NEGATIVE SYMPTOMATOLOGY AND SCHIZOPHRENIA: A CONCEPTUAL AND EMPIRICAL REVIEW

MICHAEL F. POGUE-GEILE AND JOSEPH ZUBIN

The negative symptom syndrome has become an increasingly important organizing construct for research on schizophrenia in recent years. The present issue of the International Journal of Mental Health, along with a recent special issue of the Schizophrenia Bulletin [1] devoted to the topic, attest to this growing impact. In addition, two major conferences and their published proceedings have had negative symptomatology as their focus [2,3]. A number of reviews have also recently discussed various aspects of negative symptoms [e.g., 4–11]. These integrative efforts reflect a growing empirical literature. A computer search of titles in which the key terms negative symptoms and schizophrenia both appeared found no such titles published between the years 1966 to 1974; however, from 1975 to 1981, an average of four articles a year bore such titles. The rate of increase has been even greater in the past several years, with 13 such titles in 1982 and steady increases each year to a total of 39 such titles appearing in 1986.

We seek here to critically review the English-language literature in order to understand what all this excitement is about, what we have learned from it thus far, and what may be promising directions for future study. Although much of the recent work on negative symptoms has been from the perspective of a positive/negative symptom duality, for reasons of space and clarity we shall discuss only negative symptoms.

Dr. Pogue-Geile is Assistant Professor in the Department of Psychology and the Department of Psychiatry, University of Pittsburgh. Dr. Zubin is Research Career Scientist at the Veterans Administration Medical Center and Distinguished Research Professor in the Department of Psychiatry, University of Pittsburgh. Reprint requests may be addressed to: Dr. M. F. Pogue-Geile, Clinical Psychology Center, Department of Psychology, University of Pittsburgh, 4015 O'Hara St., Pittsburgh, PA 15260.
further integrate assessment of negative symptoms with the general systematic measurement of behavior.

The current empirical status of the primary questions regarding negative symptoms will be systematically reviewed below.

Association of negative symptoms with schizophrenia

Prevalence of negative symptoms in schizophrenia

Whether negative symptoms characterize all currently diagnosed schizophrenic patients or only some subset has important theoretical implications. Crow's 1980 model predicts that only a portion of patients diagnosed as schizophrenic according to current diagnostic criteria, which emphasize positive psychotic symptoms, would present with his Type II syndrome. The results of all studies to date suggest that negative symptoms do occur in only a subsample of schizophrenic patients at any particular point in time. It is nonetheless possible, albeit perhaps unlikely, that all schizophrenic patients experience negative symptoms briefly at some time in their lives—though there are as yet no suitable longitudinal studies to confirm or refute this notion.

Because of the different rating scales and samples employed, it is not useful to try to derive some overall average prevalence of negative symptoms. It is generally reported, however, that fewer than half of schizophrenic patients show prominent negative symptoms at any one time. These findings suggest, then, that schizophrenic patients differ markedly from each other in the extent to which they display negative symptoms.

Specificity of negative symptoms to schizophrenia

Although it is a basic question, few studies to date have investigated the relative frequency of negative symptoms in schizophrenia and other disorders. Five studies have compared schizophrenic and depressed hospitalized patients [43, 51, 65–67] and have generally reported overall negative symptom ratings in depressed patients that were at least as high as, or higher than, those shown by schizophrenic patients. Although item- and factor-level analyses have found a few individual items that discriminate between schizophrenic and depressed inpatients, they have not been generally consistent across studies [e.g., 51, 66]. Two exceptions to these findings in patients in treatment have been reported by Boeringa & Castellani [65] and Chaturvedi and associates [66], who found significantly higher levels of flat affect among schizophrenic compared with depressed patients. Pogue-Geile & Harrow [46], in the only comparative study of subjects not currently in treatment, reported that schizophrenic subjects had significantly higher levels of negative symptoms one year after hospital discharge than did depressed subjects.

As might be expected, researchers have consistently observed that negative symptoms are significantly less common among manic inpatients than among schizophrenic inpatients [28, 42, 51, 65, 68, 69]. In addition, Alpert & Rush [70] have demonstrated that flat affect is more common among patients with schizophrenia than in those with Parkinson's disease. More such studies of negative symptoms in defined neurological samples are needed.

Clearly, ratings of negative symptoms are not specific to schizophrenia. The results of these studies suggest that negative symptom rating scales distinguish poorly between depressed and schizophrenic patients during episodes that require hospitalization. The discrimination appears to be much easier to make in depressed patients who are not currently in an episode requiring inpatient treatment [i.e., 46]. It is not clear whether this lack of discrimination between depressed and schizophrenic patients during episodes is due to: (1) inability of current rating scales to distinguish between two truly different phenomena (i.e., depression and negative symptoms), (2) the presence of depression among schizophrenic inpatients, or (3) the presence of negative symptoms among depressed patients. Much more work is required to clarify the complex relationship between negative and depressive symptoms.
Conceptual background

In trying to understand the recent rise in its importance, one must ask, What is new about the negative symptom construct? The term itself is certainly not a new one. It played an important part in the hierarchical theory of the nervous system proposed in the 19th century by the British neurologist Hughlings Jackson, who conceived of negative symptoms as directly reflecting basic brain lesions [12] and hypothesized that positive symptoms were secondary release phenomena resulting from the disinhibition of other cortical centers by the basic lesion. As Berrios [13] has pointed out, Reynolds, in 1857, employed the terms even before Jackson; in fact, current usage is related less to that of Jackson than to that of Reynolds, who hypothesized no functional relationship between negative and positive symptoms. Thus, the term negative symptom is not a new one, and its current meaning is largely unrelated to that given it by its most influential early theorist.

The phenomena that are generally classified as negative symptoms also have a long history. All current definitions and rating scales of negative symptoms include as constituent items only signs and symptoms that have long been a part of descriptive psychopathology. No new signs or symptoms have been described in the recent work on negative symptomatology. Blunted affect, amotivation, and psychomotor retardation were considered crucial aspects of schizophrenia by Kraepelin [14] and Bleuler [15]. Similarly, grouping these individual signs together under a higher-order concept was not novel. These signs, such as flat affect and emotional withdrawal, had been repeatedly found to load together on the same or similar higher-order factors in an impressive series of factor analytic studies of psychotic patients undertaken in the 1960s [e.g., 16–18].

What does seem to be new in the negative symptom concept is not only an emphasis on the existence of different symptom syndromes in schizophrenia but the possibility that these syndromes might reflect different pathophysiological processes. Venables’s work with the psychopathological correlates of social withdrawal can be viewed as an early conceptual forerunner of later developments in this area [19,20]. Depue and colleagues’ extension of this research and their hypotheses concerning the presence of brain damage among withdrawn schizo-
abnormality also produces other behavioral manifestations, such as various cognitive deficits, but that it does not directly produce positive psychotic symptoms. Crow [5] has recently extended this notion to include abnormal involuntary movements as an additional hypothesized manifestation of the putative structural brain abnormality.

