PSYCHOSIS AND TEMPORAL LOBE EPILEPSY

by

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INTRODUCTION

The question of the relationships existing between the epileptic psychoses and the functional psychoses is of particular interest not only because the circular, periodic or manic-depressive states first described by Falret (1794-1870) and Baillarger (1809-1890) were for almost fifty years widely believed to be manifestations of latent or larval epilepsy on account of the regularity of symptom-fluctuation common to both conditions but also because 'dementia-praecox' introduced by Morel and fully categorised by Kraepelin, who incorporated within its boundaries Kahlbaum's catatonia and Hecker's hebephrenia, was, soon after its definition, also associated with epilepsy which was believed, notably by Kraepelin, to be a relatively common concomitant of dementia praecox. Thus, historically, the problem of the functional psychoses was from the outset intimately connected with the problem of the mental correlates of epilepsy and with that of the epileptic psychoses.

By 1900 the concept of larval epilepsy had fallen into disfavour, however, the question of the role of epilepsy in the genesis of the functional psychoses arose anew with the introduction of the wider concept of schizophrenia established by Bleuler. There followed over the next 30 years or so the fascinating swing of opinion whereby from the belief that dementia-praecox and epilepsy were commonly associated it came to be thought

that their combination was so rare that the one state must protect against the other leading to the "antagonism" theory enunciated by Glaus in 1931, the theoretical background which made possible the introduction of artificially induced convulsions for the treatment of psychotic states.

As it was subsequently recognised that electro-convulsive therapy was almost specifically effective in arresting affective psychoses but without action on the fundamental symptoms of schizophrenic disorders and following Giese and Verkastner (1914), as Esser in 1938, Follin in 1941, Hill in 1953, Pond in 1957 and Slater in 1963 described with increasing precision how far from protecting against schizophrenia certain forms of epilepsy on the contrary predisposed to chronic paranoid hallucinatory psychoses in fact undistinguishable from schizophrenia, the antagonism theory in its original and general formulation was clearly shown to be incorrect.

It is to be noted that many recent studies on the phenomenology of epileptic psychoses on the whole agree that from a clinical point of view the symptomatology of an "epileptic" psychosis cannot be differentiated from a comparable non-epileptic psychosis, in contrast to the views of many of the classical workers, Krafft-Ebing, Samt, Christian, Kraepelin and Krisch amongst others who considered

that there were specific characteristics by which an epileptic psychosis might be recognised, (apart from epilepsy) or, more recently of Hill and Pond, who emphasised the presence of warmth of affect in the chronic paranoid hallucinatory psychoses associated with temporal lobe epilepsy.

The last major study published on epileptic psychoses is that of Slater, Beard and Glithero on the "schizophrenia-like" psychoses associated with temporal lobe epilepsy in which the authors conclude that the emergence of psychosis is related to the duration of the epilepsy and to brain-damage but is independent of the severity of the epilepsy. This is a very important conclusion for it implies that epileptic psychoses are fundamentally non-specific organic psychoses where epilepsy plays a part only in so far as it may lead to brain-damage.

There is a large body of clinical evidence which suggests that, for the individual patient there is, in fact, an inverse relationship between convulsive manifestations and mental state, psychotic episodes without fits alternating with sane periods with fits; psychotic episodes on the one hand terminating by spontaneous or artificially induced convulsions or on the other being induced by excessive anti-convulsant medication; phenomena which have been verified electrophysiologically, in particular by Dongier who finds statistically that there is a disappearance of anterior

temporal discharges for the duration of certain paranoid psychoses occurring with temporal lobe epilepsy, an inverse correlation between epilepsy and psychosis independently demonstrated by Landolt who labels it "forced normalization".

If certain forms of epilepsy predispose to certain forms of psychosis, while, at the same time, convulsive attacks protect against the psychotic manifestations made more probable by the epilepsy and, furthermore, if epileptic psychoses are undistinguishable from non-epileptic psychoses, then the whole question of the relationship of epileptic psychoses to the functional psychoses again arises, this is of great theoretical importance. Are epileptic psychoses simply organic psychoses related to brain damage? Are they true "epileptic" psychoses intimately related to the epileptic process? Are convulsive seizures and psychosis antithetical manifestations of the same underlying neurophysiological disturbance of cerebral function? Can a relationship be found between epileptic variables and the form of the psychosis?

The present investigation is an attempt to elucidate some of these problems.

HISTORICAL

(a) Epilepsy and manic-depressive psychosis.

(b) Epilepsy and confusional psychosis.

(c) Epilepsy and schizophrenia.

(a) Epilepsy and manic-depressive psychoses

Morel, in 1860, introduced for the first time the idea that those mental disorders which, in their symptomatology, resemble pre-ictal or post-ictal states are epileptic in origin (1). Labelling those disorders "épilepsie larvée", or "latent" epilepsy he emphasised that the term should be restricted to describe mental phenomena of an abnormal kind occurring in individuals not otherwise considered epileptic; in other words free from convulsive attacks. In this way episodic depressions, explosive attacks of senseless and motiveless aggression, progressive intellectual deterioration were understood to be epileptic in origin although non-ictal in form; a view which Morel justified by noting how frequently in these cases epilepsy revealed itself after a prolonged "incubation" by "crude" convulsive features (2).

Falret (3) essentially in agreement with Morel, preferred to call these conditions "petit and grand-mal intellectuel", both authorities assuming a hereditary genesis (4,5,6). The concept of latent epilepsy became then widely accepted, "épilepsie de l'intelligence" for Legrand du Saulle (7), "epilepsia simplex" for Berenstein (8) at a later date; soon the notion was extended to cover not only epileptic-like mental abnormalities in

non-epileptics but also to similar ones in epileptics themselves, as for instance was done by Tuke and Maudsley (9), and Magnan (10,11,12) who raised the warning that psychoses found in epileptics were not necessarily epileptic psychoses but who, curiously, did not recognize the independent existence of Falret's "folie circulaire" which he believed, with increasing knowledge into the nature of epilepsy would become eventually included with the epileptic disorders.

The basic importance of the concept of latent epilepsy was that it represented an attempt to isolate a pathological entity as specific as G.P.I. to account for the aetiology of the conditions that were later to be grouped under the equally vague rubric of "functional" psychoses. Although generally well received it should not be thought that informed opinion in the second half of the XIXth Century universally approved of "larval" epilepsy as an explanatory scheme; Delasiauve (13) in 1872 objected that no matter "however seductive the hypothesis .... of Mr. Morel it is important not to get carried away", to which Christian (14) added in 1878: "larval epilepsy does not exist ... it is merely undiagnosed epilepsy".

Retrospectively it is now clear that most of the symptoms of latent epilepsy were those of ictal

psychic disorders, characterised by sudden onset and sudden disappearance, brief duration, confusion, complete amnesia and periodicity.

One of the principal concerns of psychiatry between 1860 and 1899 was to differentiate and clarify the relationships between epilepsy, circular insanity, "folie à double forme" and intermittent madness: a relatively unprofitable discussion which ended with the emergence of the manic-depressive polarity of Kraepelin in 1899.

Nonetheless the Kraepelinian fusion whereby a large number of previously heterogeneous periodic states were reduced to alternative manifestations of a unitary underlying psychosis was not accepted without resistance and, with a shift of emphasis, the question continued to be debated. Of particular interest is the fact that, historically, one can view manic-depressive insanity as a rival construct to "larval epilepsy" both being theoretical models designed to account for mental abnormalities exhibiting periodicity.

Since Morel had refused to accept as valid either Baillarger's "folie a double forme" (15,16), or Falret's "folie circulaire" and Griesinger (17) grouped with epileptic disorders certain outbursts of mania that were of brief duration, the central problem became then one of differential diagnosis: how to distinguish non-epileptic periodic disorders from ictal ones? Morel lay stress on

the sudden onset of the explosion, the periodicity of the disorder, the presence of hallucinations; Falret emphasised the explosive violence, the complete amnesia and the terrifying nature of the hallucinatory experience. Epileptic mania was held to be always very brief, rarely lasting more than a few days and Billod (18) maintained that only by the presence or absence of amnesia could one differentiate between epileptic and non-epileptic mania. Krafft-Ebing (19), Samt (20), and Christian generally accepted the conclusion that in some epileptics madness might take the form of circular insanity but remarked that the frank, spontaneous, exalted expansiveness of pure mania was not encountered in epilepsy where a sombre element was thought to be always present. Opposing these views Heilbronner (21), Gurewitch (22), held that pure mania might be undistinguishable from epileptic mania and Meynert (23), speculated that cerebral anaemia followed by hyperaemia was at the root of both epilepsy and mania. Notwithstanding the popularity of Morel's views in the second half of the XIXth Century critics such as Delasiauve, Christian, quoted above, Billod and Witkowski (24), amongst others, continued to express their dissatisfaction with the tendency that made of epilepsy the fulcrum of all periodic mental abnormalities. In spite of which further observations demonstrating the co-existence of mental

illness with epilepsy or showing the alternating substitution of insanity for convulsive phenomena continued to be made by Falret, Tuke, Magnan; but neither the latter, nor Charcot (25), fully accepted the assimilation of periodic insanity with epilepsy. Magnan, over-emphasising the theories of hereditary degeneration considered that if several types of "délires" co-existed in a given individual this could be explained by a multiple genetic aetiology.

The introduction of two new nosological entities towards the end of the XIXth Century modified the problem still further: Chaslin (26), in 1895, described what were in effect the (symptomatic) confusional psychoses and Kraepelin four years later delineated the manic-depressive psychoses. The recognition of confusional psychosis had the consequence that many cases of so-called intermittent manias were seen to be in fact post-ictal states presenting with confusion, stupour or agitation and did not belong to the category of periodic or intermittent insanity. Similarly the comprehensive doctrine of Kraepelin, by defining the fundamental features of mania, depression and mixed states at the same time incorporated many cases of periodic mental disorders within its framework. The relationship between periodic psychic epilepsy and manic-depressive insanity now came to attract attention. Following Magnan, by and large, the importance of hereditary predisposition continued to be

stressed.

Aleksandrow (27), Kaldewey (28) in 1927 postulated a link between cyclothymic constitution and epileptoid characteristics in the following manner: M.D. --> emotional discharges --> twilight states --> seizures whilst Kleist (29) denied that any affinity could be found between twilight states and manic-depressive psychosis.

Notkin (30), Krisch (31) and Heinrichsen (32) were impressed on the other hand by the rarity of convulsive phenomena in manic-depressive psychoses and also point out that even if manic and depressive episodes are common in epileptics these episodes differ from true manic-depressive states. Lange (33) compared attenuated forms of manic-depressive psychosis with mood disorders in epileptics. As was done two generations before for circular insanity the differential diagnosis between manic-depressive insanity, manic-phase and epileptic mania was then explored. Kraepelin and his school held that manic or depressive episodes in epilepsy were always associated with delusions or hallucinations in a setting of clouding of consciousness and whilst Kraepelin believed that flight of ideas was not encountered in epileptic mania, Heilbronner thought that this feature was sometimes present. Clouding of consciousness and amnesia are important pointers in the differential diagnosis of epileptic versus functional

psychosis which would be widely considered valid today, to which Krisch adds the perhaps more questionable observation that in manic-depressive psychoses, depressed phase, the individual views himself as guilty whereas in epileptic depressive conditions he accuses others, projecting externally his morbid ideas.

Marchand and Ajuriaguerra (34), after a very detailed and thorough review of the problem of epilepsy and manic-depressive psychosis conclude that any association between the two conditions is fortuitous and that all cases with (1) deterioration of personality, (2) schizophrenia, (3) phases of very short duration, (4) clouding of consciousness, must be excluded from the category of manic-depressive psychosis. The above authors emphasise further that epileptics with (1) psychic auras with depressive or expansive quality, (2) post-ictal depression, (3) post-ictal excitement or confusion, (4) pre-ictal affective prodromata, (5) confusional episodes of short duration, (6) affective changes, psychic "equivalents" or mood disturbances resulting from anti-convulsant medication, should not be confused with manic-depressive states as the associated affective components are there all related to epilepsy. One perhaps might remark that the criteria of exclusion proposed by Marchand and Ajuriaguerra are, in fact, all characteristic criteria

of epilepsy, so that the argument is circular. Since it assumes that manic-depressive psychosis must be a pure, "uncontaminated" condition it necessarily follows, by definition, that any association or coincidence of the two disorders must be the result of chance as, by an arbitrary nosology, epilepsy is automatically excluded.

During the ictal phase, anxiety, euphoria, agitation or depression are commonly met as affective components of the seizure complex. When intensified to the point of violence, furore, or agitated hallucinatory experience the affective disturbance during ictus amounts to epileptic mania. Aschaffenburg, in 1906 (35), Krisch in 1922 as previously mentioned, and the German school in general have repeatedly drawn attention to the persecutory aspects of affective disorders occurring in association with epilepsy while Lewis, N. (36) in 1939 focusses on the nihilistic component.

Studying a population of chronic, hospitalised epileptics, Lempériére (37), in 1953, is impressed by the high incidence of depressive states, 25 of her 67 patients exhibiting depressive swings and 14 making suicidal attempts. In view of the general characteristics of chronic institutionalised patients these findings are perhaps not surprising and to argue a specific epileptic aetiology here is unconvincing. Agitated and exalted states have been rather more widely studied in epilepsy

than depressive ones and there is after all only a small gap separating the "tachypsychie comitiale" of Picard (38) from manic flight of ideas. As already mentioned Kraepelin had denied the reality of flight of ideas in epilepsy against which Heilbronner, after a thorough study in 1903 concluded that the two conditions were clinically inseparable. Picard (39) presented a number of such cases in 1946. Doutrebente (40), in a paper entitled "manie rémittente, double forme, épilepsie larvée" published in 1886 pondered over a patient whose first illness was intermittent mania, from which he suffered for 14 years, who then became subject to manic-depressive swings for 2 years culminating in convulsive seizures, later giving rise to further manic-depressive episodes. He concluded that manic-depressive states should be included within the field of epileptic psychoses. Without reaching this extreme conclusion, Ey (41), who reports this case, is impressed by the frequency with which manic-depressive states can substitute themselves for epileptic convulsive phenomena and sees in this phenomenon the expression of an underlying unity: the cerebral dysfunction being manifestable either through convulsive features or by alterations of the structure of consciousness, ("déstructuration de la conscience").

(b) Epilepsy and confusional psychoses

The salient characteristics of confusional psychoses are clouding of consciousness and disorientation associated with sudden explosions of extraordinary violence, "epileptic furore" but more often are outbursts of extreme agitation of variable but short duration, lasting hours or days and exhibiting anterograde or retrograde amnesia which may be complete or lacunar. Acutely agitated and stuporous forms are encountered, often as post-ictal phenomena precipitated by serial attacks. Confusional psychoses merge imperceptibly into the epileptic twilight states which have been viewed as intermediary stages between manic-depressive and confusional psychoses. Epileptic twilight states, the "états confuso-oniriques" of the French School, have been widely studied on account of their great medico-legal importance, notably by LeGrand du Saulle (7), in 1877 and by Krafft-Ebing in 1875 (42). Confusional psychoses are polymorphous and may present with depressive, hypomanic or predominantly paranoid hallucinatory features. Epileptic twilight states are really a sub-group in which the disorientation is less florid, presenting some analogies with hypnagogic phenomena such as somnambulism or even night-terrors. If associated with fairly prolonged and apparently purposive behaviour it has to be differentiated from depressive, hysterical

and other fugues. The E.E.G. examination may not be helpful as in the epileptic fugue it may become "normalised", however, twilight states generally are followed by a phase of somnolence analogous to post-ictal sleep and the amnesia is irreversible in contrast to hysteria where it may be overcome by abreactive techniques. Further, the dissociation is of a different quality in the two conditions. In epilepsy regressive dissociation in the Jacksonian senses operates, the personality functions on a coarser, simpler, more elementary level, in hysteria the personality remains well organised and complex but becomes "other" in a manner reminiscent of an actor exchanging roles.

P. Schmidt (43) gives an interesting analysis of the "idiot" and of the "Brothers Karamozov" in which he traces the anguished introspection so characteristic of Dostoievski's world to the author's personal experience of epileptic twilight and confusional states.

Confusional psychoses associated with epilepsy as will be shown later appear to belong to two different categories - (1) post-ictal or related to serial seizures or petit-mal status in centrencephalic epilepsy of which they are the characteristic psychotic manifestation and (2) pre-schizophrenic in temporal lobe epilepsy.

(c) Epilepsy and schizophrenia

Morel had observed the melancholic religiosity that so often affects some epileptics at the onset of their illness. Dupain (44) in his "études cliniques sur les délires religieux" published in 1888 was particularly interested in this problem and although neither Magnan nor Kraepelin had much to comment on the topic, mystical states with overtones of megalomania or pathological culpability, abnormal "passion" states with persecutory flavour and ideas of influence were described in epileptics towards the end of the XIXth Century. A special study of abnormal religious experiences in epilepsy was made in 1918 by Boven (45). It is a tenuous thread which marks the dividing line between abnormal mystical states of this kind and schizophrenia, nevertheless Gruhle (46,47) in 1923, is of the opinion that the combination of dementia praecox and epilepsy is very rare, and by 1936 becomes convinced of the primary nature of epileptic delusional states. Giese (48) and Vorkastner (49) in 1914, demonstrate the close relationship existing between the chronic hallucinatory psychoses of epilepsy and schizophrenia from a phenomenological point of view, Gruhle, Giese and Vorkastner being on the whole agreed on the relative rarity of the association: 8% of Gruhle's 92 cases; 8.6% of Giese's 347 and 4.6% of Vorkastner's patients. As Ey (41) shrewdly reminds us, the importance attached

to epileptic insanity depends partly on the clinical material available and partly on the doctors assessing it: "it can be minimised by neurosurgeons and neurologists or maximised by psychiatrists especially when dealing with institutionalised epileptics". Over the last century the following incidences of insanity occurring in association with epilepsy have been variously reported:-

Moreau de Jonnes (1843)	- 11.2% of insanity in epileptics	(50)
Parchappe (1843)	- 3.5% - ditto -	(51)
44th Annual report of the Department of Mental Hygiene, U.S.A. 1931 - 1932	- 1,247 of 56,804 cases of psychoses or 2.2%	(52)
Sutter (Algiers, 1937)	- 7.7% in North Africans	(53)
Ey, in his own hospital, 2,000 psychotics over 20 year period encountered about 100 epileptics with psychoses, or 5%.		(41)

As in the XIXth Century psychiatrists had concentrated their interest on depressive or intermittent manifestations of psychosis attention in the XXth centred on the chronic, hallucinatory and persecutory states found in association with epilepsy. Kraepelin touches on the problem in his "lehrbuch" enumerating 16% of dementia praecox in his Munich clinic and 18% from the Heidelberg clinic. Morawitz in 1900 (54), discusses epilepsy and catatonia; Masoin at

the Congrès des Aliénistes held in Bruxelles, 1903, reports 4 instances of epileptic fits taking place in patients diagnosed as dementia praecox; Giese (48) in 1914 is preoccupied by the relationship between epilepsy and schizophrenia, Thomas (55) in 1923, Neven (56) in 1925, speculate on the meaning of schizophrenia secondary to epilepsy and of epilepsy secondary to schizophrenia, respectively. In Germany, Krapf (57) in 1928, concentrates on epilepsy and schizophrenia claiming that epileptic attacks in schizophrenia are "accidental" or "hysteroid" while Notkin (30) in what appears to be the first notable contribution in the Anglo-Saxon literature (1929), presents a general review of the problem of epilepsy in relationship to the functional psychoses and contributes 5 cases of his own: three manic-depressives and two schizophrenics with concomitant epilepsy.

With the gradual abandonment of the concept of dementia praecox and the more precise definition of the schizophrenic syndrome, together with the increasing sophistication of the clinical diagnosis of epilepsy the incidence of epilepsy in schizophrenic populations steadily declined:

INCIDENCE OF EPILEPSY IN SCHIZOPHRENIA		
Urstein (1909)	13.5%	380 schizophrenics
Kraepelin (1910)	18%	
Urstein (1912)	3.5%	2,700 schizophrenics
Giese (1914)	8.6%	347 schizophrenics
Vorkastner (1918)	0.9%	217 schizophrenics
Gruhle (1923)	8%	92 schizophrenics
Strauss (1929)	0.33%	6,000 schizophrenics
Glaus (1931)	0.13%	6,000 schizophrenics
Kat (1937)	0.33%	50,000 schizophrenics
Esser (1938)	1.6%	701 schizophrenics
Hoch (1943)	0.4%	500 schizophrenics

INCIDENCE OF SCHIZOPHRENIA IN EPILEPSY		
Gauter (1925)	1 schizophrenic (0.2%)	487 epileptics
Wyrsch (1933)	10 schizophrenic (0.1%)	10,000 epileptics
Hoch (1943)	10 schizophrenic (10.0%)	100 epileptics

Many authors have, for a variety of reasons, critically commented on the above findings. The chief objections have been based on the loose criteria of epilepsy, the diagnosis of schizophrenia and the heterogeneous nature of the populations studied. Urstein (58), after a careful analysis of cases of dementia praecox (200 females and 180 males), discovered attacks of loss of consciousness or of "twitchings" in 13.5% of the combined group. Of note is a differential incidence according to sex, females being more susceptible to epilepsy, 19.5% versus 8% in males. Reviewing 2,700 such patients in 1912 he obtains

the lower incidence of 3.5% (59). The gross heterogeneity of Vorkastner's material has been frequently pointed out by critics for he includes typical epileptics with deteriorated schizophrenics, atypical epileptics with chronic schizophrenics, atypical epileptics with atypical chronic psychoses and confuses schizophrenics with migraines with true epileptics. Krapf (57) is not impressed by the German work up to 1928 purporting to support the simultaneous occurrence of epilepsy and schizophrenia. In particular he reacts unfavourably to the diffuse criteria of epilepsy that were adopted by Kraepelin who included fainting and vertigo with true epilepsy. Investigating 1,506 schizophrenics in Munich he concludes that there is no demonstrable genetic or clinical connection between epilepsy and schizophrenia*. Nevertheless Esser, 10 years later, (60) found that 11 out of 701 schizophrenic patients had convulsive attacks which, as they occurred in very agitated patients, he attributed to raised intracranial pressure and concluded that there were more epileptics in

*Krapf's systematic scepticism on this question is so extreme that it becomes humorous. Analysing the 20 cases of "combination" contributed by Vorkastner, Morawitz, Giese & Buchald he eliminates all but 2 as worthy of discussion, only to reject them as "doubtful". In his own material he is unwilling to accept those patients who might show the combination on the grounds that these could be considered as "true" epileptics!

a schizophrenic population than could be expected by chance and was, perhaps, the first to delineate clearly the paranoid hallucinatory syndrome common to both. He accounts for the discrepancy between his and Krapf's conclusions as being the result of the different nature of his cases, chronic psychotics as opposed to the acute cases reported by Krapf. The contribution of Notkin has already been referred to, he quotes Heinrichsen (61), who in 1911 made the penetrating observation that "whilst a true convulsive attack makes the diagnosis of epilepsy secure, a manic-depressive state in itself does not prove manic-depressive psychosis but may be part of the symptom-complex of epilepsy"; adding that manic or depressive features are common in epileptic psychoses but convulsions rare in manic-depressive psychosis. Ritterhaus (62) is said to have been of the opinion that epilepsy and manic-depressive psychoses frequently combine on account of common aetiological factors, which are not otherwise specified. Notkin dismisses the 5 cases of Krisch (31) on the grounds that they correspond to either pre- or post-ictal euphoric/depressive reactions but similarly one might argue that Notkin's own 5 cases of manic-depressive or schizophrenic psychosis are confusional or schizophreniform psychoses with affective or paranoid components. Hoch (63), investigating 500 unselected chronic schizophrenics from Manhattan State Hospital in 1943 only

finds two cases with convulsions and, screening 100 epileptics, obtains 10 with schizophrenic symptoms. Basing his conclusion on the twin studies of Conrad (64) for the genetics of epilepsy and Kallmann (65) for schizophrenia he rejects a genetic relationship between the two conditions since there is no excess of epilepsy in the families of schizophrenics and no excess of schizophrenia in the families of epileptics. From this Hoch deduces that where the association of schizophrenia and epilepsy occurs it represents either (a) symptomatic epilepsy in schizophrenia or, (b) symptomatic schizophrenia in epilepsy.

It is clear that the general trend after almost a quarter of a century of research and speculation into the interaction of epilepsy and schizophrenia, by the mid-1930's, was that with every major survey the incidence of schizophrenia in epileptics appeared to become smaller. Similarly the incidence of epilepsy in schizophrenics appeared to follow the same pattern. Not taking into account the numerous pitfalls of epidemiological investigations that compare statistics of one country with those of another, that presuppose equivalent diagnostic criteria in the various centres and homogenous populations,

that confuse incidence with prevalence Glaus*(66), noting the inverse relationship often found in individual cases between fit-frequency and hallucinatory state, the psychotic state becoming manifest during periods of few or absent seizures; the psychosis "alternating" with the convulsive phase, confirmed the "antagonism" theory which implied that epilepsy and schizophrenia were mutually exclusive.

In this manner the stage was set for Meduna (67), Nyiro and Jablonszky and for the introduction of artificially induced convulsive therapy for the management of psychotic states (1937). As early as 1924 Meduna had been impressed by the contrast or "antagonism" that he believed differentiated on histological examination, using Weigert stain, brain sections of epileptics from those of schizophrenics: hypertrophic glial proliferation in the former and atrophy in the latter. It is fascinating to note that in 1939 Meduna observed that schizophrenics not

*Investigating 5,000 schizophrenics in Zurich, Glaus finds 8 cases with associated epilepsy, in 4 of whom the illnesses were successive, the schizophrenia appearing after the epilepsy had "died-out". The remaining 4 patients showed either waxing and waning of the two processes in alternate phases, progressive deterioration of schizophrenia as epilepsy improved or the transformation of a schizoid constitution into a schizophrenic state. Emphasising the important contribution of hereditary or constitutional factors Glaus concludes that as a consequence of the interplay of the former the "combination" indubitably occurs although he holds it to be very rare and sees it rather as a "colouring" due to pre-existing constitution.

responding to treatment were much more resistant to seizures than those who responded favourably* and considered the possibility that the induced convulsions were not necessarily causally related to recovery but might only define a group of schizophrenics with good prognosis who were characterized by a spontaneous tendency to exhibit convulsive phenomena. Curiously it was apparently on the evidence of two cases reported by Mueller, 1930 (68) "of catatonics being healed after spontaneous convulsions" that Meduna was in 1935 moved to inject camphor then cardiazole in an attempt to cure schizophrenia, an innovation based on shaky evidence that was to revolutionise psychiatric therapy.

As insulin replaced cardiazole as a convulsive agent (69), as coma rather than seizures came to be emphasised as the parameter of cure in schizophrenia and as electro-convulsive-therapy became widely applied for the

*

Cured	Not cured
Weight = 55 kg.	Weight = 58 kg.
Camphor = 70 gm.	Camphor = 129 gm.
Fits = 6	Fits = 2

Mean figures for first ten patients

the management of depressive psychoses (70), paradoxically, the "antagonism" theory gradually fell into disfavour precisely as it was more and more convincingly demonstrated that artificial convulsions dramatically improved depressive, catatonic, stuporose, confusional and even manic psychoses.

Although by 1940 less topical a controversy, the problem of epilepsy, schizophrenia and the role of constitutional factors; of epilepsy and the atypical psychoses; of the relationship between schizophrenia and induced convulsions - continued to engage the interest of certain workers: for instance of Minkowska (71), Follin (72), and Yde, Edel-Loshe and Faurbye (73), for the above inter-relationships, respectively. Minkowska undertook a very detailed genealogical study of the families of two brothers admitted to the Burgholzi with atypical psychosis, manic-depressive type in the one, schizophrenic in the other. Although interrupted by the first world war, the investigation was carried out over a period of 5 years. Minkowska came to the conclusion that constitutional factors were responsible for the atypicality of the psychotic manifestations and noted the association of epilepsy and schizophrenia in 3, and of epilepsy and manic-depressive psychosis in 2 members of these families. Later (1944), the author became well-known for her emphasis on "viscosity" as a characteristic of the

personality structure of the epileptic, labelling it "glischoroidie". Yde and his collaborators studied 715 patients with schizophrenia in Viborg mental hospital and their investigation illustrates the type of evidence which emerged in the 1940's and appeared to disprove the antagonism theories. From the 715 schizophrenics they only found 20 patients who developed seizures and, with a very restrictive definition of epilepsy, only retained 5 of these as being true epileptics, a figure nevertheless leading to an incidence of epilepsy in this group of the order of 0.7%, or twice that of the Danish population.

For this reason, and also because they note that cardiazole induced convulsions differ from spontaneous convulsions in that the former are associated with a rise in the convulsive threshold, increasing amounts of the drug being necessary to induce serial seizures, in contrast to epilepsy where there may be a progressive tendency to attacks after a seizure, the Danish workers consider that the antagonism theory is not supported by the facts.

The question of the degree to which induced seizures differ from, or coincide with, spontaneous seizures remains unsolved to this day although it is known that induced seizures in epileptics do not necessarily reproduce the autogenous fits; nevertheless

the conclusions of Yde are open to a number of objections: in the incidence analysis incidence is confused with prevalence; the incidence of epilepsy in a hospitalised population being compared to the prevalence of epilepsy in the general population; it is implicitly assumed that epilepsy in the group is symptomatic epilepsy secondary to schizophrenia, the possibility of epilepsy with secondary schizophrenic symptomatology not being seriously considered; it is a matter of common observation that in epilepsy a fit is frequently followed by a state of relative fit-resistance and it is possible to argue that on this basis induced fits are, in fact, analogous to spontaneously occurring ones. Since the mechanism of status epilepticus and the phenomena associated with fit resistance are largely unknown no theoretical conclusion can legitimately be drawn from speculations concerning the attributes of induced seizures.

The Danish study is, however, an important one for it is one of the first of the contemporary investigations to demonstrate that schizophrenia and epilepsy cannot be viewed as mutually exclusive states in the general sense, as Glaus and Meduna had done, and as broadly it confirmed the work of Esser, suggesting that at a certain level epilepsy and schizophrenia were associated. As previously mentioned Hoch maintained that any association between

schizophrenia and epilepsy was fortuitous, evenwhen 10% of the epileptics in his own series exhibited schizophrenic symptoms. At about this time Follin (1941), after Esser, is amongst the first to demonstrate that certain epileptics may progress to schizophrenia. Ey, from his own hospital, finds that 5% of his epileptics evolve towards a paranoid hallucinatory state with visual hallucinations, oneiroid and fantastic elaborations that he compares to "post-encephalitic schizophrenia".

E.E.G. AND DEPTH E.E.G. STUDIES AND THEIR CONTRIBUTION TO THE PROBLEM OF PSYCHOSIS

With the increasing sophistication of electro-encephalographic techniques and interpretations that derived from the seminal centres of Harvard, shortly to be followed by the Montreal and Marseilles schools, it was natural that E.E.G. investigations should be directed on the combined problem of epileptic activity and schizophrenia. The early work of Berger (1931, 1936), of Travis and Malamud (1937), of McMahon and Walters (1938) discovered no abnormalities in the E.E.G. of schizophrenics. However, Lemere (74) found "poor activity" and Davis and Davis (75), three years later, "observed more seizure discharges in schizophrenics than in normals". Gibbs, Gibbs and Lennox (76) in 1938 and 1941 still preoccupied by the "psychomotor wave" which turned out to be artefactual, believed that schizophrenia-like immaturity or psychopathy was reducible to "cerebral dysrythmia" of psychomotor pattern. In the first systematic E.E.G. inquiry into the question of mental abnormality and epileptic background, Jasper, Fitzpatrick and Solomon (77) in 1939 compared the E.E.G. records of three populations: schizophrenics, epileptics and normals. The 82 schizophrenics, including catatonics, paranoid, hebephrenic and simplex ranged in age between 12 and 68. 51 epileptics with clinical epilepsy and complete ictal and non-ictal E.E.G. records were matched for age. The controls consisted

students and staff. A very careful technique designed to ensure maximal relaxation and minimal artefact was utilised. The schizophrenics and epileptics fell at opposite ends of a scale based on α-frequency with normals occupying the median range and 23% of the patients diagnosed schizophrenics showed clinical or E.E.G. evidence of epileptic activity; six of these having convulsions. The great variability of individual records, overlapping with normals or controls, was noted in the schizophrenic group. Although Jasper and his colleagues are unfavourably disposed towards the antagonism theory which they dismiss as "confused", the above results nonetheless can be interpreted as supporting the notion that epilepsy and schizophrenia are phenomena correlated in an antithetical manner. P. Davis (78) in 1940 and Grey Walter in 1942 (79), state that even if many schizophrenics have normal E.E.G's, as a group they have a tendency to exhibit paroxysmal activity of epileptic type, particularly in the catatonic forms. Gibbs (80) in 1951 published a very interesting paper entitled "Ictal and non-ictal psychiatric disorders in temporal lobe epilepsy". Analysing 458 cases with focal seizure discharges, including 163 with anterior temporal foci (95% of whom had psychomotor seizures), Gibbs concludes that "the epileptic and psychiatric components of psychomotor epilepsy are independent and anti-thetical, though anatomically associated". Administration of phenurone (phenylacetylurea)

showed that if the psychomotor seizures were blocked the psychiatric disorder became intensified. Following temporal lobectomy both the epileptic and psychiatric components were relieved in the experience of this author. Hill, Pond, Mitchell and Falconer (81) in 1957 similarly find improvement in epilepsy following this operation and also in certain parameters of personality, particularly a reduction of aggressivity and a marked improvement in the warmth of social relationships. In agreement with Gibbs they found the inverse relationship between seizures and inter-ictal psychiatric state holding in 1/3rd of their 27 cases. They note, however, that the psychotic features become aggravated rather than improved after temporal lobectomy, severe depressions of psychotic intensity appearing post-operatively in 11 cases. Gibbs impressed by the frequency with which discharges in the occipital, parietal or frontal lobes produce neurological symptoms contrasting to the psychiatric manifestations resulting from foci in one or both temporal lobes, makes the striking phrase: "the Sylvian fissure is one of the chief boundaries between neurology and psychiatry". Disturbance of neuronal organisation in the posterior-temporal, middle-temporal or mesial aspect of the temporal lobes leads to the misinterpretation of specific afferent streams, visual, auditory and olfactory, respectively. These, as micropsia, macropsia, auditory or visual

hallucinations or as disturbances of temporality, ("déja-vu, deja percu"), are subjective representations common to both schizophrenia and epilepsy. The subjective distortions of inner space resulting from interference with the functions of the anterior aspect of the temporal lobe are postulated by Gibbs as being more global in character, altering the total afferent stream (or experience). If the distortion is biased towards unpleasantness, a depressive picture will follow, if towards malevolence, a paranoid one, or if towards hedonism, a euphoric state will be experienced. This neuro-physiological model for psychoses is based on a not inconsiderable body of experimental and clinical data and cannot legitimately be dismissed as mere, fanciful speculation. Further it has the merit of providing a link between schizophrenic and manic-depressive psychoses since distortions in the subjective experience of time (retardation, the blankness of the "future") or its euphoric acceleration in mania are cardinal features of manic-depressive states, together with delusions of "badness" with paranoid components of varying intensity.

Hill (82) confirms that some 25% of catatonics show paroxysmal activity of an epileptic nature in 1948, adding in 1952 (83), that no specific E.E.G. pattern could be correlated with a specific psychotic mode. In

a thorough and critical review of the "electroencephalogram in schizophrenia" published in 1957 (84) Hill is careful to point out that the presence of abnormal cortical or subcortical discharges in psychotics does not necessarily imply an "organic pathological process in the biochemical or histological sense" in the setting of a progressive, genetically determined, pathological alteration of brain-function.

Hoenig & Leiberman (85) subjected 5 catatonics to photometrazol activation over a period of several weeks to determine variations in the convulsive threshold. In all cases there was an inverse relationship present, the threshold being maximal during stupour and minimal during remissions: in other words the process of recovery coincided with increasing tendency to convulsive phenomena.

The technique of recording cerebral activity from the depth of the brain by means of depth, or implanted electrodes was initiated in England by Walter and Dovey (86), for the investigation of brain tumours in 1946. Between 1953 and 1958 a group of workers, principally in the U.S.A., applied this method to the study of psychotic and epileptic disorders. Perhaps the most notorious of these is "studies in schizophrenia" carried out by Heath (87) in Tulane who, in 1952, implanted electrodes in the hypothalamus, caudate, mesencephalic tegmentum a few milimetres ventral to the aqueduct, hippocampus and

amygdaloid nucleus of 20 schizophrenics for "therapeutic" stimulation. The theoretical model proposed to justify this procedure was based on the assumption that the basic defect in schizophrenia was one of cortical impairment producing as a secondary consequence abnormal sub-cortical firing. It was further postulated that stimulation of the septal region might "stir the cortex into more normal activity". Heath and his co-workers estimated that the application of recording and stimulating techniques showed that there existed some correlations between electro-physiological cerebral abnormalities and pathological mental representations and that both psychological stress and electrical stimulation could reproduce these effects. In a very severe review criticising the ethical basis, the inacceptable theoretical construct, the coarseness of the surgical techniques employed (open method of electrode implantation by direct vision through the ventricles) Lilly (88) pointed out that half of the 20 patients had been sick for less than 4 years, that there were 3 failures for technical reasons, complications such as coma, seizures or fever in 12 cases and that 2 were operated on twice. Of the remaining 5 patients not one was well enough to leave the hospital and after 1 year all suffered from post-traumatic epilepsy.

