Schizophrenia Bulletin vol. 32 no. 2 pp. 250–258, 2006
doi:10.1093/schbul/sbj011
Advance Access publication on October 12, 2005

Negative Symptoms and Cognitive Deficits: What Is the Nature of Their Relationship?

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Negative symptoms and cognitive deficits in schizophrenia share many features and are correlated in their severity on a cross-sectional basis. The question arises as to the nature of this relationship: are these symptoms the same, caused by the same factor (or factors); or is the nature of their relationship determined by other factors, such as definitional issues and common correlates? In this article we provide a conceptual overview for addressing this question and provide a selective review of the literature on the cross-sectional and longitudinal relationships between these two features of the illness. We describe 4 different models of the "true" relationship between these variables. Some data suggest that the relationship between these variables is determined by the definition of negative symptoms employed and that, in general, the correlation is moderate at the most. Further, path modeling suggests the possibility, to be addressed with later research, that correlations between negative and cognitive symptoms and everyday functional outcomes may influence the observed correlations between these variables. Thus, we conclude that negative and cognitive symptoms may be separable, if not conceptually independent, domains of the illness and that it might be possible to develop treatments that target negative symptoms and cognitive deficits independently.

Key words: path analysis/longitudinal studies/ neuropsychological functioning

Negative and cognitive symptoms in schizophrenia share many characteristics, at least superficially. Their prevalence, course, prognostic importance, and correlation with various aspects of everyday functional skills performance appear similar. Further, negative and cognitive symptoms have been reported to be correlated in their severity in cross-sectional assessments of patients with schizophrenia. In addition, they are reported to be uncorrelated with the same features of illness, namely, the cross-sectional severity of psychotic symptoms.

The question is whether the data regarding the cross-sectional relationship between negative and cognitive symptoms suggest that the two are intrinsically related to each other. If they are, there are important etiological and treatment implications, in that it may not be possible to develop treatments that specifically target one symptom or the other. Further, there are issues in the definition of negative and cognitive symptoms that blur the conceptual boundaries between these constructs, and the correlation between cognitive and negative symptoms may vary as a function of the definition of the negative symptoms construct. Negative symptoms are typically defined in terms of clinical observations of behavioral features, while cognitive symptoms are defined in terms of performance on various tasks. Negative symptoms also appear to be more etiologically complex than cognitive impairments, in that psychosocial and environmental factors may impact on the expression of negative symptoms.

Models of the Relationship of Cognitive and Negative Symptoms

In this article we provide a perspective on the issues regarding how to determine the "true" relationships between these variables; we evaluate the impact that variation in definition of the different symptoms on the correlation between negative and cognitive symptoms; and we provide 4 theoretical models regarding the nature of the relationships between negative and cognitive symptoms (Figure 1). The first model proposes that these 2 dimensions are in fact identical features of the illness, or alternate manifestations of the same basic underlying process, and would therefore be improved by the same treatments. The second model holds that these features of the illness are, in fact, separable but that they share similar underlying etiological factors, which leads to observed correlations between variables and suggests that treatments for one may also impact the other.

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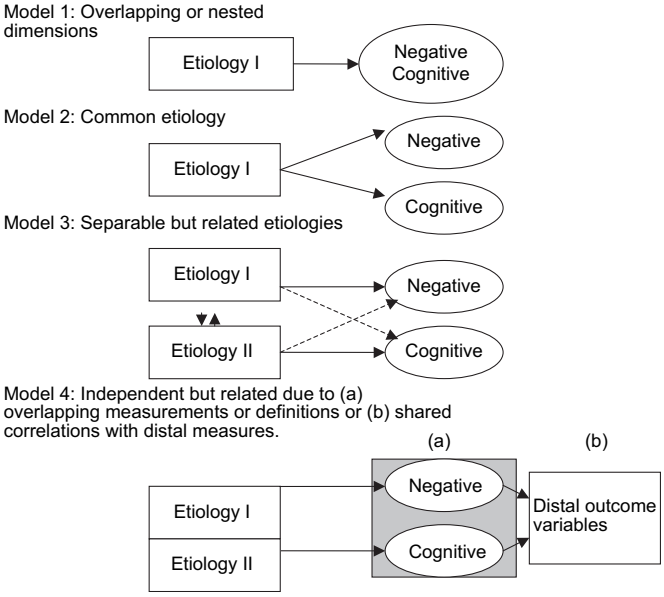

Fig. 1. 4 Theoretical Models of the Nature of the Relationships Between Negative and Cognitive Symptoms.