These basic ideas lead to a number of derivative hypotheses, outlined below, many of which have been examined empirically.

1. To the extent that the hypothesized structural abnormality is more common in schizophrenia than in other conditions, negative symptoms should be more common among schizophrenic patients.
2. Negative symptoms should be present in other disorders in which similar structural abnormalities are present.
3. To the extent that the hypothesized structural abnormality can be detected with the different imaging technologies, negative symptoms should correlate with imaging abnormalities within a group of schizophrenic patients.
4. To the extent that the hypothesized structural abnormality is stable over time, negative symptoms should be stable over time.
5. To the extent that medications cannot compensate for the hypothesized structural abnormality, negative symptoms should be resistant to currently used neuroleptic medications.
6. Negative symptoms should be correlated with cognitive deficits that are also manifestations of the hypothesized structural abnormality.
7. Negative symptoms should be correlated with abnormal involuntary movements, which are also hypothesized to be manifestations of a structural brain abnormality.
8. To the extent that persisting negative symptoms and associated cognitive deficits interfere with social and occupational functioning, negative symptoms should predict later, poor long-term functioning among schizophrenic patients.
9. Since the putative structural abnormality is hypothesized not to produce positive symptoms directly, negative and positive symptoms should be statistically independent when assessed concurrently within schizophrenia.

Definition and measurement

Before reviewing the research findings and their bearing on these hypotheses, we must comment on the conceptual and operational definitions of negative symptomatology. Most researchers in the area employ a very general conceptual definition of negative symptomatology that emphasizes observed deficits in behavior. Most would subscribe to some variant of the definition proposed by Strauss, Carpenter, & Bartko [27], in which negative symptoms “involve primarily the absence of normal functions.” Although heuristic, this presents difficulties as a formal definition in that it provides little help in deciding a priori which deficits in behavior should be considered negative symptoms. However, despite the inclusiveness of this conceptual definition, research has not focused on any and all deficits in behavior. Rather, a core group of signs, composed primarily of flat affect and poverty of speech, appears in most operational definitions, such as those proposed by Wing & Brown [24], Strauss and associates [27], and Crow [31]. This informal consensus appears to be based mainly on convention and tradition rather than on any explicit theoretical rationale.

Negative symptoms are usually contrasted with positive symptoms, which are defined as behavioral excesses, and include the core psychotic phenomena of delusions and hallucinations. It has been said that negative symptoms may be thought of as behaviors that patients do not engage in, but that normal persons do, whereas positive symptoms are behaviors that patients do engage in, but normal persons do not.

Despite this consensus on some of the core symptoms, the ambiguity of the conceptual definition has allowed a wide variety of operational definitions to flourish. The accompanying table lists the different symptoms and signs included in the major rating scales of negative symptoms. As the table illustrates, current operational definitions of negative symptoms differ markedly from each other in the symptoms that are included in each scale, some scales including such varied items as loose associations [36], inappropriate affect, distractibility [37], and memory deficits [38]. In general, the earlier definitions tended to emphasize ratings of the core symptoms flat affect and poverty of speech, based on behavior observed during an interview, whereas some
of the more recent definitions have tended to broaden the construct considerably. Although the eventual choice among such definitions is an empirical matter, it should be obvious that such variation in operational definitions makes replication of research results difficult.

Contrary to some earlier concerns [e.g., 50], all of the scales in the table have been able to demonstrate adequate interrater reliability. In addition, they generally have been shown to be internally consistent, although the method variance shared among items (i.e., all are ratings of behavior) and lack of blindness among ratings of the different items (i.e., the same person rates all items) make such results somewhat suspect. In contrast to these findings, several recent studies that have investigated the factor structure of some of the negative symptoms scales have identified multiple factors [51–53; cf. 54]. A few studies have also investigated the correlations among some of these scales. Lager and colleagues [38] found that despite different item contents, their Negative Symptom Rating Scale (NSRS) correlated reasonably well in a small heterogeneous sample with Andreasen’s Scale for the Assessment of Negative Symptoms (SANS), Abrams & Taylor’s Emotional Blunting Scale, the Brief Psychiatric Rating Scales (BPRS), and the Manchester Scale. The SANS has also been found to correlate well with the BPRS [54,55] and with the Positive and Negative Syndrome Scale (PANSS) [56]. However, to date there have been no studies of the relative construct validities of these different scales; and until such data are available, there is little empirical basis for preferring one scale over another. Until that time it may be that a strategy emphasizing conservative measures of the core symptoms of flat affect and poverty of speech rather than a proliferation of broader measures may better ensure communication among researchers and facilitate cumulative findings.

Although there has been a recent growth in the number of rating scales for negative symptoms, they have all employed the traditional rating-scale methodology and have not represented innovations in the basic measurement of negative symptoms. Promising approaches in this area seem to lie instead in other techniques that actually quantify behavior [6], such as vocal acoustic analysis [57–61], ratings of facial movements [62,63], and measures of speech quantity and rate [64]. These construct validation approaches may increase reliability and
Association of negative symptoms with background and historical characteristics

Sex differences in negative symptoms

Many of the hypotheses that have been proposed to explain the consistent sex differences in the clinical manifestations of schizophrenia have postulated an increased rate of neurological impairment among male compared with female schizophrenic patients [71]. These hypotheses parallel those concerning the role of structural brain abnormalities in negative symptoms. However, despite this theoretical convergence, relatively few studies of negative symptoms have reported sex differences; and in contrast to expectation, no study published to date has reported a significant excess of negative symptoms in male compared with female schizophrenic patients [46, 59, 67, 72–76]; in fact, Lewine & Meltzer [77] have reported that females showed significantly more negative symptoms than males. These studies employed a variety of measures of negative symptoms and patient samples ranging from acutely ill and long-stay inpatients to patients followed up in the community.

The only exception to this unanimity is a report by Kay, Opler, & Fiszbein [74], who found a significant male excess of negative symptoms in a chronic inpatient sample after statistically adjusting their findings for age and extrapyramidal symptom (EPS) ratings, although there was no sex difference in the unadjusted scores. In addition, although they found no sex differences in levels of negative symptoms, Pogue-Geile & Harrow [46] reported that the correlation of negative symptoms with other deficits was significantly higher in males than in females. These findings suggest that there may be subtle sex differences in the correlates of negative symptoms, and that further studies of sex differences are needed.

Negative symptoms and prehospitalization functioning

Many of the recent hypotheses concerning negative symptoms have much in common with earlier work on individual differences in "pre-morbid" functioning of schizophrenic patients [e.g., 78]. It is therefore both theoretically and practically important to consider the degree to which patients' level of functioning before hospitalization can predict the later presence of negative symptoms. It is, of course, not at all clear that functioning before hospital admission, even in a sample of only first-admission patients, reflects "premorbid" characteristics, not prodromal signs. Furthermore, unless the sample is composed solely of first-admission patients, such analyses also include the potential effects of already established chronicity. Such assessments of pre-hospitalization functioning are also, by their nature, retrospective and potentially open to retrospective biases in reporting. With these caveats in mind, let us review the data on this question.

