

ABSTRACT

Title of Document: TAXOMETRIC ANALYSIS OF NEGATIVE SYMPTOMS IN AN INTERNATIONAL SAMPLE OF TEN COUNTRIES

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Negative symptoms have emerged as a replicable factor of symptomatology within schizophrenia. Although rating scales provide assessments along dimensions of severity, categorization of a negative symptom subtype is typically concluded. Despite an accumulation of findings that support categorical conceptualization, the data are also consistent with a dimensional-only model where negative symptom subtypologies simply reflect an extreme on a continuum of severity. Previous studies (Blanchard, et al, 2005) have used taxometric statistical methods to confirm the existence of a negative symptom subtype; however, the nature of taxometric methods requires replication (Waller & Meehl, 1998). The current investigation is a taxometric analysis of the World Health Organization Ten-Country Study of Schizophrenia. Data from a subset of 694 individuals were analyzed using the taxometric methods of maximum covariance analysis (MAXCOV) and mean above minus below a cut (MAMBAC) and a latent class with a base rate of approximately .14 - .16 was

identified.

TAXOMETRIC ANALYSIS OF NEGATIVE SYMPTOMS IN AN
INTERNATIONAL SAMPLE OF TEN COUNTRIES

By

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Dedication

This is dedicated to my husband, Steve Wu. He has stood with me and provided unending support. throughout my graduate school career. I love you.

Acknowledgements

I would like to acknowledge the help of my adviser, Jack Blanchard in helping me with this writing process. I would also like to acknowledge the help and support that my classmates have provided me with throughout my graduate school career. Finally, I'd like to acknowledge the love of my family; without their help and support, this would have been a much more difficult journey.

Table of Contents

List of Tables	v
List of Figures	vi
Chapter 1: Introduction	1
Chapter 2: Negative Symptoms in Schizophrenia	3
Section 1: The Concept of Negative Symptoms in Schizophrenia	3
independent of one another, it is possible for them to co-occur.	5
Section 2: The Structure of Negative Symptoms in Schizophrenia.....	5
Section 3: Course and Symptom Correlates	7
Section 4: Criticisms of the Current Conceptualization	11
Chapter 3: Rationale for the Current Study	15
Chapter 4: Method	16
Section 1: The WHO Ten-Country Study of Schizophrenia	16
Section 2: Measures	16
Section 3: Statistical Method	17
Section 1: Factor Analysis	19
Section 2: Mean Above Minus Below A Cut	21
Section 3: Maximum Covariance.....	23
Section 4: Group Comparisons	27
Section 5: Post Hoc Comparisons.....	31
Chapter 6: Discussion	35
Bibliography	44

List of Tables

Table 1: <i>PSE Items Related to Negative Symptoms</i>	20
Table 2: <i>Factor Loading of the PSE Negative Symptom Items</i>	21
Table 3: <i>Base Rates Calculated for Individual Curves and for Average of the Curves</i>	27
Table 4: <i>Group Comparisons</i>	27
Table 5: <i>PSE Items Related to Depression</i>	28
Table 6: <i>PSE Items Related to Positive Symptoms</i>	29 - 30
Table 7: <i>Correlation Between Depression and Negative Symptoms Across Sites</i>	32
Table 8: <i>Correlation Between Negative Symptoms and Depression: Individual Items</i>	33
Table 9: <i>PSE Syndrome Associated with Each Item</i>	39

List of Figures

Figure 1: <i>MAMBAC (Mean Above Minus Below a Cut) Curves for Factors 1 and 2</i>	22
Figure 2: <i>MAXCOV (Maximum Covariance) Curves for Each Item and for the Mean Across All Pairings</i>	24 - 26

Chapter 1: Introduction

Schizophrenia is a serious mental illness that affects people world wide. It is recognized in every culture with an estimated prevalence rate of between 1.4 and 1.6 per 1000 people (Jablensky, 2000). The diagnostic criteria for schizophrenia include delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms (including flattened affect, apathy, and reduced speech output; American Psychiatric Association, 2000). Schizophrenia is associated with profound functional impairment, including joblessness (for a comprehensive review, see Marwaha & Johnson, 2004) and homelessness (for a review, see Folsom & Jeste, 2002). The estimated annual cost of the illness in the United States has been estimated at \$32.5 billion (Rice & Miller, 1998). These costs are comparable to the annual costs of depression-a far more prevalent illness (Hu, 2006).