The third model proposes that each of these symptom dimensions has a separate etiology but that these etiologies might be related, which would suggest that treatments for one domain might impact the other, but not to the same extent as in Model 1 or 2. The final model views these symptom dimensions as distinct from each other, with separate etiologies. Thus, correlations between these domains, if detected, are influenced by measurement and definitional issues or "third variable" relationships with other features of the illness, which could induce an observed correlation that is actually indirect.

We will evaluate the extent to which these models are supported by the data and what kind of data are needed in order to further clarify the issue of the potential differentiation between these 2 aspects of schizophrenia. Clarification of this matter is, of course, particularly important from the perspective of treatment of these different features of the illness.

Background Issues Regarding Negative and Cognitive Symptoms

Definitions of Negative Symptoms. While this topic is addressed elsewhere in this issue, some brief discussion of the implications of the varying definitions of negative symptoms is important. Following from the early definitions of Hughlings-Jackson, negative symptoms reflect a pathological deficit, representing the absence of some normal functions. It may be easier to define the presence of some abnormal behavior, belief, or perceptual experience (ie, positive symptoms) than the relative absence of normal experience. For instance, some of the domains currently considered negative symptoms are more easily delineated and defined than others. While the absence of normal affective expression or experience can be quantified and falls within the classical realm of negative symptoms, it becomes more difficult to straightforwardly decide if other behavioral deficits should be referred to as negative symptoms, as cognitive deficits, or as limitations in everyday life skills. For instance, should reduced memory performance, concentration ability, or problem-solving aptitude, even if assessed clinically rather than by performance on tests, be considered a negative symptom or a cognitive deficit? Likewise, should deficits in social competence (as compared to social motivation) or in the specific performance of occupational skills (as compared to motivation to seek employment) be considered negative symptoms? Should behaviors directly resulting from or maintained by extrinsic factors be considered negative symptoms (eg, what role do social limitations/barriers play in social withdrawal and avolition)? If the boundaries of negative symptoms are expanded to include cognitive functioning, the correlation between negative symptoms and other aspects of cognition will be increased, due to the fact that many cognitive abilities are themselves intercorrelated. While we are not offering special answers to these questions, which are addressed in other articles in this issue, we will evaluate some data suggesting that variations in the definition of negative symptoms are associated with variation in the correlations between performance deficits on neuropsychological (NP) tests and the severity of negative symptoms.

Similarities in the Characteristics of Negative and Cognitive Symptoms. Cognitive and negative symptoms have several, apparently similar features. These include onset, temporal course, correlations with other aspects of the illness, and prognostic importance. Each will be described briefly.

Onset. Deficits in social and emotional functioning are present prior to the diagnosis of psychotic symptoms.[1–4] Considerable evidence also indicates that cognitive impairments are present in cases well before the onset of psychotic symptoms.[2,5] As a group, future schizophrenia patients manifest cognitive impairments of a magnitude of about one-half a standard deviation compared with controls. The large majority of future patients, however, do not have extraordinarily poor premorbid social functioning and perform within the normal range on tests of intellectual abilities—ie, having a premorbid IQ greater or equal to 85. Thus, both cognitive and negative symptoms could be reasonably characterized as "early symptoms," and these may also be conceived as the indicators of the *developmental* (ie, premorbid to prodromal) component of schizophrenia.