Education level before hospitalization is one of the most objective and most frequently studied prehospitalization characteristics. Of the 12 studies on this question, 5 report a significant association between education level before hospitalization and degree of negative symptoms [46, 67, 72, 79, 80], the less-educated patients showing more negative symptoms, and 5 studies report nonsignificant associations [22, 76, 81–83]. Lindenmayer, Kay, & Opler [75] reported that in a sample of acutely ill patients, those with only negative symptoms had less education than those with only positive symptoms; however, a reanalysis using negative symptoms as a continuous dimension found no significant association after controlling for EPS ratings, although there was a trend in the expected direction [84]. In contrast, Kay and associates [74] found a significant association between prehospitalization education and negative symptoms in a large sample of chronically ill patients after controlling for extrapyramidal symptoms and age, but not before. Pogue-Geile & Harrow's [46] results were significant only for males.

All of these findings are difficult to reconcile with one another. These studies differ substantially in the chronicity of their samples, sex ratio, phase of assessment, and measures used; but these differences do not appear to be related in a simple fashion to the findings observed. Although it is likely that lower educational level is related in some manner to the occurrence of negative symptoms, additional research with large, representative samples is required to resolve this issue.

Several studies have also investigated measures of social functioning
before hospitalization. They have generally not found marital status to be significantly associated with negative symptoms [72,74,75], perhaps because of the young age of the patients before their first admission and the generally low base-rate of marriage among schizophrenic patients. However, in retrospective ratings of social function (e.g., number of friends), three studies have found that patients who were “less social” before admission had higher rates of negative symptoms during or after hospitalization than those who were “more social” [22,46,72]. Although such ratings of prehospitalization social functioning are potentially sensitive to retrospective bias and the effects of established chronicity, Pogue-Geile & Harrow [46] observed this association to be especially strong among first-admission patients. Moreover, they found the relationship to hold only for males. Therefore, overall it appears that schizophrenic patients, particularly males, who are markedly asocial before admission tend to show elevated rates of negative symptoms later, during and after their episode of illness.

These studies suggest that there is some degree of continuity between social and instrumental deficits before hospitalization and later negative symptoms. It is unclear, however, whether this is due to the influence of truly premorbid characteristics that persist following the onset of disorder or represents the early prodromal signs of a particularly severe form of schizophrenia that is also marked clinically by negative symptoms.

Associations of negative symptoms with other symptoms

Crow [31,32] has hypothesized that negative and positive symptoms represent independent dimensions within schizophrenia, meaning that they do or do not co-occur at chance levels. Andreasen & Olsen [72] have suggested that the two might be negatively related, or at opposite ends of the same bipolar continuum. A third possibility is that negative symptoms are positively related to positive symptoms and that both reflect a general symptom-severity dimension. These conflicting hypotheses make data on the cross-sectional relationship between negative and positive symptoms at one point in time of considerable interest.

A number of studies have investigated this question, and most have found that negative and positive symptoms represent independent dimensions when assessed cross-sectionally within schizophrenia (i.e., there was no significant correlation between scales) [36,46,56,74,76,79,81,85-88]. Kay and colleagues [74] reported a significant positive relationship between their positive and negative scales, and also between Andreasen's positive and negative scales in another sample [56]. However, when the level of other symptoms was controlled for, the relationship became negative [56,74]. The meaning of such a relationship in the latter case is unclear. Andreasen & Olsen [72] have reported a significant negative relationship between negative and positive symptoms.

Factor analyses of individual negative and positive scale items present a similar picture. Three studies using principal components analysis have disclosed two or more independent dimensions, one loading primarily on negative symptoms, such as flat affect and poverty of speech, and another loading primarily on positive psychotic symptoms, such as hallucinations and delusions [67,85,89]. In contrast, in the principal components analysis reported by Andreasen & Olsen [72], a major bipolar factor with positive and negative symptoms loading in opposite directions was observed.

The association between negative and positive symptoms depends to a considerable extent on the marginal distributions of each kind of symptom, which in turn depends on the sample selection criteria and phase of the disorder. Almost all of the studies cited above have involved inpatients who were in an acute episode and who were selected on the basis of the presence of positive psychotic symptoms. In such samples, variation in positive symptoms is in degree only, in contrast to negative symptoms, which may be completely absent. With such an attenuated range in positive symptoms among inpatient samples, findings of no correlation between positive and negative symptoms may not be surprising. However, the few studies of patients followed up at some time after hospital discharge, when both positive and negative symptoms may vary, also find that positive and negative symptoms are statistically independent [46,86]. The period of assessment is a potentially important factor in these results, one that requires further study.

The weight of these findings suggests that positive and negative
symptoms are generally independent dimensions when assessed cross-sectionally among schizophrenic patients, particularly in the acute phase, although in some samples there may be some positive relationship. This suggests that the direct pathophysiologies of the two syndromes differ. However, an important point that is often overlooked is the positive longitudinal relationship between the two—that is, negative symptoms are generally more common in patients who have at some time experienced positive psychotic symptoms, which, by definition according to current criteria, would include all schizophrenic patients. The potential mechanisms involved in such longitudinal associations, which nonetheless display cross-sectional independence, require further theoretical consideration. Such findings suggest that negative symptoms may result from the cumulative effect of positive symptoms over time in some patients.

**Association between negative and depressive symptoms**

There is a considerable literature on the occurrence of depressive symptoms among schizophrenic patients, referred to as "postpsychotic depression" [e.g., 90] and "schizoaffective disorder—depressed type" [e.g., 91]. Given the similarity between many negative and depressive symptoms, it is important to understand their interrelationship and whether current negative symptom rating scales can discriminate between them.

Of the seven studies that have investigated the association between ratings of negative and depressive symptoms among schizophrenic patients, five have reported no significant correlation between them [38,46,55,74,92]. In addition, a number of factor analyses of the BPRS in schizophrenic samples have repeatedly produced separate factors for depression and withdrawal-retardation [e.g., 18,93]. Lewine and colleagues [36] found no significant relationship between their SADS-C negative symptom scale and ratings of depression among male schizophrenic patients, but a significant positive association among females. This result is generally compatible with some of the other findings. Most of the studies that have found no association between negative and depressive symptoms have employed all male [55,92] or predominantly male samples [38,46,74] and have not analyzed the data separately by sex. More analyses that are stratified by sex are required to resolve this point.

