The prevalence of psychiatric disorders in epilepsy: a critical review of the evidence

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Summary

Psychopathology has long been associated with epilepsy and should not be overlooked as it could exacerbate the epilepsy itself and impair the health-related quality of life of sufferers. A higher prevalence of psychiatric disorders has frequently been demonstrated amongst patients with epilepsy compared both with the general population and with individuals presenting neurological or non-neurological conditions. This review critically evaluates selected studies on the prevalence of psychiatric disorders in epilepsy patients compared with the general population and controls. Heterogeneity exists across the research methodologies, therefore further research, using less selected groups, should be undertaken to allow valid comparisons and the identification of more precise prevalence rates.

KEY WORDS: behaviour, epilepsy, methodology, prevalence, psychopathology

Introduction

Psychiatric disorders are common amongst patients with epilepsy (PWE), arising in 50-60% of this population (1). Psychopathology, particularly depression, occurs more frequently in PWE than in the general population, neurological controls, and those affected by non-neurological conditions (2). Symptoms can be seizure-related (ictal psychopathology) or independent of seizure activity (interictal psychopathology). This paper reviews the available evidence on the prevalence of interictal psychopathology in PWE, as this is the most frequent psychiatric comorbidity in this patient population. The results of 13 selected studies on the prevalence of psychiatric disorders in PWE are here presented, their methodological quality examined and a conclusion established.

Research findings

Kogeorgos et al. (3) assessed psychiatric comorbidity in 66 chronic epilepsy outpatients using two self-rating psychopathology questionnaires of established reliability and validity. About half of the sample (45.5%) were considered psychiatrically affected, compared with 21.6% of individuals randomly selected from the community. Compared with a group of chronic neurological outpatients, the PWE showed higher rates and greater severity of psychiatric comorbidities. Depression, anxiety and hysteria were the predominant conditions. Edeh and Toone (4) examined 88 PWE from South London general practices using the Clinical Interview Schedule (CIS). A substantial proportion of patients (47.7%) were psychiatrically affected; 19% exhibited depressive neurosis and 13% anxiety.

Manchanda et al. (5) performed a standardised psychiatric examination on 300 treatment-resistant PWE who were considered probable surgery candidates. Of these, 47.3% met the DSM-III-R criteria for psychiatric comorbidity; 29.3% exhibited Axis I diagnoses, primarily anxiety (10.7%), while 18% had Axis II diagnoses. These researchers focused on point prevalence instead of lifetime prevalence, and thus found lower mood disorder rates compared with those recorded in other studies.

Swinkels et al. (6) compared data relating to 209 Dutch PWE from a tertiary referral centre with data, representative of the Dutch general population, drawn from epidemiological records. All the patients were administered a structured diagnostic interview based on DSM-III-R criteria. Twelve-month and lifetime prevalence rates were obtained: the PWE displayed last-year anxiety and mood disorder rates of 24.9% and 18.7% respectively, compared with general population values of 12.4% and 7.6% respectively.

Piazzini et al. (7) administered two reliable and sensitive self-rating questionnaires, measuring depression and anxiety, to 220 PWE seen at a specialist epilepsy clinic and to 100 controls. The patients had not previously received psychiatric treatment and the controls were screened to exclude neurological conditions. Patients with a diagnosis of partial epilepsy exhibited increased impairment on the questionnaires compared with the controls. A subset of temporal lobe epilepsy patients displayed the highest depression and anxiety levels, although no psychiatric diagnosis was made in this study.

Gaitatzis et al. (8) conducted a cross-sectional, population-based investigation using records from an extensive, validated UK general practitioner (GP) database. Psychiatric comorbidities were found to present twice as frequently amongst PWE as amongst the general population. Specifically, 41% of PWE received a psychiatric diagnosis. The most frequent psychiatric diagnoses were depression (18%), anxiety (11%) and psychosis.
(9%). Organic and non-organic psychoses, alcohol dependence and schizophrenia were 4-6 times more likely to occur amongst the PWE than amongst the general population. With the exception of obsessive compulsive disorder and hysteria in older patients, all the psychiatric conditions investigated were significantly more likely to occur amongst the epileptics.

Ettinger et al. (9), through administration of a community-based self-report mail survey, compared 775 PWE, 395 asthma sufferers and 362 healthy controls. Positive depression scores were most frequent in the PWE (36.5%) followed by the asthma patients (27.8%) and the controls (11.8%). The majority of consultations and treatments for depression were recorded in the PWE. It was found that many depression-positive PWE and asthma patients had not previously been screened for this condition.