Temporal Course. Psychotic symptoms in schizophrenia tend to vary over time in most patients. This was true even prior to the neuroleptic treatment era because some patients recovered from their psychotic episodes, experiencing spontaneous remission.[6] Currently, even chronic patients often have a variable course of psychotic symptoms, with the longitudinal correlations close to zero.[7] In contrast, the longitudinal stability of negative and cognitive symptoms is considerably greater, leading some to conclude that both are "trait" features of schizophrenia. Even in cases where there is relative remission of psychotic symptoms, negative and cognitive symptoms are often found to be persistent.[8] Thus, cognitive and negative symptoms appear to share a similar course. Similar courses do not provide evidence of similar origin of symptoms and could even suggest that both types of symptoms are influenced by similar external factors rather than similar illness-related factors. Further, there is some evidence that negative symptoms may vary as a function of substance abuse history, with patients who abuse substances having greater variability in their symptoms than nonabusers.[9] Interestingly, more severe cognitive impairments were associated with more stable negative symptoms in that study.

Relations to Other Aspects of Illness. Cognitive and negative symptoms also have similar relationships to other symptoms and features of the illness. For example, the typical cross-sectional correlation between the severity of negative and cognitive symptoms and the severity of positive symptoms is low to zero.[10–11] This would not be surprising, as noted above, because the typical course of psychotic symptoms is variable over time, and both cognitive and negative symptoms appear to be more temporally stable. As a result, even within the same patient, the correlation between positive symptoms and the other two domains would be expected to be variable.

Prognostic Importance. Even more important, however, is the relatively similar relationship of negative and cognitive symptoms and both global and specific indicators of prognosis and everyday life skills. For instance, it has been appreciated for years that the presence of negative symptoms early in the illness is associated with a more adverse course, including more psychotic episodes[12] and greater impairment in adaptive life skills.[13] Patients who are completely disabled and rely on others for their survival are more likely to have more severe negative symptoms than less disabled patients, while the severity of positive symptoms is similar across these groups.[14] Further, patients who meet criteria for the deficit syndrome have more severe functional impairments and more generalized disability than nondeficit patients.[15]

Similar relationships between course of illness, disability, and cognitive impairments have been detected. For instance, cognitive impairments early in the illness also predict a more adverse course of illness and greater lifelong disability.[12] In fact, cognitive deficits have been shown to be the consistently largest cross-sectional predictor of deficit in specific functional skills in schizophrenia.[16–17] So, the concurrent correlations of negative and cognitive symptoms appear to be quite similar, and from the perspective of concurrent validity, negative and cognitive symptoms appear to have very similar validators. However, similar relationships between outcome and symptoms can be multiply determined. As noted above, the presence and severity of cognitive impairments can influence the presentation of negative symptoms. Further, as also noted above, negative symptoms have the potential to be more multiply determined than cognitive deficits. If cognitive impairments led to disability, it is at least theoretically possible that apathy and disinterest might be the result of this disability and not the cause.

Cross-Sectional Data on Negative and Cognitive Symptoms. Multiple studies have suggested that, when examined cross-sectionally, the severity of negative and cognitive symptoms are correlated. These findings are relatively consistent across age and the course of the illness, from the first episode[18] to patients with a chronic course of illness and extended institutional stay. These correlations are generally moderate and in the range of $r = .30$. For instance, at the time of the first episode, moderate correlations are found between the majority of cognitive domains and affective flattening, alogia, and apathy as measured with the Scale for Assessment of Negative Symptoms (SANS),[19] versions of the Positive and Negative Syndrome Scale (PANSS) factor-analytically derived negative symptom domain,[20] and the PANSS summed negative scale.[21] A study of consecutively admitted hospitalized patients found modest negative correlations between severity of negative symptoms and performance on list-learning, paired-associate and paragraph memory, set shifting, and verbal fluency.[22] Associations between negative symptoms with verbal fluency and set shifting deficits are found in clinically stable patients as well.[23] Somewhat different correlations with negative symptoms were found in higher functioning (ie, community-dwelling) schizophrenia patients, where verbal learning and verbal fluency, but not set shifting, as measured with the Trail Making Test, part B, were correlated with negative symptom severity.[24] However, some of the variance in these patterns of correlations may be related to the negative symptom definition and rating methods employed. This level of correlation has been supported by the results of large-scale meta-analytic studies, in that the Heinrichs and Zakzanis[25] review concluded that symptom severity has a small to moderate correlation with severity of neuropsychological impairment.