In contrast to the other studies, Kay & Lindenmayer [94] reported a significant positive association in a 60% male sample between their negative symptom scale and the BPRS depression factor scale at both the acute inpatient and the follow-up phase [53]. The investigators' suggestion that their findings are due to the young age and acute phase of the sample is consistent with other findings in that most of the other studies had older samples. The Pogue-Geile & Harrow [46] study had an equally young sample, but the patients were assessed at follow-up a year and a half after hospital discharge. Therefore, in general, the association between negative and depressive symptoms may be affected by the phase, age, and sex of the sample, although further study is required to confirm this hypothesis.

The independence within schizophrenia that is generally observed between negative and depressive symptoms, particularly in older male patients, is initially somewhat surprising, given the similarity of some of the individual symptoms. In some sense, negative symptoms can be considered a subset of depressive symptoms—that is, although poverty of speech, psychomotor retardation, and expressionless facies are generally included as severe signs of depression, ratings of depression also include many other, much more frequent symptoms, such as sad mood, sleep and appetite disturbance, and worry. It is the weak association between the former behavioral signs and the latter subjective symptoms in samples that include few severe depressives that may explain the frequent independence of negative symptom and depressive ratings among schizophrenic patients. Therefore, because of this overlap between negative symptoms and overall indices of depression, it might be useful in future studies to separate items that are common to both syndromes and to examine only the correlation between items that differ between syndromes. It may also be an important theoretical point that the severe signs of both schizophrenia and depression are so similar.
Association between negative symptoms and cognitive deficits

One of Crow’s [31] primary hypotheses concerning negative symptoms as the manifestation of some structural brain abnormality was that such symptoms should correlate with cognitive deficits, which also were hypothesized to reflect structural abnormalities. Both before and since 1980, considerable effort has been made to evaluate this hypothesis and to characterize the specific nature of potential cognitive deficits associated with negative symptoms. This research is difficult to summarize because of the variety of tests used and their uncertain relationship to one another. Therefore, we shall review studies according to the type of test employed: general intelligence test, neurological examination, mental status examination, neuropsychological test, and information-processing task.

Studies have generally not found a significant correlation between estimates of general verbal intelligence and negative symptoms [73,85]. However, in samples of the chronically ill, Pogue-Geile & Harrow [76] and Kay and colleagues [74] reported significant associations, although the association in the latter study was no longer significant after controlling for age and EPS. Despite this inconsistency, a tendency may still exist for greater associations between negative symptoms and general intellectual deficit in the chronically ill.

Three studies have examined the association between negative symptoms and findings from a formal neurological examination. Two reported a significant positive association [82,83], and one did not [79]. Most of the neurological signs found in the studies by Owens & Johnstone [83] and Johnstone and colleagues [79] consisted of abnormal involuntary movements. The studies differed in the age and chronicity of the samples, but not in any systematic fashion. Nevertheless, it may also be that such associations between neurological signs and negative symptoms tend to be stronger in the more chronically ill, in whom the base rate of neurological abnormalities is probably higher.

More consistent results have been found in studies that correlated the results of structured mental status testing of cognitive abilities [95,96] with negative symptoms. All four studies of mental status have found significant associations with negative symptoms [35,72,79,83], although none of them provide any item-level analysis of the results. The mental status examinations are so heterogeneous that total score analyses provide little indication of which functional deficits might be relevant.

Studies using traditional neuropsychological tests, which have known brain correlates in neurological populations, are particularly interesting for exploring specific cognitive deficits correlated with negative symptoms. Four studies using batteries of traditional neuropsychological tests have found a range of cognitive deficits associated with negative symptoms [60,81,82,85], although the deficits were not consistent across studies. Similarly, several other studies, employing a variety of other specialized tests, have found cognitive deficits associated with negative symptoms, but with little replication among studies [33,74,80,94,97,98]. Much of this inconsistency may be due to variation across studies in the tests used, the chronicity of the samples, and the negative symptom rating scales employed [e.g., 84].

Tests inspired by the information-processing approach to cognitive psychology have also been used in an effort to characterize the nature of deficits associated with negative symptoms in schizophrenia. Green & Walker [73,99] reported that in order to identify a visual target correctly, schizophrenic patients with negative symptoms required a longer interval between the presentation of the visual target and a mask than did other schizophrenic patients, which suggests that schizophrenic patients with negative symptoms process visual stimuli more slowly than those without such symptoms. Nuechterlein and colleagues [100] have similarly reported that deficits on the Continuous Performance Task (CPT) and the Span of Apprehension Test were concurrently correlated with negative symptom ratings among schizophrenic inpatients. Negative symptoms during the inpatient phase were also predictive of CPT deficits after hospital discharge. Both of these tasks are dependent on speed of visual processing and employment of active, effortful processing strategies.

Two studies have also investigated the effect of auditory distraction on performance. Green & Walker [101] found no association between ratings of negative symptoms and performance on either a dichotic listening task or a digit span task. Similar findings have also been reported by Allen [102]. Using a different task, Clareblatt and associ-
M. F. Pogue-Geile & J. Zubin

NEGATIVE SYMPTOMS AND SCHIZOPHRENIA

ates [103] found no correlation between negative symptoms and performance in the presence of auditory distraction, although there was a significant correlation with recall of the “distracting” information.

The findings from these information-processing studies are consistent with the presence of deficits in speed and efficiency of effortful processing of information among schizophrenic patients with negative symptoms. This interpretation makes sense considering that the behaviors included in negative symptom rating scales emphasize psychomotor slowness.

In summary, Crow’s hypothesis concerning the relationship between cognitive deficits and negative symptoms has received considerable general support. However, more specific characterization of these cognitive deficits has just begun. Deficits in speed of complex processing appear to be most frequently associated with negative symptoms, although the relevant studies are not consistent on this point. It may be that differences across studies in the chronicity of the samples is important in the inconsistency of the results.

Longitudinal characteristics of negative symptoms

A most important assumption that is both implicit and explicit in most theorizing about negative symptoms is that negative symptoms are persistent once they develop. This is a basic corollary of Crow’s 1980 hypothesis that negative symptoms might reflect some structural brain abnormality. In addition, negative symptoms have been hypothesized to be prognostic of later poor functioning and to increase in frequency over the course of the disorder. The empirical findings on these three hypotheses are reviewed below. (For a more detailed review, see [104].)

Persistence of negative symptoms

Few studies have investigated the persistence of negative symptoms in a systematic fashion. In one of the earliest studies on this topic, Knight, Roff, and colleagues [105,106] reported that ratings from hospital charts of affective deficit were significantly correlated over a 22-year period. This study has been recently replicated, and the findings over a seven-year follow-up were similar [6]. In contrast, Lindenmayer and colleagues [86] studied negative symptoms assessed at the time of inpatient admission and then 2 years later at follow-up in a sample of 19 young schizophrenic patients. Over this period, the test-retest correlation for negative symptoms was not significant. The percentage of patients who had negative symptoms at admission and also at follow-up was not reported; although to some extent arbitrary, this figure would have been useful in that the correlation coefficient is sensitive to both the number of patients whose symptoms persist and the number of patients who do not show negative symptoms at either assessment. These are somewhat different issues.

