

Primary Versus Secondary Schizophrenia: A Theoretical Review

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Abstract

The present review presents a conceptualization of dividing schizophrenia into a primary versus a secondary type. Primary schizophrenia is that which is caused by primarily genetic factors, while secondary schizophrenia has an environmental etiology such as occurs in brain injury. The research dealing with schizophrenia is reviewed, and suggests that this formulation can be helpful in dealing with the etiology of schizophrenia.

Introduction

The presently proposed conceptualization is that of dividing schizophrenia into primary versus secondary such as epilepsy is sometimes divided. In secondary epilepsy there is some sort of brain injury or medical condition that produces the epilepsy. In primary epilepsy no such specific cause can be identified, and it is assumed that the patient is more constitutionally, perhaps genetically, predisposed to epilepsy.

It is here proposed that secondary schizophrenia is a function of an injury or acquired disorder of the brain. Primary schizophrenia has more of a constitutional, probably genetic, basis. In primary process schizophrenia, brain anomaly appears at an earlier age and with more of an intrinsic as opposed to extrinsic origin. Although this conceptualization is being presented as a dichotomy, it is recognized that a continuum may better characterize schizophrenic Psychopathology.

It is not here claimed that this conceptualization is radically innovative. Other similar conceptualizations have been developed. In fact, a major purpose in this present paper is to tie the present formulation to other proposed dichotomies and continua,

as well as to tie the formulation to possible etiological factors.

Process versus reactive schizophrenia

The process versus reactive distinction, which moved more toward a continuum conceptualization during the massive amount of research on the topic of schizophrenia in the 1950's and 60s, has a resemblance to the primary versus secondary formulation here proposed. In process schizophrenia, the disorder has an earlier age of onset, is more insidious in its onset, and shows less adequate premorbid psychosexual and psychosocial functioning. This type of schizophrenia shows evidence of fewer environmental precipitators, and produces a less favorable prognosis (Phillips, 1953).

The main difference between the reactive-process formulation of schizophrenia and the current primary-secondary formulation is that in the era of process-reactive research, environmental assaults were viewed to be in the psychosocial realm. Buttressed by the impressive evidence in the last two decades on the biological nature of schizophrenia etiology, the assault in secondary schizophrenia would appear to be on the brain. The primary-secondary formulation here presented suggests that psychosocial factors play a very minor role.

Brain atrophy

A disproportionate number of schizophrenics have been found to have enlarged ventricles (Johnstone, Crowe, Frith, 1976; Weinberger, Bigelow, Kleinman, Klein, Rosenblatt and Wyatt, 1980; Rieder, Donnelly, Herdt, 1979; Golden, Moses & Zelazowski, 1980; Famuyiwa, Eccleston, Donaldson, 1979; Huag, 1962; Huber, 1957; Nagy, 1963). It has been found that

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schizophrenics with brain atrophy have had less favourable premorbid adjustment, especially in childhood (Weinberger, Cannon-Spoor, Potkin & Wyatt, 1980.) Schizophrenics with larger ventricles have more negative symptoms of schizophrenia, e.g. affective flattening, avolition, and anhedonia. In contrast, schizophrenics with the smaller ventricles show; more "positive" symptoms of schizophrenia such as delusions, hallucinations, and bizarre behavior. Thus the schizophrenic with larger ventricles has symptoms placing him in the process or primary category. Those with smaller ventricles appear to be more like the secondary schizophrenic.

Also consistent with the formulation is the significant negative correlation found between drug abuse and ventricular size in one sample of schizophrenics (Andreasen, Olsen, Dennert & Smith, 1982). Andreasen et al. expressed some surprise at this negative correlation since the correlation was calculated to rule out the possibility that the brain atrophy was caused by the drug abuse. However, it could be argued that the drug abuse contributed to the etiology of the secondary schizophrenic with the smaller ventricles. Such a person could have developed schizophrenia in part because of the effects of drugs on the brain.

Thickened corpus callosum

A disproportionate percentage (20%) of schizophrenics have thickened corpus callosi (Rosenthal & Bigelow, 1972). Hare (1980) has suggested that this thickening results from prenatal damage, possibly from a virus. There is an inverse relationship between corpus callosum thickening and brain atrophy in schizophrenics (Bigelow, Nasrallah & Rauscher, 1983).