Possible Factors Influencing Cross-Sectional Correlations Between Negative and Cognitive Symptoms

Definitions of Negative Symptoms. There are several factors that influence the correlation between negative and cognitive symptoms in schizophrenia. Possibly the most robust of these influences is that of the definition of negative symptoms employed. As noted above, the breadth of the definition of negative symptoms ranges quite widely, from experimental measures of affect, emotion, and communication, to clinical rating scales that designate cognitive impairments and functional deficits as negative symptoms. Further, some definitions of negative symptoms carefully distinguish between negative symptoms that are primary and those that could be accounted for by external factors, such as the severity of positive symptoms or medication side effects.

Patients who meet criteria for the deficit syndrome, a carefully defined syndrome where extraneous causes of negative symptoms are excluded, appear to have a specific signature of cognitive impairments. Deficit patients had greater impairment than nondeficit patients in functions typically attributed to the frontal and parietal cortex and similar patterns of performance on tests sensitive to dysfunctions in the temporal cortex.[26] Thus, the correlation between negative symptoms and cognitive impairments may be contingent on primary versus secondary nature of the negative symptoms seen in the patients. This may be consistent with the results of Lysaker et al.,[9] who found that the stable negative symptom severity, as is seen in the deficit syndrome, was associated with increased cognitive impairments and found less potential influence of extraneous factors such as drug abuse.

One of the most commonly used clinical rating scales for schizophrenia is the PANSS.[27] This scale examines 30 different symptoms of schizophrenia. Interestingly, several aspects of the illness that clearly appear to be cognitive in nature (eg, deficits in abstract thinking, stereotyped thinking, poor attention) are defined as negative or general symptoms of schizophrenia by the PANSS and contribute to total scores on those symptom dimensions. In addition to designating several cognitive features of schizophrenia as negative symptoms, the PANSS does not have an extensive assessment of reduced verbal productivity, as compared with other clinical rating scales, which might also impact its correlational structure. Factor analytic studies have not supported the negative symptom factor of the PANSS as initially defined. However, a negative symptom factor emerges from typical exploratory factor analyses of the PANSS, at least one of which found that the best-fitting model required exclusion of the difficulty in abstract thinking item.[28]

The other commonly used rating scale of negative symptoms, the SANS,[29] also has some item definitions that have the potential to impact correlations with NP performance. For instance, the SANS designates a number of social, occupational, and educational performance deficits as negative symptoms. Since NP performance has been shown to be consistently related to impairments in social, occupational, and educational outcomes, designation of these behavioral deficits as negative symptoms has the potential to influence the correlation with overall negative symptom severity. Further, the SANS also designates attentional abnormalities as negative symptoms. One of the problems with clinical ratings of cognitive symptoms on negative symptom scales is that clinicians' ratings of cognitive dysfunction in schizophrenia are often poorly overlapping with NP performance measures,[20,30] so it is unclear what clinicians might be rating.

Correlations between similar domains of cognitive abilities and negative symptoms can vary depending on the symptom rating scale used. For example, Berman et al.[23] reported that problem-solving deficits measured by the Wisconsin Card Sorting Test (WCST), as well as impairments in processing speed, were correlated with the severity of PANSS negative subscale scores. Verbal fluency deficits did not appear to be correlated with PANSS negative subscale scores in that study. In contrast, other research has found that negative symptoms measured by the SANS correlate with deficits in executive functioning, estimated by WCST performance, verbal memory, and verbal fluency.[31] While Bozikas et al.[24] found that memory deficits and semantic knowledge were correlated with negative symptoms rated by the PANSS, they found that executive functioning was not. One possibility for these differences in correlations across studies is that the SANS has a more extensive assessment of verbal underproductivity (ie, alogia) than the PANSS, which uses a single item. Further, patients who refuse to talk because they are concerned about the content of the information are rated the same on this PANSS item as patients whose failure to talk is a not due to refusal.

Rating Method. Most rating scales for negative symptoms require inferential ratings of various negative symptoms, including affective experience and motivation, and these inferences are necessarily limited by the patients' level of communication, meaning that patients who are less verbally productive may also be difficult to rate on other symptoms. It is possible, however, to measure affective expression directly. Direct measures have the benefit of not relying on self-report and not requiring awareness of illness. Direct studies of emotional changes relevant to negative symptoms have found results that suggest minimal correlations between direct measures of emotional experience and neuropsychological performance.