In spite of which the technique continued to be applied, by Sem-Jacobsen, Petersen, Bickford and others,

with increasing refinements. Bickford (89,90) reduced the size of the implanted electrodes from the 1-2 mm or 2-3 mm silver spheres utilised by Heath to 37.5 microns, Dodge (91) demonstrating that no pathological and minimal histological damage to cerebral tissue then took place.

Following the implantation of depths electrodes in patients prior to leucotomy, Bickford, Sem-Jacobsen et al., (92,93) note three main characteristics in the electrical activity of the infero-medial aspect of the frontal lobes: (a) arythmic 2-4 c/s activity, (b) high voltage, 2-5 c/s paroxysmal activity and (c) episodic activity in relation to transient, acute, psychiatric manifestations.

The arythmic slow activity is considered to be non-specific, encountered in all diagnostic categories and to represent an intrinsic property of the infero-medial aspect of the frontal lobes while the paroxysmal high voltage activity, found in half of the patients, unrelated to physiological or psychological factors, is bilaterally synchronous for the frontal lobes and is interpreted as secondary to activity in the temporo-parietal areas. The episodic discharges coinciding with acute hallucinations or anxiety are slow, rhythmic waves or spikes of a non-propagating kind which last for the duration of the psychiatric episode. They may arise either in the depths of the frontal lobe or in

the temporal lobe and underline the intimate relationship existing between the infero-medial areas of the frontal lobe and the mesial aspect of the temporal lobes. Similar findings are reported by Kendrick & Gibbs (94), who confirm the temporo-frontal connections in man by strychnine neuronography (95). It is important to note that Delgado (96) applying similar techniques to psychologically normal patients leucotomised for intractable pain, encounters similar phenomena and consequently considers that these phenomena are all non-specific.

In an interesting paper entitled "Rhinencephalic activity during thought" Lesse (97) shows that distinct, reproducible changes restricted to the amygdaloid or rostral hippocampal areas could be evoked or terminated at will during interviews, regular high voltage waves in these areas being correlated with the spontaneous or suggested recall of emotionally significant memories. Olfactory stimuli or the memories of smell elicited similar discharges. An analoguous observation is made by Groethuysen, Robinson & Haylett (98), who induce a major seizure in a female schizophrenic patient, starting with an amygdaloid discharge, when they question her about her father who had attempted to rape her in her childhood.

At least two communications suggest that intoxication

with psychotomimetic drugs implicates the same areas: Schwartz (99), observing the action of mescaline (400 mg); L.S.D.25, (50-150 ug) and adrenochrome (50-75 mg) on 5 patients, two of whom epileptics with psychosis and three, chronic schizophrenics, report the presence of polyphasic spike discharges in the occipital area associated with musically driven visual (synesthesias) hallucinations. This effect was reversed after 50 mg of chlorpromazine. In another patient also given mescaline (as well as L.S.D.), activation of temporal depths was produced in conjunction with auditory and visual hallucinations; the electrical disturbance taking place in the neighbourhood of a region from which similar discharges were recorded during spontaneous hallucinations. Curiously it is reported that in the epileptics the hallucinogens had a quieting effect on spike and sharp wave foci in the depth electrodes. Monroe and the Tulane group, continuing their "therapeutic" stimulation experiments, implanted electrodes in the cortex, rhinencephalon, diencephalon of 6 chronic schizophrenic patients, one acutely disturbed and one with Parkinsonism. The predominant response after mescaline and L.S.D. was the appearance of paroxysmal activity, usually limited to the septal, anterior hypothalamic or amygdaloid-hippocampal regions (100). Again, the activity in those sites was associated with psychotic manifestations and the limbic "arousal" patterns

were blocked by chlorpromazine. Comparable results are obtained by Sem-Jacobsen (101) continuing the Rochester study in Oslo (a single case). Previously (102) the above worker had found a close relationship between acute episodes of psychotic behaviour and subcortical activity in 15 chronic psychotics who had no signs of convulsive phenomena.

Before attempting to evaluate the above findings, a characteristic sample of depth E.E.G. studies producing positive results, correlating electrophysiological activity in the limbic system with abnormal mental phenomena, it is important to note parallel studies where no such relationship was observed.

Comparing epileptics and psychotic-patients with implanted, multi-stranded depth electrodes in subcortical regions, Bickford et al. (103a) can find no real difference between the two groups apart from non-specific slow waves emanating from the deep frontal areas of schizophrenics. Spiegel & Wycis (103b) in Philadelphia are equally unable to detect any difference in the subcortical records of schizophrenics, manic-depressives and severe anxiety neuroses studied prior to thalamotomy. Delgado, Hamlin and Chapman (104) in 1952, Delgado and Hamlin (105), two years later again find that schizophrenics (6 cases) and non-psychotic

controls have analogous spikes, sharp and slow waves derived from subcortical structures. After stereotaxic recordings from the frontal and from the temporal lobes of psychotics and epileptics, Sherwood (106), in one of the relatively few English studies on this problem, notes that paroxysmal disturbances in psychotic epileptics are not restricted to the rhinencephalon (5 cases, temporal lobe epilepsy), that in schizophrenics paroxysmal or reduced activity occurs randomly in a variety of places (8 cases; frontal 5; temporal 3) and concludes that "electrographic findings are more closely related to pattern of behaviour abnormality than to nosological concepts".

It would be without profit to further enumerate examples of the often conflicting results and interpretations of the depth E.E.G. studies carried out in the years 1950-1960. The early investigations were vitiated by the crudeness of the techniques employed and by the catastrophic brain damage that ensued; however, it is now generally accepted that structural cerebral lesions with the use of non-irritative metals such as gold or stainless-steel introducers is negligible or nil. Focal brain damage at the site of implantation of buried electrodes similarly has vanished when spheres of the order of 40 microns are utilised. More serious is the difficulty created by the heterogeneous nature of the patient populations under

observation: it seems clear that in some instances the conclusions drawn about differences betweenpsychotics and epileptics are meaningless as from the clinical data provided the psychotics themselves may also be epileptic. From an epileptological point of view the very limited area tapped by a buried electrode leads to major difficulties in generalising about the intimate mechanisms involved in intra-cerebral epileptic processes; on the other hand this very defect becomes an advantage when psychiatric phenomena are considered for, in the presence of definite associations between subjective events and corresponding localised alterations of subcortical activity, one may then with reasonable justification deduce that the two phenomena are fundamentally related keeping in mind that a certain imprecision in the localisation of buried electrodes is a limiting factor imposed by present techniques which depend on either direct, visual placing or on stereotaxic devices with A.E.G. control.

Understandably, the ethical basis of such experimentation on human beings has caused widespread concern in medical circles. The problem was discussed at a round table discussion at the Fifth International Congress of E.E.G. and Clinical Neurophysiology held in Rome in September, 1961. It was generally agreed that the indications were threefold: in the case of certain epileptics presenting focal abnormalities with equivocal lateralisation

and where neuro-surgery might be beneficial; in dyskinesias and in intractable chronic mental disorders for which selective multifocal leucotomy (pre-frontal) was considered. No one has expressed better than Lilly (88) the true dimension of themoral problem when he wrote: "Workers, before they contemplate such procedures on humans should contemplate carefully what he would want done and what he would want to know, beforehe had it done on himself as a subject".

It is of some interest to note that after 1960 there is no mention of depth investigations appearing in the Journal of E.E.G. and Clinical Neurophysiology and that at the VIth International Congress of E.E.G. and Neurophysiology (Vienna, 1965), no communications on the topic were discussed.

Allowing for the sources of error outlined above one may conclude that depth studies, relatively disappointing so far for the elucidation of fundamental processes in epilepsy, have made a tremendous contribution towards the understanding of the locus of certain psychotic mechanisms in man for which they have provided the beginning of a neurophysiological basis. The overall evidence is by now extremely suggestive that abnormal phenomena in psychoses, such as visual and auditory hallucinations are the subjective manifestations of disturbed function in the limbic system, that the so-

called "model" psychoses induced by psychotomimetic drugs, although they are toxic psychoses not otherwise comparable with spontaneously occurring psychoses involve the same, or parts of the same system and that psychological stimulation directly activates or inhibits these same subcortical structures, as shown for instance by Driver (107) and conversely that subcortical stimulation may directly elicit psychotic symptoms indistinguishable from spontaneously occurring ones. The objection, that in the absence of controls any conclusion is premature, is not here relevant, since these conclusions are derived from a context in which the patient acts as his own control.

TEMPORAL LOBE EPILEPSY AND PSYCHOSIS

Leaving the contributions made by electrophysiology to the problems of epilepsy and psychosis aside and returning to the clinical question of epileptic psychoses we recall that with Esser (1938) and Pollin (1941), after incidence studies such as was published by Yde et al. (1941) the "antagonism" theory of Glaus (1931) seemed more and more untenable as it became evident that far frombeing protected against schizophrenia epileptics seemed on the contrary to be particularly susceptible to a chronic, paranoid, hallucinatory form of that illness.

In 1953 Hill (108) confirmed that certain epileptics, temporal lobe epileptics, were susceptible to a chronic paranoid psychosis in middle age, as their fits declined in frequency. This syndrome was further characterised by Pond (109) four years later, who differentiates it from post-ictal confusional states with paranoid ideas and hallucinations and from certain complex auras occurring in individuals with schizoid personalities. Pond considers that temporal lobe epileptics with complex auras are particularly prone to this illness on the grounds that the remembrance of the repeated intrusion into consciousness of abnormal ideational and emotional events taking place in spite of or against the conscious will of the subject will forms the psychological "anlage" of a subsequent psychosis. The group defined by Pond and Hill generally preserves a

warm affect contrasted to the affective blunting of non-epileptic schizophrenias and in the premorbid personality is characterised by an absence of schizoid personality structure. From the point of view of epilepsy these individuals have few major seizures, tend to have epilepsy of a few years' duration, the psychosis being often inversely related to the seizure-frequency.

The aura is the remembered experience of the onset of a seizure, the prototype of conscious epilepsy and, indubitably, in its strangeness, it is analogueous to dreamy states or hypnagogic phenomena or transient psychotic experiences. The classical authorities are agreed on its relative incidence: it occurs in 56% of epileptics (Delasiauve, 1854); an equal figure is given by Lennox and also Ajuriaguerra who provides the estimate of 50%. The Montreal school has worked out the first precise classification of auras in terms of their neuro-physiological correlates (110,111):-

(a) frontal foci; (10 cases): sudden loss of consciousness.

(b) frontal and temporal (20%); (16 cases): alteration of consciousness with adversive seizures.

(c) motor and premotor (29 cases): Jacksonian, vocalisation, adversive.

(d) post-central: sensory, somatic.

(e) occipital: visual.

(f) temporal and parietal: auditory and vestibular.

(g) uncus: olfactory.

(h) sylvian fissure: gustatory.

(i) sylvian fissure, frontal (22 cases): automatisms and epigastric.

(j) temporal (29 cases): psychic, hallucinations.

(k) temporal and frontal: illusional.

(l) frontal: forced thinking and aphasia.

Even if in minor details, the above scheme is somewhat misleading: for example forced thinking and illusions are associated with temporal rather than frontal foci, its overall validity remains uncontested today. It illustrates the fact that aural phenomena that duplicate the psychotic mode of subjective experience: hallucinations, forced-thinking, illusions are all derived from foci originating in or involving the temporal lobes. As early as 1940, Weber (112) and Jung, impressed by the striking similarity existing between the psychotic and the epileptic aural alterations of the subjective awareness of self and of reality had, logically, described the aura as representing a "micropsychosis". Hill states that the "doubling of consciousness", an aural distortion reminiscent of heautauscopy at the psychological (although not at the epileptic) level is due unilateral discharges restricted to one hemisphere and in 1953 (113), undertakes a detailed study of the content and transformations of

temporal auras. Studying 50 patients he finds that these fall into three categories: in the first the experiences are complex, highly organised, predominantly visual they have the quality of dreams and are associated with a (usually) unpleasant affective component. The second category is more fragmentary with the intrusion into consciousness of single words usually in two's or three's; a past memory may appear but as a reminiscence not as a reliving experience as in the first group. Parasitic words or forced thinking is encountered. The third type consists of the well-known "deja-vu" or familiarity illusion and includes visual or sensory hallucinations. Auras are not necessarily constant and may alter or disappear with time however it appears that the content is always psychopathologically meaningful to the patient and when apparently incomprehensible it is rendered so by processes of condensation similar to those found in dreams. Of great interest is the observation that attempts to re-activate into consciousness the full content of a fragmented aura by direct abreactive techniques is potentially dangerous, inducing a psychosis in two of Hill's patients and triggering repeated suicidal attempts in several others.

A very detailed phenomenological comparison of the mental disturbances resulting from temporal lobe epilepsy and from schizophrenia was carried out in 1955

by Karagulla & Robertson (114). Ten cases of temporal lobe epilepsy were selected from 105 patients at the Montreal Neurological Institute and their ideational disturbances were compared with those occurring in schizophrenic patients hospitalised in the Edinburgh Royal Hospital for Nervous and Mental diseases. The experiencing of indefinite or formulated thoughts; the hearing of voices either within the mind or projected externally; auditory and visual hallucinations are considered here to be all variants of the same phenomenon: the abnormal derivatives of thought characteristic of temporal lobe epilepsy are, as the authors convincingly underline, analogous to thought disorder in schizophrenia where a continuous graduation is encountered between slightly abnormal thoughts, a "mute voice", to "écho de pensée", proceeding to the full eruption into consciousness of formulated phrases leading to frank internal or external hallucinations. Especially awe-inspiring is the vague, undescribable nature which surrounds the epileptic aura for the individual who experiences it: its weird, terrifying, ominous overtones, its inexplicable foreigness to the personality. The epileptic who experiences feelings and harbours thoughts that, not only incomprehensible and meaningless, do not appear to belong to him, is not far removed from the ideas of influence and passivity delusions of the schizophrenic who shares with the

epileptic characteristic symptoms such as depersonalisation and derealisation.

A rather unique investigation was undertaken in 1956 by Dongier (115) through questionnaires distributed to thirty psychiatrists in several countries who later considered their findings in a colloquim held in Marseilles. A statistical analysis was then carried out on the clinical, psychiatric and E.E.G. (inter-ictal) data derived from observations on 536 psychotic episodes occurring in 516 epileptics. The clinical symptomatology, the E.E.G. manifestations, the psychiatric classification of the psychotic behaviour and the electro-clinical definition of the epilepsy were recorded on separate item sheets, later transferred on perforated cards. The salient findings were as follows:-

(a) excess of confusional states in centrencephalic epilepsy;

(b) confusional states with agitation and visual hallucinations more common in temporal lobe epilepsy;

(c) affective, (mood-swing) or "dissociative", (hebephrenic, paranoid, catatonic) disorders more common in temporal lobe epilepsy: 67% versus 42%, sig. at 0.01 level;

(d) all subjects with bi-synchronous spike-wave discharges were confused;

(e) where the E.E.G. was unchanged during, before, or after psychotic episode, mood-swing and depression were

common (46% versus 26% of total);

(f) paranoid features were common when the discharges disappeared during psychotic episodes: 35% versus 17% of total, sig. at 0.05 level.

Dongier concludes that there are few specific correlations between type of epilepsy and type of psychotic episode; one cannot diagnose the epilepsy from a given psychotic episode and one cannot predict what kind of a psychotic episode will characterise a given type of epilepsy. Certain generalisations can nevertheless be made from the Marseilles study: centrencephalic cases are on the whole characterised by brief, frequent psychotic episodes, that do not progress to chronicity or deterioration, and which are confusional in form. The psychotic episodes here often begin but seldom end with a seizure and have E.E.G. correlates which are analogous to those seen post-ictally after grand-mal seizures, being always modified, with diffuse slow-wave dysrythmia, spike-wave discharges or petit-mal status. The picture seen with temporal lobe epilepsy is different: the psychotic episodes are longer, lasting days or weeks rather than hours, are rarely ushered in by seizures although they may terminate in a fit and disturbance of affect, often anxiety in a setting of clear consciousness replaces the confusion encountered in the former category. Spike-wave discharges are seldom

seen, the E.E.G. background being frequently unmodified or alternately showing the disappearance, often of normal as well as of pathological rhythms, "forced normalization" or even its opposite with reinforcement of focal temporal discharges.

The above study is open to the criticism that the cases are extremely heterogenous from the point of view of selection, an inevitable consequence of the methodology employed but this is to some extent compensated by the very precise and unambiguous questionnaire. It seems to be the first large scale, systematic statistical treatment of epileptic psychoses in terms of the combined variables of epilepsy, clinical picture, electro-physiology and psychiatric symptomatology.

Whereas petit-mal status can be induced by the cessation of anti-convulsant drugs, no matter how frequent before, petit-mal status is said never occur during epileptic twilight states; an observation which led Gibbs to remark in 1951 that "the epileptic and psychiatric components of psychomotor epilepsy are physiologically anti-thetical". Landolt, H. in Zurich (1953) reports a number of cases of epileptic twilight states (including acute psychotic episodes) in which the epileptic focus disappears during the attack, to reappear later. Where previously normal, there was no E.E.G. alteration. The clinical correlates are that

during the abnormal psychic state the epileptic attacks stop, the convulsive threshold rises and reduction in anti-convulsant medication has a favourable effect on the mental state, sometimes dissolving the psychosis. The author believes that the syndrome may imply a "super-normal breaking action" of the central nervous system in keeping with the theories of Morel. The matter of forced normalisation of epileptic activity during abnormal mental state is discussed at length in "Lectures on epilepsy" edited by Lorentz de Haas (116) in Amsterdam, 1958. The regression or complete disappearance of epileptic activity during twilight states is confirmed and the variations in focal temporal activity during the course of the psychotic process is commented upon: paroxysmal foci active before and after the psychotic episode disappear during period of mental disturbance, the record then being "normalised". In the same study cases are described where experimentally induced tension and rage leads to normalization of the E.E.G. in a few subjects; similar mental and E.E.G. changes being brought about by an increase in anti-convulsant medication: the control of the seizures and the normalization of the E.E.G. having both an unfavourable action on the psychic state. Waada & Lennox (1954) find that in children with petit-mal there is more epileptic activity in the mentally healthy than in the disturbed or

psychotic individuals who show more slow-wave activity but consider that an abnormal E.E.G. in the first instance is a pre-requisite for forced normalization; on the other hand Verdeaux (1956) comes to the conclusion that, from a statistical point of view the E.E.G. of psychotic conditions associated with epilepsy is more "normal" than those of mentally healthy populations. These findings contrast with those of Hill & Watterson (1942) who showed that E.E.G. abnormalities were more frequent in the psychotic groups which they studied than in control populations.

Glaser (117), in 1963, discusses inter-ictal psychosis in psychomotor-temporal lobe epilepsy (22 females between the ages of 17-45) to whom he adds later in the same year 15 males within the same age-range. The psychotic reactions are defined as "paranoid, depressive, confusional and hallucinatory" lasting from "one to many days"; the confusional element is emphasised as is the short duration of epilepsy (mean: 6 years). No relationship is observed between psychotic state and fit-control or frequency and the absence of psychological triggers is noted.

Slater, Beard and Glithero (119) published in 1963 a detailed analysis of 69 patients who presented with "schizophrenia-like" symptoms associated with epilepsy. After reviewing some aspects of the classical German

literature on the subject, the conclusion of Bartlet (120) that schizophrenia is no more likely in epileptics than in the population as a whole is rejected as being based on a confusion between prevalence and incidence. Convincingly the authors disprove the hypothesis that epilepsy and schizophrenia coincide purely as a chance phenomenon, "both conditions being common" by calculating the random probability of epilepsy (expectation: 0.005), and schizophrenia, (expectation: 0.008) coinciding; this being of the order of 40 per million. Since the mean age of their probands at the onset of psychosis was 29 years and since the total births in England and Wales 28 years earlier was 660,000 it is calculated that some 20 new cases of schizophrenia and epilepsy could be expected per annum on a chance hypothesis (or 4 to 5 in London with a population of 10 millions). Yet in a few years they were able to obtain 69 fresh cases from 2 hospitals, suggesting that epilepsy predisposes to schizophrenic psychoses. 80% of the patients had temporal lobe epilepsy and a full genetical investigation showed that there was no loading for schizophrenia of a familial type. In more than half of the group objective evidence of organic cerebral disease was found, on the basis of neurological, A.E.G., otological or psychological investigations. Finding a positive correlation between the age of onset of epilepsy and the

age of onset of psychosis but an average frequency of grand-mal seizures of the order of 1 per month comparable to that of epileptics in general. Slater, Beard & Glithero conclude on the above evidence that the aetiological factors which underly psychosis in epilepsy are:-

(a) Duration of epilepsy (mean: 14.1 years).

(b) Organic cerebral disease.

(c) Temporal lobe epilepsy.

Their important negative conclusions are that genetic predisposition, previous personality; seizure frequency or lateralisation of foci are non-related variables.

Discussing the above paper at a meeting of the Royal Society of Medicine (121), Symonds agrees that the association between epilepsy and psychosis is not fortuitous but is not convinced that, on a chance hypothesis, the relevant epileptic history should be confined to early years since temporal lobe epilepsy does not subside with age. He further expresses the caution that too much stress should not be placed on the atypical features sometimes seen in epileptic psychoses as anomalous psychotic manifestations are not restricted to epilepsy. Moreover Symonds does not share the belief of Slater that brain-damage in itself can be related to the psychosis since neither the severity

nor the frequency of the seizures correlates with psychosis. Epileptic seizures and E.E.G. changes according to this speaker should be understood as epiphenomena of disordered neuronal activity of which fits are occasional "peaks"; fundamentally a disturbance of excitation/inhibition at the synaptic level that occurs either consecutively or simultaneously. Concluding that the schizophrenic features of auras, of the gliomas affecting the temporal lobes, of psychosis associated with temporal lobe epilepsy all suggest that the physiological circuits underlying schizophrenia are contained within the temporal lobes, Symonds emphasises that it is not brain damage as such but the disordered activity of neurones which is responsible for psychosis.

At the same session of the R.S.M. Hill stated that the chronic paranoid hallucinatory psychoses of epilepsy can be differentiated from schizophrenia by the absence of schizoid traits in the previous personality; the preservation of warm affect and the absence of social and affective deterioration. Since head injury is a rare cause of temporal lobe epilepsy in the young he does not consider that the high incidence of brain damage in the Slater study is relevant to the genesis of psychosis. Pond added that the years of epilepsy, together with episodic or continuous partial clouding of consciousness

might well predispose to psychosis and noting the absence of non-psychotic temporal lobe epileptics as controls suggested that the introduction of a control group in the study of psychosis associated with temporal lobe epilepsy might bring new factors to light.

INVESTIGATION OF THE CORRELATES OF PSYCHOSIS IN TEMPORAL LOBE EPILEPSY

(a) Methodology

(b) Results

(a) Methodology

With the aim of further defining the correlates of psychosis in temporal lobe epilepsy the following retrospective study was undertaken: 50 cases of temporal lobe epilepsy who had, at any time, also been classified as psychotics were studied over 71 variables considered to be of possible aetiological relevance and compared with 50 cases of temporal epilepsy, non-psychotic controls, over the same variables.

The fifty psychotics were selected from the archives of the Maudsley Hospital admitted over a 15 year period between the years 1950 - 1965. Cases with clinical evidence of dementia were excluded (n:4). As the combination of psychosis and epilepsy is relatively rare no attempt was made in the first instance to isolate schizophrenics, manic-depressives, confusional or schizo-affective ("mixed") conditions: a documented psychotic episode observed in a hospital setting was sufficient for inclusion in the psychotic group. The actual diagnosis of psychosis was, with a few exceptions, the diagnosis made on discharge; the diagnostic criteria being essentially the traditional Kraepelinian ones: briefly schizophrenia hinged on the presence of thought disorder and disturbance of affect with or without secondary symptoms such as hallucinations; manic-depressive states

on euphoric or depressive alterations of mood exhibiting periodicity and leaving the personality intact between phases; states in which the psychotic episodes were of short duration with schizophrenic, manic-depressive or mixed features and where clouding of consciousness and disorientation dominated the clinical picture were called confusional. The exceptions referred to above relate principally to the group defined as mixed or schizo-affective in this study. Case note diagnoses of schizophrenia with atypical features were included in the mixed group when these atypical aspects were affective in nature. In a small proportion of cases if the atypicality was the result of either the preservation of normal affect, the absence of social deterioration or the admixture of clouding of consciousness, variable in intensity and duration, these were included in the schizophrenic category.

Reliability

In order to evaluate the reliability of the diagnosis of psychosis, a second assessor was asked to independently diagnose 30 of the psychotics chosen at random. Because epileptic psychoses often exhibit atypical features which may make it difficult to allocate them definitely to a given classification an alternative diagnosis of psychosis were made in each case where this appeared necessary.

The degree of agreement was as follows:-

Reliability of diagnosis of psychosis

	Agreement	Disagreement	% agreement
1st choice	22	8	73%
2nd choice	30	0	100%

S.E. of proportion = $\sqrt{\frac{pq}{n}} = \sqrt{\frac{22 \times 8}{30}} = \sqrt{5.8} = 2.4$

(See Appendix)

The diagnosis of temporal lobe epilepsy was made on the basis of a history of epileptic attacks with symptoms and signs suggestive of temporal lobe epilepsy confirmed in ALL cases by E.E.G. evidence of abnormal activity in the temporal lobes.

The fifty controls were selected at random: patients admitted to the Maudsley Hospital and to the Guys-Maudsley Neurosurgical Unit for investigation and treatment of temporal lobe epilepsy. In all instances except one (who presented with classical symptoms and signs of psychomotor - temporal epilepsy but who had a normal E.E.G. throughout the period of observation in hospital), the temporal origin of the epilepsy was confirmed by the E.E.G. records. Of the controls 26 came from the Maudsley and 24 from the Neurosurgical Unit. This was carried out in order to allow for a within-control analysis to ascertain the presence of any possible

selection bias that might have made the Maudsley non-psychotic material non-representative. The mechanism of referral of epileptic patients to the psychiatric hospital and to the neurosurgical department, apart from a certain overlapping group analysed in detail, is independant. The only matching done was for sex, in the last 10 patients selected from the N.S.U. controls and this was for the purpose of having an exactly identical sex-ratio in the psychotic and control groups. In the groups randomly selected for sex there was no appreciable difference in the sex distribution of either psychotics (males 26: females 24) or controls (Maudsley, males 15: females 11); N.S.U. males 11; females 13.

The two populations were then studied in terms of 71 variables designed to evaluate the sociological, personality, epileptic, psychiatric, genetic, neurological, electrophysiological and psychometric characteristics of the two populations. The data was transferred from the item sheets drawn up for each of the 100 patients on to I.C.T. perforated cards for mechanical sorting. At the same time the distribution of the variables in the different categories was analysed by inspection. The statistical analysis relied exclusively on the Chi-square, t-tests for significance and on the Chi-square testing for the significance of trends.

In the sociological parameters occupational history was classified as stable or unstable from an impressionistic evaluation of the individual's work record, taking into account the number of jobs held, the duration of jobs and the rate of change of type of work along the lines indicated by Taylor, D. (122) but without rigidly adhering to an arbitrary cut-off point.

The previous personality, the assessment of a normal or abnormal childhood, of factors, emotional or environmental leading to admission to hospital was again judged impressionistically from the history. Childhood "normality" or "abnormality" was not defined by strict operational criteria but by taking into account the family background, its financial status, the degree of parental discord or harmony, the relationship between parents and patient and between the patient and his siblings. In one or both parents were absent, abnormality would be found only in the absence of satisfactory parental substitutes.

The traditional criteria were adopted to delineate the personality type, schizoid referred to withdrawn, isolated, unsociable, affectless individuals; where impulsivity, egocentricity, irritability and particularly explosive aggressiveness, perseveration and "stickiness"

or "adhesiveness" was emphasised the personality structure was considered to be "epileptic". Abnormal personalities not falling in the above categories were called "non-specific abnormal".

When hospitalisation was brought about mainly for the control of seizures which had become either more severe, more frequent or had altered in pattern the precipitating factors leading to admission were described as "physical". If abnormality of the mental state (including psychosis) was the reason for admission this was labelled as being "emotionally" precipitated; disruption of the hitherto maintained adjustment resulting from social causes, i.e. loss of a relative or of employment was defined as "environmental". It will be appreciated that these 3 factors are not necessarily mutually exclusive and in epilepsy are often inextricably correlated, the control of epilepsy being intimately connected with emotional state quite apart from the nature of the epilepsy or the precise pharmacological management.

In the estimation of familial loading for psychosis only parents and siblings were taken into account. The diagnostic terms are the familiar ones and apart from the functional psychoses and confusional psychoses "others" refers to G.P.I.; epileptic and organic psychoses.

The parameters of epilepsy were categorized more rigorously. The presence, absence, disappearance, and

content of aural manifestations was noted. The seizures were classified into (a) majors or "grand-mal"; generalised convulsive fits with tonic and clonic phase; (b) minors of the "absence"; type which in this material corresponds to minor temporal seizures and not to the 3 c/s bilaterally sunchronous spike and wave discharges of centrencephalic epilepsy; (c) psychomotor seizures; characterised by automatisms ranging from the purposeless repetition of simple movements to complex patterns of coordinated behaviour or alternatively manifested by purely psychosensory attacks.

The degree of amnesia for the psychomotor seizures was noted in a three-point scale: complete (or total); partial or none. Seizure frequency was estimated from all the available data in the records and arbitrarily divided into three categories:

(a) More frequent than one month, one a month or less than one a month for majors and psychomotor seizures.

(b) More frequent than once a week, once a week or less than once a week for minors.

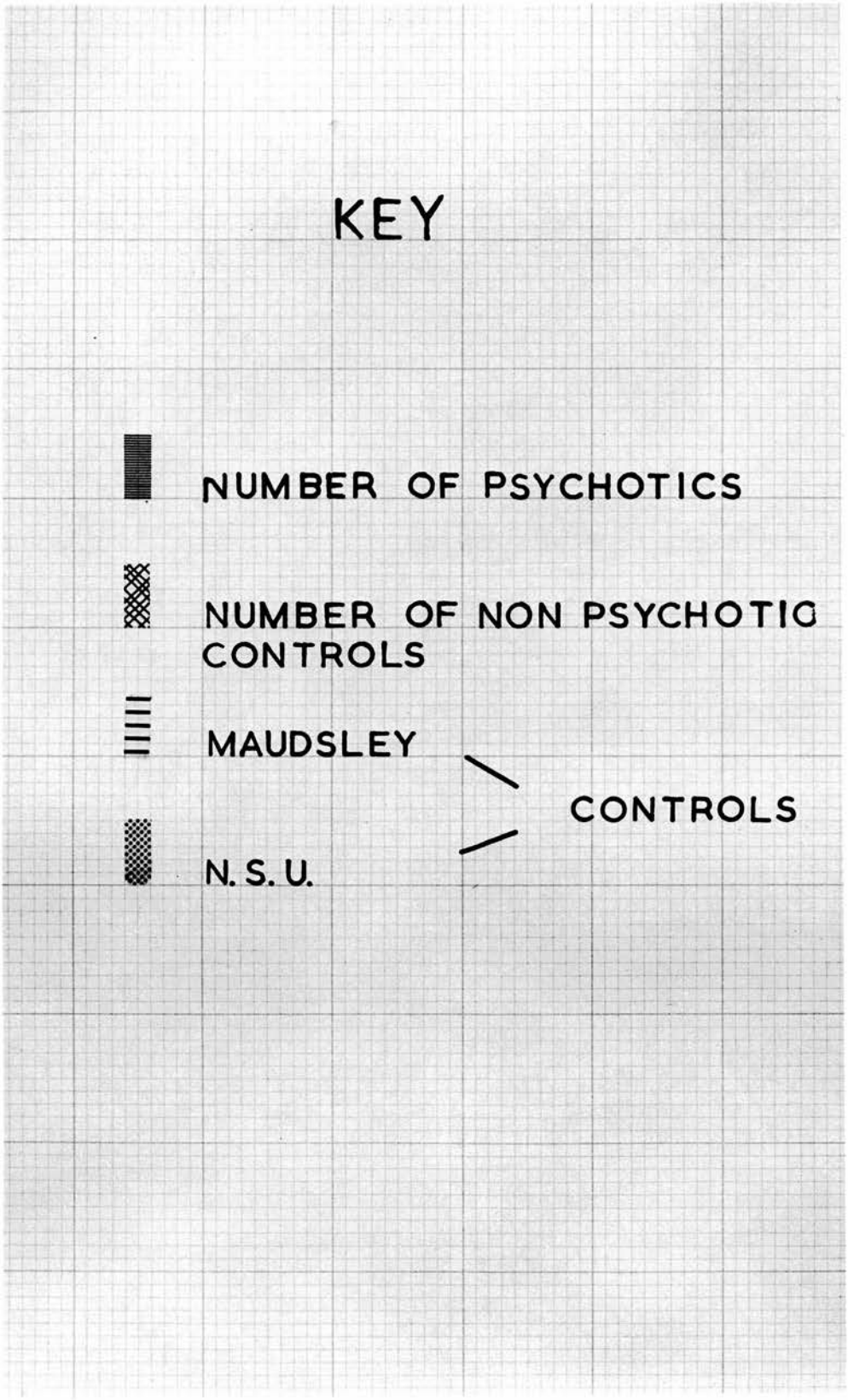
Subsequently in order to facilitate the statistical analysis the above frequency data was converted into the dichotomy: (a) more than one a month; (b) less than one a month for the first two groups and (c) more than one a week or less than one a week for the minor seizures.

Dominance was assessed from clinical handedness, it being assumed that right handedness was correlated with left-brainedness and reciprocally. Although this assumption is misleading in the case of left-handed individuals in whom the distribution of right or left cerebral dominance is approximately equal (123), the fact that only 5% of the material is left-handed enables one to make this assumption here with a 95% probability of being correct. (In 98% of right-handed individuals the dominant hemisphere is the left).

The E.E.G. characteristics are largely self-explanatory, normal and abnormal refers to background activity, abnormal usually being the result of alpha asymmetry or irregular slow-wave or intermediate mixed anomalies. The term specific was restricted to spike and wave discharges of centrencephalic type, bilaterally synchronous in distribution. Foci, overwhelmingly in the anterior temporal region, but also if definitely emanating from a focus on the temporal convexity were called "focal"; foci originating in other parts of the brain, parietal, occipital or, more usually frontal, were grouped under the rubric "others". Bilateral discharges clearly secondary to demonstrable focus were labelled "secondary bilateral hypersynchrony" if of spike and wave form.

The lumbar air-encephalography findings were divided into four groups: normal, diffuse where the abnormality involved the whole ventricular system on at least one side or focal if only one of the horns (nearly always one of the anterior temporal horns) was displaced, irregular or indented. The A.E.G. had been done in 85% of the series. In the 11 psychotics and 4 controls who were not subjected to this investigation the A.E.G. was described as "unknown".

The Wechsler Adult Intelligence Scale was the intrrument utilised by the psychology department in the assessment of cognitive functions. Eight, or 16% of the psychotics and 5 or 10% of the controls had not been tested.


