

## Epilepsy and Psychiatric Disturbance A Cross-sectional Study

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One hundred patients with cryptogenic epilepsy and normal intelligence and 100 age- and sex-matched controls were submitted to psychiatric interview using the Clinical Interview Schedule. Nineteen patients and 15 controls were identified as having psychiatric disorders. Anxiety and depression were the predominating diagnoses in both groups. Personality disorders were occasionally present in subjects with epilepsy. The study shows that patients with cryptogenic epilepsy and normal neuropsychological abilities should not be considered at any higher risk of psychiatric disturbance than a non-neurological patient population.

It is commonly accepted that patients with epilepsy have more psychiatric problems than normal individuals. However, despite the extensive literature on interictal behaviour of epileptic patients (Whitman *et al*, 1984; Dodrill & Batzel, 1986; Mendez, 1989; Robertson, 1989), the prevalence rate of psychiatric disturbance tends to vary across studies, and the type and degree of emotional and psychiatric impairment in epilepsy is subject to different interpretations.

In the majority of studies definite conclusions are impeded by serious methodological limitations. First of all, the subjects with epilepsy (in general, patients with mixed seizure disorders, from psychiatric series, or with temporal lobe epilepsy) may not be representative of the epileptic population at large. Secondly, individuals selected for controls – when present – are often drawn from different, selected series (mostly medical and psychiatric populations). Thirdly, a large sample (not found in most instances) is required in order to uncover true differences between groups. Fourthly, the assessment methods may not be comparable, accurate, or validated, and interpretation of the accumulated data is sometimes subjective. Finally, the diagnosis of psychiatric disturbance may not fit standardised classification criteria.

With these problems in mind, this study was undertaken with the purpose of defining the prevalence and characteristics of psychiatric disturbance in a fairly representative sample of adult patients with epilepsy and normal controls using standardised testing and diagnostic procedures.

### Method

The study population included all subjects aged 17 years and older seen as out-patients at the Regional Epilepsy Centre of the University Hospital of Monza, Milan, between

30 April 1987 and 30 May 1990. Epilepsy was defined as a history of two or more unprovoked seizures (not associated with brain insults or acute metabolic disorders). A patient was excluded if he/she had a progressive clinical disorder or a documented brain lesion, which might be responsible for mental impairment or epileptic seizures. In addition, in order to exclude subjects in whom mental impairment might prevent a correct investigation of psychiatric disturbances, only patients scoring 80 or higher for IQ on the full-scale Wechsler Adult Intelligence Scale (WAIS; Wechsler, 1981) were admitted.

Controls matched for age ( $\pm 5$  years) and sex were selected from otherwise healthy individuals undergoing minor surgery, as out-patients, in the same hospital.

During the day of the visit, patients with epilepsy and controls had their IQ measured and were then submitted to psychiatric interview using a slightly modified version of a standardised 23-item questionnaire, the Clinical Interview Schedule (CIS), which has been used as a screening instrument for the detection of psychiatric disorders in the general population (Goldberg *et al*, 1970) and was recently employed in a validation study in Italy (Fontanesi *et al*, 1985). The CIS comprises four sections and provides individual scores for 12 reported symptoms, ten psychiatric abnormalities detected at interview, and three summary scores: the reported symptoms score, the observed abnormalities score and the total weighted score. For each item, an overall severity rating is devised on a five-point scale, ranging from 0 (no psychiatric disturbances) to 4 (marked psychiatric illness). A total score of 13 is used as the best standard for case identification.

Patients with epilepsy and controls with positive ratings were then classified diagnostically on the basis of DSM-III-R (American Psychiatric Association, 1987) by a board-certified psychiatrist.

In order to assess the correlation between socio-economic factors, psychiatric disturbance and epilepsy, the main demographic variables (age, sex, schooling, marital status and occupation) were recorded for epileptic patients and controls. Then for each patient the main characteristics of the disease (duration of epilepsy, seizure type(s), time from last seizure, number and type of drugs) were recorded and

correlated with the results of the psychiatric interview. These predictor variables were recorded by three board-certified neurologists (EB, GB, VC) with special expertise in epilepsy who were blind to all psychiatric data. The interviews with all the epileptic subjects and controls were conducted by a psychologist (EF) who was also an expert in psychodiagnostic testing.

