

Organic Brain Disorders in the Aetiology of Schizophrenia

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Introduction

During the present century a considerable literature has grown up reporting the association of trauma or illness of the central nervous system with the appearance of an illness closely resembling schizophrenia. However, these reports have been scattered and the possibility that organic trauma of the brain could cause schizophrenia in the absence of a heredity or premorbid personality indicative of this illness has been ignored by most psychiatrists.

In 1963 Dr. Eliot Slater and his colleagues published an important paper on the schizophrenia-like psychoses of epilepsy.¹ They found that an illness indistinguishable from schizophrenia was found in epileptic patients and especially in those with temporal lobe epilepsy, with a frequency that was much greater than the expectation based on chance expectation alone Through the initiative of Dr. Slater, a major review of the literature on the association of schizophrenia-like conditions with all kinds of organic disorders of the central-nervous system, including epilepsy, was undertaken by Davison and Bagley.¹*

* The relationship between childhood epilepsy and childhood schizophrenia is also much greater than chance expectation.²

Some reprint copies of the review by Davison and Bagley³ are still available. Interested workers should contact the author of the present article.

This study undertook to translate, abstract and review as much as possible of the literature on the subject published in English, German, French and Russian during the present century. Over a thousand articles and monographs were studied in this way and some 780 of them were found to be relevant. The results of this review were published in 1969. The findings of the review seem as yet to be generally unknown amongst North American workers and in the present article we summarize the results of the major study. Full references are given in the original review.

Selection of Material

In order to delineate the material for review it was necessary to attempt the difficult task of defining schizophrenia. For our purpose phenomenological criteria are the most appropriate as this avoids pre-judging the question of aetiology. Such criteria have already been formulated by the 1957 World Health Organization (WHO) committee on schizophrenia as follows:

In the presence of clear consciousness;

- (1) Unmistakable change of personality or accentuation of schizoid traits.
- (2) Autism.
- (3) Thought disorder—bizarre statements, abnormal syntactical, grammatical and other linguistic usages;

incapacity to pursue a sustained train of thought; use of private symbols.

- (4) Shallow or incongruous affect.
- (5) Hallucinations and delusions.
- (6) Behaviour anomalies—peculiarities of posture, gesture and movement (catatonia).

In the presence of organic brain disorder items 1, 2 and 6 lose much of their diagnostic specificity. They have therefore not been used as *sole* criteria of selection. The WHO committee deliberately refrained from defining too strictly the type of hallucinations and delusions so quite a wide range of psychoses can be subsumed under the label "schizophrenia." Paranoid psychoses are included for whose retention in the schizophrenia category cogent arguments have been adduced.

The material to be reviewed has therefore been selected according to the following criteria:

- (1) The presence of an unequivocal organic disorder of the central nervous system (CNS).
- (2) The presence, at some stage, of at least one of features 3, 4 and 5 listed as characteristic of schizophrenia by the 1957 WHO committee.
- (3) The absence, at the stage when these psychotic features are displayed, of features which would reasonably lead to a diagnosis of affective psychosis, dysmnesic syndrome, delirium or significant dementia.

The bulk of the cases have some form of structural brain disease but also included are organic cerebral disorders which usually have no definite structural basis, e.g. narcolepsy.

Epilepsy

From the evidence examined (contained in 133 references) the following conclusions were drawn:

- (1) An inter-ictal psychosis resembling

schizophrenia occurs more often in epileptic patients than chance expectation.

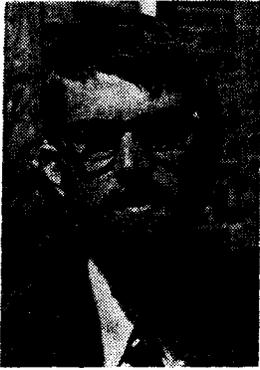
- (2) The epilepsy is usually secondary to a cerebral lesion, particularly in the temporal lobe, and the psychosis is aetiologically related to the lesion rather than the fits.
- (3) The psychosis is genetically distinct from "true" schizophrenia but claims that distinction can be made on personality, psychopathological or prognostic grounds are insecurely based.
- (4) There probably exists a separate group of episodic epileptic psychoses which are psychopathologically similar but related to changes in medication and/or the suppression of EEG epileptiform activity.