KEY
NUMBER OF PSYCHOTICS
NUMBER OF NON PSYCHOTIC CONTROLS
MAUDSLEY
N. S. U.
CONTROLS

Aetiological factors in the genesis of psychosis occurring with temporal lobe epilepsy

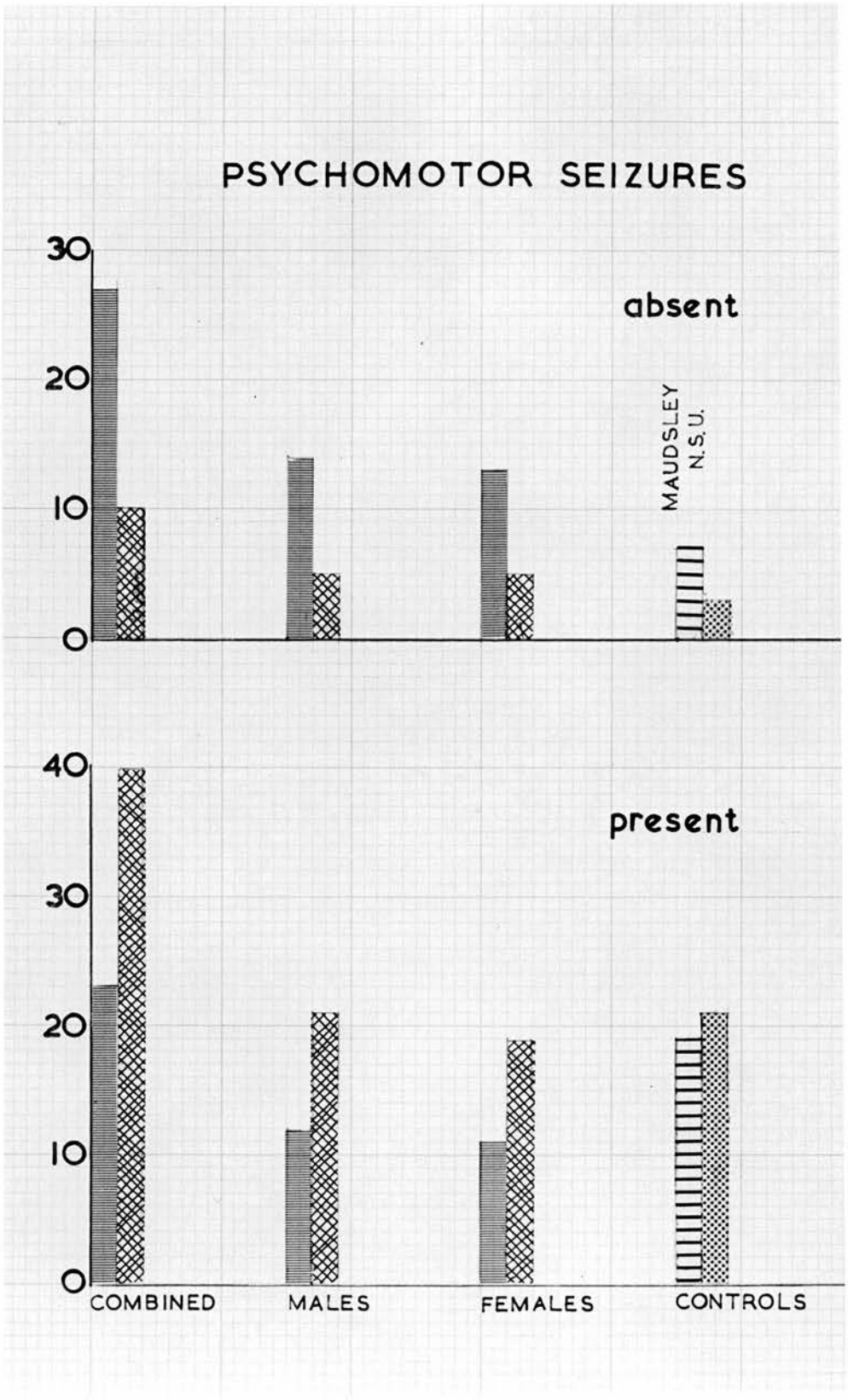
(b) Results

In temporal lobe epilepsy, irrespective of the form of the psychosis, the psychotics are, when compared with a randomly selected group of non-psychotic controls with temporal lobe epilepsy, characterised by the following features:

1) They have a lowered susceptibility to psychomotor seizures.
2) They have a tendency to infrequent seizures: as a group the psychotics have less frequent overall attacks and specifically less frequent minor temporal seizures and, when these are present, less frequent psychomotor seizures. The frequency of majors, however, is similar to that found in the non-psychotic control group.
3) The psychotics are particularly liable to have epilepsy involving the dominant temporal hemisphere.

(1) Lowered susceptibility to or relative absence of psychomotor seizures

Only 23 of the psychotics exhibit psychomotor seizures as opposed to 40 of the controls. This is a highly significant difference: X^2 : 13.07 holding at the 0.001 level of probability. To put it another way only 10 of the 50 controls do not have psychomotor attacks


PSYCHOMOTOR SEIZURES
30
20
10
0
absent
MAUDSLEY
N.S.U.
40
30
20
10
0
present
COMBINED
MALES
FEMALES
CONTROLS

while in 27 of the 50 psychotics psychomotor seizures are absent.

Breaking down the psychotic group according to sex, this difference is maintained for the males:

	Psychotics	Controls	
Psychomotor seizures present.	12	21	$X^2 = 8.12$
Psychomotor seizures absent.	14	5	$P < 0.01$
and for females:			
Psychomotor seizures present.	11	19	$X^2 = 5.70$
Psychomotor seizures absent.	13	5	$P < 0.05$

(Incidence of psychomotor seizures by sex)

In the sub-analysis of the controls no significant difference emerges between the Maudsley and N.S.U. groups, 19 of the 26 (Maudsley) and 21 of the 24 (N.S.U.) controls exhibiting psychomotor seizures. Bingley (123), in his series of 90 patients with temporal lobe epilepsy, had observed that psychomotor seizures were not associated with the laterality of the lesion but with bilateral, shifting foci. It follows that if there was an excess of bilateral foci in the control group the above finding could, in principle, be artefactual. The distribution of epileptic foci according to the unilaterality or bilaterality of the lesion in the two groups is as follows:

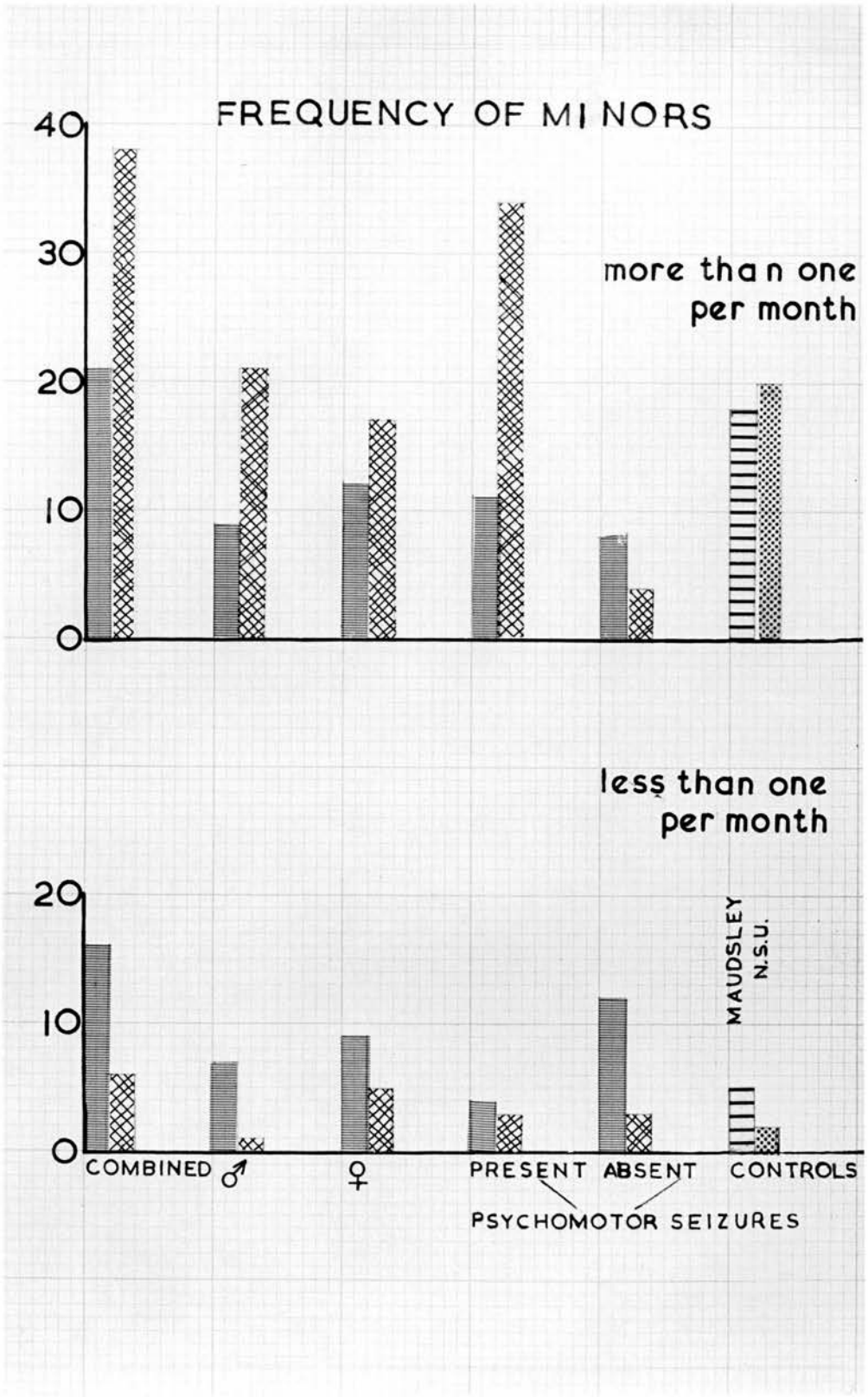
Distribution of unilateral and bilateral foci

Epileptic foci	Psychotics	Controls
Bilateral	22	11
Unilateral	28	38

Holding psychomotor seizures constant:

	Psychotics	Controls
Psychomotor seizures present:		
Bilateral	10	7
Unilateral	13	33
Psychomotor seizures absent:		
Bilateral	13	4
Unilateral	14	6

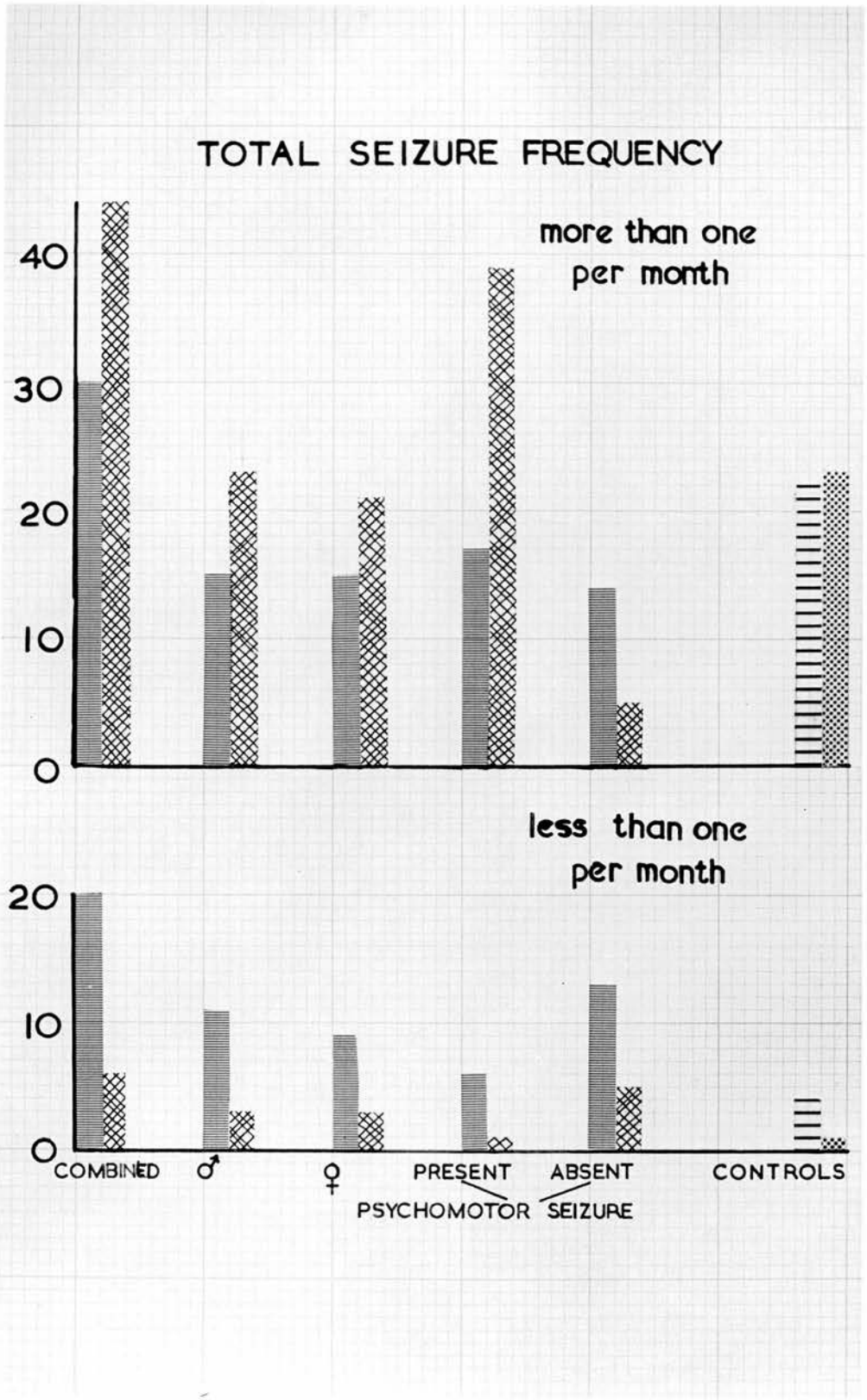
It is seen from the above tables that the psychotics in fact, with an <u>excess</u> of bilateral foci (22 out of 50 as opposed to 11 out of 50 in controls), have <u>fewer</u> psychomotor fits. Of the controls with bilateral foci, 7 out of 11 (or 64%) have psychomotor seizures while 13 out of 22 psychotics with bilateral foci (or 59%) have psychomotor seizures. The difference here is not significant. If, on the other hand, one examines psychomotor seizure susceptibility in relation to the presence of unilateral foci, then only 10 of 28 psychotics with unilateral foci are found to exhibit psychomotor fits (or 35%) in contrast to 33 out of 38 controls with unilateral foci who experience


FREQUENCY OF MINORS
40
30
20
10
0
more than one per month
less than one per month
20
10
0
MAUDSLEY N.S.U.
COMBINED
♂
♀
PRESENT
ABSENT
CONTROLS
PSYCHOMOTOR SEIZURES

such attacks (or 87%). This last difference becomes very highly significant indeed ($X^2 = 17.4$), valid at the 0.001 level. In other words in the presence of unilateral foci the psychotics are resistant to psychomotor seizures or, alternatively, the liability to experience psychomotor seizures with a unilateral temporal focus appears to protect against psychosis. When psychomotor seizures are present in both psychotics and controls, then there is an excess of bilateral foci in the psychotics.

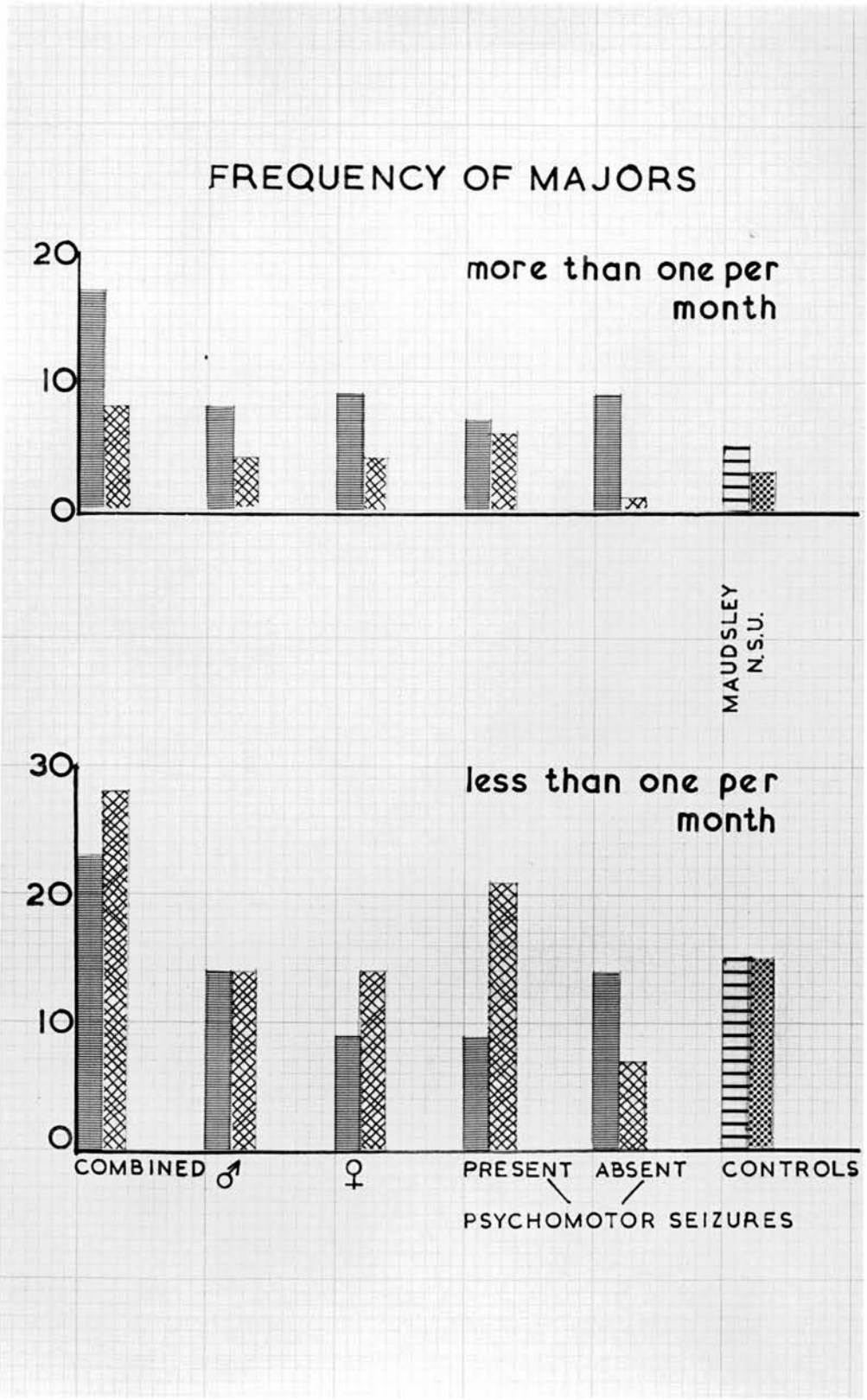
(2) Tendency to infrequent seizures

The non-psychotic group has significantly more frequent minor temporal seizures than the psychotics. 38 of the 44 controls subject to minor attacks have these more than once a week while only 21 of 37 psychotics have these as commonly ($X^2 = 8.89$; $p < 0.01$). In the sub-grouping (males, females, psychomotor seizures held constant) the difference remains significant for the males but disappears for the females, nevertheless the same trend is preserved. Similarly psychomotor seizures are much more frequent in the non-psychotics than in psychotics: 35 of the 40 controls have psychomotor attacks once a month or more against 14 of the 23 psychotics who experience these as commonly ($X^2 = 5.38$; $p < 0.05$). As was observed for minors the difference is statistically maintained for the males ($X^2 = 5.45$; $p < 0.05$), but does not reach significance for the females, although once again the trend

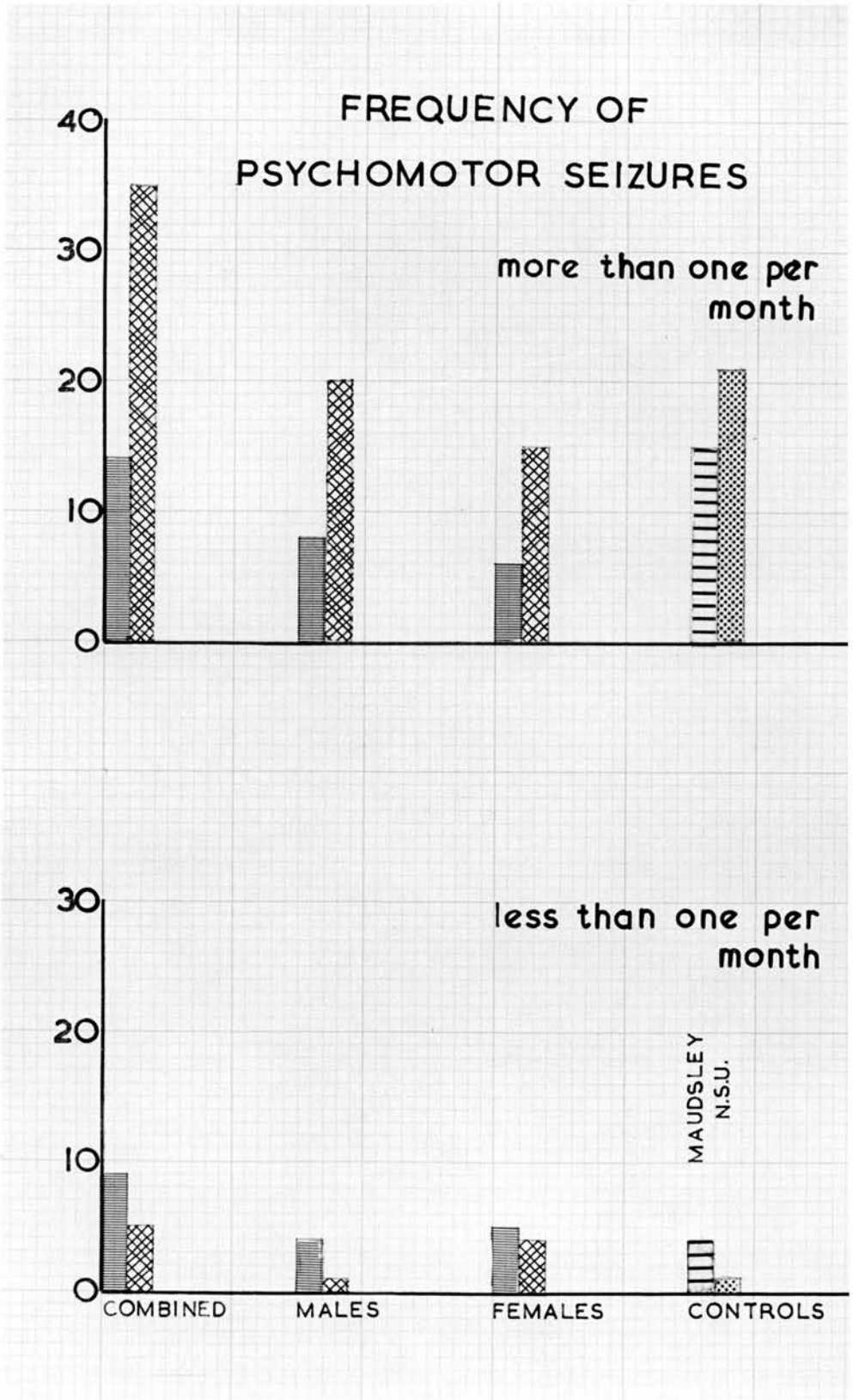

TOTAL SEIZURE FREQUENCY
more than one per month
40
30
20
10
0
less than one per month
20
10
0
COMBINED
♂
♀
PRESENT
ABSENT
PSYCHOMOTOR SEIZURE
CONTROLS

is kept. Even although the psychotics are as prone as the non-psychotics to major generalised tonic-clonic attacks, the overall (majors, minors and psychomotor fits combined) characteristic of psychotics to have less frequent convulsive or ictal manifestations than the control group remains. Globally 44 out of the 50 controls have fits once or more than once a month while only 30 of the 50 psychotics fall in the same category. Phrasing it differently, 6 out of 50 controls have infrequent seizures of the order of less than one a month while 20 out of 50 psychotics fall in the same frequency distribution. With a X^2 of 10.16 ($p < 0.01$) this is a significant finding. The difference is maintained in the sub-categories for males ($X^2 = 6.24$; $p < 0.05$); for females ($X^2 = 5$; $p < 0.05$) and where the presence of psychomotor seizures is held constant for both groups, psychotics and controls (male and female continued) ($X^2 = 8.11$; $p < 0.01$).

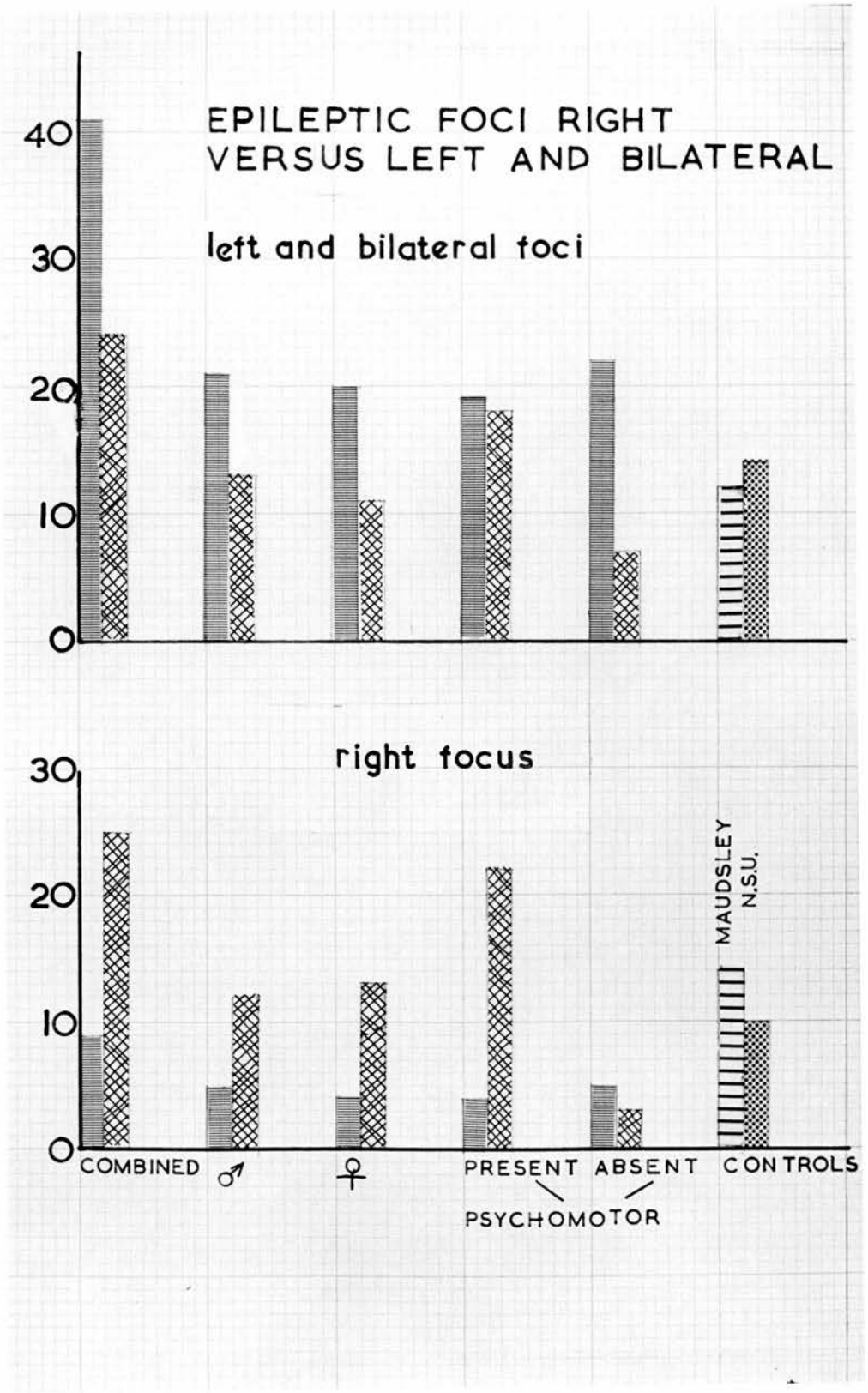
Because of the small numbers involved amongst the controls not experiencing psychomotor attacks, this sub-group where the absence of psychomotor seizures (N:10) is held constant does not indicate any difference in any of the variables under consideration. It has already been mentioned that the fit-frequency of generalised convulsive attacks did not vary in the psychotic and non-psychotic groups. Contrary to what might have been


FREQUENCY OF MAJORS
20
10
0
more than one per month
MAUDSLEY N.S.U.
30
20
10
0
less than one per month
COMBINED
♂
♀
PRESENT
ABSENT
CONTROLS
PSYCHOMOTOR SEIZURES

expected had the controls been unwittingly chosen from a special biased population of temporal lobe epileptics supposedly admitted to hospital merely because of "bad" and frequent epilepsy as opposed to the psychotics admitted on account of insanity, the trend is for the controls to have infrequent major seizures. This does not reach significance in the total population of psychotics versus controls (X^2 = 3.53, not significant at 0.05 level) nor in the male or female sub-groups. With the presence of psychomotor seizures held constant however, it reaches the 0.05 level of significance (X^2 = 4.26). Why the controls, who have much more frequent minors, psychomotor attacks and overall seizures should tend to have less frequent major convulsive phenomena than the psychotics is not immediately obvious. Those in both groups who have psychomotor attacks have significantly less frequent majors than the others. Serafetinides and Dominian (124) studying 51 consecutive admissions of epilepsy of "late" onset (after the age of 25) concluded that frequency of attacks was related to the type of seizure, being greatest in psychomotor seizures. This is confirmed for the psychotics as a slight trend in the present material, for in the presence of psychomotor fits 17 of 23 psychotics have attacks more than once a month whereas in their absence 14 out of 27 have the same frequency pattern. At a level


FREQUENCY OF
PSYCHOMOTOR SEIZURES
more than one per month
40
30
20
10
0
less than one per month
30
20
10
0
MAUDSLEY N.S.U.
COMBINED
MALES
FEMALES
CONTROLS

reaching significance a similar phenomenon occurs in the controls, in the presence of psychomotor attacks, 39 out of 40 patients have fits once a month or more while in their absence the frequency distribution is evenly distributed, five in excess of one per month and five cases below this average. So that the observation of Bingley's that psychomotor seizures are associated with bilateral foci is not confirmed although the present findings are in agreement with those of Serafetinides and Dominian relating psychomotor seizures to relatively frequent epilepsy. However, it must be noted that the characteristic of psychotics to have infrequent attacks is not simply a reflection on the fact that they also have few psychomotor seizures since when the presence of psychomotor attacks is held constant in both psychotics and control groups the psychotics still have significantly fewer seizures per month than the matched controls. Be that as it may the observation that there is no overall difference in the incidence of majors (40 of 50 psychotics had experienced majors and 35 of 50 controls), nor in their frequency is important for it indicates that the differential seizure frequency rates in the psychotics and non-psychotics is probably not the artefact resulting from preferential referral of non-psychotics to hospital on account of severity of epilepsy. It suggests further


EPILEPTIC FOCI RIGHT
VERSUS LEFT AND BILATERAL
left and bilateral foci
40
30
20
10
0
right focus
30
20
10
0
COMBINED
♂
♀
PRESENT
ABSENT
PSYCHOMOTOR
CONTROLS
MAUDSLEY
N.S.U.

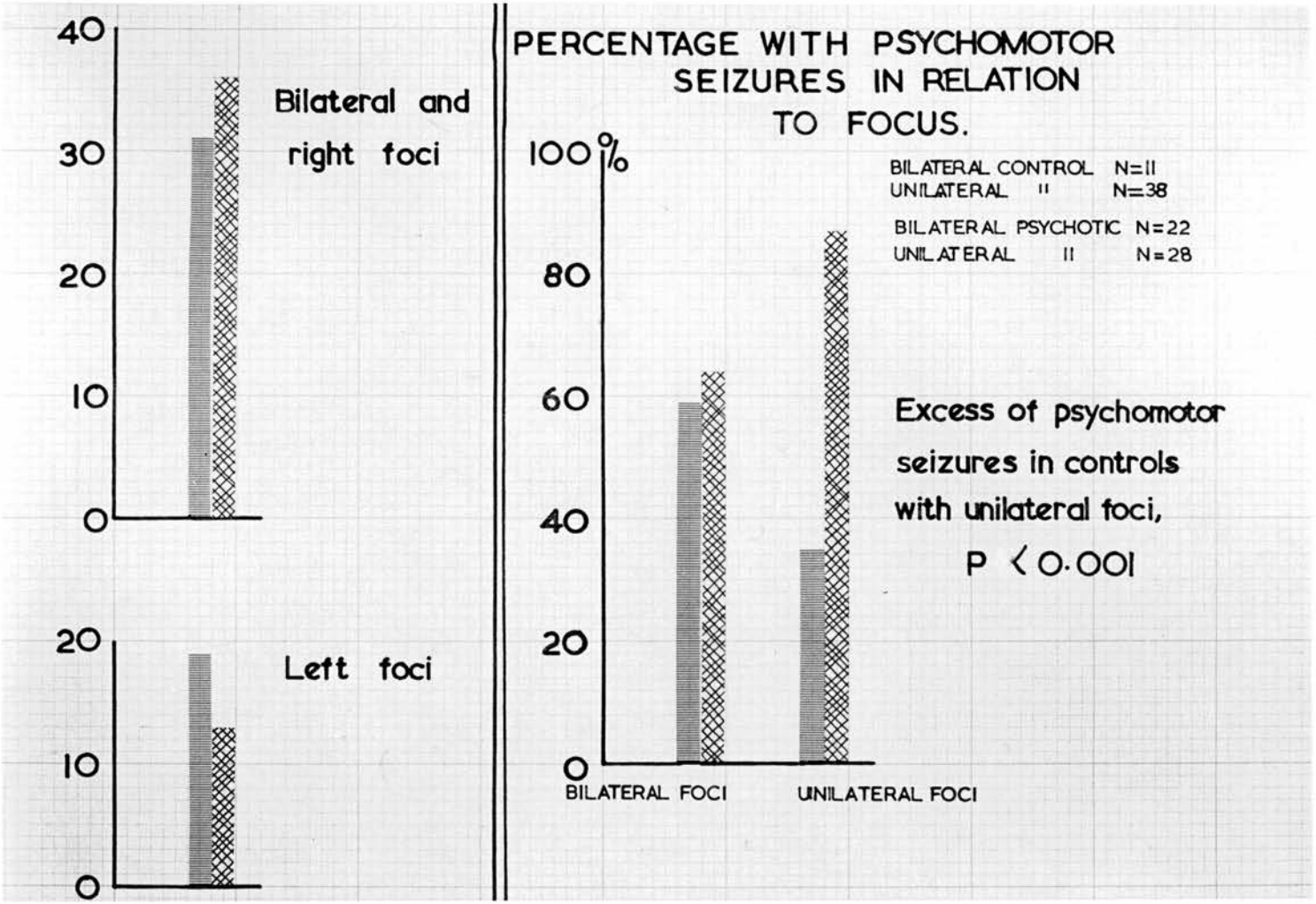
that the "anti-psychotic" function of epileptic seizures in temporal lobe epilepsy is intimately concerned with abnormal activity the locus of which is specifically contained within the temporal system and its projections; abnormal activity which is in some way diminished by the presence of temporal ictal activity and by frequent manifestations through temporal seizures.