Two studies have reported data on the persistence of negative symptoms that were initially assessed after hospitalization. Pogue-Geile & Harrow [107], who first assessed negative symptoms one year after hospital admission and then a second time two years later, reported that 55% of those patients who initially showed negative symptoms also displayed them two years later. An initial report from the Mannheim center of the “Study on the development of disability in schizophrenics,” sponsored by the World Health Organization (WHO), has also presented data on the stability of negative symptoms when assessed six months after hospital admission, and then later several times over a five-year period, in a representative sample of first-admission psychotic (predominantly schizophrenic) patients [108]. Although preliminary, this report indicated significant stability of negative symptom ratings at six months and one, two, and three years after admission. The association between six-month and five-year assessments did not appear to be significant. Further reports from this very important study should provide data crucial for hypotheses concerning the longitudinal characteristics of negative symptoms.

Although based on few data, these studies suggest, thus far, that negative symptoms during the acute inpatient phase may be quite different from negative symptoms assessed during other phases of the disorder, as Kay and colleagues [84] have hypothesized. However, when assessed during the postacute phase, negative symptoms appear to be relatively persistent, although not completely so, remission occurring in some patients. These speculations are quite tentative, how-
ever; and further data, such as those from the WHO disability study, are required.

In addition to these studies of young patients, there are two studies of schizophrenic patients much later in the course of their disorder. Both, of necessity, employed very unrepresentative samples of chronic patients who had been hospitalized continuously for a number of years. Pfohl & Winokur [109] studied patients who had been continuously hospitalized for at least 12 years and reported that once negative symptoms occurred in this select group, they rarely remitted (e.g., remission rates for flat affect, 6%; for avolition, 4%; for decreased speech, 29%). In a similar study, Johnstone and colleagues [110] twice assessed patients who had been continuously hospitalized for at least four years. They also found substantial persistence over time, although not as much as that reported by Pfohl & Winokur (e.g., remission rates for poverty of speech, 19% for flat affect, 35%).

These studies represent designs that are most conducive to revealing extreme stability, because any patient who remitted enough to be discharged would not be studied. Therefore, it is all the more remarkable that even in these studies, negative symptoms were not always persistent. These studies and those of younger patients suggest that although negative symptoms are often persistent, they are definitely not immutable. Such findings are inconsistent with a simple model that views all negative symptoms as being due to persisting structural brain abnormalities.

The prognostic value of negative symptoms

Flattened affect, currently considered a negative symptom, has long been hypothesized to be a prognostic sign of poor later functioning [e.g., 111], and earlier follow-up studies supported such notions [e.g., 112, reviewed in 78]. Three more recent studies have also found that the presence of affect deficit at hospital admission significantly predicted poor functioning several years after discharge [6,105,113]. However, two recent studies did not find that negative symptoms at hospital admission predicted later posthospital functioning [114]; in fact, the study by Lindemayer, Kay, & Friedman [86] found that negative symptoms predicted good functioning two years after discharge. Two other recent studies that assessed negative symptoms after the acute inpatient phase found, however, that they were significantly predictive of later functioning [107,108]. These findings may suggest, again, that negative symptoms at the acute phase mean something different from when they are assessed following the inpatient period, but further study is needed on this point.

How might negative symptoms acquire this prognostic value? As pointed out by Pogue-Geile and Harrow [107], it appears that negative symptoms generally appear in patients who are already functioning poorly in social and instrumental roles, and that these patients tend to continue to function poorly. This observation has been confirmed by other research [86,108,114], which also finds that negative symptoms, particularly when assessed during a postacute phase, are concurrently correlated with poor community functioning. These findings suggest that negative symptoms indicate current poor functioning in some patients that tends to persist.

Age-related changes in the prevalence of negative symptoms

Crow [31] and others have speculated that negative symptoms should be more frequent during the later phases of schizophrenia, although to date few longitudinal studies have evaluated this hypothesis over the long term. In samples of young patients who are still at an early stage in the course of their disorder, one study has reported no significant mean change in negative symptoms between admission and two years postdischarge [86]. Studies in which the assessment was made after hospital discharge suggest that negative symptoms decrease, on average, during the early posthospital period [107,108], but then increase through five years after discharge [108]. Two studies during the later periods of disorder have reported mixed results. Pfohl & Winokur’s [115] study of patients hospitalized for at least twelve years found that negative symptoms in this select cohort tended to increase during the first several years of the disorder and then to maintain a steady prevalence. Johnstone and associates’ [110] study of patients, approximately thirty years after their first hospitalization, who had been hospitalized at least four years found that poverty of speech increased and flat affect
decreased significantly during the four-year period.

These studies suggest that the early course of negative symptoms may fluctuate considerably, particularly during the inpatient period. It may be that negative symptoms during an acute episode reflect processes different from those during other periods. There is also some evidence that after this initial period, negative symptoms may gradually increase over time and perhaps becomes more stable. However, even during the later periods of the disorder, remission may occur. Further study is required to confirm these interpretations.

**Association of negative symptoms with biological characteristics**

**Structural brain abnormalities**

As noted above, one of the basic tenets of Crow's 1980 model was that negative symptoms, such as flat affect and poverty of speech, represented a behavioral manifestation of some structural brain abnormality. A number of studies have since investigated this issue by means of computed tomography (CT) scanning techniques, which, although not sensitive to all possible structural abnormalities, have been used to study a range of cerebral measurements and their relationships to negative symptoms.

Five studies have found significant positive associations between structural abnormalities on CT scan (generally, lateral ventricular enlargement) and negative symptoms [69,116–119]. Gross, Huber, & Schütte [120] have reported a significant positive association between lateral ventricular enlargement and their concept of "pure defect," which is similar in many respects to negative symptoms. However, most studies have reported no significant association between a range of CT scan abnormalities and negative symptom ratings [34,87,121–127]. Andreasen and colleagues [128] reported no significant difference in negative symptom ratings between patients with extremely large or small ventricles, although, based on the same sample, patients with only negative symptoms showed greater ventricular enlargement than those with some positive symptoms [72]. Besson and colleagues [129], using magnetic resonance imaging (MRI), have also reported no significant association between ventricular enlargement and negative symptoms. Moreover, three studies have even found negative symptoms to be significantly related to reduced ventricular size on CT scan [130–134].

These studies have employed a range of samples, negative symptom rating scales, and CT measurements, which may explain some of the variation in results. However, overall, it appears likely that for most samples, there is little association between CT scan abnormalities, particularly lateral ventricular enlargement, and negative symptoms. This contradicts a major tenet of Crow's original hypothesis, and has led the Northwick Park group to propose that this relationship is much more complex than was originally hypothesized [124].

