 (17.05)	17.88 (7.11)	14.96 (3.1)	16.02 (5.53)	19.93 (6.56)
Symptomatic	69.25 (18.48)	17.48 (6.84)	14.75 (4.11)	16.46 (5.92)	20.57 (6.94)
Cryptogenic	67.13 (17.4)	16.66 (6.2)	14.38 (3.78)	16.39 (5.62)	19.69 (6.46)
p-Value one-way[a]	0.4299	0.1529	0.2049	0.6360	0.7023
p-Value adjusted for age and gender[b]	0.8985	0.4333	0.7397	0.2555	0.8472
Concurrent diseases					
No	68.01 (18.12)	17.43 (6.87)	14.67 (3.8)	16.18 (5.73)	19.72 (6.55)
Yes	68.96 (16.62)	16.4 (5.74)	14.54 (3.8)	16.83 (5.58)	21.19 (6.86)
p-Value one-way[a]	0.4478	0.3071	0.7422	0.3324	0.0280
p-Value adjusted for age and gender[b]	0.0766	0.9397	0.6209	0.0793	0.0089
Number of medications					
Monotherapy	67.09 (20.89)	18.09 (5.34)	14.82 (5.1)	16.64 (6.9)	17.55 (6.83)
Polytherapy	66.87 (17.14)	17.05 (6.38)	14.53 (3.53)	16.02 (5.55)	19.26 (6.57)
p-Value one-way[a]	0.0903	0.8234	0.5799	0.2377	0.0051
p-Value adjusted for age and gender[b]	0.0408	0.6498	0.2963	0.1849	0.0028
Adverse treatment events					
Yes	67.95 (16.94)	16.05 (5.57)	14.43 (3.71)	16.11 (4.9)	21.36 (7.27)
No	68.26 (17.85)	17.29 (6.71)	14.66 (3.81)	16.36 (5.77)	19.95 (6.59)
p-Value one-way[a]	0.9155	0.3448	0.6922	0.9935	0.2032
p-Value adjusted for age and gender[b]	0.8424	0.6257	0.8738	0.8302	0.1880
Intellectual function					
Normal	67.3 (17.45)	16.93 (6.55)	14.56 (3.76)	16.03 (5.63)	19.77 (6.64)
Mildly or severely compromised	72.54 (18.77)	18.29 (6.88)	15.02 (4.01)	17.79 (5.88)	21.44 (6.56)
p-Value one-way[a]	0.0145	0.0553	0.2781	0.0107	0.0534
p-Value adjusted for age and gender[b]	0.0100	0.0320	0.2496	0.0092	0.0494
Psychiatric disturbances					
Yes	75.31 (18.55)	17.84 (7.47)	15.95 (3.76)	18.8 (6.02)	22.72 (6.72)
No	66.74 (17.23)	17.04 (6.43)	14.36 (3.75)	15.82 (5.49)	19.52 (6.51)
p-Value one-way[a]	<0.0001	0.3093	0.0003	<0.0001	<0.0001
p-Value adjusted for age and gender[b]	<0.0001	0.0319	<0.0001	<0.0001	<0.0001
Disability status					
Yes	71.36 (18.5)	18.01 (6.79)	14.76 (4.07)	16.99 (5.92)	21.6 (6.89)
No	66.49 (17.01)	16.71 (6.47)	14.56 (3.63)	15.98 (5.55)	19.25 (6.36)
p-Value one-way[a]	0.0044	0.0203	0.5936	0.0805	0.0002
p-Value adjusted for age and gender[b]	0.0009	0.0034	0.3428	0.0448	0.0001

Data are mean (SD), unless otherwise indicated.
AQ, Aggression Questionnaire; SD, standard deviation; ANOVA, analysis of variance.
[a]p-Values were obtained from separate one-way ANOVA models including overall or single-domain scores as the dependent variable and a single clinical characteristic as the independent variable.
[b]p-Values were obtained from separate multivariate ANOVA models including also age (in categories) and gender, when appropriate, as independent variables.

Table 3. Overall AQ and single-domain scores by sociodemographic characteristics (n = 503)

