Perceived stigma is a critical factor for interictal aggression in people with epilepsy

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ABSTRACT

Purpose: Aggression in people with epilepsy (PWE) is not well understood. We investigated interictal aggression in PWE and clarified predictors and the interrelationships among them.
Method: This was a case–control study. Eligible subjects who consecutively visited the epilepsy clinic completed several questionnaires including the Aggression Questionnaire (AQ), the Revised Stigma Scale (RSS), the Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E), and the Generalized Anxiety Disorder-7 (GAD-7).
Results: PWEs had higher overall AQ scores and anger and hostility subscale scores than controls. Patients with uncontrolled epilepsy also had higher physical and verbal aggression subscale scores than controls. Univariate analyses revealed associations between the overall AQ score and job, household income, marriage, antiepileptic drug (AED) load, seizure control, co-administration of psychiatric drugs, the RSS score, the K-NDDI-E score, and the GAD-7 score. Multivariate analyses indicated that the strongest predictor for the overall AQ score was the RSS score ($\beta = 0.346$, $p < 0.001$), followed by the GAD-7 score ($\beta = 0.244$, $p = 0.003$), and the K-NDDI-E score ($\beta = 0.172$, $p = 0.047$). The RSS score exerted a direct effect on the overall AQ score under the influences of the GAD-7 score and the K-NDDI-E score. The GAD-7 score also exerted a direct effect on the overall AQ score, but the K-NDDI-E score only had an indirect effect on the overall AQ score through the RSS score.
Conclusion: The degree of interictal aggression is higher in PWE than controls. Perceived stigma is a critical factor for aggression under the influence of depression and anxiety.

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1. Introduction

Aggression is overt, often harmful, social interaction which is intended to inflict damage or other unpleasantness upon another individual [1]. Aggression takes a variety of forms including aggression-related feelings such as anger or hostility, and aggression-related behaviors such as physical or verbal aggression [2]. Overall, data from human and animal studies suggest that subcortical brain regions, particularly the limbic system and more specifically the amygdala, are associated with aggression [3].

Epilepsy is a model for brain–behavior relationships because seizures affect behavior, and behavior affects seizures [4]. Patients with temporal lobe epilepsy (TLE) frequently have damage to the limbic area, which might lead one to predict that they would show more aggression than patients with other forms of epilepsy. It has been reported that interictal anger is more frequent in patients with TLE than in healthy controls [5]. Blumer described an interictal dysphoric disorder in patients with TLE, which is characterized by marked irritability and troublesome loss of control [6].

Although it has been reported that patients with TLE are more aggressive than healthy controls during the interictal period, there is no clear evidence that the overall people with epilepsy (PWE)

are more aggressive than people without epilepsy during that period. Numerous potential predictors of aggression have been suggested, e.g. seizure-related factors, medical factors and psychosocial factors [4], but there has been no investigation into which of these potential predictors are more critical. The aims of our study were to investigate interictal aggression in PWE and to clarify predictors for aggression and the relationships among them.

2. Methods

2.1. Subjects

We included consecutive participants from PWE who attended our epilepsy clinic between October 1, 2013 and January 31, 2014 and were taking antiepileptic drugs (AEDs). Patients were over 19 years old, had a current diagnosis of epilepsy, had been taking one or more AEDs for at least 1 year and were capable of providing informed consent and understanding the study protocol. Patients with an intellectual disability or serious medical, neurological or psychiatric disorders, or problems with alcohol or drugs that prevented them understanding the questionnaire and cooperating in study procedures were excluded as were patients who declined to answer the questionnaires. We also excluded patients who had an overt seizure in the four days preceding the start of the study. We recruited age- and gender-matched controls as a comparison group; most controls were parents, siblings, offspring or relatives of patients although some were medical students or hospital employees. Control subjects were free of epilepsy and had no history of loss of consciousness.

2.2. Study design

This case–control study was approved by the institutional review board of Kyungpook National University Hospital and all subjects provided written informed consent before participation. Epilepsy was diagnosed according to the International League Against Epilepsy classification of seizures and epileptic syndromes [7,8]. All subjects were interviewed by a trained epileptologist (SP Park) who collected demographic, socioeconomic, and clinical information from patients' medical charts; this information was entered into a computerized database.