Data were processed using the Statistical Package for the Social Sciences (SPSS, 1986). Statistical analysis was done using Student's *t*-test and the  $\chi^2$  method where appropriate. In patients with epilepsy, the degrees of correlation between psychiatric disturbance and demographic and clinical characteristics were expressed as relative risks and estimated as odds ratios (OR) and confidence intervals (CI) according to the Mantel-Haenszel method (Mantel & Haenszel, 1959). All the clinically relevant variables were assessed by univariate and multivariate logistic regression analysis.

Assuming that the proportion of subjects with psychiatric disturbance in the general population, as assessed by the CIS, lies in the range 11–47% (Harding *et al.*, 1980; Mari & Williams, 1984; Fontanesi *et al.*, 1985), a risk among epileptic patients of 2.5 times the normal would have implied the recruitment of 80–150 diseased individuals and matched controls, taking  $\alpha = 0.05$  and  $\beta = 0.20$ .

### Results

During the study period a total of 100 patients with epilepsy and 100 age- and sex-matched controls were considered suitable and submitted to psychiatric interview. There were no refusals or incomplete examinations.

There were 54 men and 46 women in each group. Mean age was 33.6 (s.e.m. 1.4) years in patients with epilepsy and 34.2 (s.e.m. 1.3) years in the controls. Twenty-six patients had less than 6 years of education, 28 had 6–8 years, and 46 had more than 8 years. The corresponding figures for the controls were 14, 29 and 57. Forty-nine patients and 52 controls were married; included in this category were those who were widowed (3 in each group) and divorced (3 patients). Sixty-five patients and 64 controls were, or had been, involved in specific occupations. Of these, 11 and 9 were retired or housewives. Unemployed persons included students (5 patients, 8 controls).

The mean disease duration was 12.5 (s.e.m. 1.1) years (< 2 years, 12 patients; 2–5 years, 20 patients; 6–10 years, 16 patients; > 10 years, 46 patients; unknown, 6 patients). Generalised (mostly tonic-clonic) attacks were the most common seizure type (67 cases). Partial seizures of presumed temporal origin were present in 28 cases and multiple seizure types in ten. In ten patients (five untreated), seizure remission lasting for 2 years or more had been recorded. Seventy-five patients received monotherapy. Carbamazepine was the most common drug (50 cases), followed by phenobarbital (21), phenytoin (14), valproate (10), primidone (6), clonazepam (6) and diazepam (1).

A total of 19 patients with epilepsy and 15 controls were identified as having psychiatric disorders ( $\chi^2 = 0.57$ ;  $P = 0.45$ ).

The psychiatric diagnoses based on the DSM-III-R classification included anxiety disorder (not otherwise specified (NOS)) (3 patients, 6 controls), depressive disorder

(NOS) (3 patients, 5 controls), generalised anxiety disorder (3 in each group), dysthymia (or depressive neurosis) (3 patients), borderline personality disorder (3 patients), histrionic personality disorder (1 patient), somatoform disorder (NOS) (2 patients), simple phobia (1 patient), and somatisation disorder (1 control).

When the individual items were assessed, emotional problems tended to prevail in both groups (Table 1). In addition, more epileptic patients than controls complained of irritability (17 v. 10) and/or impaired attention (9 v. 4) and/or fatigue (10 v. 6).

Among patients with epilepsy, the variables which were correlated with higher risk of psychiatric disturbance were lower educational status, number of seizure types, polytherapy and – to a lesser extent – female sex and lack of occupation (Table 2). Number of seizure types (OR 3.58; CI 2.03–5.13) and polytherapy (OR 3.01; CI 1.78–4.24) maintained significance when multivariate analysis of data was completed after adjusting for age, sex and educational level.