In response to these data, Crow [5] has revised his original hypothesis and has suggested that the pathology underlying negative symptoms is located in the temporal lobes, citing studies finding reduced peptide concentrations in the hippocampus and amygdala from postmortem brains of patients with negative symptoms [133]. In contrast, Seidman [135], Andreasen [134], Carpenter, Heinrichs, & Alphs [4], and Weinberger [136] have suggested that structural abnormalities in the frontal lobes may be more relevant for negative symptoms. Both temporal and frontal structures are poorly visualized on CT scan. Although specific structural abnormalities that are not well imaged on CT scan may still be implicated in negative symptoms, the weight of the evidence suggests that diffuse atrophy probably does not account for most instances of negative symptoms.

**Neurochemical correlates**

Neurochemical hypotheses of the pathology of negative symptoms are of three general types. One important corollary that Crow drew from his notion that negative symptoms reflect structural brain abnormalities is that negative symptoms are not related to abnormalities in dopaminergic neurotransmission, and that therefore they should be unresponsive to neuroleptic medications or to dopamine agonists. In addition to this position, some have hypothesized that negative symptoms reflect hypodopaminergia [e.g., 137], which implies that neuroleptic medications will worsen negative symptoms and that dopamine agonists will
ameliorate them. A related notion is that negative symptoms are primarily one of the side effects of antipsychotic medication (i.e., akinesia) [e.g., 138,139], in which case improvement of negative symptoms should follow neuroleptic dose reduction and/or the addition of EPS side-effect medications. In contrast, others have suggested that negative symptoms, along with positive psychotic symptoms, benefit from neuroleptic medications [e.g., 140].

Controlled trials have yielded evidence that neuroleptic medications may improve (see recent reviews [8,140]), have no significant effect [e.g., 33,141], or exacerbate negative symptoms [142–144]. This conflicting evidence may be due to differences in the measurement of negative symptoms and the chronicity of the samples. It may well be that neuroleptic medications are beneficial for negative symptoms during an acute episode, yet have little, or a deleterious, impact during a postepiode period. Moreover, most of these studies predate the recent interest in negative symptoms, and their results regarding "negative symptoms" are interpreted post hoc. Thus, the measurement of negative symptoms in these studies may differ from current practice.

Studies of the effects of dopamine agonists, such as L-dopa and amphetamine, have also produced mixed results, some studies finding modest beneficial effects [e.g., 145,146; review, 8], and others not [e.g., 141]. Again, these studies are primarily early studies, and their measurement of negative symptoms may differ from current practice.

In addition to these controlled trials, a number of more recent studies have examined the correlation between neuroleptic medication dosage and negative symptoms in samples in which administration of medication is not experimentally controlled. Significant associations (either positive or negative) in such studies are difficult to interpret, because they could arise either through selective dosing or some medication effect on negative symptoms. However, although not as convincing as controlled studies, the finding in these studies of nonsignificant associations between neuroleptic medications and negative symptoms nevertheless suggests that medications do not primarily either increase or decrease negative symptoms. Six of the seven such studies have found nonsignificant correlations between neuroleptic dosage and negative symptoms [46,65,79,83,86,92], and one reported a significant negative correlation, patients with negative symptoms having received lower neuroleptic doses than those with positive symptoms [80]. Although not based on controlled trials, such evidence is consistent with the notion that negative symptoms are not primarily side effects of neuroleptic medications or primarily improved by neuroleptics.

Similar uncontrolled data are also relevant to the hypothesis that negative symptoms are primarily side effects of neuroleptics. Several studies have found significant correlations between traditional EPS ratings and negative symptoms [60,74,83,86,92], although some have not [55,79,80]. From such data it is not clear whether such associations arise because both traditional EPS and negative symptoms are due to neuroleptic medications, or whether some abnormal movements and negative symptoms share a common pathophysiology that is not necessarily related to neuroleptics [5]. Recall that negative symptoms are not generally positively correlated with neuroleptic medication dose and that, in addition, anti-Parkinsonism medications may be of little benefit in countering negative symptoms [147,148].

These studies raise more questions than they answer. Although the data generally contradict the notion, it nevertheless seems intuitively likely that neuroleptic medications can increase negative symptoms, and the question is what proportion of negative symptoms may be induced by drugs. Further controlled studies of the effect on negative symptoms of neuroleptic dosage and anti-Parkinsonism medication are needed to address this issue.

Future uncontrolled studies of negative symptoms should also assess EPS, anti-Parkinsonism medication dosage, and the anticholinergic properties of patients' neuroleptic medications in order to examine these issues. It also seems clear that in some cases, neuroleptic medications can improve negative symptoms. Further study of this question that examines the effect of phase of illness is needed. Overall, the data suggest that, contrary to Crow's original suggestion, negative symptoms are generally not completely unaffected by pharmacological challenges. Rather, it appears that a variety of pharmacological influences can affect some negative symptoms. What needs to be more precisely determined is how often and when negative symptoms are sensitive to which pharmacological challenge.
Etiological studies

Twin and family studies

Although the etiology of negative symptoms has not been the focus of much theorizing, some genetically oriented studies have been reported. These investigations have yielded the following three general kinds of data.

Two studies of the homotypia of negative symptoms have been reported, both studies using Gottesman & Shields’s [149] twin sample, although with different ratings of negative symptoms. Berenbaum, Olmanns, & Gottesman [150] have reported a significant correlation (0.74) for ratings of anhedonia between MZ twin pairs discordant for schizophrenia. McGuffin, Farmer, & Gottesman [151] have similarly found a high degree of homotypia (although not complete) for ratings of Crow’s Type I/Type II dichotomy for both concordant MZ (73% similar) and concordant DZ (75% similar) twin pairs. Thus, 73% of MZ pairs discordant for schizophrenia were also discordant for the Type I/Type II rating (i.e., either both members of a pair were Type I, or both members were Type II). These data suggest that there is some tendency (although not complete) for schizophrenic patients with or without negative symptoms to “breed true” in both MZ twins and first-degree relatives.

Such results in MZ twins could arise from at least the following three potential sources:

1. The etiology of schizophrenic patients with negative symptoms could differ qualitatively from those without negative symptoms.
2. Schizophrenic patients with negative symptoms could differ quantitatively from those without negative symptoms (see below).
3. Patients with negative symptoms could differ from others on modifying characteristics that are relevant to negative symptoms, but not to schizophrenia (see below).

Although, of necessity, based on very few pairs, the high degree of homotypia shown by concordant DZ twins would tend to argue against the third possibility that negative symptoms are due to genetic factors unrelated to risk for schizophrenia, although the DZ data are also consistent with a modifying effect due to shared family experiences (see [152] for details). More such information on DZ twins or siblings is needed to further resolve this point.