For instance, Blanchard, Kring, and Neale[32] found essentially no significant correlations between any aspects of a neuropsychological assessment battery and direct

measures of facial affect expression. These affect expression measures, however, were found to be well correlated with other direct experimental measures of affect expression and perception. This study was particularly systematic in that neuropsychological measures of left and right hemisphere functioning, as well as frontal lobe functioning, were included. Alpert et al.[33] suggested that the general patterns of correlation between cognitive impairments and negative symptoms may be related to the tendency of raters to focus on global clinical features and then rate the individual items in the rating scales according to their global impression, instead of the reverse (ie, generating a global scale from the sum or average of the individual items). If this is the case, raters may be sensitive to global impairment features in the emotional/negative symptom domains or in the cognitive impairment domains, influencing their ratings in both areas and subsequent correlations as well.

Specificity of the Negative/Cognitive Relationship. It may be the case that symptoms other than negative symptoms are most strongly correlated with NP performance as well. Bilder et al.[34] reported that performance scores on a comprehensive neuropsychological battery were more strongly correlated with disorganized than with negative symptoms. Similarly, Liddle[35] found that disorganization syndrome was associated with different cognitive impairments than the psychomotor poverty syndrome, suggesting that negative and cognitive symptoms are not intrinsically liked.

Longitudinal Studies. As noted by Addington[36] five years ago, there are relatively few longitudinal studies of the correlations between negative and cognitive symptoms. The few studies that have been published are largely based on a large cohort of very severely ill, chronically institutionalized patients in the Mt. Sinai cohort. These data may not be representative of the course of negative symptoms in better outcome patients. Still, there may be some information to guide our evaluation of the relationships between negative and cognitive symptoms. In the first, we[37] reported that negative and cognitive symptoms were correlated with each other at each of 2 assessments in a 1-year follow-up, with no significant cross-lagged correlations between the two variables. One reason for the lack of longitudinal correlations may be the stability and resulting lack of variance of both of these variables across the short follow-up: there is little change and little possibility of correlation of the change scores. Longer follow-ups (up to 6 years), where patients declined in the cognitive functioning, again found the same pattern, however: significant correlations at each of the successive assessments and little correlation over time.[38–39] In a 6-month follow-up study of much better outcome patients, Hughes and colleagues[40] found essentially the same results: correlations between negative symptoms and cognitive deficits at time 1 but a failure of negative symptom change to predict cognitive change at follow-up, regardless of how the negative symptom dimension was defined. In a treatment study of initially clinically stable patients with schizophrenia,[41] clinical improvements in negative symptoms were detected, as were improvements in NP performance. While negative symptom changes were correlated with other aspects of clinical change (ie, positive and disorganized symptoms, hostility), there was no correlation between improvements in negative symptoms and cognitive performance. Thus, the limited data from longitudinal studies of various samples of patients with schizophrenia, as well as a single treatment study, have indicated that changes in cognition and negative symptoms can be dissociated. Interestingly, functional declines were associated with cognitive declines in the studies of poor outcome geriatric patients, while the course of negative symptoms was uncorrelated with functional declines.

Relationships with Distal Outcomes. Several previous cross-sectional studies have suggested that differential correlations between negative and cognitive features of the illness and everyday outcomes can be identified. In fact, in 2 separate studies, it has been shown that when negative and cognitive symptoms are considered simultaneously, cognitive impairment is more strongly correlated with real-world outcomes than are negative symptoms.[42,43] As noted above, cognitive change, but not negative symptoms change, predicted functional decline. While this finding might have important implications for improving functional outcomes, there may also be implications regarding the relationship between negative and cognitive symptoms.