(4) Gross excess of foci involving the dominant hemisphere

It is a remarkable fact that only 18% (9 out of 50) of the psychotics have temporal discharges localised to the right, or non-dominant hemisphere while 25 patients (or 50%) in the non-psychotic group have abnormalities in the temporal region lateralised to the minor cerebral hemisphere. Conversely the psychotics are, collectively, characterised by having more foci involving the left, or dominant hemisphere, (left-sided foci, psychotics: 19; controls: 13) a trend which becomes highly significant statistically if cases with bilateral foci are included. If one compares the psychotics and controls in terms of laterality of epileptic activity:

	Psychotics	Controls
Right	9	25
Left	19	13
Bilateral	22	11

Distribution of foci


40
30
20
10
0
Bilateral and right foci
20
10
0
Left foci
PERCENTAGE WITH PSYCHOMOTOR SEIZURES IN RELATION TO FOCUS.
100 %
80
60
40
20
0
BILATERAL CONTROL N=11
UNILATERAL " N=38
BILATERAL PSYCHOTIC N=22
UNILATERAL " N=28
Excess of psychomotor seizures in controls with unilateral foci,
P < 0.001
BILATERAL FOCI
UNILATERAL FOCI

Combining bilateral epilepsy with unilateral left-sided epilepsy the following distribution is obtained:

Laterality of focus in psychotics and controls

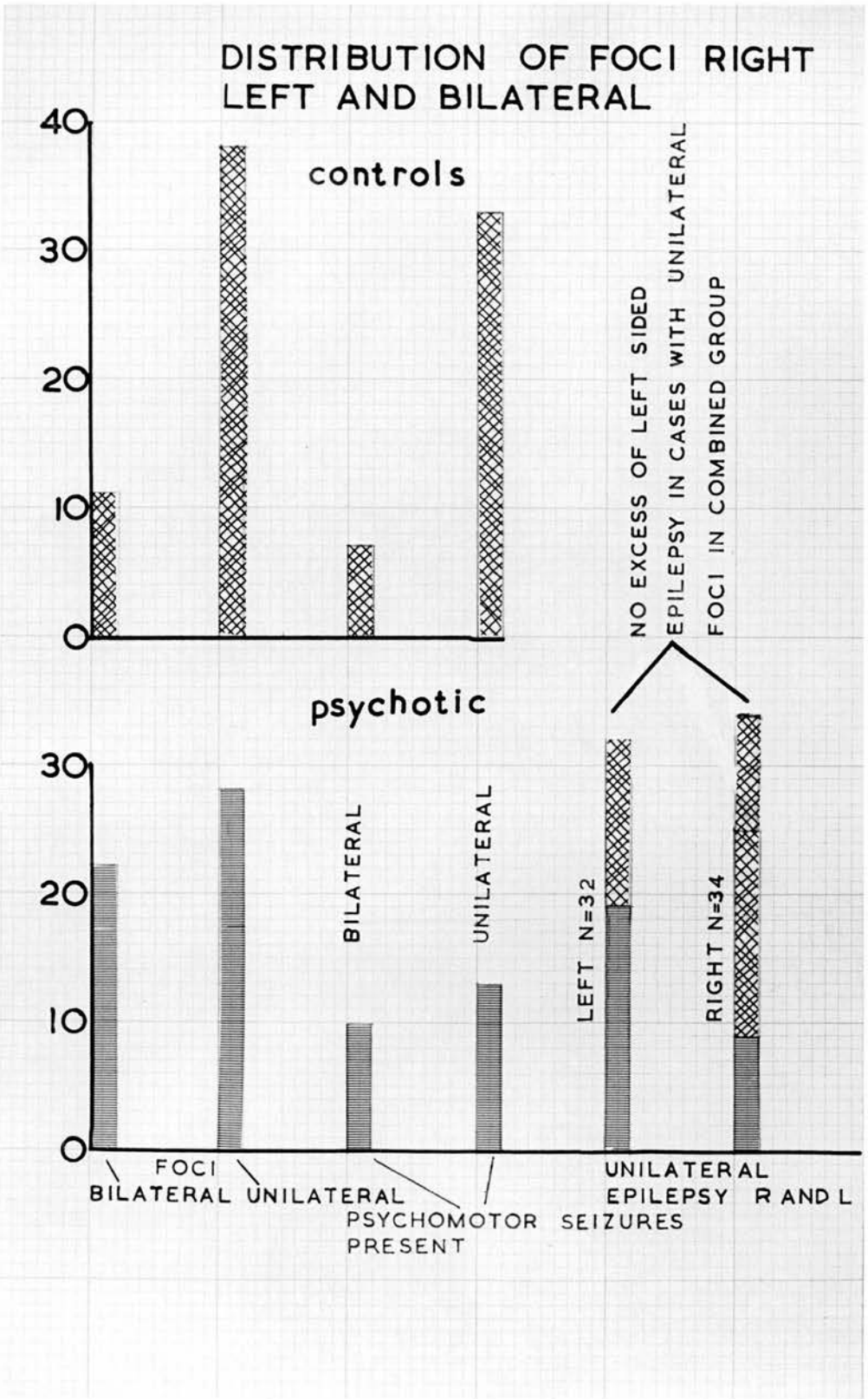
Epileptic foci	Psychotics	Controls	
Right	9	25	$X^2 = 11.96$
Left (including bilateral)	41	24	$p < 0.001$

That the interpretation of differential incidence of laterality of foci in psychotics hinges on a striking excess of dominant temporal foci in the psychotics or conversely, on a striking preponderance of non-dominant hemisphere involvement in the non-psychotics is shown by the following, symmetrical operation: if left-sided epilepsy is compared to right-sided epilepsy (bilateral and right foci combined) there is then no significant difference. This is an expression of the fact that the

Laterality of focus in psychotics and controls

Epileptic foci	Psychotics	Controls	
Left	19	13	$X^2 = 1.2$
Right (including bilateral)	31	36	not significant

higher incidence of dominant hemispheric pathology in the psychotics is not an artefact, the product of a non-specific excess of left-sided epilepsy in the material. This can be demonstrated in another way. If the 100 cases


DISTRIBUTION OF FOCI RIGHT LEFT AND BILATERAL
controls
40
30
20
10
0
NO EXCESS OF LEFT SIDED EPILEPSY IN CASES WITH UNILATERAL FOCI IN COMBINED GROUP
psychotic
30
20
10
0
BILATERAL
UNILATERAL
LEFT N=32
RIGHT N=34
FOCI
BILATERAL
UNILATERAL
PSYCHOMOTOR SEIZURES PRESENT
UNILATERAL EPILEPSY R AND L

are analysed in terms of right versus left-sided epilepsy:

Laterality of unilateral foci in psychotics and controls

	Unilateral foci left	Unilateral foci right
Psychotics	19	9
Controls	13	25
Total	32	34

It is seen that the distribution of foci is virtually the same on either hemisphere and that there is no preferential involvement of the dominant or left side. The idea that left-sided epilepsy might be more common than right-sided epilepsy can be traced back to Hughlings Jackson's observation that the sensory march related almost invariably to the right side of the body. Rey et al. (125) in 82 cases selected from 3,000 E.E.G. records for temporal abnormality finds that on the whole there is more abnormal activity on the left, although there are more right-sided abnormalities in the males. However, in 18 patients with automatisms Liddell (126) finds 12 with right-sided focus as opposed to 4 patients with a focus on the left side and quotes Gibbs (127), who found that right-sided foci were more frequent than left (1948) and Gastaut (128), who in 1950, although he encountered more left-sided abnormalities did not think there was

any significant difference between the two sides in susceptibility to epileptic abnormality. In the light of the available evidence it appears that the probability of either hemisphere acquiring an epileptogenic lesion is the same and that the historical emphasis on the left hemisphere was related to the well-known phenomenon of suppression or extinction of symptoms or deficits associated with minor hemisphere involvement. The population described by Rey is a biased one with respect to lateralisation since it consists predominantly of behaviour disorders or psychopaths who are characterised by immaturity patterns and it is known that maturational abnormalities are last to disappear from the left side.

The greater incidence of dominant hemispheric lesions in the psychotics is also reflected in the pattern of verbal performance score discrepancy found in the two groups. It is established that lesions of the dominant temporal lobe lead to a specific decrement of verbal intelligence while lesions of the minor hemisphere affect selectively performance ability, as indicated by tasks essentially tapping the capacity to organise coherently spatial configurations. It has also been shown by clinico-pathological correlations in temporal lobe epileptic populations that a discrepancy of more than 7 I.Q. points (cut-off actually 7.5), differentiates at a statistically significant level between lesions of the minor or major hemisphere.

Mean distribution of intelligence in psychotics and controls

	Psychotics	Controls
Males		
F.S.	100.9	106.7
Verbal	99.6	107.5
Performance	101.7	104.7
Females		
F.S.	92.89	97.7
Verbal	92.11	97.7
Performance	90.73	97.6
Males & Females		
F.S.	96.8	102.2
Verbal	95.8	102.6
Performance	96.2	101.1

One remarks in the above table representing the mean I.Q. distribution that the psychotics have lower verbal than performance intelligence and the non-psychotics, agreeing with expectations show the opposite trend with mean performance lower than verbal. It must be remembered that it is a discrepancy of more than 7 I.Q. points which accurately discriminate the laterality of cerebral lesions involving the temporal lobes.

	Psychotics (N:50)	Controls (N:50)
Verbal/performance discrepancy of 7 I.Q. points or more	23	29

(Distribution of verbal/performance discrepancies of 7 or more I.Q. points).

If this is further broken into the following sub-categories:

Distribution of focus laterality in relation to verbal performance discrepancy

Controls	foci :	Bilateral	Left	Right	
Performance > verbal	:	5	4	6*	(N:15)
Verbal > performance	:	3*	2	9	(N:14)
Psychotics					
Performance > verbal	:	6	6	1	(N:13)
Verbal > performance	:	5	2	3	(N:10)

It is seen that the verbal/performance discrepancy here appears to follow a somewhat unexpected pattern. In the controls only 4 of the 15 cases where performance I.Q. is greater than verbal have foci in the dominant hemisphere (27%) and where verbal I.Q. is greater than performance only 9 of 14 (61%) have foci in the minor hemisphere. Amongst the psychotics when performance ability is greater than verbal, only 6 of 13 cases have foci in the major hemisphere (46%) and when verbal intelligence exceeds performance ability only 3 cases exhibit foci in the minor hemisphere (30%).

One observes in the above table that, restricting the discussion to unilateral foci, the most aberrant groups with respect to lateralisation by psychometrical analysis consist of (1) those controls who have performance ability greater than verbal, with only 40% of foci apparently in the

(* left-handed or possible right-brainedness, 1 case for each asterisk).

dominant hemisphere and (2) of those psychotics whose verbal intelligence is greater than performance score with only 60% of foci lateralised to the non-dominant hemisphere and 40% lateralised to the dominant temporal lobe. This is possibly a reflection of the fact that where dominance is mixed handedness is a notoriously unreliable index of cerebral dominance (129), and it is conceivable that this aberrant 60% (controls) and 40%) (psychotics) corresponds to mixed or right hemisphere dominant individuals who through environmental pressures have become right-handed. It is noteworthy that, on the basis of this argument, the psychotic group is the more homogeneous in this respect with 40% mixed dominance, perhaps indirectly confirming that the psychotic group is gobally more truly left cerebral dominant, as well as being right handed, reinforcing the conclusion that temporal foci implicating the dominant hemisphere predispose to psychosis.

So far only the cases with unilateral foci have been included.

Distribution of WAIS sub-scores where I.Q. difference 7 I.Q. points or more.

	Controls	Psychotics
P > V	15	13
V > P	14	10
N =	29	23

	Left + bilateral foci	R	Left + Bilateral foci	R
P > V (Dominant)	9	6	12	1
V > P (Non-dominant)	5	9	7	3

Left temporal focus and verbal/performance discrepancy

It is seen from the above tabulation that when bilateral foci are inserted and focus lateralisation (bilateral and left) versus right is compared with psychometrical lateralisation the non-psychotics behave as if bilateral foci would disturb almost equally either the right or left hemisphere whilst for the psychotics bilateral foci strikingly and selectively implicate the dominant hemisphere, confirming again that functional disorganisation of the dominant temporal lobe is correlated with psychosis.

The two populations, temporal lobe epileptics with psychosis and non-psychotic controls with temporal lobe epilepsy did <u>not</u> differ significantly in the following variables:

1) Age distribution: This was based on age at admission to the Maudsley Hospital or to the Guys-Maudsley Neurosurgical Institute for some of the controls. If the patient had been hospitalised more than once, the age at last admission was used.

Mean age distribution

	Age (Mean)	"t-test"
Psychotics		
Males (N:26)	36.92	0.48 N.S.
Females (N:24)	34.00	1.81 N.S.
Controls		
Males (N:26)	35.27	
Females (N:24)	28.40	
Psychotics (M & F)	35.46	1.46 N.S.
Controls (M & F)	31.83	
Controls		
Maudsley (N:26)	32.42	
N.S.U. (N:24)	30.40	0.8 N.S.

It is seen that although the controls are slightly younger than the psychotics, particularly the non-psychotic female temporal lobe epileptics who tend to be hospitalised at an earlier age than either of the psychotic sub-groups or the remainder of the controls, nowhere is the difference statistically significant.

2) Duration of epilepsy: Here again no significant difference is found between the two groups:

Mean distribution of epilepsy

	Duration of Epilepsy (mean in years)	"t-test"
Psychotics		
Males	23.73	1.93 N.S.
Females	17.58	1.65 N.S.
Controls		
Males	17.11	
Females	15.70	
Controls		
Maudsley	19.3	0.8 N.S.
N.S.U.	14.08	
Psychotics (M & F)	20.65	
Controls (M & F)	16.40	

One notes in the above table that the females as a group have epilepsy of lesser duration than the males, this being of the order of 16 years in contrast to the 20 years history of epilepsy in the males. This is an artefact resulting from the fact that the average age of admission for females (31 years old, approximately), is younger than the corresponding age for the male group (36 years of age approximately).

3) Age of onset of epilepsy: The age of onset of epilepsy does not significantly differ either in the two groups.

Mean age of onset of epilepsy

	Age of onset of epilepsy (mean)	"t-test"
Psychotics		
Males	13.15	0.65 N.S.
Females	16.42	1.33 N.S.
Controls		
Males	18.15	
Females	12.71	
Psychotics (M & F)	14.78	
Controls (M & F)	15.43	0.18 N.S.

The mean age of onset of epilepsy is much later (18.5 years) in the non-psychotic male sub-group and this helps to explain the otherwise somewhat anomalous discrepancy found in the duration of epilepsy for males with a 6 years difference between the male psychotics and male controls. A later age of onset of epilepsy however, is not a trend which characterises the non-psychotics as a whole since the control-females have the beginning of their epilepsy at a younger age (12.71) than the female psychotics (16.42).

4) Age of onset of psychosis and duration of epilepsy:

Since no relationship was found between psychosis and length of epileptic history in order to test whether, perhaps, an association could be found between duration of epilepsy and age of onset of psychosis, the following study was carried out. 11 cases (6 males and 5 females) were selected at random from the psychotic population and matched with non-psychotics, holding age on admission and sex constant:

the duration of epilepsy in the two groups was then compared; that is matching age of onset of psychosis with age on admission in controls:

Age of onset of psychosis in relation to duration of epilepsy

Psychotics		Controls	
Age of onset of psychosis	Duration epilepsy	Age on admission	Duration epilepsy
52	35	52	51
21	14	21	19
34	0.25	34	14
16	5	16	10
19	15	18*	13.5
27	9	28*	2
41	24	41	22
42	32	42	25
35	1	35	24
19	15	19	4
25	0.5	24*	23
	Mean:13.7 years		Mean: 18.8 years

"t-test", 0.92, degrees of freedom, 21: not significant.

If the emergence of psychotic manifestations in temporal lobe epilepsy was in any way connected with the actual duration of epilepsy then one would have expected the controls to have a shorter epileptic history when contrasted with epileptics chosen at the point in time when they first developed psychotic illness. The trend is, in fact, in the opposite direction, the non-psychotic population having more epilepsy than the psychotics, although this does not reach significance.

Distribution of age of onset of epilepsy in temporal lobe epilepsy

Psychotics		Controls	
Male	Female	Male	Female
12	40	1	17
10	8	1	2
8	1	14	11
5	23	24	0
14	7	0	1
13	16	21	34
18	48	20	0
13	11	17	31
11	29	12	2
21	23	15	0
2	32	68	38
2	15	11	5
16	9	2	2
10	14	6	7
21	21	11	27
14	18	23	12
33	5	15	21
23	15	29	2
12	13	3	25
17	6	30	26
36	10	46	19
8	4	11	5
11	18	13	17
3	18	28	1
2		30	
6		21	
Σx = 342	= 394	= 472	= 305
$\bar{x}$ = 13.15	$\bar{x}$ = 16.42	$\bar{x}$ = 18.15	$\bar{x}$ = 12.71
Σx^2 = 6335	Σx^2 = 9544	Σx^2 = 14,214	Σx^2 = 7353

Combined $\bar{x}$ (m + f) (Psychotics) = 14.78

Combined $\bar{x}$ (m + f) (Controls) = 15.43

t = 0.18 N.S.

5) Family history of psychosis: No difference is found between the two groups, one member of the immediate family (parents or siblings) being affected in each category, schizophrenia in the psychotic group and manic-depressive psychosis in the controls.

6) Childhood experiences: do not appreciably differ in the two groups and although slightly more psychotics have abnormal family relationships in their early history (15 versus 5), this figure does not reach significance.

7) Occupational stability is identical in both groups; 35% of both populations being professionally unstable.

8) Social and psychosexual adjustment as reflected by marital status and incidence of celibacy or divorce is exactly identical in both groups.

9) Precipitating stresses leading to admission: Epilepsy per se was more commonly given as the cause of referral in the controls than in the psychotics (44 cases versus 16 respectively). In another 21 cases amongst the psychotics, however, a combination of problems relating to fits and to mental state lead to admission so that a more accurate comparison between psychotics and controls is provided by these estimates:

Psychotics (combination of fits and psychological state): 37
Controls (combination of fits and psychological state): 44

To assimilate the two sets of problems leading to admission in this way is probably closer to the reality of the complex combinations of factors which converge, making hospitalisation necessary, for a given epileptic. It is clear that in the presence of gross mental abnormality this fact, rather than concomitant epilepsy will be stressed in order to ensure hospitalisation but at the same time, in the absence of psychotic disorders, there is a very intimate relationship between psychological state and degree of control of epilepsy, emotional stresses being translated into an increased liability to seizures, which, more obvious than the former, will be emphasised. Further these alterations in seizure pattern, in as much as they relate to pressures culminating in hospitalisation are restricted in time. It is well-known that frequently after admission and for the period in hospital, many patients reverse to their normal fit-pattern. There is another finding which confirms that there is no unwitting selection bias operating in the two groups, along the line that the controls being an atypical segment of theepileptic population characterised by more frequent epilepsy than the epileptic population at large, are for this reason hospitalised as opposed to the psychotics who, in the logic of this hypothesis, with a lower tendency to seizures, identical to the "epileptics at large" might be referred because of insanity. It is that globally the incidence of major fits is the same in the controls as in the psychotics.

Moreover, with presence of psychomotor seizures held constant in both psychotics and controls, possibly for the reasons discussed previously (vide supra, p.71), the controls have LESS frequent majors (X^2: 4.26; $p < 0.05$), than the psychotics. It is difficult to imagine a bias at the selection level preferentially acting so that non-psychotics with frequent minors and psychomotor seizures but with infrequent majors would on the one hand be chosen in opposition to psychotics, on the other, who would then be referred because of infrequent minors, infrequent psychomotor seizures but more (relatively) majors. These considerations confirm that the differential incidence in susceptibility to psychomotor seizures and in their frequency is in fact truly a fundamental property which differentiates temporal lobe epileptics with psychosis from those without psychosis.

10) Dominance as judged by "handedness" is similar in both groups; 96% of psychotics being left cerebral dominant, the corresponding figures for controls being 94%*. As was previously discussed (see p.79), there is some indirect evidence which can be interpreted as suggesting that cerebral dominance is more homogeneous in the psychotics than in the controls, who may exhibit more "mixed" dominance.

*This gives an average of 5% left-handedness in the combined population, in agreement with the incidence generally reported: Burt, C.L. (1921), 5.1%; Gordon, H. (1921), 7.2%; Chamberlain, H.D. (1928), 4.3%.

11) Anti-convulsant medication: Epanutin, Mysoline and phenobarbital were assessed in relation to posology arbitrarily described in terms of standard daily regime of plus or minus 300 mg a day for the first, presence or absence for the second and ± 100 mg a day for the third. "Others" referred to drugs little used at present, such as phenylacetylurea or nydrane. No difference was found in the two groups with respect to either the type or the quantity of medication.

12) Brain damage: Brain damage as indicated by abnormal neurological signs; morbid antecedents in the personal history (birth-injury, head-injury; mastoiditis; encephalitis) or abnormal findings found on air-encephalography did not appreciably differ in the two populations:

Relationship between structural brain-damage and psychosis

	Psychotics	Controls
Neurological		
Normal	39	32
Abnormal	11	18
Morbid antecedents		
Birth-injury	5	8
Head-injury	8	13
Mastoiditis	4	5
Encephalitis	3	5
A.E.G.		
Normal	13	17
Diffuse abn.	14	19
Focal abn.	12	10
Unknown	11	4

13) E.E.G. characteristics (apart from laterality of foci): the psychotics do not differ significantly from the controls in the following characteristics, which already have been defined:

Relationship between E.E.G. findings other than laterality and psychosis

	Psychotics	Controls
E.E.G. Background		
Normal	13	18
Abnormal	37	32
E.E.G. Activity		
Specific	7	6
Non-specific	43	44
Focal temporal	39	43
Others	11	9
Unilateral	28	38
Bilateral	22	11
Secondary bilateral hypersynchrony	5	2

14) Presence or absence of majors and minors: the susceptibility to a particular type of seizure is similar in both groups:

Incidence of type of seizure

	Psychotics	Control
Majors only	8	4
Minors only	10	14
Both	32	32

15) Phenomenology of aura: the incidence of auras in the two groups is as follows: 58% of the psychotics and

76% of the controls are subject to aural experience. Although this does not reach statistical significance it is noteworthy that the proportion of non-psychotics with aura is rather higher than the generally reported figure for epileptics, which is of the order of 50% (see p. 44). Excluding the purely motor masticatory auras (psychotics, 8%, controls 20%), it is found that the various aural components, hallucinations (overwhelmingly epigastic), illusions, derealization, depersonalisation occur 41 times in the psychotics and 63 times in the controls. These, of course, are not mutually exclusive. Breaking this data down further:

Aura characteristics (complexity)

	More than 1 aura component	Epigastic only
Psychotics	16 (55%)	11 (38%)
Controls	22 (58%)	15 (39%)
	1 aura component only, (excluding epigastric and masticatory)	
Psychotics	7 (24%)	
Controls	5 (13%)	

one finds that there is a trend for the non-psychotics to experience an aura more frequently than the psychotics while more psychotics than controls have a simple aura with a single component. These results do not suggest that the psychological repercussions of the aura experience in

itself plays a part in the genesis of psychotic states.

Incidence of aura

	Psychotics	Controls
Aura present	25	37
Aura disappearing	4	1
Aura absent	18	12
Aura not known	3	-

Neither does the extent to which psychomotor seizures are remembered suggest a relationship between the subjective awareness of ictal abnormalities and psychosis:

Amnesia for psychomotor attacks

	Psychosis	Control
Total	39%	17%
Partial) None)	61%	82%

since the psychotics are more amnesic for their psychomotor seizures than the controls.

EPILEPTIC PSYCHOSIS ACCORDING TO TYPE OF PSYCHOSIS

Classifying the 50 psychotics according to the conventional diagnostic scheme (see p.), the following incidence emerges:

1) Schizophrenic .... 21 cases ..... (42%)
2) Schizo-affective (mixed) ... 11 cases ..... (22%)
3) Manic-depressive ... 9 cases ..... (18%)
4) Confusional ... 9 cases ..... (18%)

Because of the small number of manic-depressive and confusional psychoses involved a systematic statistical analysis of the data is not feasible however certain trends are suggested if one examines the proportion of each diagnostic category falling into the items of the protocol.

MARITAL STATUS:	mixed	schiz.	m.d.	confus.
Married	36%	38%	66.6%	22.2%
Single	63%	47.6%	33.3%	77.8%
Divorced	-	4.7%	-	-
Separated	-	4.5%	-	-

Psychosexual adjustment and social adaptation as indicated by marriage and celibacy is seen to be maximal in the manic-depressive and minimal in the confusional group with the mixed and schizophrenic types occupying intermediary positions. The superior adjustment of the manic-depressives causes no surprise although the finding that the confusional, rather than the schizophrenic individuals should have the most abnormal distribution is

somewhat unexpected. This may be related to the fact that the confusional subcategory has the highest incidence of brain-damage on both the evidence of morbid antecedents in the personal history and air-encephalographic abnormalities and also has the highest but one proportion of deviant personality traits:

	mixed	schiz.	m.d.	confus.
a) BRAIN-DAMAGE:				
Birth-injury	18.2%	14.3%	33.3%	11.1%
Head-injury	-	14.3%	11.1%	33.3%
Mastoiditis	9.1%	-	22.2%	11.1%
Encephalitis	-	22.2%	-	11.1%
Total:	27.3%	50.8%	46.6%	66.6%
b) AIR-ENCEPHALOGRAPHY:				
Normal	27.3%	28.6%	33.3%	11.1%
Diffuse	36.3%	28.6%	22.2%	22.2%
Not known	18.2%	19%	22.2%	33.3%
Focal	18.2%	23.8%	22.2%	33.3%
Total: (Abnormal)	54.5%	52.4%	44.4%	55.5%
c) PREVIOUS PERSONALITY:				
Schizoid	9.1%	4.7%	11.1%	22.2%
Epileptic	-	14.3%	-	11.1%
Normal	81.8%	42.8%	66.6%	44.4%
Non-specific abnormal	9.1%	38.1%	22.2%	22.2%
Total: (Abnormal)	18.2%	59.1%	33.3%	55.5%
d) NEUROLOGICAL EXAMINATION:				
Normal	90.9%	71.4%	77.8%	77.8%
Abnormal	9.1%	28.6%	22.2%	22.2%
e) VERBAL/PERFORMANCE I.Q. DISCREPANCY (7 points)	55.5%	42.8%	22.2%	66.6%

Asymmetrical responses on the verbal and performance sub-items of the Wechsler Adult Intelligence Scale have been shown to be reliably related to non-dominant temporal lobe pathology, if verbal exceeds performance by 7 I.Q. points or more and, conversely to dominant if performance ability exceeds verbal by the same differential (130), (131 & 132). The above tables show that on this index of cerebral pathology, as on A.E.G. and historical evidence of brain-damage these cases of temporal lobe epilepsy that are associated with confusional psychoses are those in whom structural cerebral damage is most extensive. In the same way manic-depressive and schizo-affective disorders emerge in those psychotics with temporal lobe epilepsy who show the smallest incidence of brain-damage. The schizophrenic group occupies a position not quite, but virtually co-extensive with the confusional psychoses if viewed in terms of associated cerebral damage. This continuum of psychotic reaction which appears to be quantitatively correlated with organic brain-damage appears clearly if expressed in tabular form:

Index of brain-damage	Brain-damage (increasing % of cases)
	minimal ..... maximal
Historical	mixed --- m.d. --- schiz. --- confus.
Neurological	mixed --- (m.d. & confus.) -- schiz.
v/p discrepancy	m.d. --- schiz. --- mixed --- confus.
Personality	mixed --- m.d. --- confus. -- schiz.
I.Q.	(mixed & m.d.) --- confus. -- schiz.
A.E.G.	m.d. --- schiz. --- mixed --- confus.

The striking co-incidence of schizophrenic and confusional psychoses on the one hand and manic-depressive and mixed on the other, is best exemplified by the I.Q. distribution (mean):

Mean I.Q. distribution and form of psychosis

I.Q. (mean)	Schiz.	Confusional
f.s.	91.88	92.42
Verbal	92.05	91.57
Performance	94.66	93.42

The corresponding figures for mixed and manic-depressive psychoses being:

I.Q. (mean)	Mixed	Manic-depressive
f.s.	105	105
Verbal	102.3	103
Performance	107.4	104.4

e) AURA:

Auras appear most frequently in the manic-depressive and least commonly in the mixed or schizo-affective categories; at the same time thelatter has the highest proportion of simple auras (100%), and the former the lowest (33%). The aura is described here as a function of the presence of one, or more of the following subjective phenomena: hallucinations; derealisation; depersonalisation; illusions and mastication. Mastication is discarded as a purely motor sign, an aura being defined as simple when

any one of the above items are remembered by the patient as taking place at the onset of the seizure and as multiple when more than one is recalled.

If we examine the distribution of simple and complex auras amongst the four diagnostic groups we find that the manic-depressives have the largest amount of complicated auras, followed by the schizophrenics, confusional and schizo-affective, in that order:

Aura characteristics and form of psychosis

	Schiz.	Confus.	M.D.	Mixed	(No.of cases)
Aura present	13	5	6	5	
Simple aura	10)	4)	2)	5)	
Multiple aura	3)	1)	4)	0)	
Aura absent	7	5	2	6	
Aura not known	1	1	1	0	
% with simple aura	77%	80%	33%	100%	
Aura present, %	50%	50%	62.5%	45%	
Aura disappear	15%	-	12.5%	-	
Aura present, total	65%	50%	75%	45%	
Aura absent	35%	50%	25%	55%	

So that we obtain the somewhat surprising result that the mixed and manic-depressive psychoses, so consistently associated with minimal brain-damage here diverge to the opposite extremes of the aura continuum, with the manic-depressives having the highest incidence of auras (75%), and the greatest proportion of complex, or multiple auras and the mixed schizo-affective psychoses the lowest aura incidence (45%), but the highest representation

of simple auras (100%). It must be remembered that the numbers involved are too small for a meaningfull statistical analysis and therefore that these are only trends; trends which would possibly suggest that a complex aura is related quantitatively but not qualitatively to the psychotic manifestations, the complexity increasing pari-passu with the incidence. Alternatively one might argue that, given temporal lobe epilepsy and a comparable, minimal amount of demonstrable brain-damage, then frequent, complex, remembered ictal discharges restrict the psychosis, as it were, to the manic-depressive mode, the converse predisposing to increasing schizophrenic admixture.

h) EPILEPSY:

Turning now to the epileptic variables it is seen that over a number of items the manic-depressive group can again be opposed together with "mixed" psychotics, to the schizophrenic-confusional types:

1) The highest incidence of right-sided unilateral foci (non-dominant), is found in the manic-depressive followed by the mixed psychoses. In schizophrenic psychosis the dominant temporal lobe is predominantly involved.

Laterality and form of psychosis

Epileptic foci	M.D.	Mixed	Confus.	Schiz.	
Right	44.4%	18.2%	11.1%	9.5%	Trend statisti
(Left	22.2%	36.3%	44.4%	42.8%	cally signifi-
(Bilateral ...	33.3%	45.5%	44.4%	47.6%	cant.

$X^2 = \frac{b^2 yx}{Vnr\ byx} = 4.4$

with 1 degree freedom

p 0.05*

*See appendix.

2) The incidence of psychomotor seizures is lowest in the manic-depressives (33.3%), highest in the schizo-affective (73%), the confusional and schizophrenic occupying intermediary positions, 44.4% and 38.1% respectively. The mean frequencies of psychomotor attacks is fairly similar in all groups:

Frequency of psychomotor seizures and form of psychosis

Frequency	M.D.	Mixed	Confus.	Schiz.
Less than 1/month	100%	30%	50%	25%
More " "	0%	70%	50%	75%

The apparent excess of patients with frequent fits in the mixed and schizophrenic sub-groups is a reflection of the greater incidence of psychomotor seizures rather than an indication of differential frequency rate as such. In view of the small numbers involved, only 3 manic-depressives with psychomotor attacks, no great importance can be attributed to these trends.

3) Grand-mal or major seizures are more commonly the sole ictal manifestations in manic-depressive than in the other psychotic forms:

Type of seizure and form of psychosis

	M.D.	Mixed	Confus.	Schiz.
Majors only ..	44.4%	0	0	19%
Minors only ..	22.2%	9%	22.2%	23.8%
Both	33.3%	90.9%	77.8%	57.1%

but although manic-depressives tend to have more majors as the only clinical manifestations of epilepsy, the "mixed" psychotics are much more liable to grand-mal attacks in combination with minors, however, but with the manic-depressives have these relatively infrequently. The schizophrenic group as a whole experiences major fits most frequently.

Fit-frequency and form of psychosis

Frequency of:	M.D.	Mixed	Confus.	Schiz.
Majors				
Less than 1/month	80%	66.6%	43%	38%
More than 1/month	20%	33.3%	57%	62%
Minors				
Less than 1/week	40%	44%	50%	80%
More than 1/week	60%	56%	50%	50%
Total				
Less than 1/month	66.6%	27.3%	44.4%	23.8%
More than 1/month	33.3%	72.7%	55.5%	76.2%

The above table shows that, seen from the view-point of overall fit-frequency, the schizo-affective psychoses then merge with the schizophrenic having most frequent epilepsy, the confusional holding a transitional place between the former and the manic-depressive states with least frequent attacks. It is interesting that this data suggests that the affective psychoses are correlated with major convulsive epilepsy infrequently manifested - the affective component appearing to be associated with

infrequent major seizures but relatively independent of the overall fit-frequency if manic-depressive and schizo-affective psychoses are considered together. This would seem to imply that, since total fit-frequency of minor temporal seizure is similar in all diagnostic types that major seizures infrequently released are fundamentally related to the manic-depressive configurations. This hypothesis is further supported by the finding that the manic-depressive psychoses are more susceptible to show secondary bilateral hypersynchrony than the schizo-affective or schizophrenic forms (22% versus 9%).

4) E.E.G. characteristics

Apart from an excess of secondary bilateral hypersynchrony in the manic-depressives and a preponderance of focal temporal activity in the mixed psychotics, no difference emerges between the diagnostic categories:

E.E.G. characteristics (apart from laterality) and form of psychosis

E.E.G.	M.D.	Mixed	Confus.	Schiz.
Background, normal	33.3%	27.3%	11.1%	28.6%
" abnormal	66.6%	72.7%	88.9%	71.4%
Activity, specific	22.2%	9.1%	-	19.0%
Activity, non-specific	77.8%	90.9%	100.0%	80.9%
Focal temporal	66.6%	90.9%	55.5%	85.7%
Others	33.3%	9.1%	44.4%	23.8%
Unilateral	66.6%	54.0%	55.5%	52.4%
Second. bilat. hypersync.	22.2%	9.1%	11.1%	9.5%

	M.D.	Mixed	Confus.	Schiz.	
Age (mean)	35.33	37	31.55	36.06	years
Duration of epilepsy (mean)	19.77	20.72	19.2	21.90	years
Frequency of psychotic episodes (mean)	3.3	2.54	1.00*[1]	1.85	No.of times
Duration of psychosis (in months)	5.3	11.4*[3] (26.72)	0.87*[2] (7.40)	56.7	months

(*Uncorrected, *[1]: 3: *[2]: 2.4 and *[3]: 26.72). It is considered that a more reliable estimate is obtained by removing eccentric results, then calculating the correlated mean. In the first instance by eliminating the two cases of confusional psychosis with an abnormally long-lasting psychotic episode, 9 & 7 months respectively as opposed to 1 month or less in the remainder of the group. In the same way all confusional psychotics had in fact a single psychotic episode, excepting one member with 20. The third correction involves one of the schizo-affective group with an unusually prolonged psychosis lasting 180 months, as opposed to 36 months, the next longest).

5) Other findings

No significant difference or suggestive trend is found on analysis of the anti-convulsant medication; mixed psychotics are occupationally the most stable, schizophrenics the least and similarly normal childhood experiences is most commonly met with in the mixed and manic-depressive forms,

least frequently in the schizophrenics and confusional group. 6) The youngest (mean) age group is that of the confusional, followed by the manic-depressives, schizophrenics and schizo-affectives, in this order but the schizophrenics have the longest mean duration of epilepsy and the confusional psychotics the shortest. The duration of psychotic episodes is longest in schizophrenics, approximately half to a quarter as long in the mixed category, then equal and very short for both confusional and manic-depressives. The manic-depressives, on the other hand, are subject to the greatest number of recurring psychotic episodes, nearly equalled by the confusional, followed by the schizo-affectives with the schizophrenics having the most sustained but least fluctuating course:

Summarising the trends discussed in the preceding section it is seen that the manic-depressive psychoses which arise in association with temporal lobe epilepsy are clearly demarcated from the schizophrenic psychoses and confusional psychoses arising from the same epileptic condition. The "mixed" or schizo-affective psychoses although they share some features in common with the schizophrenic or confusional psychoses are, in fact, very much closer to the manic-depressive category.

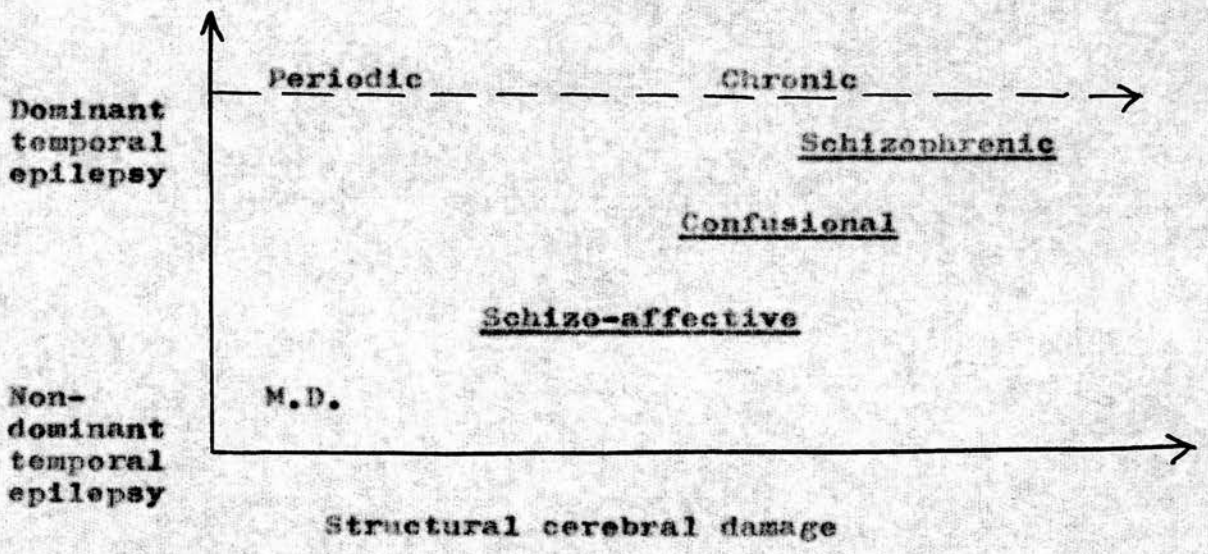
In common the manic-depressive and schizo-affective states share a normal previous personality, normal childhood

experiences, normal psycho-sexual and marital adjustment, stable occupational adaptation in marked contrast to the schizophrenic-confusional groups. Further on almost all indices of cerebral damage available, neurological, morbid antecedents in the personal history, I.Q. scores, verbal/performance discrepancies, A.E.G. abnormalities invariably the manic-depressive and fixed forms demonstrate minimal brain-damage and the schizophrenic or confusional types maximal. The mixed or transitional aspect of the schizo-affective category is suggested in the last two assessments as on both v/p discrepancy and A.E.G. abnormalities the mixed psychotics exhibit a relatively greater incidence of brain-damage than the schizophrenics; nevertheless the combined I.Q. score for manic-depressive and mixed (105), contrasted to that of the schizophrenics and confusional (92), dramatically illustrate the intellectual deterioration or deficit characteristic of the latter. The manic-depressives have more grand-mal seizures occurring as the only ictal manifestation but have these infrequently and have fewer psychomotor seizures than the other psychotics, they also have the highest incidence of auras together with the greatest proportion of complex, multiple aural components, in opposition to the mixed who not only have the lowest tendency to aura experience but have also the largest amount of simple ones. Manic-depressives in addition have fewer

seizures and specifically fewer major seizures, than the mixed or schizophrenics who, on this last criterion, almost exactly coincide. Moreover, the manic-depressive psychosis is associated with a preponderance of unilateral foci in the non-dominant hemisphere (44%), against (9.5%) for the schizophrenics with the schizo-affective form occupying an intermediary position (18%) - a trend which is statistically significant ($X^2 = 4.4$; $p < 0.05$).