Other studies have investigated the correlation in negative symptoms between MZ and DZ twins without regard to their concordance for schizophrenia. Such analyses bear on the degree to which different familial factors are important in the determination of negative symptoms. Both samples in which at least one member of each twin pair was schizophrenic and samples of normal twins have been studied. Dworkin & Lenzenweger [153] reported a significant MZ correlation (0.26) for ratings of negative symptoms based on the published case histories from previous twin studies of schizophrenia. Using data from Gottesman & Shields’s [149] twin study of schizophrenia, Berenbaum, Olmanns, & Gottesman [154] reported significant correlations for poverty of speech in both MZ (0.54) and DZ (0.60) twins. This result suggests that environmental experiences shared by twins, not genetic influences, are important determinants of poverty of speech. In contrast, these investigators found in the same sample that MZ correlations (0.53) were significantly higher than DZ correlations (–0.38) for ratings of anhedonia [150]. Dworkin & Saczynski [155] have reported similar findings in a small sample of normal twins. Although not uniform, these few studies have produced results that are consistent with the notion that negative symptoms are familial, and that some may be genetically influenced.

A number of studies have also examined the association between negative symptoms among probands and familial risk for schizophrenia in general. This analysis is relevant to the possibility that negative symptoms may indicate a quantitatively more genetically severe form of schizophrenia. One twin analysis on this issue has found the presence of negative symptoms in schizophrenic probands to be associated with increased concordance for schizophrenia in general among MZ twins [153]. McGuffin, Farmer, & Gottesman [151] also found a nonsignificant trend in this direction for MZ twins (64% vs. 53% concordance for negative-symptom vs. non-negative-symptom probands), but an opposite trend among DZ twins (0% vs. 19% concordance, respectively). A third study found that anhedonia in MZ twin probands was associated with increased nonschizophrenic diagnoses in the co-twins, but not with diagnoses of schizophrenia [150]. McGuffin, Farmer, &
Gottesman [151] have also reported an increased MZ/DZ concordance ratio among probands with negative symptoms. These twin results are generally consistent with a model in which schizophrenia with negative symptoms is a genetically more severe form of the disorder. This echoes earlier findings of Gottesman [156] in which he found an association between clinical severity and twin concordance.

Along similar lines, several studies have also examined the association between negative symptoms among probands and risk for schizophrenia in nontwin relatives. Most such studies have not found a significant association in nuclear families [69,72,79,83]. In contrast, Kay and colleagues [84] have reported that negative symptoms in probands are associated with decreased risk for major mental disorder if assessed during the inpatient phase, but with increased risk for such disorder (not schizophrenia specifically) if the probands are chronic patients. These nuclear-family studies generally contradict some of the findings based on twins. This may be due to the large sample sizes that are required to detect differences in familiality because the rate of schizophrenia among relatives of schizophrenic patients is low. In addition, the family studies have relied on family-history data from informants, rather than family interview information from each relative, which further reduces the sensitivity of these investigations.

The results of these twin and family studies of negative symptoms must be considered extremely tentative, because of the small sample sizes; but they have nevertheless provided some important leads. Despite a lack of complete consistency, the twin studies suggest that negative symptoms are familial, and there is some evidence of both genetic and shared family environmental influences. Some twin studies, although not supported by the family studies, also suggest that negative symptoms may mark a more severe form of schizophrenia. Much more information is needed, however, before these interpretations can be considered persuasive.

Influence of environmental experiences

Wing & Brown [24] have demonstrated in their study of the effect of hospital environment that increased environmental stimulation can improve some patients’ negative symptoms, although the improvements were generally not dramatic. In contrast to the results of this experimental study, others, using correlational designs, have found little effect of long-term institutionalization [76,79].

In any case, it appears reasonable to expect that extremes of environmental understimulation might produce some negative symptoms. The question, however, is, How important are such factors for most negative symptoms among young schizophrenic patients who have not had extensive hospitalizations and may live with their families in the community? Further studies of understimulating environments are needed to evaluate their current importance for most schizophrenic patients, especially young noninstitutionalized patients who may nevertheless lead secluded lives.

Summary of empirical findings

Before discussing more general theoretical models, we shall briefly summarize the findings from the studies reviewed above.

1. Negative symptoms are associated with schizophrenia, although they are clearly not specific. Moreover, negative symptoms occur in only a subset of schizophrenic patients at any single point in time.

2. Although there do not appear to be obvious sex differences in levels of negative symptoms, more subtle differences may be present. Future research should include analyses of sex differences.

3. Poor social or instrumental functioning before hospitalization appears to be associated with later negative symptoms.

4. Negative symptoms are generally not correlated concurrently with positive symptoms within schizophrenia. However, they appear to be positively correlated longitudinally, in that negative symptoms are more common among patients who have once experienced positive psychotic symptoms.

5. Negative symptoms are generally not correlated with ratings of depression during the postacute period. However, this relationship is surely a complex one, as patients in depressive episodes are rated high on negative symptoms. The overlap between "negative" and "depressive" symptoms in schizophrenia is an important area for future research, as is the meaning of negative
symptoms among depressive patients.

6. As Crow and others have suggested, negative symptoms tend to be associated with some cognitive deficits. In general, cognitive tasks that emphasize speed and effortful processing appear to be the most closely associated with negative symptoms; however, further study is required to characterize such cognitive deficits more fully. These findings suggest the importance of distinguishing between traditional negative symptoms and cognitive deficits.

7. Negative symptoms appear to be relatively stable during the postacute period. However, remission may occur at any time. During the acute inpatient period, negative symptoms appear to be unstable, and may reflect processes different from those during the postacute period. Negative symptoms assessed during the postacute period are prognostic of later poor functioning; this seems to be due to the tendency of these symptoms to occur in patients who are currently functioning poorly and who then tend to continue in this fashion. Negative symptoms occur in only a subset of poorly functioning patients.

8. Although observed in some samples, negative symptoms do not appear to be strongly associated with structural brain abnormalities as imaged on CT scans.

9. Negative symptoms can be either improved or exacerbated by neuroleptic medications. To date, however, it appears that negative symptoms are probably not overwhelmingly affected by current pharmacological challenges. This is an important area that needs further research.

10. Twin and family studies suggest that negative symptoms are familial, and perhaps genetically influenced. Negative symptoms may indicate a quantitatively more genetically severe disorder, but more research is required to confirm or reject this hypothesis.

11. It appears plausible that extreme environmental understimulation may induce negative symptoms, but the importance of such factors for most negative symptoms remains to be demonstrated.

Any summary of these studies is complicated by variations across studies in the measurement of negative symptoms. As suggested above, comparative studies of the various operational definitions and more objective measurement should be priorities for future research. An emphasis on the traditional core negative symptoms would facilitate comparison among studies. We can only echo Crow [5] when he calls for a narrow operational definition of negative symptoms before comparisons among studies become meaningless because of extremely broad and idiosyncratic ratings of such symptoms.