### Discussion

Our study showed that non-retarded patients with cryptogenic epilepsy develop psychiatric disturbances at a rate similar to that in a non-epileptic population. Our findings are at variance with several other

Table 1  
Abnormal psychiatric symptoms and signs in patients with epilepsy and controls, based on the Clinical Interview Schedule

	Patients with epilepsy (n = 100)	Controls (n = 100)
<i>Reported symptoms score</i>		
Depressive thought content	42	35
Depression	20	16
Phobias	17	15
Somatic symptoms	17	12
Irritability	17	10
Fatigue	10	6
Lack of concentration	9	4
Excessive concern with bodily functions	4	8
Sleep disturbance	5	8
Anxiety	5	1
Depersonalisation	5	–
Obsessions and compulsions	–	–
<i>Observed abnormalities score</i>		
Depressed	40	45
Histrionic	22	18
Anxious	14	10
Slow, lacking spontaneity	7	5
Elated, euphoric	4	2
Suspicious, defensive	2	–
Intellectual impairment	1	–
Flattened, incongruous	1	–
Hallucinations	–	–
Delusions, thought disorder	–	–

Table 2

For patients with epilepsy, psychiatric disturbance based on the total score of the Clinical Interview Schedule, main subject and disease characteristics, and univariate analysis

Variable	Psychiatric disturbance		Univariate analysis	
	Number of cases	%	Odds ratio	Confidence interval
<b>Age</b>				
< 25 years	6	19	1	—
25–34 years	6	20	1.08	0.49–2.42
35–44 years	4	21	1.16	0.20–6.58
> 44 years	3	16	0.81	0.02–32.18
<b>Sex</b>				
Male	8	15	1	—
Female	11	24	1.81	0.49–6.60
<b>Education</b>				
< 6 years	7	27	3.87	0.82–18.21
6–8 years	8	29	4.20	0.96–18.29
> 8 years	4	9	1	—
<b>Marital status</b>				
Single	9	18	1	—
Married	10	20	1.20	0.03–45.99
<b>Occupation</b>				
No	9	26	1.90	0.53–6.87
Yes	10	15	1	—
<b>Seizure types</b>				
Temporal	6	21	1.24	0.20–75.57
Other	13	18	1	—
<b>Disease duration</b>				
≤ 5 years	7	22	1	—
> 5 years	12	19	0.77	0.08–7.60
<b>Number of seizure types</b>				
1	15	17	1	—
2+	4	40	3.33	0.58–19.08
<b>Time from last seizure</b>				
≤ 2 years	17	19	1	—
> 2 years	2	20	1.07	0.71–1.62
<b>Number of drugs</b>				
None	1	20	1	—
1	10	13	0.62	0.01–27.73
2+	8	40	2.67	0.01–1421.47

reports which showed patients with epilepsy had more psychiatric problems than normal individuals. However, the higher levels of psychiatric problems found in previous series may be explained largely by selection bias. Most reports are drawn from clinic-based series which cannot be generalised to unselected groups of persons with epilepsy. In fact, in those series, patients most likely to show poor psychological adjustment may be over-represented.

Accordingly, the low prevalence of psychiatric abnormalities of our study fits with the results of a recent community-based survey on psychological and social adjustment to epilepsy (Trostle *et al*, 1989), which showed that psychological impairment in 125

non-retarded adults with unprovoked epileptic seizures in the community is low compared with that found in selected out-patient services.

Although in Italy patients with epilepsy, however serious, have easy access to the hospital out-patient services (including epilepsy centres) and several subjects had their epilepsy first diagnosed in our institution, the present study is not a community-based survey. Had our patients been a more representative sample of the overall epileptic population, the difference in the prevalence rates of psychiatric disturbance among epileptic and non-epileptic subjects would have been even lower.

Our data are at variance with those of Edeh & Toone (1985), who used the CIS to assess psychiatric morbidity in patients with epilepsy aged 16 years and older from a general-practice survey. In that study 37 out of 82 patients (45%) scored 13 or more. However, only patients with repeat anticonvulsant prescriptions and a history of at least three epileptic seizures in any two-year period were included. Then, individuals with brain lesions or focal neurological signs were retained.