	Overall functioning	Physical aggression	Verbal aggression	Anger	Hostility
Geographic distribution					
Northern	65.55 (16.66)	16.74 (6.64)	14.11 (3.47)	15.74 (5.49)	18.97 (6.18)
Central	65.76 (18.5)	16.21 (6.43)	15.23 (4.17)	15.41 (6.14)	18.9 (6.85)
Southern	70.01 (17.77)	17.65 (6.65)	14.66 (3.79)	16.85 (5.6)	20.85 (6.68)
p-Value one-way[a]	0.0197	0.1652	0.1854	0.0802	0.0109
p-Value adjusted for age and gender[b]	0.0463	0.3090	0.3175	0.1442	0.0153
Gender					
Male	68.65 (17.89)	18.58 (6.96)	14.6 (3.79)	16.07 (5.54)	19.4 (6.33)
Female	67.86 (17.65)	15.92 (6.04)	14.67 (3.82)	16.58 (5.84)	20.69 (6.88)
p-Value one-way[a]	0.6468	<0.0001	0.8512	0.3385	0.0287
p-Value adjusted for age[b]	0.5841	<0.0001	0.8327	0.4079	0.0340
Education					
0–8 years	69.65 (18.43)	17.77 (6.69)	14.45 (4.1)	16.52 (5.7)	20.92 (6.64)
9–13 years	67.79 (17.39)	17.07 (6.75)	14.88 (3.53)	16.37 (5.73)	19.47 (6.66)
>13 years	64.73 (16.14)	15.48 (5.64)	14.48 (3.59)	15.59 (5.62)	19.17 (6.43)
p-Value one-way[a]	0.0602	0.0112	0.8949	0.2819	0.0747
p-Value adjusted for age and gender[b]	0.0010	<0.0001	0.3578	0.0522	0.0116
Marital status					
Single	71.06 (18.43)	18.04 (6.98)	15.13 (3.7)	17.04 (5.9)	20.85 (6.74)
Nonsingle	65.29 (16.76)	16.27 (6.17)	14.14 (3.87)	15.62 (5.48)	19.27 (6.53)
p-Value one-way[a]	0.0005	0.0023	0.0035	0.0035	0.0094
p-Value adjusted for age and gender[b]	0.2319	0.7871	0.5254	0.2474	0.0522
Occupational status					
Retired	63.88 (17.63)	15.98 (5.66)	13.38 (3.72)	15.15 (5.15)	19.38 (7.06)
Housewife	66.47 (16.72)	15.72 (6.02)	14.24 (3.77)	16.27 (5.8)	20.25 (6.65)
Other	70.23 (17.3)	18.28 (7.09)	15.25 (3.5)	16.98 (5.91)	19.73 (6.09)
Student	76.15 (18.11)	19.73 (6.23)	16.27 (3.78)	18.3 (6.02)	21.85 (7.18)
Unemployed	76.7 (19.05)	20.3 (7.37)	15.61 (3.79)	18.22 (5.82)	22.57 (6.61)
White collar	61.99 (14.41)	14.93 (5.32)	13.8 (3.5)	15.13 (5.15)	18.13 (6.05)
Blue collar	70.17 (17.95)	18.81 (6.95)	15.36 (4.2)	15.66 (5.63)	20.34 (6.66)
p-Value one-way[a]	0.1660	0.0566	0.0396	0.9040	0.7836
p-Value adjusted for age and gender[b]	0.8583	0.5230	0.1449	0.4456	0.5469

Data are mean (SD) unless otherwise indicated.
AQ, Aggression Questionnaire; SD, standard deviation; ANOVA, analysis of variance.
[a]p-Values were obtained from separate one-way ANOVA models including overall or single-domain scores as the dependent variable and a single sociodemographic characteristic as the independent variable.
[b]p-Values were obtained from separate multivariate ANOVA models including also age (in categories) and gender, when appropriate, as independent variables.

significantly and consistently affected the overall AQ score and three of its single domains (Physical Aggression, Verbal Aggression, and Anger).

Disease duration significantly affected the overall AQ and Physical Aggression and Hostility domain scores, even though without a linear trend: the higher the duration, the higher the mean scores of the domain.

Discussion

We highlighted that mean aggressive behavior of patients with epilepsy is statistically different from that of the general Italian population, that is, that people with epilepsy can have slightly less aggressive responses than others. The determinants of their reactions can be found in different types of variables. Among them, cognitive impairment represents one of the most important, considering that it can provoke evident limitations on driving, high unemployment, and lack of independence. All these aspects, together with the fact that patients with neuropsychological deficits can be less aware of the significance of their reactions, can aggravate aggressive responses.

It has been hypothesized that common pathogenic pathways might exist between epilepsy and psychiatric events, and between those events and aggressiveness (Prueter & Norra, 2003). For these reasons, psychiatric disorders can facilitate aggressive behavior, which can be a direct consequence of the psychopathologic event.

Disability status carries with it a loss of autonomy, with immediate fallouts in many daily activities. The estimated prevalence of severe behavioral problems in people with disabilities is between 10% and 15%; among them aggression is the most representative one (7%) (Emerson et al., 2001).