It would appear, consequently, that the emergence of manic-depressive symptoms in association with temporal lobe epilepsy hinges on epileptic process acting on the non-dominant hemisphere predominantly provoking grand-mal rather than psychomotor fits infrequently released and in combination with a relative absence of cerebral damage. As cerebral damage extends, together with the emergence of psychomotor seizures, indicating that the temporal-limbic axis is now increasingly the seat of disturbed activity, and as the dominant hemisphere becomes involved the clinical manifestations of psychosis become hybrid, transitional, schizo-affective. Ultimately as the disorganization of the dominant temporal-limbic system progresses further, the periodicity of the psychotic phenomena disappears, leading to the classical chronic schizophrenic illness. The mean age of manic-depressives, mixed and schizophrenics on admission is virtually the same,

35, 37 and 36 respectively, while the confusional psychotics are considerably younger, with a mean age of 31 years and since the confusional group has otherwise almost exactly the same characteristics as the schizophrenics on the variables studied this raises the possibility that confusional psychotic episodes, in temporal lobe epilepsy, is a "forme fruste" of schizophrenia when it is associated with structural brain-damage.



Diagrammatic representation of the parameters of psychosis in temporal lobe epilepsy

CENTRENCEPHALIC EPILEPSY AND PSYCHOSIS

It is a remarkable fact that over a period of some 15 years, between 1950 and 1965 approximately 60 psychotics with temporal lobe epilepsy were referred to the Bethlem Royal and Maudsley Hospital as against 6 cases of psychosis associated with centrencephalic epilepsy. Keeping in mind that incidence estimates based on hospital admissions do not necessarily reflect true prevalence, there is no reason to suppose that, given a clinical picture of psychosis, a preferential referral of temporal lobe epilepsy and a segregation against centrencephalic epilepsy would operate, so that we must conclude that the emergence of psychotic states is intimately related to epileptic activity involving the temporal structures, this increasing 10 times the probability of psychosis. Unexpected also is the finding that all 6 cases of psychosis occurring against a background of centrencephalic epilepsy are females while the sexes are equally represented in the temporal lobe epilepsy group.

Compared with the temporal psychoses, the centrencephalic epileptics are younger at the time of hospitalisation, have suffered from epilepsy for a longer period and consequently have a much earlier age of onset of epilepsy. Their full scale I.Q. score is lower, the fall being brought about by relatively poorer performance ability. It is interesting to note that intellectually they are quite close to the female psychotics with temporal lobe epilepsy. Psychotic

episodes occurring with centrencephalic epilepsy are more frequent but much shorter than similar episodes in temporal lobe epilepsy and are in the present material always confusional in form. Although they are twice as likely as the temporal lobe epileptics to have majors as the only ictal manifestation and have fewer auras the fit-frequency pattern is comparable in both groups. In spite of the fact that there is a complete absence of those morbid antecedents which predispose to cerebral damage, encephalitis, mastoiditis, birth-injuries or head-injuries which are found in some 40% of cases of temporal lobe epilepsy, irrespective of the presence or absence of psychosis, the incidence of clinically demonstrable neurological abnormalities is the same in all groups, this suggests, perhaps, that brain disease in centrencephalic epilepsy is the result of epilepsy where in temporal epilepsy it tends to be the result of the lesion underlying the epilepsy. Sociologically centrencephalic epileptics with psychosis are issued from a more disturbed home environment than the temporal lobe epileptics and are occupationally more unstable: though curiously they marry more commonly.

The table following contrasts the characteristics of patients with centrencephalic epilepsy and psychosis against the combined group of psychotics with temporal lobe epilepsy and also with the female and confusional sub-groups

PSYCHOSIS WITH CENTRENCEPHALIC EPILEPSY		PSYCHOSIS WITH TEMPORAL LOBE EPILEPSY		
		Combined psychotics	Females	Confus.
SEX. Female,	100%	50%	-	44%
AGE.	31.5	35.4	34	31.5
DURATION EP.	23	20.6	17.5	19.2
TYPE OF FIT				
majors only	33.3%	16%	9%	-
minors only	-	20%	26%	22.2
both	66.6%	64%	65%	77.8%
TOTAL FIT FREQUENCY				
less1/month	33.3%	40%	46%	44.4
more 1/month	66.6%	60%	60%	55.5
AGE OF ON SET OF EP.	8.5	14.76	16.42	12.3
BRAIN DAMAGE				
neurol normal	83%	78%	80%	77.8%
abnormal	17%	22%	20%	22.2%
A.E.G. normal	17%	26%	20%	11%
abnormal	33%	52%	50%	55.5%
n.k.	50%	22%	30%	33.5%
ENCEPHALITIS etc.				
(present)	0%	40%	50%	66.6%
(absent)	100%	60%	50%	44.4%
I.Q. f.s.	89.6	96.6	92.89	92.42
verbal	94.2	95.8	92.11	91.57
performance	86	96.2	90.73	93.42
FREQUENCY OF PSYCHOTIC EPISODES	4.6 times	2.2	1.8	1.1
DURATION OF PSYCHOTIC EPISODES	6.5 months	18.5 months	39.89	0.87 x 2
FAMILY HISTORY OF PSYCHOSIS, (functional)	0	2%	0	11.1%
PREVIOUS PERSONALITY,				
epileptic	50%	6%	0	11.1%
schizoid	0	12%	10%	23.2%
non-specific abn.	16.7%	28%	35%	22.2%
normal	33.3%	54%	55%	44.4%
AURA, present	33.3%	58%	46%	50%
CHILDHOOD ENVIRONMENT,				

	CENTRENCEPHALIC	COMBINED	TEMPORAL EP. FEMALES	CORPUS
CHILDHOOD ENVIRONMENTAL, abnormal	50 %	30 %	20 %	44.4 %
OCCUPATIONAL, stable	33.3 %	65 %	60 %	77.8 %
MARRIED	50 %	40 %	30 %	22.2 %
E.E.G.				
background activity	33.3 %	26 %	32 %	11.1 %
normal				
abnormal	66.6 %	74 %	68 %	71.4 %
epileptic activity				
specific	100 %	14 %	8 %	0 %
focal (non-temp)	0	22 %	20 %	23.8 %
FORM OF PSYCHOSIS				
confusional	100 %	18 %	17 %	100 %
mixed	17 %	22 %	20.5 %	0 %
n.d.	0	18 %	20.5 %	11 %

DOMINANCE 100 %

I. GENERAL

1 uncorrected = 3
2 uncorrected = 2.44

taken independently. This clearly demonstrates that it is the underlying nature of the epilepsy which is responsible for the particular pattern of psychosis later emerging, as the female psychotics with temporal lobe epilepsy are much closer in all variables, to the combined temporal lobe epilepsy series than to the females with idiopathic epilepsy and psychosis. As was discussed previously confusional psychoses in temporal lobe epilepsy are correlated with an early age of hospitalisation and with the greatest incidence of structural cerebral damage, nevertheless, globally they approximate quite closely to the other psychoses arising from temporal lobe epilepsy. Two features, however, they tend to share with the centrencephalic cases, the young age on admission just noted and a tendency to relatively short-lived psychotic episodes.

The relationship between epileptic activity and psychosis in centrencephalic epilepsy is illustrated by the following brief descriptions.

One patient, a 27 year old female, had 10 psychotic episodes and showed normalization of the E.E.G. during the psychotic states which, associated with confusional features were variously depressive with paranoid colouring, schizo-affective, relieved by major seizures or principally characterised by paranoid excitement.

In another case, aged 26, on the other hand, the psychosis, confusional in form, was ushered in by a sudden exacerbation of the epilepsy (12 major seizures per month), and gradually cleared on increased anti-convulsant medication with consequent freedom from attacks. A third patient presented with a series of confusional episodes associated with depressive features, often precipitated by fits whilst in a fourth, aged 49, a single confusional episode lasting two months was initiated by petit-mal status. The fifth patient experienced her first psychotic episode at the age of 40, a confusional state with paranoid colouring and hallucinosis becoming manifest 7 weeks after the onset of the confusion, but not otherwise producing any change in the symptomatology. It must be repeated that the discussion of centrencephalic epilepsy and psychosis is necessarily tentative on account of the rarity of the combination. It seems probable nevertheless that the salient distinguishing aspects of the latter are:

1) Frequent psychotic episodes.

2) The psychosis invariably presents with a confusional element.

3) They are associated with diffuse brain-damage that is probably the result of the epilepsy itself rather than with, as in the temporal series, structural damage arising from the pathological process underlying the epilepsy.

4) The psychotic episodes are both more frequent and longer

than in the comparable psychosis occurring with temporal lobe epilepsy.

5) One cannot attribute the genesis of the confusional episode to specific "spike and wave" epileptic activity per se, since confusional psychosis in association with temporal lobe epilepsy have the lowest incidence of specific E.E.G. abnormalities (0%).

6) Auras are much more commonly absent, the age of onset of epilepsy is much younger and the duration of epilepsy much longer than in the temporal lobe series with psychosis.

7) The E.E.G. sometimes dramatically illustrates the inverse-relationship with normalization during the psychotic episodes however the picture in centrencephalic epilepsy is complicated by the fact that here, frequently, an excess of epilepsy precipitates a confusional episode during which irregular slow wave dysrythmia with spike and wave forms may be prominent.

PSYCHOSIS IN RELATION TO PRESENCE OR ABSENCE OF PSYCHOMOTOR SEIZURES

As the emergence of psychosis in temporal lobe epilepsy is correlated with a relative absence of psychomotor epilepsy and with infrequent psychomotor seizures, when these occur, a comparison of psychotics with psychomotor fits (N:23) contrasted to those without such attacks (N:27) was undertaken in order to see whether other factors correlating with psychosis might be found.

Relationship between variables and presence or absence of psychomotor attacks in psychotics

	Psychotics with psychomotor fits N = 23	Psychotics without psychomotor fits N = 27
Married	43%	37%
Single	52%	55.6%
Aura, present	60.8%	33.3%
absent	13%	51.8%
disappear	26%	3.7%
Seizures		
majors only	0%	26%
minors only	30%	14.8%
both	69.5%	59.2%
Amnesia		
total	43%	-
partial	47.8%	-
Aural complexity	25.[illegible] aural items	16 aural items
males	47.8%	55.6%
females	52.2%	44.4%
Seizure frequency		
Majors, less than 1/month	39%	51.8%
Majors, 1/month or more	30%	33.3%
Minors, less than 1/week	17%	44.4%
more than 1/week	17.8%	30%
Psychomotor, less than 1/month	39%	-
1/month or more	52%	-
Total fit frequency:		
Less than 1/month	26%	48.1%
More than 1/month	74%	51.8%
Epileptic foci, right	17.3%	18.5%
left	39%	33.3%
bilateral	43%	48.1%
Neurological, normal	82.6%	74%
abnormal	17.3%	26%
E.E.G., background, normal	34.8%	18.5%
abnormal	65.2%	81.5%

	Psychomotor fits present	Absent
E.E.G.		
Activity, specific	21.7%	7.4%
Non-specific	78.2%	92.6%
Focal temporal	91.3%	66.6%
Others	8.6%	40.7%
Unilateral	56.5%	51.8%
Secondary bilateral sync.	21.7%	0%
Brain-damage (history)	39%	40.7%
A.E.G.		
Normal	21.7%	33.3%
Diffuse abn.	21.7%	30%
Focal abn.	39.0%	11.1%
Not known	17.6%	26%
Previous personality		
Normal	43%	63%
Abnormal	57%	37%
Occupationally		
Stable	78.2%	52%
Unstable	21.8%	48%
Childhood		
Normal	74%	66.6%
Abnormal	26%	33.3%

It is seen that, in the absence of psychomotor seizures, the psychotics have seizures more infrequently than if psychomotor attacks are present. In nearly half of the former category the overall frequency of fits is of the order of less than once a month while only a quarter of the group with psychomotor attacks fall into this pattern, the great majority having relatively frequent attacks. The E.E.G. background is more often abnormal in the cases not manifesting psychomotor seizures and, as would be expected the incidence of focal abnormalities is reduced,

that of unilateral slow-wave dysrythmia increased. The excess of left or bilateral foci is equally distributed in the two groups and objective evidence of brain-damage does not appreciably differ either. Aura manifestations are almost three times more common in the series with psychomotor epilepsy than in the group without automatisms.

There is no significant difference in the age distribution, in the duration of the epilepsy or in the intellectual ability of the two populations.

	Psychotics (psychomotor seizures present)	Psychotics (psychomotor seizures absent)
Mean age	37.3	34 (t,1,3,n.sign)
Duration of epilepsy	21.78	19.92 (t,1,3,n.sign)
I.Q. Full scale	101	93
Verbal	100	92
Performance	102	96
Form of psychosis		
Schizophrenic	39%	48.2%
Manic-depressive	13%	22.2%
Confusional	13%	18.5%
Mixed	34.8%	11.1%

On account of the small number of controls not presenting with psychomotor attacks (N:10) no significant difference is found when they are compared with psychotics not exhibiting psychomotor seizures. If, holding the presence of psychomotor fits constant in the two groups, one compares the psychotics with the controls (psychotics, N:23;

controls, N:40) then it is apparent that the same factors operating in the total psychotic group emerge here as well as the fundamental parameters of psychosis occurring in relation with temporal lobe epilepsy:

1) Psychotics have an excess of foci involving the dominant hemisphere (X^2: 8.10; $p < 0.01$).
2) Psychotics have infrequent psychomotor seizures (X^2: 7.20; $p < 0.01$).
3) Psychotics have less frequent overall seizures (X^2: 8.71; $p < 0.01$).

CONTROLS

The non-psychotic controls, as was discussed on p.59, were selected randomly from the temporal lobe epileptics admitted to the Maudsley Hospital between the years 1950-1965 and from patients admitted for surgery of temporal lobe epilepsy in the Guys-Maudsley Neurosurgical Unit between the years 1955-1965. It is seen from the accompanying table comparing the 26 Maudsley and 24 N.S.U. temporal lobe epileptics that no significant differences emerges between the two groups, notably that the incidence of psychomotor seizures is almost exactly identical as is the frequency of psychomotor seizures and overall fit-frequency. Further the distribution of epileptic foci is evenly distributed in both categories. N.S.U. patients have a slightly higher incidence of brain damage on the evidence of morbid antecedents in the personal history and neurological and A.E.G. findings but this fails to reach statistical significance and the full scale I.Q. is slightly higher for the surgical cases. It is interesting to note that from the point of view of a verbal/performance discrepancy score of 7 or over only 46% of the N.S.U. sub-group as opposed to 69% of the Maudsley material fall into the categories consistent with dominant or non-dominant pathology and what is more the surgical cases are here predominantly non-dominant while the Maudsley patients tend to have dominant involvement. The difference is not,

however, statistically significant and is not in keeping with the equal distribution of unilateral foci (right and left) which characterises the N.S.U. population, in particular and the controls as a whole.

The epileptics admitted to the Maudsley are slightly older (33.4 years) than the N.S.U. patients (30.4 years) and have epilepsy of longer duration, 18.6 years for the Maudsley series against 14.08 for the surgical group; however, with a t-test coefficient of 0.8 for the age and 0.87 for the duration of epilepsy these figures again do not differ significantly.

The previous personality, childhood environment and sociological variables are comparable in both instances.

Falconer and Serafetinides (133) have indicated the selection criteria for suitability for temporal lobectomy which are essentially those of long-standing epilepsy relatively resistant to drug therapy, without evidence of space-occupying lesions and with clearly lateralising features.

In view of the above it may appear surprising that the Maudsley and surgical groups should, in fact, be so comparable and this might possibly suggest that the Maudsley control group is not homogeneous or that what, in fact, determines whether a given temporal lobe epileptic is referred for surgical assessment is not only the nature

of his epileptic illness but also dependent on complex sociological and psychological factors present in the patient and in his environment which permits his milieu and himself to tolerate or not tolerate his epileptic disease. A number of the N.S.U. patients were referred from the Maudsley Hospital for surgery, sothat it becomes necessary to examine these separately and compare them in turn with those N.S.U. patients directly referred from general or neurological centres. Of the 24 surgical controls 14 or 58.3% came from non-psychiatric sources of referral and 10 or 41.7% from the epileptic ward of the Maudsley Hospital.

Characteristics of controls: psychiatric and non-psychiatric referrals

	N.S.U. controls (General Hospital) or Neurology referral (N = 14)	N.S.U. controls (N:10 Maudsley referral)
Age (mean)	32.78	29.2
Duration of epilepsy (mean)	15	16.4
Age of onset of epilepsy	17.78	12.8
Males	8	3
Females	6	7
Married	10	2
Single	4	6 (1 sep.)
Aura, present	9	9
" absent	5	1
Majors seizures only	1	0
Minor seizures only	2	4
Both	11	6
Fit frequency - majors, less than 1 per month	10	6

	N.S.U. controls (General Hospital) or Neurology referral (N = 14)	N.S.U. controls (N:10 Maudsley referral)
Fit frequency, majors, 1/month or more	2	1
Minors, less than 1/week.	1	0
Minors, 1/week or more	11	10
Psychomotor seizures: less than 1/month	0	0
1 per month	3	0
1/month or more	11	10
Psychomotor attacks present	11	10
absent	3	0
Total fit-frequency, less than 1/month	1	0
more than 1/month	13	10
Epileptic foci, right	5	5
left	6	3
Bilateral	3	2
E.E.G., background normal	4	3
abnormal	10	7
activity, specific	1	0
" non-specific	13	10
Epileptic activity, focal	13	10
" " others	2	0
Unilateral epilepsy	11	8
Bilateral "	3	2
Brain-damage, morbid antecedents in the personal history	12	7
A.E.G., normal	4	2
diffuse abnormality	6	7
focal	4	2
Personality, normal	8	3
abnormal	6	7
Childhood, normal	11	7
abnormal	3	3

The above table demonstrates clearly that the factors which determine whether a (non-psychotic) epileptic eventually referred for surgery is sent in the first instance to a psychiatric or to a general or neurological centre for management does not depend only on epileptic variables but also on social and psychological considerations. Since the type of seizures, the frequency of attacks, the laterality of the epilepsy, the incidence of structural cerebral damage, the E.E.G. characteristics do not appreciably differ in the cases referred from the psychiatric to those admitted from non-psychiatric sources and in view of the finding that the differences between the two series lie in the following areas:

1) Age of onset of epilepsy (12.8 years for Maudsley group, 17.78 for the general hospital group: t-test, 0.66, degrees of freedom, 23 does not reach significance, but trend is suggestive).
2) Preponderance of females in Maudsley referral group (70% versus 43%).
3) Striking excess of unmarried individuals in Maudsley sub-group 70% versus 30% which is associated with a higher proportion of abnormal personalities (70% versus 42%).

This implies that severe, intractable or frequent epilepsy is not a general characteristic of the Maudsley controls as

a whole but only of a minority, and further confirms that it is not so much the epileptic variables but psycho-social ones as reflected by a high evidence of abnormal personalities, a preponderance of celibacy, an excess of unfavourable childhood circumstances which determine the referral or stay or epileptics to a psychiatric as opposed to a neurological centre. It appears most probable that an early age of onset of temporal lobe epilepsy has far-reaching repercussions on the personality structure of the affected individual, increasing the likelihood of personality disorders and disturbed inter-personal relationships, which are reflected in the high incidence of celibacy and it is this complex interplay of psycho-social factors which leads to psychiatric referral rather than any special attribute of the epilepsy as such. The control population, however, is not homogenous since it consisted of 36 Maudsley patients (26 non-surgical and 10 referred to surgery) together with 14 surgical patients arising from non-psychiatric sources. If the Maudsley patients referred to surgery are compared with those not referred it can be shown that the former have more frequent fits, have more psychomotor seizures, have longer duration of epilepsy with earlier age of onset and more focal activity than the Maudsley controls not referred to surgery -

they do not have more left-sided epilepsy however. If, from the 36 Maudsley controls one removes the 10 patients referred to surgery for epilepsy, one is left with a control population by definition not characterised by severe or frequent epilepsy and comparing the psychotics with this derived control population (N:26) all the previously found features significantly differentiating psychotics from non-psychotics are maintained, including infrequent epilepsy in the psychotic situation. The important consideration for the purpose of the present investigation is that one may conclude that the non-psychotic controls do not appear to have been subjected globally to a process of selection influencing the epileptic variables under consideration.

DISCUSSION OF INVESTIGATION IN RELATION TO RECENT STUDIES OF EPILEPTIC PSYCHOSES

Relating the factors found in this investigation to be correlated with the genesis of psychotic states associated with epilepsy to the other studies inquiring into this problem which have been published in the last 15 years, it is apparent that there is general agreement on the fundamental importance of temporal lobe dysfunction.

The observations of Dongier are fully confirmed, in his as in our material, centrencephalic epilepsy is associated with confusional psychoses and temporal lobe epilepsy with affective, paranoid or schizophrenic psychotic disorders in which a pronounced inverse relationship between convulsive manifestations and psychotic susceptibility clearly operates.

Landolt describes the same phenomenon in electrophysiological terms, naming it "forced normalization" and showed that it was encountered not only in schizophrenic psychoses with the temporal focus disappearing for the duration of the psychotic episode but also in the course of confusional psychoses or "twilight states" when, in the same way, spike and wave activity may regress or disappear altogether.

Lorentz de Haas and Magnus on the other hand note that in 18* of their 72 cases of epileptics with episodic

*These patients are described as psychotic or "quasi" psychotic however, of the 18 cases with sub-cortical discharges 6 are said to have a non-schizophrenic paranoid syndrome, another 6 are "unclassifiable" leaving 6 patients of whom only one was schizophrenic.

mental abnormality these episodes exhibit sub-cortical type of epilepsy as well as bilateral temporal discharges and the authors are inclined to correlate the psychosis with the former disturbance. This relationship has not been reported by subsequent studies and is conspicuously at variance with the Maudsley series where confusional psychosis, the invariable concomitant of centrencephalic epilepsy is associated with temporal lobe epilepsy in only 9% of cases and 'spike and wave' patterns occur in only 10% of psychotics with temporal lobe epilepsy. It seems reasonable therefore to view the sub-cortical activity in those patients of Lorentz de Haas either as a secondary phenomenon, in effect, secondary bilateral hypersynchrony dependent on bilateral temporal epilepsy or, more probably, in view of the absence of frank psychotic manifestations of a clear-cut nature as primary centrencephalic epilepsy with secondary spread to the temporal areas.

Gastaut (152) analysed the clinical and E.E.G. correlations in 83 epileptics presenting with interictal psychotic disturbances - these being extracted from 1,094 epileptic case histories the overwhelming majority of whom had been referred to non-psychiatric hospitals (N:1043). The overall incidence of psychotic episodes was 7.5% being lowest in the military hospital (2.9%) and highest in the

psychiatric hospital (41%) which contributed 21 of the 83 cases with psychotic episodes. Neurology clinics from which more than half of the total material was derived had an intermediate incidence of 8.8% for psychotic episodes. The mean age of onset of epilepsy was older than in this investigation (20 years as opposed to 15) but the mean duration of epilepsy to the onset of the psychosis was comparable (11 years versus 13 years). The incidence of brain damage in the personal history (head injury etc.) was high (50%) a finding which is close to the 40% found in the present study but which neither in Gastaut's or in our material can be regarded as specific to psychosis since it is equally high in non-psychotic temporal lobe epileptics. Observing that in 22 of his cases the severity of the epilepsy was of the order of less than one attack a month while in 58 others it was in excess of 1 seizure per month Gastaut concludes that the severity of the epilepsy bears no relationship to the psychotic disturbances. This is a meaningless conclusion, however, since the severity of the epilepsy is neither related to the patients, longitudinally nor to the non-psychotics, horizontally. Comparing the incidence of grand-mal attacks, psychomotor seizures and focal attacks in the psychotic series with a different group consisting of 1,000 epileptics the authors state that the type of epilepsy does not predispose to

psychotic episodes. This conclusion is not justified by the evidence cited for it is the type of seizure, not the type of epilepsy which is the variable discussed here. In agreement with Landolt, Dongier and Lorentz de Haas and this investigation Gastaut finds a positive correlation between centrencephalic epilepsy and confusional psychoses and an association between temporal foci and depression, mixed or schizophrenic psychotic manifestations, strictly defined. In 11 or exactly half of the patients showing definitive focal temporal discharges, the focus disappeared during the psychotic episode. Interestingly in another 10 patients, 4 with temporal focus, 6 with centrencephalic discharges E.E.G. accentuation of the epilepsy was invariably related to confusional episodes.

Glaser, as has already been mentioned, was unable to detect any evidence of forced normalization or of "inverse relationship" in the psychotic episodes associated with temporal lobe epilepsy which he analyses in 37 patients and he notes the absence of psychological triggers. The significance of this negative finding is limited by the scanty information given on the patients, both from a psychiatric and neurological point of view, and by the fact that the psychotic episodes are categorized simply as paranoid, depressive, confusional or hallucinatory reactions, variously combined. Further since "over half"

of the 37 cases are described as presenting with disorientation and memory disturbance the possibility arises that the conditions described are largely confusional states. Moreover, bilateral theta discharges were present in 6, diffuse theta activity in 5, bilateral spike and waves in 4 patients and the E.E.G. was normal in another 2 cases so that in more than half of this material there is the further possibility that the diagnosis is not primarily of "true" temporal lobe epilepsy but of centrencephalic epilepsy with bilateral spread to the temporal areas.

Centrencephalic epilepsy may occasionally present with psychomotor seizures which result from bilateral, symmetrical radiation from the diencephalon to the temporal lobes. If, as there is reason to believe, the psychotic manifestations related to epilepsy primarily involving the limbic or temporal system exhibit characteristics quite demarcated from the psychotic episodes encountered in centrencephalic epilepsy, then the distinction between psychomotor seizures, the result of diencephalic irradiation, from seizures that derive from epileptic activity in the cortex or depth of the temporal lobes or as a result of spread from the rhinencephalon becomes theoretically important even although clinically the fits may be undistinguishable. As approximately half of the cases described by Glaser appear to belong to this class this

may account for the absence of the "inverse relationship" since in sub-cortical epilepsy an excess of epileptic activity, not necessarily amounting to petit-mal status, may produce confusional states closely mimicking confusional psychoses. This interpretation is supported by the fact that in 9 or 25% of Glaser's series, the inter-ictal psychological disorder is associated with an intensification of temporal or spike-wave disturbance.

Non-convulsive epilepsy with psycho-sensory, somatic and autonomic coordinates had been recognised by Falret as early as 1861 and with prophetic accuracy was discussed by Magnan 20 years later. Following the detailed and precise clinical descriptions of "uncinate crises" and "intellectual auras" made by Hughlings Jackson soon afterwards (1889) little progress was made in the understanding of epileptic "automatisms" and of "psychic" epilepsy until the electro-clinical definition of psychomotor seizures was first established by Gibbs, Gibbs and Lennox (1935-38), who correlated automatisms, transient clouding of consciousness and abnormal affective states with what was then thought to be a specific dysrythmia consisting of slow waves of 6 c/s frequency, of wide amplitude with "flat top". The Harvard School interpretation was subsequently contested by the Montreal workers who objected that the E.E.G. was a method of

localisation of neuronal discharges and in no way enabled one to identify specific cerebral rhythms. Jasper demonstrated in 1941 that sharp waves, spikes and slow-waves of 6 c/s frequency arose from the temporal regions of patients subject to psychomotor seizures and emphasised that these might originate in the depth of the temporal lobes or even in the neighbourhood of mid-line structures. Pointing out that the temporal convexity was usually healthy in patients with psychomotor seizures, Lennox and Brody (1946), Gastaut (1950), produced further evidence showing that temporal abnormalities in psychomotor epilepsy are often secondary to lesions in the deeper layers of the Sylvian fissure, hippocampus, anterior insula, uncus or orbital cortex of the ffontal lobes. Animal experimentation, notably by Jasper, Delgado, Kaada unequivocally demonstrated that stimulation of rhinencephalic, mesencephalic and diencephalic structures evoked temporal discharges. Gastaut (118), in a brilliant critical review of the concept of temporal or psychomotor epilepsy proposes the most logical classification of epileptic disturbances affecting the temporal regions:-

a) Hippocampal (psychomotor) epilepsy: the most common with autonomic dysfunction during ictal phases: pharyngeal, epigastric, abdominal and associated with confusion and automatisms.

b) Diencephalic (psychomotor) epilepsy: less frequent than (a) characterised by impulsive violence and affective reactions.

c) Temporal (cortical psychomotor) epilepsy: the least common form, in which illusions, visual and auditory hallucinations and other psycho-sensory phenomena predominate.

In Gastaut's material the onset of psychomotor seizures is before the age of 30 in 80% of cases with a majority of males. Closed head-injuries, encephalitis and obstetric accidents are the outstanding factors in the pathogenesis of these seizures, antecedents which are in keeping with the "incisural sclerosis" theory of Penfield and with the high incidence of morbid antecedents of this type (40%) found in the present study.

The absence of a control population is responsible for the emphasis placed by Slater on the duration of epilepsy and the presence of organic brain-damage as being aetiologically relevant to the emergence of schizophrenic psychoses in temporal lobe epilepsy. In 56 of 69 cases, or 81%, in whom an A.E.G. investigation was carried out this latter was abnormal in 70% of cases. The corresponding incidence of A.E.G. abnormalities in the present investigation is 52% for all forms of psychosis and 52.4% for the

schizophrenic psychoses taken separately. In our material the A.E.G. was performed in 39 (or 78%) of the psychotic group and 46 (or 92%) of the controls. Since the non-psychotic controls in 58% of instances had an abnormal A.E.G. and did not significantly differ from the psychotics in the other indices of brain damage, (neurological, psychometrical, morbid antecedents), it is concluded that structural cerebral damage in itself is not aetiological for psychosis in temporal lobe epilepsy.

Open to a similar criticism is the aetiological importance attached by Beard and Slater to the duration of epilepsy before the onset of psychosis. The average duration of epilepsy to the onset of the psychosis, was 14.1 years in Slater's series and was considered significant on account of a positive correlation of 0.58 between the age of onset of epilepsy and the age of onset of psychosis. In this investigation the mean duration of epilepsy to the onset of psychosis was almost identical to that reported by Slater, 13.7 years (cf. p.84) however, although shorter did not significantly differ from a control group matched for sex and for age on admission. Further since the mean age at time of last admission (psychotics: 33.5; controls: 31.8) the mean duration of epilepsy (psychotics: 20.6 years; controls: 16.4) and the age of onset of epilepsy (psychotics:

14.8; controls: 15.4) do not differ at a statistically significant level in the current study it is concluded that neither the age of onset nor the duration of epilepsy are related to the emergence of psychosis in temporal lobe epilepsy.*

Curiously although Slater and Beard report 17 cases in whom the psychotic episodes clearly showed an inverse relationship to the presence of severity of the epilepsy (or 25% of their material), the authors, basing their statement on a consideration of fit-frequency that is restricted to major convulsive seizures alone, postulating a modal figure of one Grand-mal attack per month, conclude that the severity of the epilepsy in the psychotics is approximately the same as in epileptics in general and that consequently psychosis is unrelated to the severity of the epilepsy.

The present investigation comparing the fit-frequency characterising the psychotic and non-psychotic temporal lobe epileptics and assessing independently the frequency of Grand-mal attacks, psychomotor and minor temporal seizures confirms that psychosis in temporal lobe epilepsy does not appear to be correlated with the frequency of major seizures but shows that at a statistically significant level

* NOTE: 12 of the psychotics in this study were included in the Slater, Beard and Glithero investigations. All, independently, were allocated to the schizophrenic sub-group by the writer with one exception (case No.H1955) with centrencephalic epilepsy, diagnosed here as confusional and schizo-affective.

it is inversely correlated with the presence of psychomotor seizures and inversely correlated with the frequency of minor temporal seizures, psychomotor seizures and global fit-frequency.

One of the most striking differences found between the psychotics and the controls in this analysis is related to the laterality of the epileptic focus. At a highly significant level ($P < 0.001$) psychosis is correlated with epilepsy affecting the dominant temporal lobe in contrast to the controls who have predominantly non-dominant temporal lobe involvement and moreover, a trend reaching significance ($P < 0.05$) suggests that the more the dominant temporal lobe is involved the more schizophrenic is the psychosis. In the "schizophrenia-like psychoses of epilepsy", section (ii), dealing with the physical aspects, Beard reports "an interesting negative finding" that the lateralisation of the focus is immaterial, basing his conclusion on the following focus distribution: left-sided foci, 16; right-sided, 12 and bilateral, 20. It is worth noting here that if laterality was important this would be obscured by the high proportion of bilateral foci. In view of the known functional asymmetry of the human hemispheres established in many important areas (speech, form perception, auditory verbal learning, recognition of non-verbal auditory stimuli) it is not legitimate to assume that bilateral foci necessarily

disturbs equally the dominant and non-dominant hemisphere with respect to a given parameter of mental organisation. Some evidence has been presented which suggests that bilateral temporal foci in psychotics appear to affect the dominant more than the non-dominant temporal lobe, the converse holding for the controls (cf.p 80). Analysed in this manner then it is apparent that the figures given by Beard implicate the left hemisphere 3 times more frequently than the right: left and bilateral foci: 36; right: 12.

In agreement with the findings of Slater, Pond, Dongier and Hill, an association is found between temporal lobe epilepsy and schizophrenic psychoses, the probability of psychosis being 10 times greater in temporal lobe than in centrencephalic epilepsy and the form of the psychosis being schizophrenic, or having schizophrenic features in 82% of the cases investigated.

The observations of Slater that there is no genetic predisposition to psychosis, of Hill, Pond and Slater that there is no excess of schizoid personality structure in these patients, of Glaser that there is no obvious psychological trigger to the psychotic episodes are also confirmed in the present enquiry.

The implications of the study of Slater in the "schizophrenia-like" psychoses associated with epilepsy were that, related to temporal lobe epilepsy, duration of epilepsy

and brain-damage but independent of the severity of the epilepsy epileptic psychoses were in reality non-specific organic psychoses where the epilepsy was of importance only in so far as it was the cause or the reflection of structural cerebral damage.

In this investigation temporal lobe epilepsy is found to be aetiologically associated with schizophrenic forms of epileptic psychosis which are, themselves, directly correlated with dominant temporal involvement whilst at the same time being inversely correlated with the severity of temporal seizures. For the reasons outlined above, however, structural cerebral damage does not appear to be related to the emergence of epileptic psychoses.

In the light of these findings it is concluded that epileptic psychoses are not "organic" psychoses in the general non-specific sense of the term but are truly epileptic psychoses fundamentally related to epilepsy rather than to associated brain-damage.

CONCLUSION

SPECIFIC: AETIOLOGICAL FACTORS IN EPILEPTIC PSYCHOSES

I. Fifty cases of psychosis associated with temporal lobe epilepsy were studied and compared with randomly selected temporal lobe epileptics, free from psychosis or psychotic episodes up to the time of their last admission to the Maudsley Hospital.

It was found in this investigation that the principal factors significantly differentiating the two populations are the following:

1) Psychotics have a lowered susceptibility to psychomotor seizures; (X^2: 13.07; $p < 0.001$).
2) Psychotics with psychomotor seizures have less frequent automatisms than non-psychotics; (X^2: 5.45; $p < 0.05$).
3) Psychotics have less frequent minor temporal attacks of the "absence" variety; (X^2: 8.89; $p < 0.01$).
4) Psychotics have less frequent seizures, if all varieties of attacks are taken into account (majors, minors and psychomotor seizures) although the frequency of majors does not significantly differ in the two groups; (X^2; 10.16; $p < 0.01$).
5) Psychotics have a gross excess of epileptic activity related to the dominant hemisphere; (X^2; 11.96; $p < 0.001$).
6) Non-psychotic controls have a very significant excess of psychomotor seizures with unilateral temporal foci; (X^2: 17.4; $p < 0.001$); conversely psychotics with unilateral epilepsy are refractory to psychomotor seizures.