Jones et al. (10) administered a concise standardised psychiatric interview to 174 PWE from five tertiary centres. Of these, 48.9% exhibited DSM-IV Axis I conditions, principally anxiety (30.4%) and mood disorders (21.8%). Among the mood disorders, major depressive disorder was the main diagnosis, showing a prevalence of 17.2% in the PWE versus 10% in the general population. Psychoses, including schizophrenia, were rare.

Strine et al. (11) explored data from a self-report population-based survey. Individuals categorised by a clinician as affected by seizures were significantly more likely to present psychological problems. They were more prone to report depression and anxiety within the previous year. Around 14% fulfilled criteria for serious mental illness, compared with 2.9% of the seizure-free subjects.

Kobau et al. (12) reported data from a population-based survey of 4345 adults aged 18 years or older. Self-reported PWE were twice as likely as subjects without epilepsy to report experiencing depression or anxiety during the previous 12 months. Self-reported depression was almost three times as likely (39.7% vs 15.5%) and anxiety more than twice as probable (14.9% vs 6.7%) in those suffering active epilepsy compared with the inactive epilepsy group.

Mensah et al. (13) investigated comorbid depression in 499 primary care-notified PWE through administration of a self-rating postal questionnaire within the Cardiff community. Borderline depression was found in 16.6% of the PWE, and 11.2% showed clinical depression, which was associated with unemployment, recent seizure activity and adverse effects of medication. Again, these prevalence rates were higher compared to those recorded in the general population.

Conversely, two studies found no increased prevalence of psychiatric disturbances in PWE compared with controls. Fiorielli et al. (14), using the CIS, compared 100 patients with cryptogenic epilepsy with age- and sex-matched controls from an epilepsy centre in Italy. The PWE were not more prone to psychiatric conditions compared with the non-neurologically affected individuals. Mental disorders occurred in 19 PWE and 15 controls, with anxiety and depression the most frequent diagnoses; personality disorders were also present in some of the PWE. Psychiatric disturbances were more prevalent in those receiving polytherapy.

Stefansson et al. (15) compared PWE in Iceland with age- and sex-matched controls suffering somatic illnesses. All the subjects received disability support. According to their results, 35% of PWE and 29.7% of controls had psychiatric diagnoses. Therefore, no differences in psychiatric profile emerged between these two groups.

Methodological evaluation

The prevalence data for comorbid psychiatric diagnoses in PWE show considerable variability across studies. In this paper, we have identified and reviewed 13 studies of the most rigorous methodological quality. Table I summarises the prevalence rates of the most common DSM-defined psychiatric diagnoses.

<table>
<thead>
<tr>
<th>DSM-defined diagnosis</th>
<th>Prevalence rate (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mood disorders</td>
<td>24-75%</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>10-25%</td>
</tr>
<tr>
<td>Psychosis</td>
<td>2-7%</td>
</tr>
<tr>
<td>Personality disorders</td>
<td>1-2%</td>
</tr>
</tbody>
</table>

In the following section, we critically analyse methodological aspects of these research studies. The majority of studies presented in this review used selected samples which limits the possibility of generalising the data to the entire epilepsy population. For example, studies searching GP databases introduce an admission-rate bias. Such studies, focusing on patients seen in primary care settings, are likely to include more severely affected patients with various morbidities. Those with well-managed epilepsy or older, possibly housebound patients in the community would be overlooked, as would people not registered with GPs. On the other hand, studies on surgery candidates and on outpatients from tertiary centres or epilepsy clinics contain a selection bias: a majority of these patients would suffer from temporal lobe, cryptogenic or refractory epilepsy and would likely be patients with more severe, chronic epilepsy of longer duration. Psychiatric disturbances are also argued to be more prevalent in temporal lobe epilepsies (7). A substantial proportion of PWE (46%) receive polytherapy (10), which is a known contributor to psychiatric disorders. Prevalence rates could therefore be higher amongst these selected cohorts than among non-selected, less severe or well-controlled epileptics in the community. One of the studies which found no difference in prevalence rates of psychiatric disorders between PWE and controls used participants receiving disability support (15). This selection criterion could explain the lack of difference found between these PWE and controls. Disabled individuals could be more prone to psychiatric disorders, irrespective of epilepsy, and more severely disabled patients could experience associated complications and comorbidities that mask the direct effects of epilepsy. In other studies, the PWE were more likely to be single, lower educated, unemployed and disabled (6), and to have lower incomes (9). These are all psychosocial factors that could contribute to a greater vul-
nerability to mental illness, producing exaggerated psychiatric disorder rates, irrespective of the epilepsy diagnosis. The data from the population or community-based studies reviewed can be extrapolated to non-clinical populations, thereby providing larger samples which could allow more valid estimations. However, surveying individuals from specific households, such as only those registered with survey panels, could introduce selection bias. The studies administering self-report measures also introduce several problems. Under- or over-reporting of psychiatric symptoms could generate misrepresentative prevalence rates. Between-participant differences amongst individuals completing surveys could further bias findings. Seizure type, intensity and rate cannot be confirmed. Recall bias can interfere with prevalence accuracy. Survey completion demands functional ability, therefore individuals with severe epilepsy, which impairs function, may have been excluded from taking part. Finally, although self-administration reduces the problem of stigmatisation, some individuals may still withhold information due to the stigma surrounding epilepsy.

