

## Current Literature

In Clinical Science



# Anxiety Disorders in Epilepsy: The Forgotten Psychiatric Comorbidity

## Prevalence of Anxiety Disorders in Patients With Refractory Focal Epilepsy—A Prospective Clinic Based Survey.

Brandt C, Schoendienst M, Trentowska M, May TW, Pohlmann-Eden B, Tuschen-Caffier B, Schrecke M, Fueratsch N, Witte-Boelt K, Ebner A. *Epilepsy Behav* 2010;17:259–263.

Comorbid anxiety disorders severely affect daily living and quality of life in patients with epilepsy. We evaluated 97 consecutive outpatients (41.2% male, mean age =  $42.3 \pm 13.2$  years, mean epilepsy duration =  $26.9 \pm 14.2$  years) with refractory focal epilepsy using the German version of the anxiety section of the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I). Nineteen patients (19.6%) were diagnosed with an anxiety disorder (social phobia, 7.2%; specific phobia, 6.2%; panic disorder, 5.1%; generalized anxiety disorder, 3.1%; anxiety disorder not further specified, 2.1%; obsessive-compulsive disorder, 1.0%; posttraumatic stress disorder, 1.0%). Four-week prevalence rates reported elsewhere for the general population in Germany are 1.24% for social phobia, 4.8% for specific phobia, 1.1% for panic disorder, 1.2% for generalized anxiety disorder, 1.3% for anxiety disorder not further specified, and 0.4% for obsessive-compulsive disorder. A trend for people with shorter epilepsy duration ( $P = 0.084$ ) and younger age ( $P = 0.078$ ) being more likely to have a diagnosis of anxiety disorder was revealed. No gender differences were found; however, this may be due to the small sample size. In conclusion, anxiety disorders are frequent in patients with refractory focal epilepsy, and clinicians should carefully examine their patients with this important comorbidity in mind.

### Commentary

In the last decade, epileptologists have recognized the importance of identifying and treating psychiatric comorbidities in patients with epilepsy (PWE). Yet, in clinical practice and research alike, most of the attention has been focused on depressive disorders (DD), as they are the most frequent psychiatric comorbidity (1). In addition, DD yield a negative effect on the quality of life of PWE (2), increase significantly their suicidal risk, (3) worsen their tolerance to antiepileptic drugs, and have been associated with a worse response of seizures to pharmacologic and surgical treatments (4, 5). Although anxiety disorders (AD) are the second most frequent psychiatric comorbidity in PWE (1), they remain underrecognized and undertreated despite the fact that they have as negative impact on the life of these patients as DD (see below).

In a Canadian population-based study, the lifetime prevalence of any AD in PWE was 22.8% (vs 11% in nonepilepsy subjects). Anxiety disorders are also relatively frequent in patients with treatment-resistant epilepsy, as shown in the study by Brandt et al., which accompanies this commentary and in which close to 20% of the 96 patients exhibited an AD.

Of note, AD and DD tend to occur together with a high frequency, and, in the Canadian study, a lifetime prevalence of

34.2% was found for comorbid AD and DD in PWE (vs 19.6% in nonepilepsy subjects). The clinical significance of the comorbid occurrence of primary AD and DD led the committee developing the fifth edition of the Statistical Manual of Mental Disorders (DSM-V) to create a new diagnostic category of “mixed depression/anxiety disorders.”

Patients with and without epilepsy can experience more than one AD. In a study of 188 consecutive PWE from five epilepsy centers in the United States (50% of whom had been seizure-free for the last 6 months), current AD (identified with the Mini International Neuropsychiatric Interview) were found in 49 patients (26%), with agoraphobia, generalized anxiety disorder (GAD), and social phobia being the most frequent (5). Among these 49 patients, 27 (55%) had two or more anxiety disorders while 28 (57%) were also suffering from a comorbid major depressive episode (MDE).

As in the case of DD, AD has a negative effect on the life of PWE at several levels. For example, the presence of anxiety symptoms at the time of diagnosis of epilepsy was associated with a worse response to pharmacotherapy after a 12-month follow-up period (4).

The effect of AD on the quality of life of PWE has been demonstrated in several studies as well. In one study, AD and MDE had a comparable negative effect on the quality of life measured with the Quality of Life in Epilepsy Inventory-89 (QOLIE-89) while the presence of more than one AD occurring together with a MDE had the worst effect on health-related measures of quality of life (5). In a South Korean study of 154



outpatient adults with epilepsy, the presence of anxiety symptoms was the most important factor in explaining a worse quality of life (7). In another study of 87 patients with temporal lobe epilepsy, symptoms of depression and anxiety were the strongest predictors of poor quality of life (8); of note, the effect of each class of symptoms was independent, and the psychiatric comorbidity explained more variance in the quality of life measures than did the combined groups of clinical seizure or demographic variables.

The effect of AD on the suicidality risk of PWE was illustrated in a Danish population-based study, in which AD increased the risk of completed suicides by 12-fold relative to people without epilepsy (3). Anxiety disorders have also been shown to increase the suicidal risk in people without epilepsy. For example, in a Dutch population-based longitudinal study, the presence of any AD was significantly associated with suicidal ideation and suicide attempts in both the cross-sectional analysis (adjusted OR for suicidal ideation, 2.29; 95% CI: 1.85–2.82; adjusted OR for suicidal attempts, 2.48; 95% CI: 1.70–3.62) and longitudinal analysis (adjusted OR for suicidal ideation, 2.32; 95% CI: 1.31–4.11; adjusted OR for suicide attempts, 3.64; 95% CI: 1.70–7.83) (9). Furthermore, the presence of any AD in combination with a DD was associated with a higher likelihood of suicide attempts in comparison with a DD.

The need to recognize comorbid AD in patients with DD and vice versa has significant implications with respect to the course of these two conditions and their response to treatment. For example, population-based studies have revealed that a history of primary AD in patients with DD increases their risk for hospitalization and suicide attempt, prolongs the course and worsens the severity of the DD, and decreases the likelihood of remission of the depressive disorder (10, 11). Although these studies have yet to be carried out in PWE, there is no reason to assume that AD may affect differently the course of DD in these patients.

These data clearly demonstrate the need to identify and treat comorbid AD in PWE, in particular when they occur together with DD. Selective serotonin-reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRI) have become the first line of pharmacotherapy of primary AD. Although there are no controlled trials for the treatment of AD in PWE, there is a general consensus that these psychotropic agents are equally effective and safe in PWE. Benzodiazepines are prescribed for the initial 4 to 8 weeks of therapy to achieve an early symptom remission, as the therapeutic effect of SSRIs and SNRIs may be delayed by 4 to 6 weeks. Cognitive behavior therapy (CBT) has been shown to be an effective nonpharmacologic treatment modality for primary AD. Furthermore, a combination of CBT and an SSRI or SNRI has been recommended in particular when AD and DD occur together.

Several screening instruments are available to identify patients with AD, but none have been yet validated in PWE. The most user-friendly instrument available is the Patient's Health Questionnaire-Generalized Anxiety Disorder-7 (GAD-7),

which is a seven-item self-rating scale developed to screen for GAD, one of the most frequent types of AD. It takes less than 3 minutes to complete; a score of >10 is suggestive of a GAD diagnosis. It has been widely used by general practitioners (12). An advantage of this scale for PWE is the lack of items with somatic symptoms that can be confused with adverse events of AEDs or cognitive symptoms of the seizure disorder or the underlying neurologic disorder associated with the epilepsy. In summary, identification of comorbid psychiatric disorders should not be limited to DD and should always include the screening for AD.

by *Andres M. Kanner, MD*

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