A regression result showing that one variable is much more important as a predictor than the other could be obtained if negative and cognitive symptoms were actually very highly correlated, or even alternative measures of the same ''true construct'' (see Models 1 and 2). To produce this outcome, which was obtained with regression analyses, the measure of negative symptoms would need to be only slightly less correlated with everyday functioning than cognitive impairments. It is also possible that negative and cognitive symptoms could be uncorrelated in ''true'' severity with each other, with other correlational relationships a statistical artifact. This outcome would be expected if Model 4 was true, and the correlation between negative and cognitive symptoms was induced by their joint, but independent, associations with a distal measure such as real-world functional outcomes. Finally, it is possible that negative and cognitive symptoms have different patterns of influence on real-world outcomes. It could be that NP performance is associated with the *ability* to perform everyday living skills, while negative symptoms are associated with the *likelihood* of performing these skills.

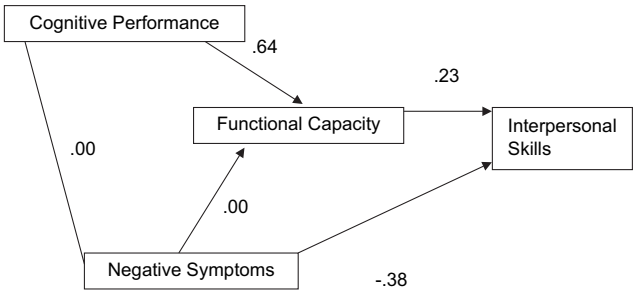

Fig. 2. Negative Symptoms, Cognitive Performance, and Everyday Skills Performance. *Source*: Bowie et al.[44]

We[44] used confirmatory path modeling to examine the partial correlations between several different aspects of schizophrenia, including ratings of everyday functioning generated by case management personnel, performance on a comprehensive NP battery, scores on a performance-based measure of functional skills (the UCSD performance-based skills assessment [UPSA][45]), positive and negative symptoms measured by the PANSS, and self-reported depression. Best-fitting path models were developed and used to determine the nature of the relationship between these features of schizophrenia and everyday functioning. While these results are presented in detail elsewhere, they were informative in terms of providing some intriguing insights about our 4 models of cognitive and negative symptoms. Zero-order correlations between PANSS negative symptoms and NP performance were quite similar to those reported in previous studies (r = –.32). However, when the simultaneous relationships between these variables were examined with path modeling, a more complex picture emerged. The most consistent predictor of several different aspects of everyday functioning was skills competence (ie, the capacity to perform these skills in an analog setting). However, negative symptoms were directly correlated with everyday functioning in the domains of social performance and everyday life skills. In the path model for social functioning (Figure 2), it can be seen that when the path coefficients between NP performance, functional capacity, and negative symptoms are examined, there is no relationship between negative symptoms and either NP performance or functional competence.

These findings suggest not only that negative and cognitive symptoms are discriminable, but that they also have considerably different functional implications. The moderate zero-order correlation detected prior to path analysis may be explained by correlations with distal outcomes. More important, however, is the functional implications of these findings. NP performance was correlated with the ability to perform everyday living skills, while negative symptoms were related to the likelihood of performing these skills.

Conclusion: Evaluation of the Models

Very few, if any, of the studies reviewed here provide direct or comprehensive evidence about all of the 4 possible models of the relationship between cognitive and negative symptoms in schizophrenia. However, this discussion shows that the existing studies provide stronger support for Models 3 and 4 than for Models 1 and 2. In the following sections we summarize the evidence pertaining to each model and indicate the kind of data that is still needed in order to further assess it.

Model 1

Evaluation. Model 1 posits that cognitive and negative symptoms are 2 alternate or nested manifestations of the same basic process. The results of many studies of the onset, temporal course, relations to other aspects of the illness, and cross-sectional correlations between negative and cognitive symptoms appear on the surface to support this model. Much of the data from these studies, however, suggests that, while both cognitive and negative symptoms are related to other aspects of the illness and occur during the same time frame, the correlation between negative and cognitive symptoms is limited in magnitude. Data from longitudinal studies, as well as factor and path analytic studies, suggest that the 2 symptom dimensions can change independently of the other due to either treatment or to the natural course of the illness. The basically small level of correlation between cognitive and negative symptoms argues that it is unlikely that they are actually the same phenomenon and suggests that more complex models may be required to explain the association between these models.