From the above it should be clear that subsequent research has not confirmed all of Crow’s 1980 hypotheses. Many have been supported, some seem untenable, and the jury is still out on many. Nevertheless, his and others’ predictions have been immensely heuristic: they have stimulated studies of a range of new questions and forced researchers to look at old data in a new light. Additional research has illuminated complexities that were initially unseen; new hypotheses have been proposed.

Etiological conjectures

In line with the expectation that new observations are stimulated by new theory, we propose below some that we believe to be promising models of the etiology of negative symptoms.

Much of Crow’s and others’ theorizing has been concerned with characterizing the underlying biological pathology of negative symptoms, and etiological questions have generally not been considered explicitly. Nevertheless, a general etiological model has been implicit in much of the theorizing to date. This implicit model might be termed the “specific-influence” model, and it is just one of several relevant etiological models that we shall describe below (also see [107, 152]).

The specific-influence model implies that some negative symptom-specific factor (either genetic or environmental) is sufficient to produce negative symptoms and also the generally accompanying positive psychotic symptoms of schizophrenia. This model assumes that negative symptoms are “indigenous” to schizophrenia. In the context of a hypothetical polygenic model of schizophrenia, such a model can be illustrated as follows. Suppose that five genes can contribute to the liability to schizophrenia (e.g., genes A, B, C, D, and E), that any triad is sufficient to produce diagnosable schizophrenia, and that gene A also produces negative symptoms. Any person with a gene triad that includes gene A would present with negative symptoms. In contrast, those with a gene triad not including gene A would not display negative
symptoms. In a case in which gene A, the negative symptom-specific factor, is sufficient to produce as well the positive psychotic symptoms that are required for the diagnosis of schizophrenia, negative symptoms would delineate a subtype of schizophrenia with an etiology different from that of other schizophrenic patients. This model seems to be the one implicitly favored in most theorizing to date.

A second etiological model is a multiple-threshold model [157]. Continuing with the polygenic example used above, in the multiple-threshold model, no genes would be specific or sufficient to produce negative symptoms. Rather, only the number of genes present would be associated with negative symptoms, not any specific gene. For example, suppose that three of five genes were required to produce clinically diagnosable schizophrenia and that an additional gene, for a total of four genes in all, would be required to produce schizophrenia with negative symptoms. In this case, no specific factor would be related to negative symptoms. This model has been extensively developed mathematically [157] and has been studied elegantly, in terms of a number of other individual differences among schizophrenic patients, by Gottesman and colleagues [e.g., 151, 156, 158].

The third model, the "modifying-influence" model, postulates a trait that itself does not contribute to the risk for schizophrenia, but interacts with a more specific schizophrenic diathesis. For example, a trait, such as low sociability, may not directly contribute to the risk for schizophrenia, but when it occurs in schizophrenic patients, may be exacerbated and lead to a negative symptom picture. It must be remembered that negative symptoms represent extremes of normal behavioral patterns that themselves show considerable variation in the general population. It is certainly possible that for persons who are at the extremes of normally distributed dimensions, such as in asociality, amotivation, and restricted emotional expressiveness, and also are schizophrenic, these characteristics might give the picture of the disorder a negative symptom color. Thus, only a subset of schizophrenic patients who are at the extremes of such relevant dimensions would show negative symptoms. In contrast, persons at the extremes of these normally determined distributions who develop nonschizophrenic disorders, such as anxiety or obsessive compulsive disorder, would not develop negative symptoms, because an interaction with a schizo-

phrenic diathesis would be required for the evolution of severe negative symptoms. This general notion has also been discussed by Meehl [159] and by Zubin & Spring [160].

A fourth, general, model postulates that negative symptoms are not "indigenous" to schizophrenia, but arise because of factors that would produce negative symptoms in anyone. Two varieties of this general model can be distinguished. First, as in the modifying-influence model above, persons at the extremes of a normally distributed dimension of negative symptoms would show negative symptoms "premorbidly" and would continue to display them after psychotic episodes. However, in contrast to the modifying-influence model, no interaction with a schizophrenic diathesis is required for the manifestation of negative symptoms. Therefore, it would be predicted that negative symptoms would be equally common in all disorders.

A second variety of this general model regards negative symptoms as side effects of the devastating experience of undergoing a schizophrenic episode. In this "iatrogenic" model, schizophrenic patients are not more susceptible to negative symptom-producing experiences than anyone else [11], but rather, because of the experience of psychosis itself, others' reaction to it, and its treatment, they are exposed to more negative symptom-inducing experiences than are most people. If non-schizophrenics were exposed to similar experiences and treatments, they also would develop negative symptoms. The shattering impact of a schizophrenic episode on the personality, the ensuing rise of self-doubt about coping ability, and the general loss of life direction might produce negative symptoms even in patients, whether schizophrenic or not, who were not premorbidity affected by them. In this model, the formation of negative symptoms might be viewed as either an active coping strategy or a residual scar of the experience of an episode. In any case, other iatrogenic effects of treatment and stigmatization might then exacerbate and reinforce the proneness to negative symptoms and thus interfere with recovery. This model would predict negative symptoms to be common also among persons who have been exposed to experiences that are similar to those that many schizophrenic patients encounter, e.g., possibly neglected nursing-home residents. In contrast to the other models, this one views negative symptoms as not being indigenous aspects of schizophrenia, although their "-atment and pre-
vention nevertheless remain important.

None of these conceptual models are entirely new. The first two of these models (i.e., specific-influence and multiple-threshold) imply that negative symptoms are somehow a "part" of some schizophrenias. In contrast, the latter two (i.e., modifying-influence and nonindigenous) models see the etiology of negative symptoms as being outside schizophrenia itself, although in the modifying-influence model "normally" determined individual differences are exacerbated by a schizophrenic diathesis. As yet little data exist to enable a choice to be made among these possibilities, although some of the family data support the multiple-threshold model and, perhaps, the modifying-influence model. Further investigations of these etiological possibilities are needed, and will not only be important in their own right but also serve to better inform the search for the underlying pathology of negative symptoms.

Acknowledgments

Preparation of this article was supported by grant BRSG RR 07086-20 from the National Institutes of Health (NIH) to Dr. Pogue-Geile and aid from the Medical Research Service of the Veterans Administration to Dr. Zubin.

The authors are grateful to Ms. Barbara Epstein, librarian at the University of Pittsburgh, for carrying out the computer search of the relevant literature, and to Mr. John Hall for assisting with the library research.

Note

1. In this case, homotypia refers to the degree of similarity in negative symptoms shown by pairs of relatives who are already concordant for schizophrenia.

References


NEGATIVE SYMPTOMS AND SCHIZOPHRENIA


view of Psychology, 30, 527.

NEGATIVE SYMPTOMS AND SCHIZOPHRENIA

ventricular enlargement in acute and chronic schizophrenia. Psychiatry Research, 9, 225.