The psychotics and the non-psychotic controls do NOT differ in the following variables:

1) Mean age on last hospitalisation; (psychotics 35.46; controls 31.83, t: 1.46; n.sig.);
2) Duration of epilepsy (psychotics 20.65 years of epilepsy; controls 16.40 years, t: 1.82, n.sig.).
3) Age of onset of epilepsy (psychotics 14.78 years; controls 15.43, t: 0.18, n.sig.).
4) Age of onset of psychosis in relation to duration of epilepsy; (years of epilepsy prior to onset of psychosis in 11 randomly selected psychotics matched for age with controls; psychotics, mean duration: 13.7 years; controls, 18.8; t: 0.92, n.sig.).
5) Family history of psychosis.
6) Social, psycho-sexual, occupational stability indices.
7) Dominance.
8) Anti-convulsant medication.
9) Incidence of brain-damage.
10) E.E.G. characteristics apart from laterality of focus.
11) Incidence and phenomenology of aura.

II. Enquiring into the form of the psychotic disturbance in this series it is found that schizophrenic psychosis is the commonest occurring in association with temporal lobe epilepsy (42%), the incidence rising to 60% if the schizo-affective disorders are included.

On the other hand the mixed or schizo-affective psychoses encountered in temporal lobe epilepsy appear to coincide on many of the variables studied, particularly with respect to minimal evidence of structural cerebral damage, with the manic-depressive group; the confusional and schizophrenic manifestations being associated with maximal brain-damage. Manic-depressive forms have the highest relative incidence of non-dominant hemisphere epilepsy and there is a striking trend, reaching statistical significance (X^2: 4.4; $p < 0.05$), indicating the possibility of a continuum of psychosis, manic-depressive psychosis occurring in association with non-dominant temporal epilepsy and minimal structural cerebral damage followed by schizo-affective disorders, also on a background of minimal brain-damage but with more dominant hemisphere epilepsy, leading in turn to the confusional and schizophrenic psychoses in which brain-damage and dominant temporal involvement is maximal: the periodicity diminishing and the schizophrenic features, with the chronicity, becoming more accentuated as the epilepsy and structural cerebral

alterations progress in the dominant hemisphere (see p.). Further, since manic-depressives are more susceptible to generalised seizures as the sole clinical manifestation of epilepsy and have major attacks infrequently whilst the more mixed, the less affective, the more schizophrenic the psychosis becomes the greater the incidence of temporal seizures, it follows that depressive psychoses also exhibits the "inverse correlation" infrequent majors standing in the same relationship to depression are infrequent temporal seizures do to schizophrenic manifestations.

III. Some factors, which appear to be specific to the disturbance of function in the temporal (dominant) region resulting from epilepsy emerge when psychotics with temporal lobe epilepsy are compared with psychotics suffering from centrencephalic epilepsy:

1) The probability of psychosis is 10 times greater in temporal lobe epilepsy than in centrencephalic epilepsy.

2) The form of psychosis is invariably confusional in centrencephalic epilepsy and predominantly schizophrenic in temporal lobe epilepsy.

3) The susceptibility to psychosis is similar in both sexes if the epilepsy involves the temporal regions; there is, however, an excess of females becoming psychotics when the epilepsy is of the centrencephalic variety; (significant at the 0.05 level of probability).

4) The evidence suggests that structural cerebral damage in centrencephalic epilepsy is the result of the epilepsy while in psychoses associated with temporal lobe epilepsy it is the result of the underlying lesion.

5) The age of onset of epilepsy is at a younger age (mean: 8.5) the duration of epilepsy is longer (mean: 23 years) in the centrencephalic group than in the temporal epileptics (mean age of onset: 14.8 years; duration of epilepsy, 20.6 years).

6) Probably related with the early age of onset of epilepsy the centrencephalic group has a higher incidence of abnormal personalities, disturbed childhood environment and abnormal inter-personal adjustment.

IV. If the presence of psychomotor seizures is held constant in the psychotics and in the controls it is found that in this sub-group, as in the total series, the same factors are related to the emergence of psychosis.

1) Psychotics have an excess of foci involving the dominant temporal lobe (X^2: 8.10; $p < 0.01$).

2) Psychotics have less frequent psychomotor seizures (X^2: 7.20; $p < 0.01$).

3) The overall fit-frequency is lower in the psychotics than in the non-psychotics (X^2: 8.71; $p < 0.01$).

Taking all the temporal epileptics together, psychotics

and non-psychotics, it is further found that the presence of psychomotor seizures "protects" against grand-mal seizures (X^2: 4.26; $p<0.05$); moreover, if the psychotics with psychomotor attacks are compared with the psychotic patients in whom such seizures do not occur the same trend operates: psychotics without psychomotor epilepsy have (naturally) a greater predisposition to grand-mal attacks as the sole manifestation of epilepsy but have these less frequently than psychotics liable to automatisms or psychosensory seizures.

V. The control, non-psychotic population, was analysed to assess in which directions it might be biased as a result of selective factors operating in connection with referral to a psychiatric hospital. For this reason almost exactly half of the controls were chosen from patients referred to the Guys-Maudsley Neurosurgical Unit for surgical treatment of epilepsy. No difference was found initially in any of the variables studied when the Maudsley and surgical patients were compared. However, if the surgical controls were separated in terms of psychiatric as opposed to General Hospital or Neurology referrals and the various control sub-groups then systematically analysed, it was found that the non-psychotic epileptics referred from the psychiatric centre (N = 10) were characterised by a younger age of onset of epilepsy (12.8 years v. 17.78); a preponderance of females (70% v. 43%) and a striking excess

of abnormal personalities (70% v. 42%) and of unmarried individuals (70% v. 30%). The important conclusion was that the control population was not based for severity of epilepsy and that generally referral of non-psychotic epilepsy to the psychiatric hospital hinged more on personality and sociological factors than in the severity or type of epilepsy are such.

It is, therefore, concluded that the parameters which are aetiologically related to the emergence of psychosis in temporal lobe epilepsy are:-

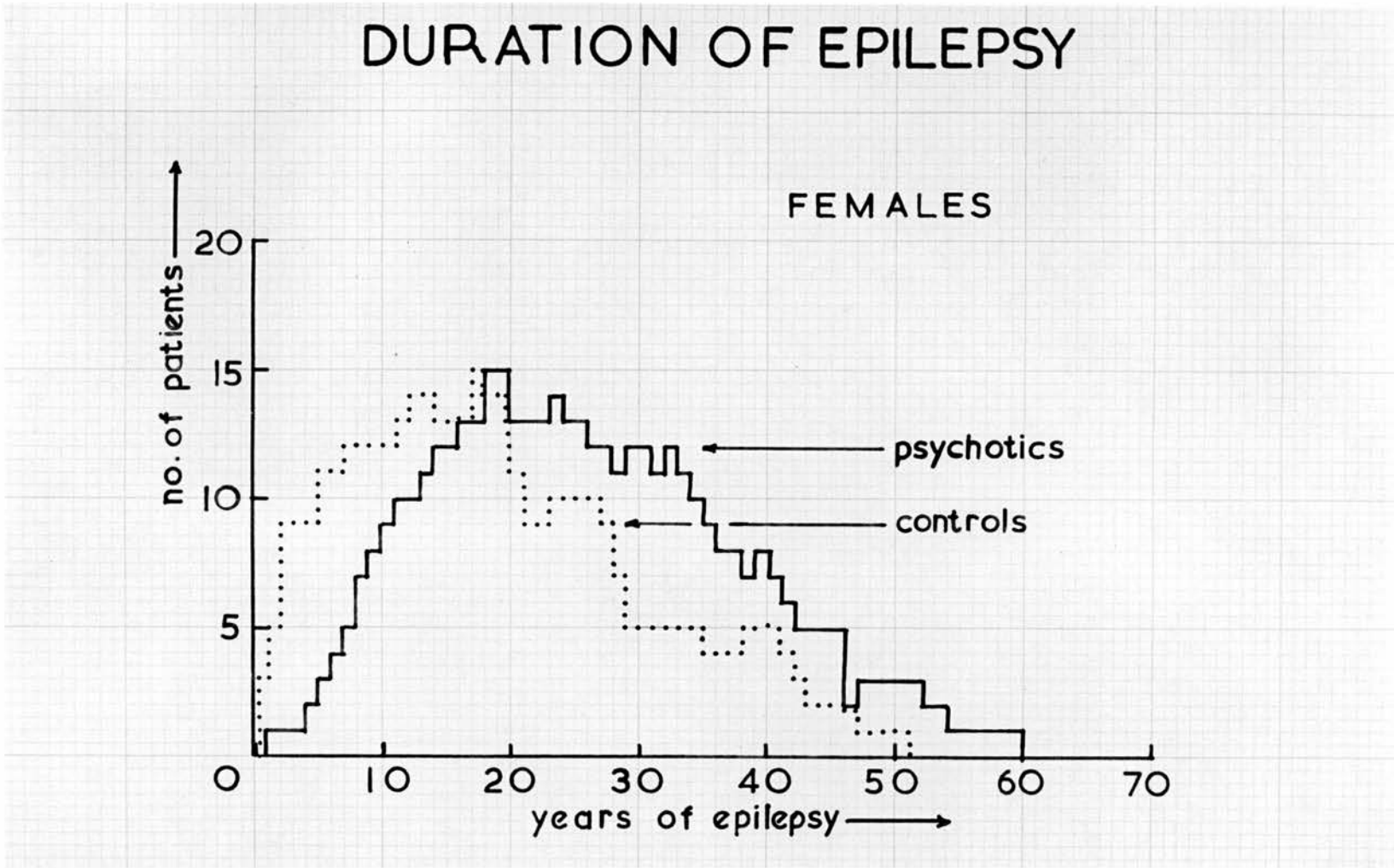
1) Temporal lobe epilepsy resistant to psychomotor seizures.
2) Temporal lobe epilepsy lateralised to the dominant hemisphere.
3) Temporal lobe epilepsy particularly resistant to psychomotor seizures in the presence of a unilateral focus.
4) Temporal lobe epilepsy with infrequent temporal seizures.

CONCLUSION

GENERAL AND SPECULATIVE: RELATIONSHIP BETWEEN THE EPILEPTIC AND THE FUNCTIONAL PSYCHOSES

These three sets of factors, temporal lobe epilepsy without or with few psychomotor seizures, lateralised to the dominant hemisphere are all very significantly correlated with psychosis and are associated with a generally lowered fit-frequency; in opposition to which the non-psychotics are particularly predisposed to psychomotor seizures not only with bilateral foci but also with unilateral foci.

Further psychosis in temporal lobe epilepsy is not aetiologically caused by structural cerebral damage as such, since the controls and psychotics are comparable in this respect, nor does it appear to be related to the duration of the epilepsy or to the age of onset of epilepsy. It is suggested that a long duration of epilepsy associated with an early age of onset does not predispose to psychosis but to personality and character disorders and disturbed interpersonal relationships. Examining more closely the question of duration of epilepsy and its relation to the consequent fate of the epileptic it is apparent from the accompanying histograms drawn for male and female temporal epileptics, psychotic and non-psychotic, that what distinguishes the psychotics from the controls is not that they have epilepsy of longer duration but that the former tend to have it at a <u>later</u> age, broadly between the ages of 15 and 30 while the latter have epilepsy starting at a younger age, roughly between 5 and 20, strikingly illustrating


DURATION OF EPILEPSY
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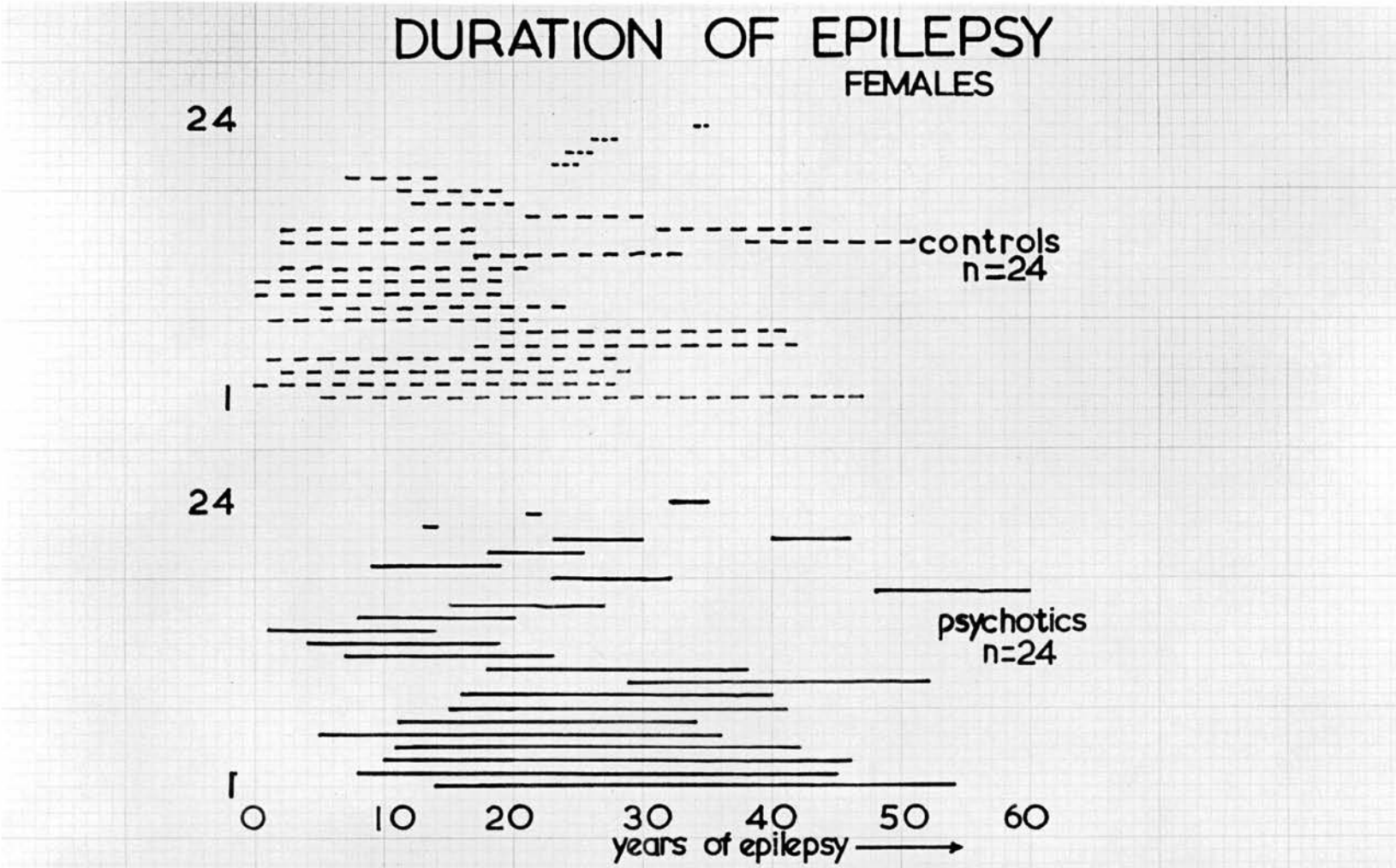
years of epilepsy
psychotics
controls


DURATION OF EPILEPSY
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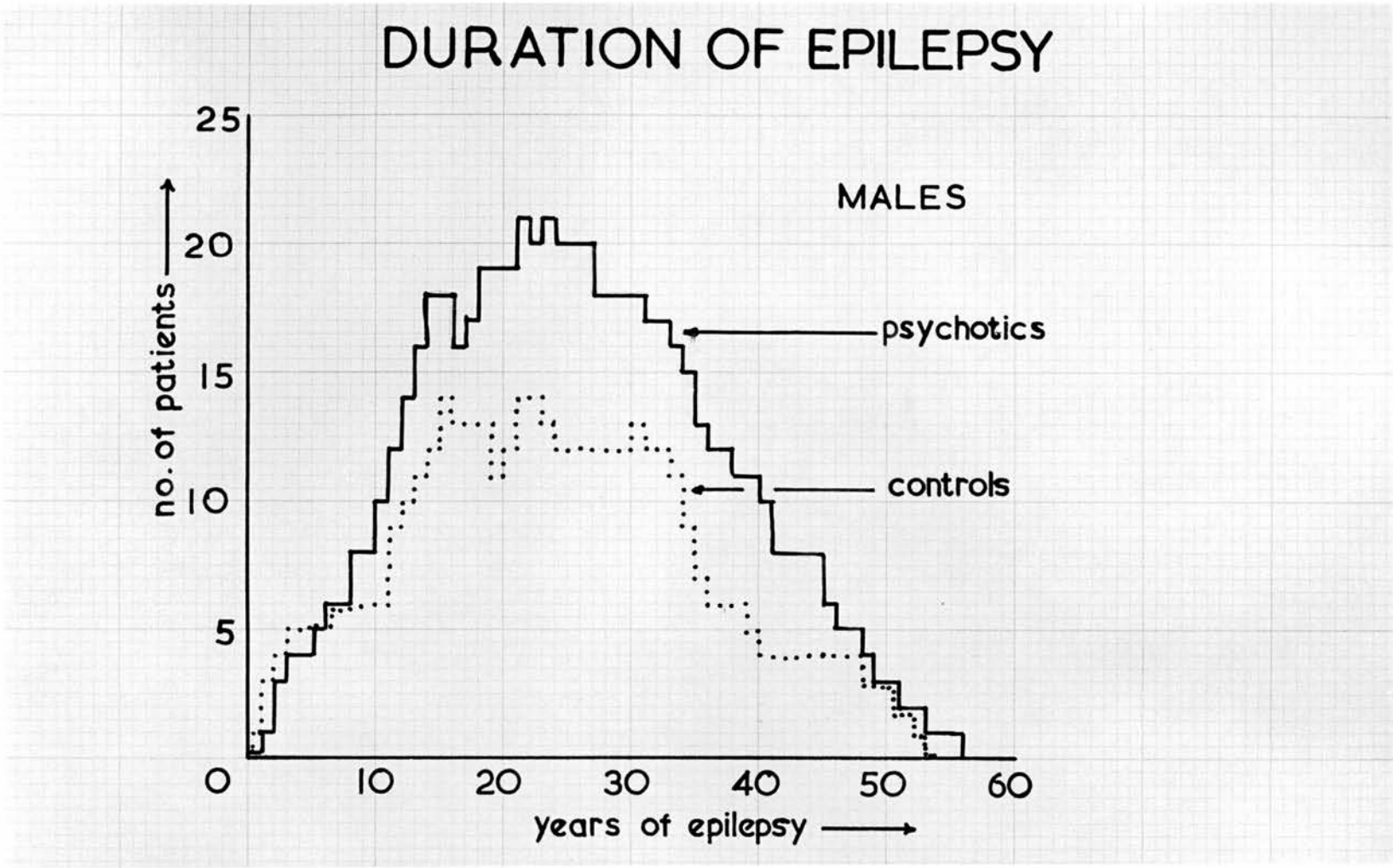
DURATION OF EPILEPSY
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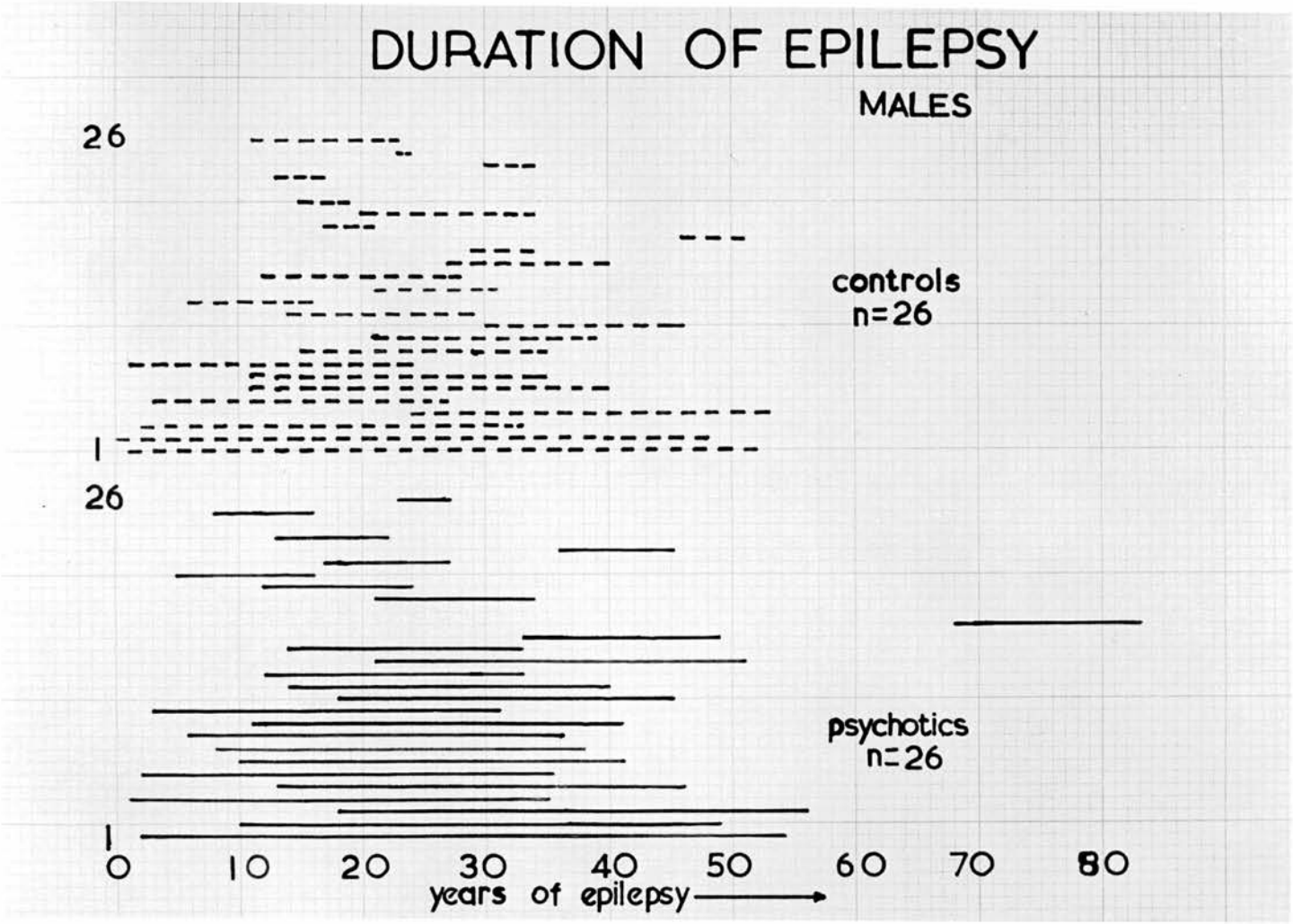
DURATION OF EPILEPSY
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years of epilepsy

the fact that the psychotics have an excess of epilepsy precisely in that period of the individual's life-span during which he is most predisposed to psychotic manifestations. That a psychotic evolution in temporal lobe epilepsy is not related to organic cerebral disease as such is an important negative finding for it implies that epileptic psychoses are not non-specific organic psychoses but truly epileptic psychoses. The degree of brain damage seems to be related to the form and chronicity of the psychosis, once it has emerged as a consequence of a specific dysfunction of the dominant temporal-limbic axis, the dysfunction being fundamentally and inversely correlated with the severity of the epilepsy, but, however, not with structural brain damage. The present investigation clearly shows that, with a highly significant statistical probability, temporal lobe epilepsy predisposes to psychosis (cf. comparative incidence of psychosis in centrencephalic and temporal epilepsy in general) and that, given temporal lobe epilepsy, it is the extent to which the dominant temporal lobe is affected which is the crucial determinant of psychosis, further that the fewer the seizures the greater the risk. There is a suggestive and consistent trend reaching statistical significance, indicating that the less the dominant temporal lobe is involved the more manic-depressive the form of the psychosis, the greater the periodicity; as

the dominant hemisphere becomes more involved and as the structural cerebral damage increases the periodicity progressively diminishes, the chronicity increases, the psychosis becoming schizo-affective, then finally culminating in a chronic, non-fluctuating, schizophrenic psychosis associated with the highest incidence of objective evidence of cerebral damage.

Since centrencephalic epilepsy is associated with confusional psychoses and temporal lobe epilepsy leads, in the majority of instances, to schizophrenic or schizo-affective disorders it follows that not only temporal lobe epilepsy particularly predisposes to psychosis as discussed above but would appear to be specifically responsible for a schizophrenic evolution. The results of the investigation confirm, in addition, that there is an inverse relationship between seizures and psychosis, in other words that frequent attacks, and more particularly frequent psychomotor attacks "protect" in a sense the individual from psychosis. It should be emphasised, however, this conclusion is only partially a return to the "antagonism" theories of Glaus, for the workers of the 20's and 30's had failed to appreciate that although infrequent seizures made psychosis more likely, and that therefore given epilepsy, frequent fits were indeed associated with a relative protection against schizophrenia nevertheless the presence of epilepsy

generally increased the susceptibility of the individual to psychosis. That temporal epilepsy predisposes to schizophrenia in such a manner that frequent ictal discharges reduce the risk strongly suggest that it is not so much the epilepsy itself but the underlying patterns of abnormal neuronal activity in the dominant temporal lobe and its connections in the hippocampal-amygdaloid-cingular gyrus complex which is fundamentally responsible for the schizophrenic-syndrome with the further implication that abnormal activity in the depth of the temporal region is inversely correlated with seizure frequency, but directly correlated with psychotic manifestations. There are observations derived from depth E.E.G. studies in man which in fact are in keeping with this hypothesis: stimulation of the depth of the temporal lobe and of the limbic system characteristically elicits hallucinatory experiences or unexpected and arbitrary affective responses rather than seizures (134); attacks with abnormal activity in the deep temporal structures are usually associated with the simultaneous depression of surface cortical activity (135), and in all types of psychomotor seizures the first electrical manifestation is a depression of background activity and of spike discharges over all the deep and surface temporal structures.

The phenomena of "forced normalisation" of the E.E.G. during psychotic episodes, documented by Landolt and Dongier,

is, perhaps, a reflection of the complex antithetical equilibrium which appears to underly the organisation of the temporal lobe: the forced normalisation of the (scalp) E.E.G. during a psychotic episode being the probable manifestation of increased disturbances in the depths of the temporal lobe(s).

To the writer's knowledge the present investigation is the first which demonstrates the inverse relationship between psychosis and fit-frequency by a horizontal, cross-sectional statistical analysis as opposed to the longitudinal study of individual patients and is also the first to show that epileptic activity in the dominant temporal lobe is highly correlated with the emergence of psychosis and that the laterality of the lesion is correlated with the forms of the psychosis. In relation to this last point Pagni et al. (134) makes the important observation that with a unilateral temporal focus the convulsive discharge can be shown by depth studies to be restricted to the ipsilateral hemisphere, a finding which, independently, confirms the significance of the excess of unilateral dominant temporal epilepsy in the psychotics with temporal lobe epilepsy when compared to non-psychotic controls.

From another approach, a recent study of Lishman (136) investigating, amongst other things, the incidence of psychiatric disability occurring after penetrating head-

injuries is of relevance here as in his large series, the probability of occurrence and extent of the subsequent psychiatric sequellae was shown to be related to structural involvement of the dominant temporal lobe.* An attempt will be made to integrate the findings reported in this study into the wider context of the functional psychoses.

It is a curious fact, historically, that from the time when they were first clearly delineated in the second half of the XIXth century the functional psychoses have been intimately associated, either positively or negatively, with epileptic disorders.

The periodicity of the syndrome which was later labelled manic-depressive immediately led Morel and Falret to assimilate it to the equally periodic epileptic disorders, of which it was thought to be a "larval" or sub-ictal form. When the schizophrenic syndrome finally emerged from its ancestor, dementia-praecox, at the beginning of the century, it was at first believed to be highly associated with epilepsy (Urstein, 1909; Kraepelin, 1910), then to be negatively correlated with convulsive disorders (Glaus, 1931) to the extent that artificial "epilepsy" was introduced by Meduna in 1937 in the hope that this might relieve the condition. It was

Ictal and sub-ictal activity and psychosis

*These findings confirmed the work of Hillbom (155), on the after-effects of head-injuries where it was found that the incidence of psychic disturbances were significantly related to the left-sided injuries and where, furthermore, 63% of the 27 cases who developed psychotic disturbances exhibited left-sided lesions. In the series, consisting of 359 cases, the appearance of temporal localisation was greatest in the psychotic group: 40%.

subsequently shown that exogenously induced convulsions were not generally effective in the treatment of schizophrenia, with the important exception of catatonic forms of the illness but that artificially induced epilepsy by means of electroplexy dramatically improved periodic psychoses of the manic-depressive variety. Although the mode of action of E.C.T. is today hardly better understood than it was when first introduced by Cerletti and Bini in 1938 (470), Ottoson (137) showed in 1960 that the therapeutic effect and the post-treatment slowing of the E.E.G. seemed to be related to the seizure discharge while the non-specific organic syndrome with amnesia was an independent variable related to current-intensity. Driver and Eilenberg in the same year (138), found that the photo-convulsive threshold in severely depressed patients was identical to that of other diagnostic categories or even normal subjects and did not alter after E.C.T.* In 1959 Chatrian and Petersen (139), examining the spread of metrazole induced convulsive activity in 5 schizophrenic patients and comparing it with E.C.T. induced convulsions concluded that, over 21 convulsive episodes, followed through by means of implanted electrodes, the E.E.G. patterns associated with the prodromal, tonic and clonic phases were constant for each individual and

*That the convulsive threshold should be invariant in depressive psychoses while it appears to be inversely correlated with the clinical manifestations of catatonic schizophrenia is a curious anomaly worthy of further study.

independent of the convulsive agent used, results which would imply that E.C.T. induced convulsions are, in fact, analogueous to spontaneous epileptic seizures.

In order to "explain" the inverse correlation between mental state and fit-frequency, between psychotic episodes and convulsive phenomena Gibbs introduced the concept of "sub-ictal irritation" and later Gastaut invoked the notion of the "continuous prodrome". There is some biochemical data which may be relevant to this problem.

The present study confirms that given temporal lobe epilepsy involving the dominant hemisphere then the less the abnormal temporal activity is able to release itself on account of the absence of psychomotor seizures or because of infrequent temporal seizures the greater the risk of schizophrenic psychosis. The finding that it is a relative absence of, or low frequency of psychomotor seizures which is correlated with psychosis but that in temporal lobe epilepsy the emergence of schizophrenic psychoses is independent of the frequency of grand-mal or major attacks is theoretically of great importance for it argues that the schizophrenic psychoses in temporal lobe epilepsy are specifically related to a disordered function of the dominant temporal-limbic system since minor seizures in psychomotor epilepsy are, in fact, restricted, short temporal attacks. If one recalls that in the present material the manic-depressive psychoses

characteristically have infrequent major seizures, although as a group they are more liable than the schizophrenic forms to generalised convulsive disorders associated with secondary bilateral hypersynchrony of spike and wave pattern and that moreover, it has been often observed clinically that depressive states in temporal lobe epilepsy are often relieved after spontaneous major convulsive attacks then we have here a possible link connecting both schizophrenic and manic-depressive psychoses and incorporating the relatively specific effect of E.C.T. in the treatment of manic-depressive states which would be the artificial analogue of temporal seizures in schizophrenic disorders. It is known (158) that the cerebral acetyl-choline content of young rats subjected to electroshock drops sharply as soon as the current is applied, being half its normal value after 2 seconds but that the convulsions begin some 8 to 15 seconds after current application only when the brain has restored its acetyl-choline concentration to normal values; ceasing again on reaching 40% of its normal level. In man the cerebrospinal fluid under ordinary conditions contains no appreciable quantity of acetyl-choline, however, after spontaneous epileptic attacks or after E.C.T. the c.s.f. acetyl-choline content rises and in addition intra-carotid injections or intracisternal instillation of the amine produces generalised convulsions in the cat while its local application on various

Biochemical Aspects

parts of the central nervous system leads to local discharges.

Tower (159) has summarised the functional changes associated with seizures in experimental animals and man:

1) Pre-ictally: rise in cerebral ammonia, fluctuations in cerebral acetyl-choline and onset of paroxysmal E.E.G. activity.
2) Inter-ictal: free acetyl-choline in c.s.f; in epileptogenic areas: decreased acetyl-choline binding capacity; increased cholinesterase activity; increased glutamic acid utilization; impaired maintainence of cellular K; spontaneous E.E.G. discharges.
3) Ictal: increase in cerebral blood flow, increase in cerebral oxygen consumption and cerebral lactic acid production; decrease in cerebral acetyl-choline, cerebral glutamic acid, cortical pH and high energy phosphate compounds. Intracellular electrolyte shift, K out of cell, Na in cell.

Both excess of free acetyl-choline and lowered intracellular potassium lead to depolarization of cell membranes, hence increase the probability of neuronal discharges and anti-convulsants and anaesthetics increase the acetyl-choline "binding" capacity of cerebral tissues.

It appears, consequently, that the biochemical evidence to date may imply that inter-ictal state in epileptic areas is characterised by an excess of free" acetyl-choline

in the brain which during seizures, spontaneous or induced, is released into the cerebrospinal fluid and it is, perhaps, this mechanism which is responsible for the beneficial effect of seizures in psychoses associated with temporal lobe epilepsy as well as being implicated in the anti-depressant action of E.C.T. the abnormal mental state being specifically associated with the excess of effective acetyl-choline in specific cerebral regions*, the anatomical site determining the form of the psychosis, epilepsy improving the mental state through the associated reduction in cerebral acetyl-choline.

Recent observations made by Grossman are compatible with the above hypothesis. Giving some of his reasons for believing that the effect is fairly specific, this worker found that a single injection of acetyl-choline in certain areas of the temporal lobe in cats led to profound behavioural changes in these animals who, from friendly began to viciously attack men or even dogs. The response to a single injection could last for months and was associated with abnormal E.E.G. discharges sometimes leading to seizures. Shorter lived disturbances in the emotional reactivity of rats followed acetyl-choline injections in the septal area as shown by the loss of fear reaction to painful stimuli. (Grossman, S.P.

*Similarly it has been shown (153), that anti-convulsants increase cerebral acetyl-choline content so that psychotic episodes induced by excessive anti-convulsant medication may be the result of the same mechanism.

"Exploring the brain with chemicals", Discovery, May 1966, 19-23).

Tentative and uncertain as the above representation may be, it is not impossible that to some extent it is, at a chemical level, at least a partial explanation of the puzzling "inverse relationship" so often observed in epileptics when emotional state is contrasted to the severity of the epilepsy.

It would further appear from the evidence of this study that the phenomenon of periodicity in psychosis hinges to some extent on the degree of cerebral damage, the milder the damage and the less the dominant hemisphere is involved the more purely affective and the greater the periodicity. The remarkable fact that, at a statistically significant level, the mixed or schizo-affective disorders in temporal lobe epilepsy stand in an intermediate position between the episodic manic-depressive and chronic schizophrenic psychoses with respect to the laterality of lesion, the degree of brain-damage involvement and from the point of view of periodicity has already been noted these parameters being the structural correlates of psychosis which appear to be modulated into florid manifestations by the "functional" propensity to specific sub-ictal discharges.

Nosological considerations

It may be objected that the separation of the functional psychosis into distinct, independent affective and schizophrenic categories established

by Kraepelin sixty years ago has been validated by generations of clinical observation and this is true; however, this division essentially relies on a system of classification based on outcome; the diagnosis in a sense being justified retrospectively once the prognosis was known and such a taxonomic system, no matter how useful practically, has in principle no aetiological implications. It may be further objected that the classical studies in the genetics of the functional psychoses carried out by Kallman, Slater, Shields and others confirm the independence of the Kraepelinian dichotomy; however, other studies have appeared suggesting that the genetic factor in the functional psychoses is not necessarily as overwhelming nor as specific as was at first believed, notably the Finnish survey of Tienari (140) where a zero concordance for schizophrenia was obtained in monozygotic twins and also, for instance the interesting finding reported by Herlofsen in 1957 (141), of an excess of manic-depressive heredity in the families of schizophrenics whose parents were first cousins when these were compared with a control population. On the Kraepelinian criteria of symptoms, course and prognosis, Clark and Mallet found, in 1963 (142) that schizo-affective disorders followed over a three-year period, were, in fact, intermediate between manic-depressives and schizophrenic controls.

The findings of the present investigation do not suggest that brain-damage as such plays an aetiological role in the genesis of psychosis but rather modify the form of the psychosis once the latter is established; in particular influencing the periodicity and the chronicity. Since the first report appeared in 1929 when Jacobi and Winkler first applied air-encephalography to demonstrate diffuse cerebral atrophy in schizophrenia some 30 papers have been published claiming to confirm the co-existence of diffuse structural brain-damage and schizophrenia; studies of which the most important perhaps is that of Huber (143) in 1957 showing that there was a positive association between the chronicity of schizophrenia and the degree of brain-damage. Storey (144), who reviews the problem of the significance of abnormal A.E.G. findings in chronic schizophrenia comments on the lack of controls in most of this work but quotes the large scale controlled survey of Peltonen (1962) which fails to find any difference in the extent of 3rd ventricle dilatation when schizophrenics are compared with non-psychotic control populations and he, himself, is unable to detect any significant difference in the A.E.G. characteristics of 18 chronic schizophrenics and those of 18 normal controls.