Data Needed. More information is needed about the reliability and stability characteristics of the measures used to assess negative symptoms. Long-term data regarding the general stability of negative, as compared with cognitive, symptoms would provide information regarding the possibility that these are not separable entities.

Model 2

Evaluation. Model 2 puts forward the assumption that cognitive and negative symptoms are indeed separate features of schizophrenia but that they share similar underlying etiology. An example of such an etiology could be a dysfunction of the thalamus, wherein abnormal activity in this region would result in cognitive impairments due to influences on temporal lobe projections and negative symptoms through influences on frontal lobe projections. This model appears to be supported by the results of cross-sectional studies that find moderate correlations between the severity of these 2 symptom dimensions and consistent correlations over time in longitudinal studies. While the lack of longitudinal correlations in

changes between the 2 domains appears not to support the model, it should be noted that many illnesses with common causes, such as diabetes and coronary artery disease, have a variable course with not all symptoms of the illness being present consistently over time.

Data Needed. More studies of the joint course of negative and cognitive symptoms would provide information about the linkage between these two symptom domains. Studies of changes in brain structure or function and their correlations with changes in these symptom domains would be helpful as well.

Model 3

Evaluation. Like Model 2, Model 3 speculates that negative and cognitive symptoms represent 2 separate dimensions of the illness. Model 3, however, posits that each dimension has its own etiology, which in turn might be related to the etiology of the other dimension due to outside influences. An example of this type of cause would be distributed neuropathology, such as white matter abnormalities, which would differentially affect brain regions depending on the normal density of white matter. Thus, pathological changes in completely separate brain regions could be the cause of the negative and cognitive symptoms, but the underlying etiologies are related to each other. We believe that Model 3 is supported by existing studies and holds promise for explaining the observed relations between cognitive and negative symptoms in schizophrenia. First, most longitudinal studies suggest a similar yet not overlapping course of negative and cognitive symptoms. Second, recent studies suggest that cognitive performance is at least as strongly related to disorganized symptoms as to negative ones, indicating that cognitive impairments may be related in severity to multiple features of the illness. Finally, negative and cognitive symptoms appear to change at different rates in studies of both the progression and treatment of the illness, but the overall level of impairment in each of these domains tends to be correlated at successive longitudinal assessments.

Data Needed. In order to discriminate Model 3 from Model 2, similar data would be required. Identification and longitudinal assessment of putative etiological factors may provide the data required for the critical tests of these 2 models, combined with carefully defined measures of negative symptoms and NP tests.

Model 4

Evaluation. Model 4 views the 2 symptom dimensions as distinct from each other, with independent etiologies. However, unlike Model 3, Model 4 attributes the observed correlations between negative and cognitive symptoms to measurement issues and correlations with distal measures. The fact that deficit syndrome patients show a different signature of cognitive impairments than nondeficit patients is also consistent with this interpretation: it may be that the deficit syndrome truly reflects a different etiology for the illness and for the associated cognitive impairments as well. Finding that objective measures of emotional experience are uncorrelated with cognitive symptoms is also consistent with this model. This model is supported by more recent path analysis studies that demonstrate that the zero-order correlation between negative symptoms and cognitive impairments is explained by correlations with distal outcome measures.

Data Needed. Evaluation of this model will be facilitated by treatments that enhance cognitive functioning. These interventions, either pharmacologically or rehabilitation oriented, may serve as a critical test of the discriminability of negative and cognitive symptoms.

In sum, negative and cognitive symptoms of schizophrenia appear to be correlated but potentially separable domains of the illness. While cross-sectional studies suggest moderate relationships, path modeling suggests that these 2 symptom domains may have critical differences in their functional relevance and that their cross-sectional correlation could be related to independent relationships with other features of the illness. As the definition of the negative symptoms construct appears to influence the correlation with cognitive performance, innovations in the assessment of negative symptoms may be required in order to truly answer the questions regarding the relationship of negative symptoms and other aspects of schizophrenia.

Acknowledgments

This research was supported by NIMH Grant Number MH 63116 to Dr. Harvey, the Mt. Sinai Silvio Conte Neuroscience Center (NIMH MH 36692; KL Davis PI), and the VA VISN 3 MIRECC.

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