Most of the studies used measures that detect psychiatric symptoms, not clinical diagnoses. Not every symptom is representative of a psychiatric disorder (16), therefore prevalence could be overrated due to the absence of a standardised clinical interview. Without additional psychiatric assessment clinical diagnoses remain invalidated in these studies. Swinkels et al. (6) used a standardised interview that has not been validated in epilepsy populations, thus reducing the reliability of their findings. Four studies reported invalidated epilepsy diagnoses (8,9,11,12). A clinical examination must be conducted to guarantee an accurate diagnosis. Patients exhibiting seizures should not be regarded as suffering from epilepsy unless appropriate clinical investigations have been undertaken. Thus, misdiagnosis (13) could further confound the estimates obtained.

Some of the controls used were unrepresentative of the general population, as they presented conditions that could, independently, exacerbate psychiatric disorders. This makes them less reliable as comparative cases. Kogeorgos et al. (3) used individuals with chronic neurological conditions. Ettinger et al. (9) included asthma patients in whom the risk of depression could already be higher than that found in healthy controls. Controls undergoing minor surgery could also experience more psychological distress (14). GP-registered patients generally (8) could be affected by other conditions increasing their vulnerability to psychiatric disorders. Between-group differences could additionally interfere with prevalence rates. The case-control studies, however, did obtain controls from within the same population as the PWE. Instead, Edeh and Toone (4) and Manchanda et al. (5) did not include controls. Therefore it remains to be established whether the psychiatric morbidity identified by these studies is higher than that present in the general population.

Certain findings (6), referring to a highly specific geographical area and setting, do not lend themselves to cross-cultural generalisation. Cross-sectional designs (8) prevent inference of causation. For example, whether psychopathology precedes or occurs after the diagnosis of epilepsy cannot be established. Psychopathology in PWE may not be equivalent to that observed in non-epileptic populations (2). In 2007 Krishnamoorthy et al. published the proposal issued by the International League Against Epilepsy Commission on Psychobiology of Epilepsy for the classification of neuropsychiatric disorders in epilepsy. The aim of this proposal was to separate psychiatric disorders comorbid with epilepsy and those that reflect ongoing epileptiform activity from epilepsy-specific disorders, and to attempt to sub-classify the epilepsy-specific disorders alone (17). For example, this classification system incorporated the affective-somatoform (dysphoric) disorder of epilepsy, characterised by symptoms of irritability, depressive moods, anergia, insomnia, atypical pains, anxiety, phobic fears and euphoric moods (18,19).

It has been shown that gender-specific neurobiological substrates can affect the prevalence of specific psychiatric comorbidities (20). Likewise, seizure-related factors such as ictal alterations of the content of consciousness can play a role in the development or exacerbation of interictal psychopathology (21,22). The epidemiology of certain behavioural problems might be difficult to ascertain and therefore large samples of PWE might be required to provide accurate estimates of their prevalence (23). Finally, it is important to consider the different prevalence types measured (point or lifetime), as estimates could differ accordingly.

### Concluding remarks

Despite heterogeneity across research methodologies, studies have consistently demonstrated an increased prevalence of mental disorders, particularly depression, in PWE compared with the general population and controls. Psychiatric comorbidity should not be allowed to go unrecognised as it could exacerbate the epilepsy syndrome and affect patients’ health-related quality of life. In future research, selected epilepsy populations should be avoided in order to allow more valid comparisons and thus more precise prevalence rates.

### References