A.E.G. studies and psychosis

It will be apparent that the conclusions of Huber taken in conjunction with the controlled studies of Peltonen

and Storey, independently confirm that brain-damage is not aetiologically related to schizophrenia (although it may precipitate it) but may be correlated with the form of the schizophrenic illness. Although dismissed by the author as "accidental", Storey finds that at a statistically significant level the paranoid schizophrenics in his series have greater dilatation of the 3rd ventricle than hebephrenics.

Phenomenology

The phenomenological similarity existing between the symptomatology of spontaneously occurring schizophrenic illnesses and the ictal manifestations of temporal lobe epilepsy, emphasised by Karagulla, Gibbs and others led Pond to postulate that the repeated experience of these abnormal mental representations might psychologically predispose the individual epileptic thus afflicted to a subsequent psychosis embodying these features. The fact that non-psychotic temporal lobe epileptics are as liable to these ictal manifestations and are as likely to be only partially amnesic for psychomotor seizures as the psychotics does not support the hypothesis that the "schizophrenomimetic" aura by a process of gradual psychological incorporation and elaboration plays a causal part in the development of psychosis. If those remembered ictal experiences, alterations of perception, thought-processes, paroxysmal and arbitrary affective disturbances which, characteristic of temporal seizures and phenomenologically undistinguishable from

schizophrenic symptomatology do not predispose to the schizophrenic psychoses of epilepsy then what do they represent?

Here the possibility arises that if the "schizophrenomimetic" aura does not predispose to psychosis then the simplest logical alternative is that, in so far as the aura of temporal lobe epilepsy is qualitatively undistinguishable from schizophrenia then it is the psychosis, a transient schizophrenia or "micro-psychosis" as Weber and Jung so strikingly labelled it in 1940; a micro-psychosis which, under certain conditions, of which laterality of lesion and susceptibility to frequent ictal discharges appear to be crucial, may become hardened, "fixed" in a relatively fluctuating (periodic) or permanent (chronic) psychosis.

In a very fine analysis of the symptomatology of early schizophrenia Chapman (145), recently draws attention to the close similarity encountered in schizophrenic thought-blocking and in epileptic alterations of consciousness associated with (minor) temporal seizures and comes to the important conclusion that the subjective changes reported by their schizophrenic patients "appear to occur in a paroxysmal fashion" and further that speech defects in their cases "bears some resemblance to the paroxysmal dysphasia" commonly met with in temporal lobe epilepsy.

Briefly recapitulating the problem of the relationship between schizophrenia associated with temporal lobe epilepsy

and the spontaneously occurring non-convulsive schizophrenias we have on the one hand factual evidence that temporal lobe epilepsy involving the dominant hemisphere predisposes to schizophrenic psychoses which are undistinguishable from non-epileptic schizophrenias at the clinical level and moreover if temporal seizures are absent or infrequent the greater is the risk of psychosis. Evidence is also presented which shows that the emergence of psychosis in temporal epilepsy is unrelated to structural cerebral damage as such which suggests that once the psychosis has emerged brain-damage modifies the form of the psychosis and is related to its chronicity.

On the other hand half a century of increasingly sophisticated research into the macro- and micro-pathology of spontaneous schizophrenias in structural or biochemical terms has been invariably inconclusive while at the same time the more finely the symptomatology of schizophrenia has been observed the more it has been shown to approximate the paroxysmal ideational, perceptual, affective and dysphasic non-convulsive disorders of temporal lobe epilepsy.

Moreover, some electrophysiological evidence argues strongly in favour of relating fragments at least of the (non-epileptic) schizophrenic syndrome to sub-ictal abnormal activity emanating from the limbic system or depths of the temporal lobes, abnormal activity which, with the psychotic

symptoms, have been reversed by chlorpromazine.

It is, therefore, suggested that in the light of the available evidence it would appear that "sub-ictal", non-convulsive neuronal abnormalities of the limbic system and of the dominant temporal lobe may be the fundamental cause of all schizophrenias, of which the schizophrenic psychoses associated with temporal lobe epilepsy would represent an extreme group, extreme not because they are qualitatively distinct but because they are complicated by convulsive phenomena which in a sense are irrelevant since they exercise in "anti-psychotic" function; but which nevertheless are epiphenomena of psychosis which are of the greatest importance as they are themselves indirect parameters of psychosis.

Manic-depressive psychoses

The classical division of affective disorders into endogenous ("incurable") and exogenous ("curable") classes which, at a later date, came to be identified with E.C.T. response, the former being thought to respond well, although relapsing and the latter poorly to electroplexy was shown in a series of papers by Lewis (146) to be untenable as the symptom-complex which correlated with endogenity were essentially those of the intensity and depth of the depression and were largely independent of the "reactive" elements.

At the present thenosology of the affective psychosis

is somewhat chaotic, partly on account of conflicting clusters which various workers extract, by factorial analysis, as being correlated with E.C.T. response or with endogenous features: a bipolar factor corresponding to the traditional endogenous/exogenous dichotomy (Carney, Roth, Garside, 147); an excess of childhood bereavement (Forrest, Fraser, Priest, 148); the inability of sleep-pattern disturbance to differentiate reactive and endogenous types (Costello and Selby, 149) and finally the conclusion of the follow-up study of Kessel and Holt (150) in which no difference emerges between reactive and endogenous groups in terms of recurrence rates or imipramine response. Pollitt (151), in a recent paper proposes a model which, hinging on the concept of hypothalamic or "functional shift" reconciles many of the observed characteristics of psychological and physiological, exogenous or endogenous, reactive or psychotic depressions in a unitary model of affective disorders, psychological depression under certain circumstances leading to an inhibition of autonomic

and hypothalamic* functions which then produces the features of psychotic depression, features which, however, may arise with apparently trivial emotional or somatic stresses in sensitive or predisposed individuals and of which the periodicity might represent a fundamental biological property

*It is true that the somatic manifestations of severe depressions sleep disturbance, appetite impairment immediately evoke the possibility of hypothalamic dysfunction however it is possible that the role of the amygdala has been insufficiently stressed in this connection. Receiving afferent input from the lateral olfactory tract, the inferior temporal gyrus, from all sensory modalities, from the thalamus, hippocampus and the brain-stem reticular formation the amygdaloid nuclei send monosynaptic efferents to the septal area, head of caudate, pre-optic area, hypothalamus, anterior temporal cortex and contra-lateral amygdaloid as well as efferents to the sub-thalamus, hypothalamus, hippocampus through multi-synaptic pathways and to the neo-cortex through the diffuse thalamic projection system (156). Bilateral ablation in animals is followed by (1) depression leading to hyperactivity; (2) anorexia leading to hyperphagia, (3) hypersexuality, (4) placidity leading to paroxysmal rage and (5) a specific learning deficit where noxious stimuli are no longer associated with fear. The analogy existing between these effects and the signs of depression may be superficial but remains nevertheless striking. More remarkable still are the effects of amygdaloid stimulation in man which elicit fear, rage, anxiety or depression in the affective sphere and in the area of motor manifestations grimaces and facial movements which are not mediated by the motor-cortex. Although again a matter of speculation it is difficult not to be impressed by the possible relevance of this functional system to the displaced affect or to the mannerisms and stereotypes of certain schizophrenics. Although difficult to evaluate, and in many ways unsatisfactory, the report of Sawa (157), is of some interest in this connection. Bilateral amygdaloidectomies were performed on 12 patients, (5 schizophrenics, 5 epileptics and 2 "hyperactive imbeciles") and resulted in rage, "childishness", hypomania, oral disturbances (phagomania and heterophagia) and hypersexuality. It is seen that interference with amygdaloid functions appears to selectively disturb the modalities of mood, appetite, activity and sex and it is suggested that the evidence is sufficiently convincing to make it not unreasonable to postulate that abnormal activity of the amygdaloid nuclei may play an important part in the genesis of affective disorders in man.

analogous to hibernation. Although emphasising the neurophysiological substrate the views of Pollitt are, perhaps, closer to those of Lewis than is at first apparent. Both authors agree in considering psychotic,manic-depressive, endogenous features as being inextricably associated with reactive elements, the individual presentation depending on the relative balance holding between the two sets of factors, in other words they share a unitary concept of depressive illness.

Would it be justifiable to extend the argument to the functional psychoses in general and ask whether in view of (1) the relative rarity of both true manic-depressive psychoses showing the alternation of mania and depression, (2) the relative rarity of "nuclear" schizophrenia restricted to the fundamental symptoms of Bleuler, and without affective admixture, (3) the increasingly recognised importance of mixed states with affective features, be they labelled schizo-affective, atypical, cycloid, schizo-manic and attempt to resurrect the now unfashionable notion of "enheitpsychose"? Might not the pure schizophrenic and manic-depressive forms be themselves the extreme manifestations of a continuum of psychosis in relation to which the schizo-affective states would stand in the same position as the mixed depressions on the continuum of endogenity and reactiveness?

Be that as it may, it is suggested that a satisfactory general theory of the functional psychoses in the present state of knowledge should account for the following central facts:

1) Manic-depressive psychoses are periodic and generally have a good prognosis.
2) Schizophrenic psychoses have a less favourable prognosis and are less or non-periodic.
3) There is a large group of mixed or schizo-affective psychoses which from the point of view of periodicity, symptomatology and prognosis lie in an intermediate position between the manic-depressive and schizophrenic psychoses.
4) That those changes in the function of the central nervous system which accompany epileptic convulsive phenomena or "artificially" induced "epilepsy" are fundamentally related to the genesis of manic-depressive states as E.C.T. is the most specific anti-psychotic agent known in the condition.
5) That the phenomenology of schizophrenia is reproduced by the phenomenology of temporal lobe epilepsy.
6) That specific epileptic activity involving the dominant temporal or limbic system protects against the schizophrenic psychoses associated with temporal lobe epilepsy; probably

in the same way as bilaterally symmetrical limbic-diencephalic grand-mal seizures protect against manic-depressive psychoses.

7) That generalised grand-mal seizures, analogous to E.C.T., similarly protect against depressive manifestations in depressive psychoses associated with epilepsy.

It is further postulated that to dismiss as incidental, trivial, or irrelevant the intimate interaction observed between convulsive phenomena and the "functional" psychoses is to neglect the possibility that it is perhaps precisely the complex consequences in specific regions of the central nervous system of factors associated with resistance to convulsive phenomena which is the fundamental locus of both the manic-depressive and schizophrenic psychoses and that if the problem of the periodicity of epileptic phenomena was resolved this might correspond to that periodicity so characteristic of manic-depressive states.

It is tentatively suggested that the present study provides some evidence making it reasonable to propose that in epileptic psychoses -

1) A neurophysiological dysfunction of the dominant temporal lobe is responsible for the symptomatology of schizophrenia.
2) The more the non-dominant temporal lobe is the seat of neurophysiological dysfunction the more schizo-affective or affective is the psychotic picture.

3) Frequent ictal discharges are both generally and specifically anti-psychotic; the neurophysiological system implicated in generalised seizures relating to manic-depressive, that in temporal seizures to schizophrenic psychoses.

4) That although brain-damage of a structural kind is not aetiological to psychosis, when present it influences its form, reducing the periodicity and being responsible for chronicity.

5) That this evidence suggests that the functional psychoses are the manifestations of neurophysiological disturbances of the limbic system; these may be fundamentally related to epilepsy, of a non-convulsive kind, in such a manner that it is the relative extent to which the limbic-system alone or the degree to which the dominant or non-dominant temporal lobes are involved which modulates the clinical picture of pure manic-depressive, mixed or schizophrenic psychosis.*

6) The above set of postulates provides a conceptual model which enables one to understand the specific therapeutic action of grand-mal seizures, converging symmetrically on the limbic system andhypothalamus in affective disorders and also accounting for the excess of hypothalamic and

*Independent evidence compatible with this hypothesis (154), is provided by the observation that the pattern of Wechsler sub-test scores in schizophrenics is characterised by impairment of verbal functions whilst depressive psychotics typically exhibit an extreme impairment of performance abilities.

autonomic manifestations found in these conditions for the centrally situated and symmetrical limbic lobe converges on the hypothalamus. It, in addition, provides a neurophysiological substrate linking on the same continuum the depressive, mixed and schizophrenic psychoses in which increasing disorganisation of the non-dominant, then dominant hemisphere is the neuronal counter-part of schizo-affective and schizophrenic states; periodicity, a fundamental property of biological organisms, decreasing with increasing structural cerebral damage which appears to impose a fixity or chronicity to otherwise fluctuating phenomena which, essentially sub-ictal, are circumscribed by specific convulsive episodes. It follows from this hypothesis that the functional psychoses would correspond to a continuum of cerebral disorganisation essentially related to the laterality and localisation of abnormal activity in the human brain, which, though anatomically symmetrical is functionally asymmetrical. Seen in a different perspective the schizophrenic psychoses associated with temporal lobe epilepsy would appear to lie at an extreme end of a continuum of schizophrenia of which they would represent the (occasionally) convulsive variant and the same might be true of the affective psychoses.

APPENDIX

(a) ILLUSTRATIVE CASE SUMMARIES

Mr. S.C. age 52: admitted 25.10.61 - 17.1.62: 13.2.65 - 8.3.65. Family history unremarkable, father a docker. Patient youngest of three brothers. A happy, healthy child with no neurotic traits apart from nightmares and fear of dogs. Left school at 14 where his scholastic record was above average and worked as a packer, then salesman until 1940 when was called up, serving as a gunner in England and Italy. Following his discharge from the Army has been occupationally stable working as a docker, earning a good salary. Married at 23, very happy with his wife with whom he had three children, only two remaining alive, a daughter having died of poliomyelitis at the age of 5. Of note in the medical history are malaria (1944 and 1945), and head injury at work in 1955 followed by brief period of unconsciousness. Personality quiet, reserved, conscientious, a man of high intelligence who is a devout catholic. Transient lapses of consciousness began in 1945 when would become vacant for brief periods with post-ictal headaches lasting 24 hours. A second attack 6 months later was followed by a third some weeks afterwards which precipitated the first confusional psychosis with clouding of consciousness, aggressive and violent behaviour which lasted several days. E.E.G. at this time (1946) showed left-sided abnormality. Phenobarbital was introduced and patient remained seizure-free for five years, when after a

few minors in 1951, became unusually quiet and depressed. Clouding of consciousness with aggressive explosions of violence ensued when he attacked his wife and smashed furniture. Psychotic episode subsided after 10 days. After an interval of another 5 years (1961), a third similar psychotic episode, exactly identical to the previous occurred during which it was noted that for the duration of the psychotic episode the right plantar response became extensor. At this time the neurological examination was otherwise normal. A.E.G. showed dilatation of the left lateral ventricle and E.E.G. a diminution of alpha-rhythm over the left hemisphere but was otherwise without lateralising features. Psychological examination, f.s. 127, verbal, 130, performance, 118. The patient was re-admitted in 1965 at the request of his wife who feared a recurrence of explosive insanity as he had become "grey, begun to stare and was very quiet". Mental state was of depression, with retardation, delusions of guilt and unworthiness, ruminating over a (imaginary) theft of a few shillings perpetrated some 20 years before, with ideas of influence and alteration of time perception, subjectively feeling that time had stopped and that everyone at work was working abnormally fast. E.E.G. during the psychotic state showed non-specific abnormalities with excess of slow components. On admission the right plantar response was again extensor, suddenly

becoming flexor 3 days afterwards, the resolution of the babinski coinciding with the disappearance of the ideas of influence. Sleep E.E.G. after recovery showed right-sided fronto-temporal abnormalities. Drugs, mysoline and, for the duration of the psychotic episode, chlorpromazine. DIAGNOSIS: early psychotic episodes: confusional psychosis; last admission: epileptic psychosis, MANIC-DEPRESSIVE TYPE. Addendum: this case, whom the writer examined during the 1965 admission, is of particular interest, as it illustrates (1) the transformation of a confusional psychosis into a depressive psychosis; (2) shows that the psychotic episode coincides with sub-ictal activity in the dominant hemisphere (r. Babinski); (3) exhibits the phenomenon of "forced normalisation"; (4) on account of the remarkable regularity of the psychotic episodes.

Mr. F. age 51: admitted 22.6.59 - 6.8.59. Patient eldest of family of 8, with whom spent a happy childhood, father an expert craftsman. No epilepsy or mental illness in antecedents. Birth uneventful with forceps delivery, developmental stages normal, no neurotic traits in childhood, above average at school. Employed on the railways most of his life. Married at 21, premarital intercourse for two years, stable, happy relationship with his wife, now menopausal. 3 children, all well. Apart from fits which

began in infancy, no illness. Attacks, which had ceased in childhood and adolescence recurred when he was 21: major convulsive seizures with vertiginous aura and deviation of head to the left, frequency 1 to 6 per annum. Anti-convulsant medication only started at 46, first post-ictal confusional episode in 1958 lasting two days, with complete amnesia.

In 1959 a psychotic episode of 10 days duration was ushered in with transient confusion during which he wandered into the street looking for tennis balls, subsequently becoming disorientated, agitated and abusive, swearing loudly. An exalted phase ensued when, laughing a great deal, he talked to himself incessantly, asserting that he was king of the world. In the later course of the psychotic episode the clinical picture became depressive, patient believing that he was dead, that he deserved to die and go to hell, accusing himself (falsely) of having sexually assaulted a child. Recovery was complete and sudden with complete amnesia for the whole 10 days. A.E.G., normal; skull x-ray, normal; E.E.G., bilateral temporal spikes at sphenoidal leads. Psychological, verbal: 98; performance: 122. Drugs: epanutin, 100 mg t.i.d; phenobarbital, 30 mg t.i.d. DIAGNOSIS on discharge: post-epileptic psychosis, manic-depressive type. DIAGNOSIS: Manic-depressive psychosis.

Mrs. E.C.A. age 30: admitted 24.11.52 - 4.3.53. Unhappy childhood as father died when patient was 5 years old and her mother subsequently remarried husband's brother, an alcoholic who was cruel to the five children. Family history negative for epilepsy or mental illness. No history of meningitis or head-injury. Left school at 15, worked in factories for 5 years and married at 20. Onset of epilepsy soon after birth of first child who was stillborn, age 21 or 22. Emotional aura, depressive in content involving memories of dead child and associated with micropsia leading into the attack when becomes blank for 2 or 3 minutes making chewing movements of mandible. Five or six fits a month related to menstruation. Post-ictal headache and somnolence. Has also experienced three generalised seizures with deviation of head to the right. Personality altered with the onset of epilepsy, patient becoming depressed, irritable and withdrawn in contrast to her previous personality which was out-going and cheerful. During a post-ictal confusional state following one of the major seizures she amputated the finger tip of her small daughter with a saw, being amnesic for the incident. On examination, right-handed, physical examination normal, mental state depressed, with retardation, full of guilt. Skull x-ray normal. Wechsler, f.s., 90, verbal, 88, performance, 94. Sphenoidal E.E.G: bilateral abnormalities at sphenoidal electrodes. Epilepsy controlled with epanutin,

100 mg t.i.d., depression dramatically responding to course of 11 E.C.T's. Diagnosis on discharge: "psychotic depression apparently endogenous with phobic contamination". DIAGNOSIS IN INVESTIGATION: manic-depressive psychosis.

Miss K, age 42: admitted 15.3.51 - 2.6.51. Mother was troubled by obsessional thoughts for many years but was able to cope with these without medical help. Two brothers died in infancy, of unknown cause, family history otherwise unremarkable. Birth normal with convulsions at 14 months (isolated), fits starting again at 15, two years after onset of menarche. She was a shy, easily frightened girl, educationally backward. Spent many years in institutions but was later taken home by her mother, against medical advice. Major convulsive seizures occurred infrequently, circa two per annum with minors about once a week. Gradually has become increasingly preoccupied by obscene threats emanating from peoples' radios and worried by obscene words uttered by strangers about her occasionally provoking an excited and disturbed response from the patient, who also ruminates obsessively about naked men, conscious at the same time that God and Christ are pondering over her problems. Skull x-ray normal. A.E.G. normal. Neurological examination normal. Pentothal sphenoidal revealed frequent spikes from left temporal lobe. Major seizures induced in hospital by

stroboscopic stimulation, causing transient cheerfulness but not influencing schizophrenic symptomatology. Diagnosis on discharge "paranoid psychosis". DIAGNOSIS IN INVESTIGATION: schizophrenic psychosis.

Mr. D.W.H. age 35: admitted 11.3.55 - 4.6.55. Father a paranoid alcoholic, depressive in character, immersed in Christian Science. Severe parental disharmony. Two younger brothers. Normal birth, health in childhood unremarkable, apart from slight feeding difficulties when aged 4 months. Left school at 16, joining the R.A.F., later becoming sergeant with ground crew in Iraq. Discharged from the forces for dyspepsia and has worked with his father ever since. Since the age of 17 has masturbated with complex fantasy of "controlled girl, riding astride a horse with whip, erect in saddle, with spurs". Married at 28, has 3 children, but s.i. only possible with above fantasy and totally impotent for 6 months prior to admission. Only illness bilateral otitis media at 16. Onset of epilepsy aged 2, this being restricted to 4 grand-mal attacks not associated with pyrexia. Onset of minors at 23 with epigastric aura, motor and sensory aphasia together with "unrecallable thought, always the same". Major fits very infrequent, 6 in the last 12 years with aura of derealization.

Personality described as socially insecure, altruistic, untidy with depressive tendencies. As a child was compelled to attend a methodist, later christian science church, which he did without great interest. In his late 'teens more actively religious going to church weekly in the company of a youth alleged to be "neat, tidy and strong-willed". Began to feel, in Iraq, that he was in communion with nature in a most fundamental sense and experienced acutely the insignificance ofman, suddenly becoming converted to "God and Church". In 1952, 24 hours after a grand-mal seizure developed a florid religious psychosis with only slight alteration of consciousness, lasting 6 or 7 days. Since has been intensely preoccupied by religious feelings, ideas of unworthiness, need for atonement, believing in the literal reality of the experience which proved that he had been chosen by God. Neurological examination normal. Skull x-ray and A.E.G. both lateralise to the left temporal lobe and E.E.G. revealed a left anterior temporal focus. Psychological testing demonstrated high intelligence with impaired learning. Following a left anterior temporal lobectomy insight improved and potency returned. Discharge diagnosis: "psychotic character disorder, religious schizophrenic state". DIAGNOSIS IN INVESTIGATION: schizophrenic psychosis.

Mr. H. age 43: admitted 26.5.53 - 15.8.53. Father, aged 72, "epileptic and neurotic", a retired police constable. Mother, 76, capable but "spiteful and quarrelsome". One sibling, an elder brother discharged from the police force because of duodenal ulcer. Birth and infancy normal, "average" at school which he left at 16, becoming a clerk with the G.P.O. but forced to resign following onset of major fits at 18. Long periods of un-employment, found work as parks gardener a year before admission. Diphtheria as a child. No head-injuries. Experienced attacks of nausea with movements of lips and tongue as a child leading to major grand-mal attacks at 18 with epigastric aura, smacking of lips, rotation of eyes to the right and generalised convulsions. Aura becoming less pronounced with time, post-ictal automatisms supervening. Married a divorcee with 16 year old daughter and has an 8 year old boy of his own. Personality said to be solitary, suspicious, irritable and unhappy. Onset of paranoid delusions 3 months before admission related to work-mates, making transfer to other park necessary where he attacked school boys "who were talking about him". Mental state on admission of depression with paranoid delusions of reference. Physical examination normal, apart from nystagmus secondary to epanutin. E.E.G. revealed bilateral, independent, epileptic discharges from temporal lobes. A.E.G. showed atrophy of left hemisphere. WAIS: f.s. 92, verbal 101,

performance 97. Skull x-ray normal. Diagnosis on discharge: "psychosis resulting from epilepsy".

On account of affective colouring, absence of fundamental symptoms of schizophrenia, presence of restricted delusional system of paranoid type, DIAGNOSIS: schizo-affective.

Mrs. C. age 32: first admission, October - December, 1951. Family history unremarkable, both parents alive and well. An only child, pregnancy and delivery were normal. No neurotic features present in childhood and scholastically and socially was average. Menarche at 14, menstruation regular, but "prudish and naive". Some marital friction, her husband, a policeman is said to be unduly dependent on his mother. Dyspareunia, children avoided by contraception. Has worked throughout her married life, hairdressing, factory work and filing-clerk lately. No convulsions in infancy, mild head-injury age 4, scarlet fever with delirium at 13. Personality described as shy, but good mixer, fond of dancing with practical interests, knitting, embroidery. Lacks initiative and is always slightly irritable although nevertheless often fairly cheerful. Attacks began at 23, initially simply "stood still" for short periods, not aware that she had had an attack, pattern changing to "tummy going over", followed by fall and loss of consciousness of 2 minutes duration with masticatory movements and mumbling but no rigidity or clonus.

frequency once a week, often nocturnal, precipitated by worry or surprise. Three major convulsive seizures between 1941-48.

For ten years prior to admission has experienced ideas of reference and hallucinations, "hearing people say that she is a crafty copper's wife, that she wets the bed ..."; depressed for the last six months with crying spells and impaired concentration. Physical examination is normal and mental state on admission is one of depression with delusions of reference and occasional auditory hallucinations. W.R. - negative; ESR: 2; skull x-ray, normal; WAIS: f.s. 90, verbal 91, performance 89. Readily discussed sexual conflicts after drug abreaction, depression lifting but hallucinations becoming more prominent. There was some disagreement on the diagnosis, one of the consultant psychiatrists feeling that the warmth of affect made the diagnosis of schizophrenia unlikely after so prolonged an illness, the other stating that the picture was unmistakably schizophrenic. Discharged with a diagnosis of paranoid psychosis and psychomotor epilepsy she was re-admitted 7 months later (4.7.52), the paranoid ideas having become more severe and the depression deepening following long interval without seizures. The mental state then was dominated by delusions of reference, suspicion, irritability but with no hallucinatory component. The E.E.G. which had not previously been lateralised now

showed a left-sided temporal focus, and sphenoidal E.E.G. revealed bilateral independent temporal discharges, most active on the left side. Drugs: epanutin, phenobarbitone and amphetamine. DIAGNOSIS: schizo-affective psychosis.

(b) STATISTICAL METHODS

The following formulae were used in the investigation:

1) Testing for the significance of the difference between two means. (Student's t-test)

$$\frac{\bar{x} - \bar{y}}{\sqrt{\frac{x^2 - \frac{(\Sigma x)^2}{n1} + y^2 - \frac{(\Sigma y)^2}{n2}}{n1 + n2 - 2}} \times \left(\frac{1}{n1} + \frac{1}{n2} \right)}$$

where $\bar{x}$, $\bar{y}$ = mean

n_1, n_2 = numbers of cases.

2) Chi-squared test (Testing for the significance of differences between proportions)

$$\chi^2 = \sum \frac{(O - E)^2}{E}$$

Where O = observed frequencies.

E = expected frequencies.

3) Chi-squared (Yates' correction)

Whenever value of O in any cell is less than 5, with 1 degree of freedom.

$$\chi^2 = \sum \frac{(O - E) - \frac{1}{2})^2}{E}$$

4) Error of proportion

$$= \sqrt{\frac{P\,Q}{n}}$$

When P = proportion

Q = (1-P)

n = number of cases.

5) Significance of trend of proportion by regression method

Assigning the arbitrary values x = 4,3,2,1 to the psychotic categories, which correspond to the increasing proportion of right-sided foci, given the value y = 1, assuming a linear relationship between x and y (i.e. y = bx + c) then the best fit is given by

$$byx = \frac{\Sigma (x - \bar{x})(y - \bar{y})}{\Sigma (x - \bar{x})^2}$$

$$= \frac{\Sigma(x - \bar{x})^2 + \Sigma (y - \bar{y})^2 - \Sigma (x - y) - (\bar{x} - \bar{y})^2}{2 \Sigma (x - \bar{x})^2}$$

$$\text{Variance of byx} = \frac{\text{Variance y}}{\Sigma (x-\bar{x})^2}$$

$$\text{Where variance y} = \Sigma\frac{(y-\bar{y})^2}{n}$$

$$X^2 = \frac{b^2 yx}{\text{Variance byx.}}$$

		M.D.	Schizo-affective	Confusional	Schizophrenic	Total
Right-sided foci	y=1	4	2	1	2	9
Left bilateral foci	0	5	9	8	19	41
		9	11	9	21	50
	x =	1	2	3	4	

Where y = numerical designation for presence of right-sided foci.

x = numerical designation of psychiatric categories.

$\Sigma(x-\bar{x})^2 = 66.7$

$\Sigma(y-\bar{y})^2 = 7.4$

Variance y = 0.148

$$\Sigma \left|(x-y) - (\bar{x}-\bar{y})\right|^2 = 87.2$$

$$byx = \frac{66.7 + 7.4 - 87.2}{2 \times 66.7} = 0.098$$

$$\text{Variance } b_{yx} = \frac{0.148}{66.7} = 0.0022$$

$$X^2 = \frac{(0.098)^2}{0.0022} = \frac{0.0096}{0.0022} = 4.4$$ Sig. with P 0.05 level

with 1 degree of freedom or the amount of total X^2 (= 5.59) due to trend.

(c) RELIABILITY OF DIAGNOSIS OF PSYCHOSIS

Thirty psychotics were selected at random and independently diagnosed by assessor in the form of first diagnosis and alternative diagnosis where indicated. Agreement on first diagnosis for twenty-two patients (73% agreement). In all cases where disagreement on first diagnosis, 100% agreement on alternative diagnosis, the second diagnosis of the assessor corresponding to the first diagnosis of the author (7 cases), or the first diagnosis assessor corresponding to second diagnosis of author in one instance.

	Author	Assessor
1	a - Schizo-affective b - Manic-depressive	a - Schizophrenia b - Schizo-affective
2	a - Manic-depressive b - Confusional	a - Confusional b - Manic-depressive
3	a - Schizo-affective b - Schizophrenia	a - Schizophrenia b - Schizo-affective
4	a - Schizo-affective b - Schizophrenia	a - Schizophrenia b - Manic-depressive
5	a - Manic-depressive b - Schizo-affective	a - Schizo-affective b - Manic-depressive
6	a - Schizo-affective b - Confusional	a - Confusional b - Schizo-affective
7	a - Schizophrenia b - Schizo-affective	a - Schizo-affective b - Schizophrenia
8	a - Confusional b - Manic-depressive	a - Manic-depressive b - Confusional

where a = 1st diagnosis
b = 2nd diagnosis

In cases with disagreement on first diagnosis

(d) PROTOCOL

COLUMNS

1-5	Hospital No.
6	1. Male. 2. Female.
7,8	Age in years.
9	1. Married. 2. Single. 3. Div. 4. Sep. 5. Cohabit.
10	Aura 1. present. 2. absent. 3. disap. 4. N.K.
11	Seiz. 1. Majors only. 2. Minors only. 3. Both.
12	Psychomotor 1. Present. 2. Absent. 3. N.K.
13	Amnesia 1. Total. 2. Partial. 3. None.
14	Hallucinations
15	Illusions
16	Depersonalisation
17	Derealisation
18	Masticatory
19,20	Duration of ep. in years
21	Epanutin 1. -300 2. 300 3. +300
22	Phenob. 1. -100 2. 100 3. +100
23	Ospolot 1. -600 2. 600 3. +600
24	Mysoline 1. Yes. 2. No.
25	Others 1. Yes. 2. No.
26	Majors 1. -1/12 2. 1/12 3. +1/12
27	Minors 1. -1 wk. 2. 1 week. 3. +1 week.
28	Psychomotor 1. -1/12. 2. 1/12. 3. +1/12.
29	Frequency seiz. 1. Less 1 month. 2. 1 month. 3. Plus 1 month.
30	Dominance. 1. r. 2. l. 3. ambid.
31	Epilept. foci. 1. r. 2. l. 3. bilat.
32	EEG background. 1. normal. 2. abnormal.
33	Epilept. activity. 1. specific
34	1. Non-specific
35	1. Focal temporal
36	1. Others
37	1. Unilateral
38	1. Secondary bilateral hypers.

39 Brain damage. 1. birth injury

40 1. Head injury

41 1. Mastoiditis

42 1. Encephalitis

43 Neurol. 1. normal. 2. abnormal.

44 AEG 1. Normal. 2. Diffuse. 3. Focal. 4. N.K.

45,46,47 f.s. I.Q.

48,49,50 verb. I.Q.

51,52,53 perf. I.Q.

54 v/p discrepancy if over 7. 1. Yes. 2. No.

55 Psychosis 1. schiz. 2. md. 3. confusional.
4. mixed. 5. own diagn.

56 Freq. psychotic episodes 1,2,3,4,5,6,7,8,9,0:9 Plus

57 Duration in months 1,2,3,4,5,6,7,8,9,0:9 Plus

58 Family history Psychosis 1. schiz. 2. M.D. 3. Other
4. None

59 Previous mental health 1. In-patient. 2. Out-patient.
3. None

60 In-patient, no. of times 1,2,3,4,5,6,7,8,9,0:9 Plus

61 Personality 1. schiz. 2. epileptic. 3. normal
4. Non-specific abnormal.

62 Precipitating stress for psychosis 1. emotional

63 1. Physical

64 1. Environmental

65 Precipitating stress for admission, non-psychotics,
1. emotional.

66 1. Physical

67 1. Environmental

68 Occupational 1. stable 2. unstable

69 Abnormal childhood 1. present 2. absent

70 1. Psychotics

71 1. Non-psychotics

(e) TABLES

	Psychotics (n:50)	Controls (n:50)
married	20	22
single	27	24
separated	2	3
divorced	1	1
co-habitee	-	1
AURA		
present	25	37
absent	18	12
disap.	4	1
n.k.	3	-
SEIZURES		
majors only	8	4
minors only	10	14
both	32	32
PSYCHOMOTOR		
present	23	40
absent	27	10
X^2 = 13.07, sig. 0.001		
AMNESIA		
total	9	7
partial	14 (12	29) 33
none	(2	4)
AURAL		
hallucinations	(22	28)
illusions	(13	20) 63
derealisation	41 (4	9)
depersonalisation	(2	6)
masticatory	4	10
DRUGS		
mysoline	16	25
others	1	2
epanutin (- 300 mg./day)	13	9
(300 ")	29	27
(+ 300mg ")	1	6
phenobarb (- 100 ")	11	4
(100 ")	9	8
(+ 100 ")	22	19
ospolot	2	3
SEIZURE FREQUENCY, MAJORS		
- 1 per month	23	30
1 "	17 (3	5) 8
+ 1 "	(14	3)
X^2 = 3.53, n.sig.		

