The psychoses of epilepsy

B K Toone FRCPsych FRCP *Department of Psychiatry, King's College Hospital, Denmark Hill, London SE5*

Keywords: epilepsy; schizophrenia; laterality; post-ictal psychosis

Paper read to Section of Psychiatry, 13 November 1990

In this article I will review some aspects of the psychoses of epilepsy and consider how a study of these relatively uncommon disorders may aid our understanding of the functional psychoses. This widely-used schema (Table 1) describes a number of disorders, all in some way related to epilepsy but by no means all psychotic in the now commonly used meaning of the word. It can be seen that these disorders fall clearly into two separate groups; a pericta group in which the close temporal association between the abnormal mental state and the ictus leaves little room for doubt regarding the aetiological relationship, and an interictal group of chronic psychotic disorders, of which it could be said the relationship with seizure disorders is one of statistical association, the two sets of disorders coexisting more commonly than chance would predict. Their causal relationship is a matter for speculation. Only the interictal psychoses of a schizophreniform type and the postictal psychoses will be considered here. The abnormal mental states that may accompany minor status fall within the category of organic confusional states and while of interest clinically bear little resemblance to the functional psychoses. There is little evidence to suggest that epileptic patients are predisposed to develop affective psychoses.

I will first deal with the interictal condition, the so-called schizophrenia-like psychosis of epilepsy (SLPE). An association between epilepsy and schizophrenia had been noted since the turn of the century[1], but there was considerable uncertainty regarding its direction. There was much debate as to the respective merits of the 'affinity' and 'antagonism' hypotheses (attention to the latter prompted the first use of ECT) but both were eventually accommodated within a conceptual framework that recognized the increased incidence among patients with epilepsy, but also that in some patients epileptic and psychotic symptoms might show reciprocity, that is, one set might wax as the other wanes. This so-called inverse relationship has attracted considerable attention in Europe, less so in this country where the phenomenon is less frequently commented on. We are indebted to Elliott Slater and his colleagues[2] for the first detailed clinical description. Elliott Slater's observations were based on the tertiary referrals seen at the Maudsley Hospital and at the National Hospital for Nervous diseases. Since that time a series of studies of the epileptic psychoses have emanated from these two centres[3-5], and a fairly consistent pattern has emerged. The principle characteristics of the schizophrenia-like psychoses of epilepsy may be summarized as follows:

(1) Among epileptic patients a schizophrenia-like syndrome occurs more commonly than chance would predict.
(2) This condition is not clearly distinguishable from schizophrenia on phenomenological grounds.
(3) Temporal lobe epilepsy is over-represented.
(4) A family history of schizophrenia occurs with no greater frequency than in the general population.
(5) The onset of seizures almost invariably precedes the development of psychotic symptoms, usually by an interval of several years.

These statements cannot be made without reservation. They have emerged from work conducted at post-graduate teaching hospitals and lack a foundation in epidemiological research. A sixth statement may be added, one that is more controversial but also of greater immediate interest in the light of current research in schizophrenia.

(6) Within the various combinations of epilepsy sub-types and psychosis sub-types, a schizophrenia-like syndrome is usually associated with a dominant temporal lobe focus.

Flor-Henry's finding[6], for it was he who first reported this association, remains controversial for although it has been largely supported by subsequent research (Table 2) there have been important negative studies. A more recent study[3] goes further and finds a more exclusive association between a nuclear schizophrenia syndrome as defined in the Present State Examination[8] and dominant temporal lobe foci.

If the laterality findings can be accepted, SLPE represents not only an excellent example of asymptomatic psychosis (ie a schizophrenic phenotype associated with and presumably causally related to

Table 1. Psychoses of epilepsy: classification

Brief psychoses
(A) Ictus-related states
  (1) Pre-ictal states
  (2) Minor status: Petit mal status
      Psychomotor status
  (3) Post-ictal confusion
  (4) Post-ictal psychosis
  (5) Other states: twilight states
      fugue states
(B) Unrelated to seizure activity
  (1) The alternating psychoses
  (2) Sub-ictal psychotic states

Chronic interictal psychoses
Schizophrenia
Paranoid
Manic-depressive

0141-0768/91/080457-03/02.00/0

*Table 2. Epilepsy discharge, lateralization and type of psychosis: a summary**†*

	Schizophrenia			*Affective disorder*		
	Left	*Right*	*Bilateral*	*Left*	*Right*	*Bilateral*
Slater *et al.* (1963)	16	12	20			
Flor-Henry (1969)	9	2	10	2	4	3
Kristensen & Sindrup (1969)	24	30	33			
Taylor (1972)	2	2	0	1	1	0
Gregoriadis *et al.* (1973)	43	0	0	0	9	0
Lindsay *et al.* (1979)	9	0	2			
Pritchard *et al.* (1980)	2	1	0	1	0	1
Hara *et al.* (1980)	6	4	0			
Sherwin (1981)	5	1	0			
Perez *et al.* (1985)	7	2	2			
Toone (1989)	6	4	11	7	3	11
Total	129	58	78	11	17	15

*The study by Jensen & Larson (1979) is not included as these authors did not refer to any numerical data relating to laterality
†Table 2 is taken from ref 7

a primary organic disorder) but also an example of a psychosyndrome associated with localized or lateralized region cerebral pathology.