If, as has been argued above, the psychoses are aetiologically related to the cerebral lesion underlying the epilepsy, the occurrence of psychoses associated with epilepsy secondary to gross brain lesions is to be expected. In fact cases have occurred with hydrocephalus, myoclonic epilepsy, tuberous sclerosis, Sturge-Weber syndrome and other forms of vascular malformation, cerebral tumour and following cerebral trauma.

Cerebral Trauma

Our conclusions were (based on 52 references) that:

- (1) The incidence of schizophrenia-like psychoses in brain-injured populations significantly exceeds chance expectation.
- (2) There is no evidence for genetic-predisposition to schizophrenia in these cases.
- (3) There is a possible association with temporal lobe lesions and an early development of psychosis is related to severe closed head injury with diffuse cerebral damage.



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(4) Information about treatment and prognosis is sparse.

Cerebral Tumour

From the evidence studied (contained in 92 references) the following conclusions could be drawn:

- (1) The association of "schizophrenia" and cerebral tumour probably exceeds chance expectation.
- (2) There is insufficient evidence to indicate whether or not these patients are genetically predisposed to schizophrenia.
- (3) Little is known of the natural history of these psychoses.
- (4) Psychoses occur in all pathological types and cerebral localizations but there is a suggestion of particular association with pituitary and temporal lobe tumours.
- (5) Epilepsy is not a significant aetiological factor.

It should be noted that the apparent irrelevance of epilepsy in the aetiology of psychoses associated with cerebral trauma and tumour is further evidence in support of the thesis that epileptic psychoses are aetiologically related to the underlying cerebral lesion rather than the occurrence of fits. In the CNS disorders about to be considered epilepsy is either rare or nonexistent.

The Encephalitides

Conclusions (based on 77 references):

- (1) Schizophrenia-like psychoses have long been accepted as sequelae of encephalitis lethargica but no firm data on their actual incidence have been located.
- (2) Parkinsonism is commonly associated with the psychosis.
- (3) Opinion is divided on the degree of resemblance of the psychosis to schizophrenia.
- (4) There is no good evidence of personality or genetic predisposition to schizophrenia in patients with postencephalitic psychoses.

Rheumatic "Encephalitis" and Sydenham's Chorea

Conclusions (based on 43 references):

- (1) There is considerable evidence that the expectation of developing schizophrenia (or a schizophrenia-like psychosis) is increased after Sydenham's chorea and acute rheumatism but probably not to the extent claimed by Bruetsch.
- (2) The alleged response of such psychoses to penicillin and steroid therapy requires confirmation.
- (2) The possible genetic association of chorea and schizophrenia is of considerable theoretical interest but also requires confirmation.

Cerebral Syphilis

Conclusions (based on 28 references):

- (1) A schizophrenic form of general paresis seems to occur more frequently than chance expectation.
- (2) The psychosis is often psychopathologically indistinguishable from "true" schizophrenia but only a minority of affected patients appear to be genetically predisposed to schizophrenia.

- (3) The psychosis may pursue a course independent of the physical disorder but no consistent prognosis has yet been determined.

Basal Ganglia Disorders

Conclusions (based on 68 references):

- (1) There is evidence to suggest that schizophrenia-like psychoses occur in association with Wilson's disease more frequently than chance expectation.
- (2) Absence of genetic predisposition and progression to dementia confirm their organic basis.

Huntington's Chorea and other Pre-Senile Degenerations

Conclusions (based on 40 references): A wide variety of psychiatric disorders is described in patients with Huntington's Chorea and their families, often before the onset of neurological abnormalities and it is generally accepted that these are all manifestations of the cerebral disorder. From the evidence presented here, particularly the lack of genetic predisposition, it seems reasonable to include the schizophrenia-like psychoses among these manifestations.

Schizophrenia-like psychoses are reported in the early stages of a wide variety of pre-senile cerebral degenerations more usually associated with dementia. The absence of a family history of schizophrenia suggests that the psychosis is a direct manifestation of the cerebral disorder.

There are contradictory reports on the occurrence of cerebral atrophy in chronic "true" schizophrenic patients. Pneumoencephalographic observations are not always adequately controlled and there are conflicting reports of the presence of macro-

scopic cerebral atrophy at post-mortem.

Friedreich's Ataxia

Conclusions (based on 12 references):

Although schizophrenia-like psychoses are reported in association with Friedreich's ataxia and in neurologically unaffected relatives the small number of reports does not permit any firm conclusion.