The demographic variables were age, gender, and education. The socioeconomic variables were employment status (employed versus unemployed), household income (at least one million Korean won (KRW) per month [equivalent to US\$ 900 per month] versus less than one million KRW/month), possession of a driving license (yes versus no) and marital status (married versus divorced, bereaved, or unmarried). The clinical variables were age at onset of epilepsy, duration of epilepsy, type of seizure, etiology, epilepsy syndrome, MRI abnormality, family history of epilepsy, history of febrile convulsions, duration of AED intake, AED therapy regimen, AED load, levetiracetam (LEV) intake and degree of seizure control. Etiology was classified as idiopathic or cryptogenic/symptomatic. Four categories of epileptic syndrome were used: TLE; extraTLE (epilepsy syndromes in which the epileptic attacks originated from the frontal, parietal, or occipital lobes); generalized epilepsy (GE) and unknown syndrome. AED regimen was classified as monotherapy or polytherapy according to the number of AEDs the patient was using. AED load was estimated as the sum of the ratios of prescribed daily dose (PDD): defined daily dose (DDD; the assumed average daily maintenance dose of the drug when used for its main indication [9]) for each AED in the subject's treatment regimen [10]. We included LEV intake as a variable because LEV has been reported to produce anger and aggression [11]. Patients who took LEV as monotherapy or polytherapy were included in the LEV intake group. We used three categories for degree of seizure

control: well-controlled epilepsy (WCE; seizure freedom in the last year); poorly-controlled epilepsy (PCE; an intermediate degree of seizure control that did not meet the criteria for WCE or UCE) and uncontrolled epilepsy (UCE; drug-refractory epilepsy i.e., failure to respond to adequate trials of two AEDs, an average of more than one seizure per month for 18 months and maximum seizure-free period of less than three months [12]). PWE were assigned to a seizure control category on the basis of information about seizure frequency obtained from their medical records. The psychosocial factors were perceived stigma, depression and anxiety. Eligible patients completed several self-report questionnaires: the Aggression Questionnaire (AQ) [13], the Revised Stigma Scale (RSS) [14], the Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E) [15] and the Generalized Anxiety Disorder-7 (GAD-7) [16].

2.3. Interview and questionnaires

2.3.1. Aggression Questionnaire (AQ)

The AQ was developed by Buss and Perry; it measures aggressive behavior and consists of 29 items in four subscales: Physical Aggression (9 items), Verbal Aggression (5 items), Anger (7 items) and Hostility (8 items) [17]. Responses to all items are given on a five-point Likert scale ranging from 'never' (1) to 'always' (5); subscale scores can be summed to obtain an overall score. Higher scores indicate greater aggression. A validated Korean version of the AQ has been produced [13]. During the validation process, a decision was taken to omit two of the original items from the anger subscale ('Some of my friends think I'm a hothead' and 'Sometimes I fly off the handle for no good reason') because they related more to verbal aggression and hostility than anger. After all, 27 items was represented for the evaluation of aggression. Cronbach's α coefficient for the Korean version of the AQ was 0.86.

2.3.2. Revised Stigma Scale (RSS)

Perceived stigma used to be measured using a three-item scale which was originally developed for the assessment of stigma in stroke patients [18], but revised and adapted for use with PWE [19]. Individuals are asked to give a yes/no response to a question which asks whether they feel that other people are (1) uncomfortable with them, (2) treat them as inferior and (3) prefer to avoid them, because of their epilepsy. A 'yes' response to an item scores 1 and an individual's score is the sum of their positive responses. Recently, it was shown that this scale is subject to a ceiling effect which probably reflects the use of binary responses [20]. Thereafter, the RSS was developed and validated [14]. The RSS uses a four-point Likert scale (0: 'not at all'; 1: 'yes, maybe'; 2: 'yes, probably'; 3: 'yes, definitely'), which may have enhanced its sensitivity to more subtle differences in perception of stigma. The RSS scores range from 0 to 9; a score of 0 indicates that the person does not feel stigmatized, scores 1–6 indicate that the person feels mildly to moderately stigmatized and scores 7–9 indicate that the person feels very stigmatized. Cronbach's α coefficient for the RSS was 0.85.

2.3.3. Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDI-E)

The K-NDDI-E is a reliable, validated screening tool for major depressive disorder (MDD) in Korean PWE [15]. Subjects are asked to rate six items using a four-point scale (1–4) to indicate how much they have been bothered by depression-related problems over the previous two weeks. Total scores range from 6 to 24; higher scores indicate more intense depression. Cronbach's α coefficient was 0.898 and a total score of 12 or more is suggestive of MDD.