The rather stately progress of research into the psychoses of epilepsy, unavoidable perhaps given both the complexity and the rarity of the disorder, has been overtaken by biological studies of the functional psychoses. Computerized tomography may only have confirmed what air encephalography had already made known about the schizophrenic brain, namely that modest but statistically demonstrable atrophy is present in a substantial minority of patients. But the ready availability of this relatively unintrusive technique rekindled interest in brain structure and set in train a series of neuropathological studies. The findings from these have in turn sought and received confirmation in the more precise reconstructions of magnetic resonance imaging (MRI). Both neuropathology and neuroimagining have identified structural abnormalities in the temporal lobes, and where lateral asymmetries have been noticed it is usually the left temporal lobe that has appeared most severely affected. Common findings in the neuropathological studies are a reduction in tissue volume, particularly in the hippocampal area[9] and parahippocampal and entorhinal cortical thinning[10,11]. MRI findings are less consistent but several studies have reported reductions in single slice temporal lobe area measures, in temporal lobe and hippocampal volume, and an increase in temporal horn size, all of these changes more marked on the left. There is thus a convergence of evidence from studies of psychotic epileptic and functional psychotic patients, implicating the dominant temporal lobe.

In schizophrenia one line of enquiry has demonstrated structural changes in the temporal regions, another has reported frontal dysfunction. Regional cerebral blood flow (CBF) and metabolic studies have demonstrated impaired function, so-called relative hypofrontality, particularly under conditions of cognitive challenge. It is thought that frontal impairment may contribute to the presence of negative symptoms in schizophrenia.

What implications does this have for the SLPE. Here we may assume there is no frontal lobe involvement and that therefore negative symptoms would not be conspicuous. Attempts to demonstrate a difference in psychotic symptomotology between the primary and epileptic schizophrenias had been largely unsuccessful[5,12], but these were carried out at a time when there was little interest in negative symptoms and before the instruments to measure them had been developed.

Finally we shall consider why, if the hypothesis that the nuclear schizophrenic syndrome is related to dominant temporal lobe pathology is correct, the laterality literature is so inconsistent. Two explanations stand out. First, the epileptic schizophrenic population is presumably of mixed aetiology. The disorder occurs more often than chance would predict, so presumably the excess arises due to a causal relationship between epilepsy and schizophrenia, that is to say, the first increases the risk of the second. This should not lead us to overlook the fact that epilepsy and schizophrenia are each common disorders and many epileptics will develop schizophrenia as a matter of chance. These cases will introduce a confounding factor into any search for explanatory hypotheses.

Second, the validity of the laterality studies leans heavily on the operational definition of a unilateral focus. The criteria are not always clearly stated. In fact, the more comprehensive the investigation, the fewer the cases. This is particularly true of EEG studies. The more often the EEG is repeated, the more often evidence of bilateral temporal involvement or of extra temporal foci will be discovered. More sophisticated neuroimaging has revealed more pathology. Using MRI, lesions can be demonstrated in over half of those cases with well controlled partial complex seizures. CBF studies demonstrate hypoperfusion extending well beyond the limits of structural abnormalities. Moreover, a battery of tests may produce conflicting evidence of lateralized abnormalities. It follows from this that a research strategy that sets out to identify a sizeable group of patients with dominant unilateral temporal foci is likely to encounter difficulties. It would be methodologically more realistic and almost as valid to define a group of patients with epileptic psychosis and to test the hypothesis that all patients with a nuclear schizophrenic syndrome showed dominant temporal lobe pathology, even though other parts of the brain might also be affected.

Finally I wish to consider the postictal psychoses, a brief psychosis that is well recognized by most specialists who work with epileptic patients, but which has attracted surprisingly little attention in the literature. In 1989 Drs Steven Logsdail and I published a brief account of 14 such patients seen mainly at the Maudsley and at King's College Hospital[13]. The diagnostic criteria were as follows: The onset occurs within one week of the seizure; the duration is one day to 3 months; the mental state is characterized by a mixture of delusions and hallucinations which may or may not occur in clear consciousness; other possible diagnoses are excluded. These include brief postictal confusion, interictal psychosis, anticonvulsant toxicity, minor status and dissociative states. Each case was comprehensively investigated. Most patients had more than one episode. The mean age of onset of epilepsy was 17 years and of psychosis 32 years. Most patients had partial complex seizures with secondary generalization. Most developed psychosis after an exacerbation of seizure activity. Of particular interest 12 exhibited a lucid interval between the cessation of seizure activity and the beginning of the psychosis. The mental state phenomenology was characterized by confusion (nine patients; sustained in five) and hallucinations (six in the visual, six in the auditory modality). Primary delusions and thought disorder were seen only in one patient. The pre-psychotic EEG showed focal sharp wave/spikes in nine and in six of these there was an increase in discharge activity during the psychosis.

What do the two forms of epileptic psychosis have in common and how does this assist us in understanding their aetiology? Both psychoses occur more commonly in patients with partial complex seizures but only after an interval of over a decade. A history of psychiatric illness is unusual. This raises the possibility of a limbic kindling process. Postictal psychoses usually follows an exacerbation of seizure activity and so may be related to the degree of disturbance in the cerebral metabolism or neurotransmission. The increase in epileptic discharge activity suggests that the psychosis may represent an active process, even conceivably a type of limbic status.

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(Accepted 29 April 1991)