Motor Neurone, Muscular Dystrophy and other Spinal Cord Diseases

Conclusions (based on 18 references):

There are several reports of schizophrenia-like psychoses occurring in association with motor neurone disease, muscular dystrophy and other neuromuscular disorders but it is not possible to draw any specific conclusion.

Demyelinating Diseases (Multiple Sclerosis, Schilder's Disease and Diffuse Encephalomyelitis)

Conclusions (based on 51 references):

Schizophrenia-like psychoses are reported in association with CNS de-myelination. In the cases of multiple sclerosis the statistical evidence suggests that their frequency is not greater than chance expectation, whereas the clustering of psychosis onsets around the time of first appearance of neurological abnormalities and the comparative rarity of a schizophrenic family history suggests that the CNS disease and the psychosis are not independent.

Narcolepsy

Conclusions (based on 27 references): (1) Schizophrenia-like psychoses occur in narcoleptic patients more frequently than chance expectation and

in the absence of genetic predisposition.

- (2) Amphetamine intoxication is unlikely to be responsible for more than a small minority of reported cases.
- (3) Sleep hallucinosis is by no means an invariable precursor.
- (4) The hypothesis that the narcoleptic syndrome and the psychosis are both manifestations of diencephalic dysfunction is preferred.

Sleep, Dreaming and Schizophrenia

Conclusions (based on 37 references):

- (1) The long recognized similarity between dreams and psychotic experience now has a physiological analogy-
- (2) The relationship between psychosis and sleep-deprivation and REM-de-privation is examined with interest, since this appears to be an important field of schizophrenia research.

Cerebro-Vascular Disease

Conclusions (based on 16 references):

- (1) Paranoid-hallucinatory psychoses are reported in association with subarachnoid haemorrhage, fat embolism, bilateral carotid artery occlusion and pseudo-calcification of small cerebral vessels.
- (2) The association of psychosis with cerebral atheroma and its complications is difficult to assess. Longstanding schizophrenics do not appear to develop cerebrovascular disease in later life more frequently than expected but there is a suggestion that late-onset schizophrenia may be significantly associated with cerebro-vascular disease.

Vitamin B₁₂ and Folic Acid Deficiency

Conclusions (based on 17 references): (1) Paranoid-hallucinatory psychoses resembling schizophrenia occur in association with pernicious anaemia and with occult B₁₂ deficiency but they are less frequent than delirium or dementia and correction of the B₁₂ deficiency does not always induce remission of the psychosis. (2) The significance of folic acid deficiency in psychiatric patients remains unclear. It may be a contributory factor in the aetiology of epileptic psychoses.

Cerebral Location and Symptoms

A review of literature (130 references) and a correlation analysis of data from 150 cases led to the following conclusions:

The main features are the association of left cerebral hemisphere and particularly temporal lobe lesions with primary delusions and catatonic symptoms; basal ganglia lesions with catatonic symptoms; diencephalic lesions (including basal ganglia) with auditory hallucinations; and brain stem lesions with thought disorder and Schneider's symptoms of the first rank.

In the light of the previous discussion on epileptic psychosis the significant correlation of affective flattening or incongruity with an early age of onset of both psychosis and CNS disorder is of particular interest. Thought disorder and catatonic-symptoms are similarly correlated but paranoid delusions are associated with later age of onset.

The high correlation of epilepsy with a long interval between onset of CNS disorder and psychosis is more likely to be related to an early age of onset of epilepsy and the selection of adult case reports than to a biological antagonism of epilepsy and schizophrenia. The association of diencephalic lesions with a short latent interval agrees with the findings

in post-traumatic psychoses.

Correlation does not, of course, necessarily imply causation and some of the associations may have occurred by chance in the large number of intercorrelations calculated. However taken at face value this material does provide some support for the general approach of Kleist.

A Conceptual Model for Schizophrenia

Our conclusion about the place of organic schizophrenia-like psychoses in relation to "true" schizophrenia is summarized in Fig. 1 which illustrates diagrammatically a somewhat over-simplified conceptual model. It seems probable that the final common path in the production of the schizophrenic syndrome is a disturbance of cerebral function but aetiological factors may be contributed by any of the facets of human experience, physical, psychological or social.