Long-term polytherapy has been associated with relevant side effects, which can affect the patients' psychological

Table 4. Overall AQ and single-domain scores by age-related characteristics (n = 503)

	Overall functioning	Physical aggression	Verbal aggression	Anger	Hostility
Age					
18–29	73.07 (18.68)	19.32 (7.55)	15.68 (3.48)	17.25 (5.84)	20.82 (6.49)
30–39	67.86 (17.61)	17.11 (6.47)	14.58 (3.74)	16.48 (5.91)	19.68 (6.86)
40–49	69.02 (17.17)	16.72 (6.19)	14.39 (3.94)	16.85 (5.65)	21.06 (6.77)
≥50	62.49 (15.43)	15.14 (5.16)	13.75 (3.78)	14.7 (5.02)	18.89 (6.3)
p-Value one-way[a]	<0.0001	<0.0001	<0.0001	0.0289	0.2091
p-Value adjusted for gender[b]	<0.0001	<0.0001	<0.0001	0.0036	0.2092
Disease duration					
≤5	65.57 (16.52)	16.86 (5.82)	14.67 (3.81)	15.41 (5.09)	18.63 (6.55)
6–15	68.53 (17.82)	17.13 (7.12)	14.68 (3.46)	16.9 (6.01)	19.82 (6.07)
16–29	70.31 (17.61)	17.83 (6.95)	14.9 (3.78)	16.61 (5.6)	20.98 (7.05)
≥30	66.76 (18.23)	16.55 (6.14)	14.02 (4.07)	15.9 (5.79)	20.3 (6.49)
p-Value one-way[a]	0.7582	0.4414	0.3261	0.9520	0.0257
p-Value adjusted for age and gender[b]	0.0373	0.0381	0.7844	0.2659	0.0084
Age at onset					
<10	73.29 (18.73)	18.41 (7.25)	15.33 (3.87)	17.73 (5.91)	21.83 (6.66)
10–19	67.31 (17.44)	17.13 (6.9)	14.47 (3.85)	15.87 (5.94)	19.84 (6.2)
20–29	70.21 (18.39)	18.03 (6.72)	15.04 (3.57)	16.7 (5.73)	20.44 (7.27)
≥30	63.08 (15.01)	15.24 (5.27)	13.76 (3.76)	15.37 (5.05)	18.71 (5.89)
p-Value one-way[a]	0.0032	0.0036	0.0288	0.0834	0.0078
p-Value adjusted for age and gender[b]	0.0976	0.1413	0.4856	0.5024	0.0480

Data are mean (SD) unless otherwise indicated.
AQ, Aggression Questionnaire; SD, standard deviation; ANOVA, analysis of variance.
[a]p-Values were obtained from separate one-way ANOVA models including overall or single-domain scores as the dependent variable and a single age-related characteristic as the independent variable.
[b]p-Values were obtained from separate multivariate ANOVA models including also age (in categories) and gender, when appropriate, as independent variables.

and psychiatric profiles. Long-term polytherapy may influence higher-order cortical functions, and can provoke behavioral dysfunctions, in particular aggression. These negative side-effects worsen with increasing dosages and anticonvulsant blood levels.

The overall AQ score was also affected by geographic distribution, with people living in Southern Italy showing higher scores on aggression than Northern patients. This fact can be explained considering that the stigma related to epilepsy is still more severe in the South than in the North of Italy (Colombatto, 2002). Higher material deprivation, the difficulty of getting adequate and effective medical care, lack of employment, and discrimination at work may all contribute to making epilepsy a significant hindrance for social and labor-market inclusion of patients, thus prompting higher levels of frustration and aggressiveness. In another study of ours, it emerged that the quality of life perceived by patients with epilepsy living in the South of Italy was more compromised than that of the Northern population, mainly because patients felt strongly isolated due to sociocultural reasons (Piazzini et al., 2008).

Education also has a significant effect on AQ score. Previous investigations have found that people with a higher school degree may show not only larger cognitive reserves, but also more adequate behavior than those with fewer years of formal education (Ming-Chyi & Jing-Jane, 2005).

Age seems to be a key factor influencing the overall AQ score and three of its single domains: the older the age, the lower the mean scores indicating aggressive behavior. It is likely that aggressive responses are more often expressed in younger individuals; as patients become older they tend to accept their condition, and to have a lower frequency of aggressive reactions.

We found that disease duration affected the overall AQ and the Physical and Hostility domain scores; some reports provided similar results, suggesting that disease duration might be related to some personality disorders and aggressive traits (Delgado-Escueta et al., 1981).

This study has some limits and strengths. One of the limits is that we did not distinguish between Axis I and Axis II factors in the psychiatric disorders evaluation, but we intend to provide an investigation specifically devoted to it in the future.

We considered aggression only during the interictal phase, because we believe that the examination of aggressive reactions in the ictal and postictal phases requires different clinical considerations and instruments.

This study showed that patients with epilepsy can be frustrated, but they resort to aggressive responses like other nonclinical patients, or even less often. We think that this result should be deeply studied to identify more detailed information on its potential determinants. Being aware of the fact that patients with epilepsy are less aggressive than others can contribute to eliminating

prejudices, and can represent a useful resource for clinical and research issues.

In conclusion, our data offer a springboard for further investigations aimed at analyzing mechanisms related to aggression. A clearer understanding of the complex relationship between epilepsy and aggressive responses might open up possibilities for exploiting this research beyond its original purpose, in light of a wider exploration of the neurologic basis of aggression.

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Disclosure

None of the authors have any conflict of interest to disclose. All authors confirm that have read the Journal's position on issue involved in ethical publication and affirm that this report is consistent with those guidelines.

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