	PSYCHOTICS (n:50)		CONTROLS (n:50)	
SEIZURE FREQUENCY, MINORS				
-1 per week		16		6
1 "	21	2		11
+ 1 "		19		27
				38
χ^2=8.89, sig. at 0.01				
SEIZURE FREQUENCY, PSYCHOMOTOR				
- 1 per month		9		5
1 "	30	2		6
+ 1 "		12		29
				35
SEIZURE FREQUENCY, TOTAL				
- 1 per month		20		6
1 "	30	3		4
1 "		27		41
				45
χ^2= 10.16 sig. at 0.01				
DOMINANCE right		2		3
left		48		47
EPILEPTIC FOCI,				
right		9		25
left	44	19		13
bilateral		22		11
				24
χ^2 = 11.96, sig at 0.001				
NEUROLOGICAL.				
normal		39		32
abnormal		11		18
E.E.G. BACKGROUND				
normal		13		18
abnormal		37		32
specific		7		6
non-specific		43		44
focal temporal		39		43
others		11		38
unilateral		28		38
secondary bilateral		5		2
hypers.				
BRAIN DAMAGE (Historical)				
birth-damage		5		8
head-injury		8		13
mastoiditis		4		5
encephalitis		3		5
A.E.G.				
normal		13		16
diffuse		14		19
focal		12		10
not known		11		4

		PSYCHOTICS (n:50)	CONTROLS (n:50)
FAMILY HISTORY, PSYCHOSIS			
	m.d.	-	1
	schiz.	1	-
	others	4	-
	none	45	49
PREVIOUS PERSONALITY			
	schizoid	6	-
	epileptic	3	9
	normal	27	27
	non-specific abn.	14	14
PREVIOUS MENTAL HEALTH			
	in-patient	32	9
	out-patient	3	2
	none	15	29
PRECIPITATING FACTOR FOR ADMISSION:	emotional	9	6
	physical	16	44
	environmental	4	-
	environmental and mental state	21	-
OCCUPATIONAL HISTORY,			
	stable	32	33
	unstable	18	17
CHILDHOOD,			
	normal	35	41
	abnormal	15	9

~~66/66~~
SINGLES

	PSYCHOTICS n: 24	CONTROLS n:24	
married	7	10	
single	16	12	
separated	1	-	
divorced	-	1	
co-habitee	0	1	
AURA,			
present	11	18	
absent	10	3	
disap.	3	-	
n.k.	-	3	
SEIZURES,			
majors only	2	1	
minors only	6	6	
both	16	17	
PSYCHOMOTOR,			
present	11	19	
absent	13	5	
$\chi^2 = 5.70$ significant at 0.05			
AMNESIA,			
total	4	19	
partial	7	15	16
none	-	1	
AURAL,			
hallucinations	12	13	
illusions	6	10	
derealisation	2	7	
depersonalisation	-	4	
masticatory	3	6	
DRUGS,			
mysoline	6	12	
others	1	2	
epamitin - 300mg/day	8	5	
300mg "	14	13	
+ 300mg "	-	4	
phenobarb - 100 "	7	2	
100 "	3	1	
+ 100 "	12	10	
osopolet	-	-	
SEIZURE FREQUENCY MAJORS,			
$\chi^2 = 3$ - 1 per month	9	14	
1 "	3	2	4
not sig. + 1 "	6	2	
SEIZURE FREQUENCY, MINORS,			
$\chi^2 = 1.97$ - 1 per week	9	5	
not sig 1 "	1	5	17
+ 1 "	11	12	

FEMALES

		PSYCHOTICS (N:24)	CONTROLS (N:24)
SEIZURE FREQUENCY, PSYCHOMOTOR			
$\chi^2 = 1.17$	- 1 per month	5	4
not sig.	1 "	6 { 1	2 } 15
	+ 1 "	{ 5	13 }
SEIZURE FREQUENCY, total			
$\chi^2 = 4$	- 1 permonth	9	3
sig. at 0.05	1 "	15 { 2	3 } 21
	+ 1 "	{ 13	18 }
DOMINANCE,	right	-	2
	left	24	22
EPILEPTIC FOCI,			
$\chi^2 = 7.36$	right	4	13
sig. at 0.01	left	20 { 10	4 } 11
	bilateral	{ 10	7 }
NEUROLOGICAL	normal	19	14
	abnormal	5	10
E.E.G. BACKGROUND,			
	normal	8	7
	abnormal	16	17
	specific	2	4
	non-specific	22	20
	focal temporal	19	21
	others	5	4
	unilateral	14	17
	secondary bi. hypers.	2	1
BRAIN DAMAGE:(historical)			
	birth- injury	5	6
	head-injury	2	3
	mastoiditis	4	2
	encephalitis	1	3
A.E.G.	normal	4	6
	diffuse	8	10
	focal	4	6
	n.s.	8	2

FEMALES

		PSYCHOTICS (n:24)	CONTROLS (n:24)
FAMILY HISTORY, PSYCHOSIS			
	m.d.	-	-
	schiz.	-	-
	others	-	-
	none	24	24
PREVIOUS PERSONALITY,			
	schoziod	2	-
	epileptic	1	7
	normal	13	9
	non-spec.abn.	8	8
PREVIOUS MENTAL HEALTH,			
	in-patient	16	6
	out-patient	2	2
	none	6	16
PRECIPITATING FACTORS FOR ADMISSION:			
	emotional	6	5
	physical	9	19
	environmental	1	-
OCCUPATIONAL HISTORY,			
	stable	15	15
	unstable	9	9
CHILDHOOD	normal	20	17
	abnormal	4	7

MALES

		PSYCHOTICS n: 26	CONTROLS n:26
married		13	12
single		11	12
separated		1	2
divorced		1	-
co-habitee		-	-
AURA	present	14	18
	absent	8	7
	disap.	1	1
	n.k.	3	-
SEIZURES	majors only	6	3
	minors only	4	8
	both	16	15
PSYCHOMOTOR,	present	12	21
	absent	14	5
$\chi^2 = 8.12$, sig at 0.01			
AMNESIA,	total	5	4
	partial	6 { 5	14 } 17
	none	1	3
AURAL,	hallucinations	10	15
	illusions	7	10
	derealisation	2	2
	depersonalisation	2	2
	masticatory	-	4
DRUGS,	mysline	10	13
	others	-	-
	epamutin (-300mg/day)	5	4
	" (300 ")	15	14
	" (+300 ")	1	2
	phenobarb (-100 ")	4	2
	" (100 ")	6	7
	" (+100 ")	10	9
	ospolot	2	3
SEIZURE FREQUENCY, MAJORS			
	- 1 per month	14	14
	1 "	8 { 0	3 } 4
	+ 1 "	8	1
SEIZURE FREQUENCY, MINORS			
$\chi^2 = 8.55$	- 1 per week	7	1
	1 "	9 { 1	6 } 21
sig. at 0.01	+ 1 "	8	15

MALES

		PSYCHOTICS (n:26)		CONTROLS (n:26)	
SEIZURE FREQUENCY, PSYCHOMOTOR					
X 2= 5.45	- 1 per month		4		1
sig. at 0.05	1 "	8	1		4
	+ 1 "		7		16
					20
SEIZURE FREQUENCY, TOTAL					
X 2= 6.24	- 1 per month		11		3
sig.at 0.05	1 "	15	1		-
	+ 1 "		14		23
					23
DOMINANCE,	right		2		1
	left		24		25
EPILEPTIC FOCI,					
X 2 = 4.76	right		5		12
sig at 0.05	left	21	9		9
	bilateral		12		4
					13
NEUROLOGICAL,	normal		20		18
	abnormal		6		8
E.E.G. BACKGROUND,	normal		5		11
	abnormal		21		15
	specific		5		2
	non-specific		21		24
	focal temporal		20		22
	others		6		5
	unilateral		14		22
secondary bil. hypers.			3		1
BRAIN-DAMAGE (Historical)					
	birth-injury		-		2
	head-injury		6		10
	mastoiditis		-		3
	encephalitis		2		2
A.E.G.	normal		9		11
	diffuse		6		9
	focal		8		4
	n.k.		3		2

MALES

		PSYCHOTICS	CONTROLS
FAMILY HISTORY, PSYCHOSIS			
	n.d.	-	1
	schiz	1	-
	others	4	-
	none	21	25
PREVIOUS PERSONALITY,			
	schizoid	4	-
	epileptic	2	2
	normal	14	18
	non-specific abn.	6	6
PREVIOUS MENTAL HEALTH,			
	inpatient	16	3
	out-patient	1	-
	none	9	23
PRECIPITATING FACTORS FOR ADMISSION:	emotional	3	2
	physical	7	25
	environmental	5	-
OCCUPATIONAL HISTORY,			
	stable	17	18
	unstable	9	8
CHILDHOOD,	normal	15	24
	abnormal	11	2

sig. at 0.05

CONTROLS		(Males = 14 (Female = 12	(Males = 11 (Female = 13
		Maudsley N:26	N.S.U. N:24
Married		9	13
Single		14	10
Separated		1	-
Divorced		1	1
Co-habitee		1	-
AURA,	present	18	18
	absent	5	5
	disap.	-	1
	N.K.	3	-
SEIZURES,	majors only	3	1
	minors only	8	6
	both	15	17
PSYCHOMOTOR,	present	19	21
	absent	7	3
AMNESIA,	Total	4	3
	partial	12	19
	none	3	1
AURAL,	hallucinations	12	16
	illusions	8	12
	derealisation	4	5
	depersonalisation	2	4
	masticatory	7	4
DRUGS,	mysoline	14	11
	others	6	1
	epanutine (-300 mg/day)	7	2
	(300 ")	16	11
	(+ 300 ")	1	5
	phenobarb.(-100 ")	4	-
	(100 ")	8	1
	(+100 ")	4	16
	Depolet	1	1
SEIZURE FREQUENCY, Majors			
- 1 per month		15	15
1 " "	5	4	1 } 3
+1 " "		1	2 }
SEIZURE FREQUENTY, Minors			
- 1 per week		5	2
1 " "	18	6	2 } 20
+1 " "		12	18 }

CONTROLS

		MAUDSLEY		N.S.U.	
SEIZURE FREQUENCY, PSYCHOMOTOR					
- 1 per month		4		1	
1 "		3	15	1	21
+ 1 "		12		20	
SEIZURE FREQUENCY, TOTAL					
- 1 per month		4		1	
1 "		2	22	2	23
+ 1 "		20		21	
DOMINANCE	Left	23		24	
	Right	3		-	
EPILEPTIC FOCI,					
	Right	14		10	
	Left	5	12	10	14
	Bilateral	7		4	
NEUROLOGICAL,					
	Normal	21		18	
	Abnormal	5		13	
N.S.G. BACKGROUND					
	normal	11		8	
	abnormal	15		14	
	specific	4		2	
	non-specific	22		22	
	focal temporal	22		23	
	others	7		2	
	unilateral	19		20	
Rocontary bil. hypers.		-		2	
BRAIN-DAMAGE (historical)					
	birth-injury	2		5	
	head-injury	8		5	
	mastoiditis	2		3	62%
	encephalitis	1		2	
A.E.G.	normal	9		7	
	diffuse	9		11	
	focal	5		5	
	N.K.	3		-	
V/P discrepancy (10 or more) present:		14		5	
	7 or more) "	18		11	
DISCREPANCY	Verbal greater than perf.	11	69%	3	46%
	Perf. greater than verbal	7		8	

CONTROLS

	MAUDSLEY	N.S.U.
FAMILY HISTORY, PSYCHOSIS		
absent	26	23
n.d.	-	1
PREVIOUS MENTAL HEALTH		
in-patient	4	5
out-patient	2	2
none	22	17
PERSONALITY		
epileptic	3	7
normal	15	12
non-spec-abn.	8	6
schizoid	-	-
PRECIPITATING STRESS FOR ADMISSION		
emotional	9	2
physical	22	22
ep. and environmental	5	-
OCCUPATIONAL		
stable	16	17
unstable	10	7
CHILDHOOD		
normal	23	17
abnormal	3	7

PSYCHOMOTOR SEIZURES PRESENT

		PSYCHOTICS (n:23)		CONTROLS (n:40)	
married		10		22	
single		12		17	
separated		1		-	
divorced		-		1	
co-habitee		-		-	
AURA,	present	14		30	
	absent	6		7	
	disap.	3		1	
	n.k.	-		2	
SEIZURES,	majors only	-		1	
	minors oly	7		13	
	both	16		26	
PSYCHOMOTOR,	present	23		40	
	absent	-		-	
AMNESIA,	total	10		7	
	partical	12 (11		29)	33
	none	(1		4)	
AURAL					
	hallucinations	12		23	
	illusions	8		20	
	derealisation	2		8	
	depersonalisation	3		6	
	masticatory	4		11	
DRUGS,	mysoline				
	others				
	epanutin males	11		21	
	phenoberb females	12		19	
	ospelot				
SEIZURE FREQUENCY, MAJOR					
X2 = 4.26	- 1 per month	9		21	
sig. at 0.05	1 "	7 (2		2)	6
	+ 1 "	(5		4)	
SEIZURE FREQUENCY, MINORS					
	- 1 per week	4		3	
	1 "	11(1		9)	34
	+ 1 "	(10		25)	

PSYCHOMOTOR SEIZURES PRESENT

		PSYCHOTICS (n:23)	CONTROLS (n:40)
SEIZURE FREQUENCY			
χ^2 = 7.20	- 1 per month	9	5
	1 "	12 (1	5) 35
sig. at 0.01	+ 1 "	12 (11	30) 35
SEIZURE FREQUENCY, TOTAL			
χ^2 = 8.71	- 1 per month	6	1
	1 "	17 (4	2) 39
sig. at 0.001	+ 1 "	17 (13	37) 39
DOMINANCE,	right	-	2
	left	23	38
EPILEPTIC FOCI	right	4	22
	left	19 (9	11) 18
	bilateral	19 (10	7) 18
χ^2 = 8.10			
sig.at 0.01			
NEUROLOGICAL	normal	19	24
	abnormal	4	16
E.E.G. BACKGROUND,			
	normal	8	17
	abnormal	15	23
	specific	5	3
	non-specific	18	37
	focal temporal	21	34
	others	2	6
	unilateral	13	33
secondary bil. hypers.		5	1
BRAIN DAMAGE (historical)			
	birth-injury	2)	7
	head-injury	4)	13
	mastoiditis	1)	1
	encephalitis	2)	2
A.E.G.	normal	5	14
	diffuse	60% 5	15
	focal	9	9
	n.k.	4	2

PSYCHOMOTOR SEIZURES PRESENT		PSYCHOTICS (n:23)	CONTROLS (n:40)
FAMILY HISTORY, PSYCHOSIS			
	m.d.	-	1
	schiz.	-	-
	others	1	-
	none	22	39
PREVIOUS PERSONALITY,			
	schizoid	3	-
	epileptic	3	8
	normal	10	23
	non-specific abn.	7	9
PREVIOUS MENTAL HEALTH,			
	in-patient	15	6
	out-patient	1	2
	none	7	32
PRECIPITATING FACTORS FOR ADMISSIONS			
	emotional	2	8
	physical	8	32
	environmental	1	-
OCCUPATIONAL HISTORY			
	stable	18	27
	unstable	5	13
CHILDHOOD	normal	17	34
	abnormal	6	6
	TYPE OF PSYCHOSIS		
	schizophreniform:	9 - 39 %	
	manic-depressive:	3 - 13 %	
	confusional	3 - 13 %	
	mixed	8 - 34.8 %	

PSYCHOMOTOR SEIZURES ABSENT

		PSYCHOTICS n:27	CONTROLS n:10	
married		10	2	
single		15	6	
separated		2	1	
divorced		-	1	
co-habitee		-	-	
AURA?	present	9	6	
	absent	14	3	
	disap.	1	-	
	n.k.	3	1	
SEIZURES,	majors only	7	3	
	minors only	4	2	
	both	16	5	
PSYCHOMOTOR	present	-	-	
	absent	27	10	
AMNESIA	total		1	
	partial		1	
	none		-	
AURAL,	hallucinations	9	5	
	illusions	5	-	
	derealisation	2	1	
	depersonalisation	-	-	
	masticatory	-	-	
DRUGS	males	15	5	
	females	12	5	
SEIZURE FREQUENCY				
	- 1 per month	14	7	
	1 "	9 (-	1)	1
	+ 1 "	(9	-)	
SEIZURE FREQUENCY MINORS				
	- 1 per week	12	3	
	1 "	8 (-	1)	4
	+ 1 "	(8	3)	

PSYCHOMOTOR SEIZURES ABSENT			PSYCHOTICS	CONTROLS
SEIZURE FREQUENCY PSYCHOMOTOR	- 1 per month			
	1 "			
	+ 1 "			
SEIZURE FREQUENCY TOTAL				
X2 = 0.009	- 1 per month		13	5
	1 "	14	-	1 } 5
not sig.	+ 1 "		14	4 }
DOMINANCE,	right		2	1
	left		25	9
EPILEPTIC FOCI	right		5	3
X 2 = 0.58	left	22	9	3 } 7
not sig.	bilateral		13	4 }
NEUROLOGICAL	normal		20	7
	abnormal		7	3
E.E.G. BACKGROUND.	normal		5	2
	abnormal		22	8
	specific		2	4
	non-specific		25	6
	focal temporal		18	8
	others		11	2
	unilateral		14	6
secondary bil.hypers.			-	1
BRAIN DAMAGE (historical)				
	birth-injury		3	2
	head-injury		4	-
	mastoiditis		3	-
	encephalitis		1	1
A.E.G.	normal		9	3
	diffuse		8	4
	focal		3	1
	n.k.		7	2

PSYCHOMOTOR SEIZURES ABSENT			
		PSYCHOTICS	CONTROLS
FAMILY HISTORY, PSYCHOSIS			
	m.d.	-	-
	schiz.	-	-
	others	3	-
	none	24	10
PREVIOUS PERSONALITY			
	schizoid	3	-
	epileptic	1	1
	normal	17 - 63%	5
	non-specific abn.	6	4
PREVIOUS MENTAL HEALTH,			
	in-patient	15	3
	out-patient	2	-
	none	10	7
PRECIPITATING FACTORS FOR ADMISSION:			
	emotional	6	4
	physical	7	9
	environmental	3	-
OCCUPATIONAL HISTORY,			
	stable	14 - 51.8 %	6
	unstable	13	4
CHILDHOOD	normal	18 - 66.6 %	8
	abnormal	9 - 33.3 %	2
	TYPE OF PSYCHOSIS:		
	schizophreniform:	13 - 48.1 %	
	manic-depressive:	3 - 22.2 %	
	confusional:	5 - 18.5 %	
	mixed:	3 - 11.1 %	

CONTROLS, (Male and Female), MAUDSLEY: (N:26)

AGE	DURATION EPILEPSY	AGE OF ON SET	I.Q.	VERBAL	PERFORMANCE	
52	51	1	101	102	99	
24	23	1	95	105	89	
29	15	4	112	107	114	
53	29	24	97	88	110	
48	48	0	90	86	97	
31	10	21	131	130	124	
34	14	20	111	116	104	
21	4	17	87	97	80	
28	16	12	111	124	94	
19	4	15	109	108	106	
83	15	68	109	122	95	
35	24	11	125	124	120	
33	31	2	72	85	61	
16	10	6	-	-	-	
40	29	11	103	96	111	
28	27	1	123	127	114	
42	25	15	92	93	84	
47	42	5	95	89	104	
41	22	19	108	109	106	
28	2	26	76	70	88	
27	2	25	94	95	94	
17	15	2	102	98	106	
30	9	21	103	111	93	
20	8	12	96	102	92	
29	2	27	93	93	94	V/P
14	7	7	99	108	90	
$\bar{x}$ = 33.42	= 18.61	= 373 = 14.34	101.36	103.4	98.76	

Σx = 869 = 484

Σx^2 = 34,573 = 13,820

CONTROLS, (Male and Female), N.S.U.: (N:24) (Maudsley Ref. 10) (General Hospitals) (Neurology 14)

AGE	DURATION EPILEPSY	AGE OF ON SET	I.Q.	VERBAL	PERFORMANCE
19	19	0	60	61	68
17	15	2	80	86	78
21	20	1	111	106	114
17	4	13	77	76	83
21	19	2	67	69	72
23	12	11	99	96	107
29	27	2	-	-	-
27	24	3	118	115	117
35	1	34	129	126	128
51	5	46	127	130	117
34	4	30	105	98	111
40	12	28	-	-	109
46	16	30	109	103	115
34	5	29	126	126	122
43	12	31	101	104	99
51	13	38	-	-	-
33	16	17	104	98	108
35	20	15	130	134	121
40	19	21	111	108	112
28	28	0	103	98	109
24	1	23	-	-	-
24	19	5	105	105	104
19	8	11	103	105	99
19	19	0	100	96	104
		= 392			
$\bar{x}$ = 30.4	= 14.08	= 16.3	103.2	= 102	= 104.6
Σx = 750	= 338				
Σx^2 = 24,796	Σx^2 = 6180				

AGE (Maudsley and N.S.U.) T = 0.8

d.f. = 49, not sig.

DURATION OF EPILEPSY (Maudsley / N.S.U.)

T. = 0.87, not sig.

Comparison between psychotics and control sub-group with infrequent epilepsy

	Psychotics % (N: 50)		Maudsley Controls % (N:26)
			(Excluding surgical referrals with frequent ictal manifestations)
Married	40 %		36 %
Aura present	50 %		72 %
Psychomotor present	46 %		76 %
Majors only	16 %		12 %
Minors only	20 %		32 %
Both	64 %		60 %
Seizure frequency			
Majors -1/12	46 %		60 %
" +1/12	34 %		20 %
Minors -1/52	32 %		20 %
" +1/52	42 %		72 %
Psycho-motor -1/12	18 %		6 %
" +1/12	28 %		60 % age 33.3
Total fit frequency -1/12	40 %		16 % duration Ep. 18.6
" +1/12	60 %		88 %
Epileptic foci			
right	18 %		56% age onset Ep. 14.3
left	38 %	82 %	20 % 48 %
bilateral	44 %		28 %
Brain damage, historical	40 %		52 %
A.E.G., normal	26 %		36 %
diffuse	28 %		36 %
focal	24 %		20 %
n.k.	22 %		12 %
Previous personality: Normal	54 %		60 %
Occupationally stable	64 %		64 %
Childhood normal	70 %		92 %

Characteristics of controls; psychiatric and non-psychiatric referrals

Controls, N.S.U. patients

N = 10 Maudsley referrals			N = 14 Neurology referrals		
AGE	DURATION Ep.	ONSET EP.	AGE	DURATION Ep.	ONSET EP.
17	15	2	33	16	17
19	19	0	40	12	28
27	24	3	34	4	30
41	12	29	35	1	34
19	19	0	23	12	11
28	27	2	35	20	15
46	16	30	51	13	38
51	5	46	21	20	1
19	8	11	34	5	29
24	19	5	40	29	11
			28	28	0
			40	19	21
			28	27	1
			17	4	13
Σx, 292	164	128	459	210	249
$\bar{x}$, 29.2	16.4	12.8	32.78	15	17.78
		$\Sigma_x 2 = 402$			$\Sigma_x 2 = 6493$

t-test for distribution of age of onset; t:0.66 with 23 degrees of freedom; not sig.

Characteristics of controls referred to surgery from psychiatric hospital

	N.S.U. Controls, Maudsley referrals (N = 10)	
Married	20%	
Aura present	90%	
Minors, more than 1 per week	100%	
Psychomotor seizure more than 1/month	100%	
Psychomotor seizure present	100%	
Total fit-frequency: over one per month	100%	
Epileptic foci, right	50%	
left	30%	50%
bilateral	20%	
Epileptic activity, focal	100%	
A.E.G. normal	20%	
diffuse abn.	60%	
focal abn.	20%	
Personality abn.	70%	
Childhood abn.	30%	
Age of onset of epilepsy: (mean): 12.8		
Duration of epilepsy: 16.4 years		
Mean age of group: 29.2		

TEMPORAL LOBE EPILEPSY: PSYCHOTICS, (MALES, N:26)

AGE	DURATION EPILEPSY	I.Q.	VERBAL	PERF.	FREQ. OF PSYCHOTIC EPISODES	DURATION PSYCHOTIC EPISODES (in months)
24	12	117	121	110	1	0.2
41	31	87	91	83	2	6
38	30	112	102	121	3	1
16	11	71	70	77	1	60
33	19	-	-	-	1	9
22	9	120	125	110	3	7
45	27	112	108	115	5	8
46	33	100	93	110	1	36
36	25	120	116	121	1	180
34	13	-	-	-	1	1
35	33	126	124	124	12	3
54	52	91	92	89	1	1
56	38	87	95	83	1	48
49	39	100	85	116	1	1
51	30	115	98	122	1	1
40	26	93	88	99	1	9
49	16	127	130	118	5	2
27	4	76	89	64	1	4
33	21	119	114	119	10	3
27	10	61	61	66	3	9
45	9	108	103	113	2	-
16	8	-	-	-	1	48
41	30	115	111	115	1	36
31	28	69	73	69	1	60
35	33	125	122	124	1	6
36	30	70	74	70	20	7
$\bar{x}$ =36.92	=23.73	100.2	99.6	101.7	3.1	23.28
Σx = 960	= 617					
Σx^2=38,138	Σx^2 = 18.145					

AGE, t = (PSYCHOTIC/CONTROLS) = 0.48, d.f. = 51 - not sig.

DURATION OF EPILEPSY, (PSYCHOTIC/CONTROLS) t = 1.93, not sig.

AGE OF ON SET OF EPILEPSY: $\bar{x}$ = 13.15 (Σx = 342, Σx^2=6335)

(PSYCHOTIC/CONTROLS) t = 0.65, not sig.

TEMPORAL LOBE EPILEPSY: CONTROLS : (MALES, N: 26)

AGE	DURATION EPILEPSY	I.Q.	VERBAL	PERF.
52	51	101	102	99
24	23	95	105	89
29	15	112	107	114
53	29	97	88	110
48	48	90	86	97
31	10	131	130	124
34	14	111	116	104
21	4	87	95	80
28	16	111	124	94
19	4	109	108	106
83	15	109	122	95
35	24	125	124	120
33	31	72	85	61
16	10	-	-	-
40	29	103	96	111
24	1	-	-	-
35	20	130	134	121
34	5	126	126	122
27	24	118	115	117
46	16	109	103	115
51	5	127	130	117
23	12	99	96	102
17	4	76	76	83
40	12	-	-	109
34	4	105	98	111
40	19	111	108	113
$\bar{x}$ = 35.27	= 17.11	= 106.7	107.5	104.7
Σx = 917	Σx= 445			
Σx^2= 37.004	Σx^2=11,751			

AGE OF ON SET OF EPILEPSY $\bar{x}$ = 18.15 (Σx = 472) (Σx^2 = 14,214)

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TEMPORAL LOBE EPILEPSY, PSYCHOTICS, (FEMALES: N:24)

AGE	DURATION EPILEPSY	I.Q.	VERBAL	PERF.	FREQ.OF PSYCHOTIC EPISODES	DURATION PSYCHOTIC EPISODES
46	6	99	97	100	1	12
20	12	96	103	89	1	1
14	13	82	76	92	1	1
32	9	90	91	89	1	15
23	16	115	117	110	4	20
40	24	92	-	-	1	72
60	12	121	116	123	1	24
42	31	110	105	113	1	8
52	23	93	99	89	1	4
30	7	90	88	94	1	6
35	3	98	87	105	1	1
27	12	-	-	-	1	6
19	10	85	88	85	3	4
54	40	78	77	83	9	444
22	1	-	-	-	1	12
38	20	97	87	108	1	3
36	31	-	—	-	1	1
42	27	81	81	85	1	4
14	1	-	-	126	3	18
34	28	73	74	69	1	84
46	36	75	82	74	1	204
19	15	89	89	89	4	5
25	7	101	101	101	3	7
46	38	-	-	-	1	6
$\bar{x}$ = 34	= 17.58	= 92.89	92.11	90.73	1.8	39.89
Σx = 816	= 422					
Σx^2= 31,622	Σx^2= 10,688					

AGE, t (PSYCHOTIC/ CONTROLS) = 1.81, d.f. = not sig.

DURATION EPILEPSY, (PSYCHOTIC/CONTROLS) t = 1.65. not sig.

AGE OF ON SET OF EPILEPSY, f = 16.42 (Σx = 394) (Σx^2=9544)

(PSYCHOTIC/CONTROLS) t = 1.33, not sig.

TEMPORAL LOBE EPILEPSY: CONTROLS, (FEMALES: 24)

AGE	DURATION EPILEPSY	I.Q.	VERBAL	PERF.
33	16	104	98	108
29	27	-	-	-
19	8	103	105	99
19	19	100	96	104
21	20	111	106	114
35	1	129	126	128
19	19	60	61	68
43	12	101	104	99
21	19	67	69	72
28	28	103	98	109
51	13	-	-	-
24	19	105	105	104
17	15	80	86	78
14	7	99	108	90
29	2	93	93	94
20	8	96	102	92
30	9	103	111	93
17	15	106	98	106
27	2	94	95	94
28	2	76	70	88
41	22	108	109	106
47	42	95	89	104
42	25	92	93	84
28	27	123	127	114
$\bar{x}$ = 28.4	= 15.7	97.7	97.9	97.6
Σx = 682	= 377			
Σx^2 = 21,796	Σx^2 = 8249			

AGE OF ON SET OF EPILEPSY

$\bar{x}$ = 12.71

Σx = 305)

Σx^2 = 7353)

PSYCHOTICS : PSYCHOMOTOR SEIZURES PRESENT (N:23)

AGE	DURATION EPILEPSY	I.Q.	VERBAL	PERF.
38	20	-	-	-
38	30	112	102	121
14	13	82	76	92
23	16	115	117	110
22	9	120	125	110
36	25	120	116	121
46	38	-	-	-
32	9	90	91	89
46	6	99	97	100
16	11	71	70	77
45	27	112	108	115
20	12	96	103	89
40	24	92	-	-
33	19	-	-	-
46	33	100	93	110
34	13	-	-	-
56	38	87	95	83
35	33	126	124	124
42	31	110	105	113
52	23	93	99	89
54	52	91	92	98
30	7	90	88	94
60	12	121	116	123
$\bar{x}$ = 37.30	= 21.78	= 101	100	102
Σx = 858	Σx^2 = 13.740			
Σx^2 = 34.447	Σz^2 = 901			

AGE t = 1.4, d.f. = 62 not sig.

DURATION OF EPILEPSY, t = 1.50, d.f. = 62 not sig.

PSYCHOMOTOR SEIZURES PRESENT: CONTROLS (N:40)

AGE	DURATION EP.	I.Q.	VERBAL	PERF.
33	31	72	85	61
19	4	109	108	106
34	5	126	126	122
34	14	111	116	104
35	20	103	134	121
52	51	101	102	99
51	5	127	130	117
29	15	112	107	114
53	29	97	88	110
48	48	90	86	97
28	16	111	124	94
16	10	-	-	-
40	12	-	-	109
40	29	103	96	111
83	15	109	122	95
24	23	95	105	89
24	1	-	105	89
46	16	109	103	115
23	12	99	96	102
27	24	118	115	117
40	19	111	108	112
28	27	123	127	114
33	16	104	98	108
30	9	103	111	93
21	19	67	69	72
20	8	96	102	92
41	22	108	109	106
19	8	103	105	99
21	20	111	106	114
29	27	-	-	-
51	13	-	-	-
24	19	105	105	104
28	28	105	98	109
43	12	101	104	99
35	1	129	126	128
17	15	80	86	78
19	19	60	61	68
29	2	93	93	94
27	2	94	95	94
19	19	100	96	104
$\bar{x}$ = 32.82	= 17.12	= 103	104	100.6
Σx = 1313	= 685			
Σx^2 = 49.614	Σx^2 = 16.609			

PSYCHOTICS : PSYCHOMOTOR SEIZURES ABSENT (N:27)

AGE	DURATION EPILEPSY	I.Q.	VERBAL	PERF.
40	26	93	88	99
27	4	76	89	64
19	10	85	88	85
36	30	70	74	70
34	28	73	74	69
41	30	115	111	116
31	28	69	73	69
41	31	87	91	83
45	9	108	103	113
27	10	61	61	66
33	21	119	121	119
14	1	-	-	126
46	36	75	82	74
35	33	125	122	124
25	7	101	101	101
27	12	-	-	-
49	39	100	85	116
16	8	-	-	-
36	31	97	87	108
22	1	-	-	-
49	16	127	130	118
51	30	115	98	122
35	3	98	87	105
42	27	81	81	85
54	40	87	77	83
19	15	89	89	89
24	12	117	121	110
$\bar{x}$ = 34	= 19.92	= 93	92	96
Σx = 918	= 538			
Σx^2 = 34.480	Σx^2 = 14.732			

PSYCHOMOTOR SEIZURES ABSENT : CONTROLS (N:10)

AGE	DURATION EPILEPSY	I.Q.	VERBAL	PERF.
-	-	-	-	8
42	25	92	93	84
47	42	95	89	104
28	2	76	70	88
35	24	125	124	120
34	4	105	98	111
14	7	99	108	90
17	15	102	98	106
21	4	87	95	80
31	10	131	130	124
17	4	77	76	83
$\bar{x}$= 28.6	$\bar{x}$ = 13.7	$\bar{x}$ = 98.9	98.1	99
Σx= 286	Σx= 137			
Σx^2= 9314	Σx^2= 3391			

AGE, t = 13, d.f. = 36. not sig.

DURATION EPILEPSY t = 1.30 d.f. = 36 not sig.

PSYCHOTICS WITH:

PSYCHOMOTOR FITS PRESENT		PSYCHOMOTOR FITS ABSENT	
Frequency of psychotic episodes	Duration of psychotic ep. (in months)	Frequency	Duration (months)
1	8	3	9
1	180	10	3
1	20	1	5
1	36	4	5
3	7	5	2
1	24	2	6
5	8	1	12
1	1	1	1
12	3	3	7
1	6	1	4
1	6	1	48
1	12	1	84
1	72	1	36
1	48	1	1
3	1	3	4
4	20	1	6
1	60	9	444
1	4	3	18
1	9	1	4
1	1	1	17
1	1	2	-
1	1	1	1
1	1	20	7
		1	9
		1	1
		11	1/8
= 45	: 529	: 79	: 732
$\bar{x}$: 1.9	$\bar{x}$ = 23	$\bar{x}$: 3.1	$\bar{x}$ = 29.2

= (529 - 120)
= 409

= 409/22
$\bar{x}$ = 20.4

= 732-444
= 288

= 288/24
$\bar{x}$ = 12

EPILEPTIC PSYCHOSES, ACCORDING TO TYPE OF PSYCHOSIS

	% MIXED (n:11)	SCHIZOPHER. (n:21)	M.D. (n:9)	CONFUS. (n:9)
married	36%	38%	66.6%	22.2%
single	63	47.6	33.3	77.8
divorced	-	4.7	-	-
separated	-	9.5	-	-
co-habittee	-	-	-	-
AURA, present	45	47.6	55.5	55.5
absent	54	33.3	22.2	33.3
disap.	-	14.3	11.1	
n.k.	-	4.8	11.1	11.1
SEIZURES:				
majors	-	19%	44.4	-
minors	9	23.8	22.2	22.2
both	90.9	57.1	33.3	77.8
PSYCHOM TOR SEIZ.				
present	73.0	38.1	33.3	44.4
absent	27.0	57.1	66.6	44.4
n.k.		4.7	-	11.1
DOMINANCE				
left	81.8	100	100	100
right	18.2	-	-	-
BRAIN-DAMAGE				
birth-injury	18.2	14.3	33.3	11.1
head-injury	-	14.3	11.1	33.3
mastoiditis	9.1	-	22.2	11.1
encephalitis	-	22.2	-	11.1
FAMILY HISTORY PSYCHOSIS		14.3	-	11.1
PREVIOUS MENTAL HEALTH				
in-patient	72.7	57.1	55.5	55.5
out-patient	9.1	4.7	-	11.1
none	18.2	38.1	44.4	33.3
PREVIOUS PERSONALITY				
schizoid	9.1	4.7	11.1	22.2
epileptic	-	14.3	-	11.1
normal	81.8	42.8	66.6	44.4
non-spec.abn.	9.1	38.1	22.2	22.2
PRECIPITATING STRESS				
emotional	18.2	14.3	22.2	22.2
physical	18.2	23.8	44.4	55.5
environmental	-	19	-	-

	MIXED		SHIZOPHR.		M.D.		CONFUS%	
DRUGS,								
mysoline	18.2		28.6		22.2		55.5	
others	36.3		22.2		-		33.3	
epanutin - 300mg.	27.3		23.8		44.4		II.I	
300mg.	63.6		61.9		33.3		55.5	
+ 300mg.	-		4.7		-		-	
phenobarb -100mg.	I8.2		22.2		44.4		22.2	
I00mg.	36.3		22.2		II.I		22.2	
+ I00mg.	45.4		57.I		33.3		II.I	
espolot	-		II.0		-		-	
CONTROLS OF EPILEPSY								
majors, less I/month	66%		38%		80%		43%	
I/month)	-		-		20%		57%	
+ more I/month)	33%		62%		-		-	
MINORS, less I/week	44%		50%		40%		50%	
I/week)								
more 1/week)	55%		50%		60%		50%	
PSYCHOMOTOR,								
less I/I2	30%		25%		I00%		50%	
I% I2)								
more 1/I2)	70%		75%		-		50%	
A.E.G.								
normal	27.3		28.6		33.3		II.I	
diffuse	36.3		28.6		22.2		22.2	
n.k.	18.2		19.0		22.2		33.3	
focal	I8.2		23.8		22.2		33.3	
OCCUPATIONAL								
stable	81.8		47.6		66.6		77.8	
unstable	I8.2		52.4		33.3		22.2	
CHILDHOOD								
normal	81.8		66.6		77.8		55.5	
abnormal	I8.2		33.3		22.2		44.4	
NEUROLOGICAL								
normal	90.9		71.4		77.8		77.8	
abnormal	9.1		28.6		22.2		22.2	
EPILEPTIC FOCI								
right	18.2		9.5		44.4		II.I	
left	36.3	81.3	42.8	90.4	22.2	55.5	44.4	88.8
bilateral	45		47.6		33.3		44.4	
TOTAL SEIZ. FREQUENCY,								
- I/I2	I.3		23.8		66.6		44.4	
I/I2	27.3		-		-		-	
+ I/I2	36.3							
	36.3	72.I	76.2		33.3		55.5	

	MIXED	SCHIZOPHR.	M.D.	CONTROLS %
E.E.G.				
background	27.3	28.6	33.3	11.1
normal	27.3	28.6	33.3	11.1
abnormal	72.7	71.4	66.6	88.9
specific	9.1	19.0	22.2	-
non-specific	90.9	80.9	77.8	100
focal temporal	90.9	85.7	66.6	55.5
others	9.1	23.8	33.3	44.4
unilateral	54	52.4	66.6	55.5
sec.bil. hypers.	9.1	9.5	22.2	11.1
AGE (mean: in years)	37	36.04	35.33	31.55
DURATION EP. (mean: in years)	20.72	21.90	19.77	19.2
P.S.I.Q.	105	91.88	105	92.42
V.S. "	402.3	92.05	103	91.57
F.S. "	107.4	94.66	104.4	93.42
FREQUENCY, (P) (No. of times)	2.54	1.85	3.3	3 (with correction, :0.87)
DURATION, (P): (mean in months)	26.72 (with correction, :11.4)	56.7	5.3	2.4 (with correction 0.87)

(P) = Psychotic Episodes.

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