The model fits the genetic findings but it

could be further validated by a comparison of social and psychological variables in organic and non-organic psychotic cases. A corollary is that organic cerebral cases should be rigorously excluded from any series of patients with "schizophrenia" being investigated for physical (extra-cerebral), social, psychological, genetic or biochemical factors.

General Summary

The following general conclusions are drawn:

- (1) In many organic CNS disorders the association of "schizophrenia" exceeds chance expectation.
- (2) Lesions in the temporal lobe and diencephalon are particularly significant in the genesis of these psychoses.
- (3) Small but significant correlations between individual psychotic symptoms and specific sites of brain lesion are noted.
- (4) These psychoses have a range of symptoms similar to the general run

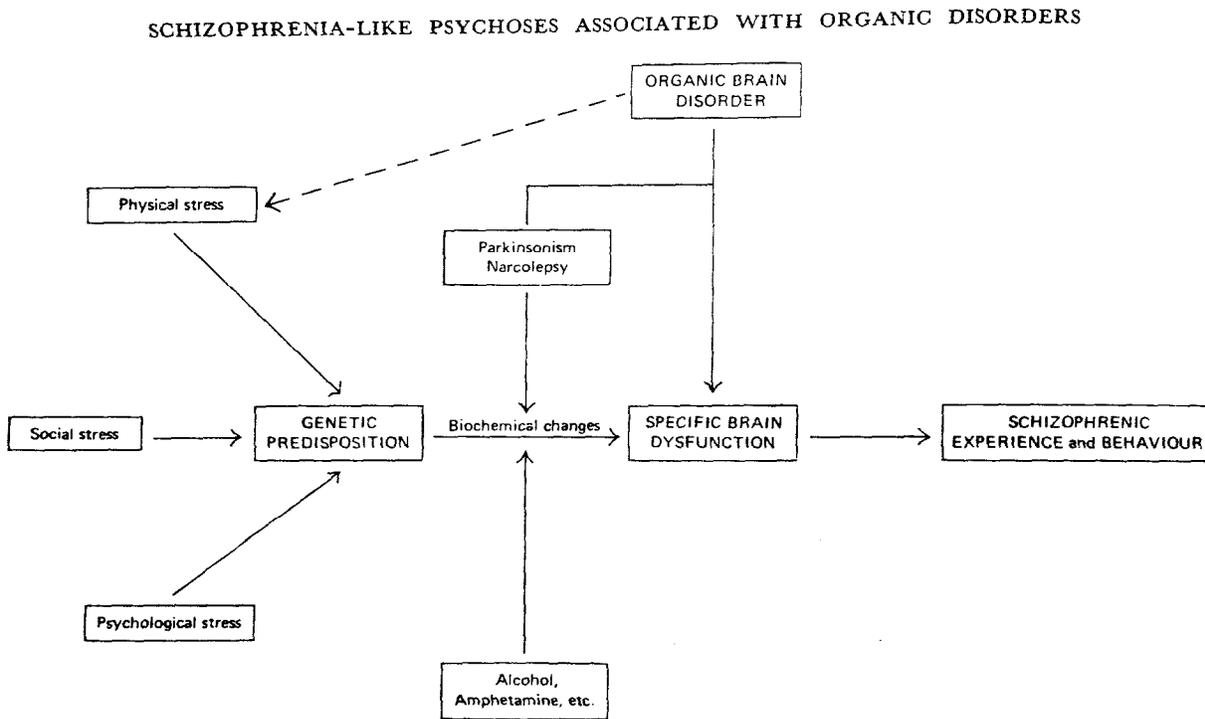


FIG. 1.—The place of organic brain disorder in the aetiology of schizophrenia.

of psychoses diagnosed as schizophrenia.

- (5) Alleged distinguishing clinical features between these psychoses and "true" schizophrenia are largely illusory.
- (6) There are insufficient data to reach any conclusion on the response to treatment and ultimate outcome in these psychoses.
- (7) The psychoses usually occur in patients without genetic loading for schizophrenia.
- (8) The site of the brain lesion appears to be more important than the predisposition of the patient in the genesis of the psychosis.
- (9) In most cases the organic CNS disorder appears to be both a necessary and a sufficient cause of the psychosis. (10)

Organic disorder of the CNS occurs in a substantial minority of patients with a diagnosis of schizophrenia, and is of particular importance in the psychoses of childhood and possibly old age.

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