Since brain atrophy is consistently associated with the sort of Psychopathology manifested in primary schizophrenia, it is proposed that a thickened corpus callosum is associated with secondary schizophrenia. Consistent with such a contention is the finding in one study of a negative relationship between the width of the corpus callosum and age (Bigelow, Nasrallah & Rauscher, 1983). In other words, the older schizophrenics had a corpus callosum less thickened than the younger schizophrenics. The authors conjecture regarding this negative correlation:

This finding could be consistent with a pathological process such as a sub-clinical viral

infection leading initially to a slightly increased tissue volume and later resolving after cell loss, thereby leading to a relatively normal dimension. ..It is tempting to speculate that increased thickness of the corpus callosum would be found in schizophrenics having active thought disturbance and be a reflection of disordered neural communication. The later course of chronic schizophrenia, as the individual becomes 'burned out', might coincide with a resolution of that process leaving some disruption in communication between the hemispheres.

It is interesting to note that they speculate that the schizophrenics with a thickened corpus callosum have more "active thought disturbance", a conceptualization clearly agreeing with the present formulation of secondary schizophrenia.

Cerebral asymmetry

A disproportionate number of schizophrenics have a reversal of the normal cerebral asymmetry. That is, they have greater right sided than left sided cerebral mass. This is in contrast to the asymmetry of the normal person who typically has greater left sided mass (Luchins, Weinberger, & Wyatt, 1979; Nasser, Levine & Benson, 1981; Luchins, Weinberger, & Wyatt, 1982). In view of the fact that reversal of the typical asymmetry is also associated with language, development, and learning disorders (Hier, Lemay, & Rosenberger, 1978; Rosenberger & Hier, 1980), it is here suggested that reversal of normal cerebral asymmetry in schizophrenia is associated with secondary schizophrenia. Consistent with this position is the finding that it is the schizophrenics with the normal asymmetry that tend to have cortical atrophy, which has already been associated in this formulation with primary schizophrenia.

Deficit sensory gating

Research indicates that schizophrenics have a deficit in sensory gating, that is, the ability to filter and disregard extraneous stimuli. The schizophrenic's excessive responding to a bombardment of various stimuli is said to account for his or her poor performance on tasks that require concentration or attention. In one experiment using auditory evoked responses it was not only

found that schizophrenics responded excessively to the less relevant of a pair of auditory stimuli but that 50% of their first degree relatives had this same gating deficit. The relatives who had the more pathological scores on the MMPI were more likely to have this filtering difficulty (Siegel, Waldo, Mizner, Adler & Freedman, 1984). Thus it appears that deficient sensory gating is associated with primary schizophrenia to the degree that this type of schizophrenia is genetically based.

Atypical schizophrenia

Atypical schizophrenics obviously have less incapacitation and better prognosis than typical schizophrenia. In one study in which schizophrenics had larger ventricles than the control subjects, the "borderline (i.e., atypical) schizophrenics actually had smaller ventricles than the control subjects" (Schulsinger, Parnas, Peterson, Schulsinger, Teasdale, Mednick, Moller & Silverton, 1984). The fact that it has long been recognized that schizophrenics with an affective component have a better prognosis also supports the contention that atypical cases of schizophrenia also have a better prognosis.

In another study, schizophrenic patients who were non-suppressors on the dex-amethasone suppression test, thus exhibiting the response ordinarily observed in endogenously depressed individuals, displayed more favorable outcomes than those who were suppressors (Targum, 1983). It would appear that atypical cases of schizophrenia would tend to be in the general domain of secondary schizophrenia. Both the symptoms and the prognosis of these schizophrenics more closely match that of the secondary schizophrenic than the primary schizophrenic.

Seasonality of schizophrenic birth

It has been well established that schizophrenics tend to be born in the colder months of the year (Torrey, 1980). The bulk of the evidence seems to support the "harmful effects" hypothesis, that is some sort of harmful influence, e.g. infection, associated with cold weather is responsible for the development of schizophrenia (McNeil, Raff, & Cromwell, 1971). Such evidence includes the greater seasonality of schizophrenia in Europe than in the United States where technology has provided more protection from the elements in the 20th

century (Templer, Halcomb, Bartlow, & Ayers, 1978). It also includes the decrease in seasonality from 1900 to 1960 in Missouri (Templer & Austin, 1980).

More immediately relevant to the present model is the finding of greater seasonality in paranoid schizophrenics than in either catatonic or hebephrenic schizophrenics. Catatonic and hebephrenic schizophrenics collectively have been referred to as "kernal" or "nuclear" schizophrenics and have more of a genetic predisposition. In addition, these two groups have greater personality and cognitive deterioration and less adequate psychosexual and psychosocial premorbid functioning than the paranoid type schizophrenics. Also relevant is the research showing greater seasonality of births to be associated with later age of onset, a variable long recognized as often indicating a reactive as opposed to process schizophrenia (Corgiat, Regier & Templer, 1983). It is therefore suggested that the sort of schizophrenia caused by the harmful effects associated with seasonality of birth tend to have a greater secondary schizophrenic element.