In general, abnormal interictal behaviour is more likely to be correlated with an epileptogenic brain lesion, as recently confirmed (Dodrill & Batzel, 1986). The prevalence of emotional and psychiatric problems among patients with epilepsy is similar to that among subjects with other neurological disorders (Dodrill & Batzel, 1986), suggesting that the poor psychiatric adjustment may be more properly linked to an underlying overt encephalopathy than to epilepsy *per se*. This concept is in keeping with the results of Matthews & Klove (1968), who showed that patients with epilepsy of known aetiology had worse psychiatric adjustment, by the Minnesota Multiphasic Personality Inventory (MMPI), than patients with cryptogenic epilepsy.

Our findings merit some comments in the light of the controls employed, and the methods for ascertainment of psychiatric disorders.

First of all, a control group of individuals undergoing minor surgery may actually involve a higher rate of emotional problems. This could help explain the higher degree of mood impairment in our controls, as the structure of the interview cannot differentiate between state and trait anxiety (Spielberger, 1966, 1972a,b). However, the proportion of psychiatric disorders found in our reference population, similar to that found in primary-care investigations in developing countries (11–18%) (Harding *et al*, 1980), was lower than that reported using the same screening instrument in other samples of the general population (46–47%) (Mari & Williams, 1984; Fontanesi, *et al*, 1985). This difference

is probably attributable to the validity and reliability of the screening instrument used. In fact, as shown in the validity study (Fontanesi *et al*, 1985), the sensitivity and specificity of the CIS were only 75% and 54% respectively, with a misclassification rate of 35%. Therefore, this standardised interview is only a rough instrument for screening for psychiatric disorders, and some individuals with positive symptoms in the two groups may have escaped notice here. However, it was not the main goal of the present study to calculate the prevalence rate of psychiatric disorders in epilepsy; the study simply aimed at comparing the psychopathology of patients with epilepsy and normal individuals.

The psychologist who conducted the interview was not blind to patient groups. However, this bias may not have affected our data, as our negative results contrast with the common belief that patients with epilepsy are at higher risk of psychiatric morbidity.

As in the general population, the prevailing psychiatric disorders were anxiety and depression (Regier *et al*, 1988). This is in keeping with several reports that dysthymia is the most common condition among epileptic patients assessed with different screening instruments, including the CIS (Kogeorgos *et al*, 1982; Mendez *et al*, 1986; Edeh & Toone, 1987; Robertson *et al*, 1987; Mendez, 1989), and provides evidence that the psychopathology of epileptics is by and large similar to that of the general population.

The few individuals with personality disorders were only among patients with epilepsy. However, patients classified as having personality disorders in our sample did not conform to the general characteristics of the 'epileptic personality' seen in patients with temporal lobe epilepsy (Bear & Fedio, 1977). The small sample size (which included an even smaller number of subjects with temporal lobe epilepsy) and the controversial issue of the psychopathology of temporal lobe epilepsy (Dodrill & Batzel, 1986) may also explain our negative findings.

The correlation between the number of seizure types and the presence of psychiatric problems is worth noting. This is in agreement with other reports (Rodin *et al*, 1976; Hermann *et al*, 1982; Dodrill, 1984) and does suggest that some unknown biological factors may play a role in the origin of emotional/psychiatric symptoms in epilepsy.

Psychiatric disturbances were more prevalent among patients with multiple drug regimens. The behavioural and cognitive toxicity of phenobarbital and, to a lesser extent, phenytoin and carbamazepine is well known (Meador *et al*, 1990). In our sample 27 patients were treated with barbiturates (including primidone), which are frequently accompanied by symptoms and signs of mental impairment (Wolf &

Forsythe, 1978; Reynolds, 1983). Anti-epileptic drugs also alter neurotransmitter and other monoamine levels, which have been implicated in the pathophysiology of depression (Robertson, 1989). However, as multiple drug therapy often couples with combined seizure types, which affect interictal behaviour, the independent contribution of drug treatment cannot be clearly assessed in our sample. This issue must be addressed at the study-design stage by matching patients with epilepsy for number of drugs and their types.

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