Brain syndromes producing schizophreniform psychosis

Davison and Bagley (1969) provided an excellent and most comprehensive review of schizophrenic-like psychoses produced by brain conditions. These brain conditions include a myriad of disorders within the more general categories of degenerative disorders, narcolepsy, cerebrovascular disease, metabolic and toxic brain disorders, nutritional deficiencies, trauma, encephalitis, basal ganglia disorders, and epilepsy. Genetic predisposition does not generally seem to be associated with the schizophreniform disorders in association with these brain conditions. Davison and Bagley presented a table of Astrup, Fossum, and Holmboe (1962) which provided symptom comparisons of schizophrenic patients and brain disorder patients with psychosis.

Differences included the schizophrenics having significantly greater flatness of affect, pre-morbid schizoid personality, and family histories of schizophrenia. Perhaps "true schizophrenia" corresponds to our primary schizophrenia, and that psychosis in persons with organic brain disorder diagnoses cor-

responds to secondary schizophrenia.

Response to treatment

Research indicates that schizophrenic patients with enlarged ventricles and process symptom characteristics respond less well to antipsychotic medications (Weinberger, Bigelow, Kleinman, Klein, Rosenblatt & Wyatt, 1980). Also, it has been reported that the process schizophrenics are less likely to exhibit improvement after megavitamin treatment. Pfeiffer (1976) differentiated between schizophrenics with an abnormally high histamine level and those with an abnormally low level and that appear to require different megavitamin therapy regimens. The former, who sit for hours and stare, would appear to be primary schizophrenics, in contrast to the latter who appear to be secondary schizophrenics and feel tormented by evil spirits and have other positive symptoms of schizophrenia such as "...thoughts hurdling and somersaulting so rapidly through their distraught minds that ideation and speech processes become distorted and bizarre" (p. 398). It would therefore appear that primary schizophrenics respond less well to treatment than do secondary schizophrenics. It is of interest to note that persons found diagnosed as schizophrenic, but later found to have brain tumors responsible for their conditions, responded favorably to antipsychotic drugs (Binder, 1983).

Limitations of the model

All factors do not seem to mesh perfectly with the proposed conceptualization. For example, in the study of Schulsinger et al. (1984) with offspring of schizophrenics, ventricular size correlated with birth complications. Thus we have a positive correlation between a measure presumably associated with our postulated primary schizophrenia and conditions presumably producing secondary schizophrenia. However, few authorities on schizophrenia would doubt that some sort of interaction between inherited (genetic) predisposition and harmful effects increase the probability of schizophrenia. In regard to the Schulsinger et al. findings, the authors reported that "these results are interpreted as being consistent with the hypothesis that neurological insult may decompensate schizotypal individuals toward florid schizophrenia."

It is to be borne in mind that we have

acknowledged the distinct possibility that primary versus secondary schizophrenia is a continuum. However, we do not wish to suggest that it is a continuum in which predisposition and primary schizophrenia imply less (in an absolute sense) of harmful effects and secondary schizophrenia. This conceptualization is not an either/or unipolar dimension. Rather it is a two-dimensional concept which implicates the relative contributions of both primary and secondary elements in combination. Whether or not a person becomes schizophrenic is positively associated with **both** primary and secondary elements.

Summary

Table 1 presents the features associated with primary and with secondary schizophrenia. It is not here maintained that the evidence or the logic for all of these features being found in the predicted direction is overwhelming. The determination of the fit of facts and conceptualization awaits research on this model. Nevertheless, the increasing evidence that schizophrenia is a disorder associated with an array of brain structural and functional abnormalities found at various points of the lifespan lends evidence to our postulation.

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Table 1
Features associated with
primary and secondary schizophrenia

Primary schizophrenia

Process
 Brain atrophy
 Normal brain asymmetry
 Corpus callosum not thickened
 Sensory gating deficit
 "Typical" schizophrenia
 - symptoms
 Affective flatness
 Lower IQ
 Less seasonality of birth
 No head trauma
 No epilepsy
 More genetic involvement
 Insidious onset
 Poor premorbid functioning

Secondary schizophrenia

Reactive
 No brain atrophy
 Abnormal brain asymmetry
 Corpus callosum thickened
 More normal sensory gating
 "Atypical" schizophrenia
 + symptoms
 Affective component to illness
 Higher IQ
 More seasonality of birth
 Head trauma
 Epilepsy
 Less genetic involvement
 Rapid onset
 Good premorbid functioning

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