Despite many years of intensive study, the causes of schizophrenia remain a mystery. One of the single biggest reasons for this failing is the heterogeneous nature of the illness. The presentation of schizophrenia can vary widely between patients. One patient can present with flagrant hallucinations and delusions, while another can appear with disorganized speech and inappropriate affect. Yet both of these individuals will receive a diagnosis of schizophrenia.

The subtypes of schizophrenia recognized by the American Psychiatric Association are an attempt at reducing this heterogeneity, by grouping patients based on similar characteristics (i.e. – paranoid delusions, disorganized thinking, and catatonic behavior; [American Psychiatric Association, 2000]). However, these categories have been found to have limited temporal stability (Fenton & McGlashan,

1991) which has reduced their utility in this regard. The consequences of this heterogeneity are not trivial and have lead directly to a poor understanding of the genetic etiology of the illness.

Despite the high heritability of schizophrenia (Owen, O'Donovan, Gottesman, 2002) scientists have been unable to determine the genetic underpinnings of the illness (DeLisi, 1997). Jablensky (2006) notes that genetic heterogeneity (one illness caused by multiple genes) is a common cause for human illnesses. Further, he argues that other disciplines have had success in resolving genetic heterogeneity by dividing diverse illnesses into subtypes; something that schizophrenia researchers have attempted, but never satisfactorily resolved. In order to make substantive progress in understanding schizophrenia, valid subtypes must be identified. Persons (1987) has argued that the best way to delimit phenotypic heterogeneity is to divide the patient population based on a characteristic of interest so that patients with the symptom can be compared to patients without the symptom. This allows for a within-group comparison that controls for several variables that have a likely impact on results (such as a history of inpatient hospitalization and use of antipsychotic medications). Consistent with this approach, some have argued for the utility of negative symptoms as a valid subtype within schizophrenia (Buchanan & Carpenter, 1994) as these symptoms have important implications for the course of the illness (Kirkpatrick, Buchanan, Ross, & Carpenter, 2001) and show greater temporal stability than the DSM identified subtypes (Fenton & McGlashan, 1991).

Chapter 2: Negative Symptoms in Schizophrenia

Section 1: The Concept of Negative Symptoms in Schizophrenia

The symptoms of schizophrenia have been bifurcated into positive and negative symptoms. Positive symptoms are the most clearly recognized symptoms of schizophrenia and include hallucinations and delusions. Positive symptoms are often thought of as a release of higher order cognitive controls (Hughlings-Jackson, 1931). Negative symptoms, on the other hand, represent a deficit of normal functioning (Hughlings-Jackson, 1931). Typically, the symptoms that are recognized in this category include diminished emotional expression (flat affect), poverty of speech, lack of pleasure from social or physical stimuli (anhedonia), lack of drive (avolition), and apathy (McGlashan and Fenton, 1992). The consensus on this list of symptoms was hampered, in part, by a lack of reliable assessments for certain types of negative symptoms (Johnstone, 1989). However, with the introduction of measures such as Andreason's Scale for the Assessment of Negative Symptoms (SANS; Andreason, 1983), the validity of negative symptoms could be confirmed. Once accurate measurement tools were available, theories about the structure and causes of negative symptoms in schizophrenia began to develop rapidly. Two such theories of historical significance are Andreason's theory of positive and negative schizophrenia (1982) and Crow's theory of type I and type II schizophrenia (1980).

Andreason's early theory of positive and negative schizophrenia divided patients into three groups: positive, negative, and mixed. Patients with predominantly positive symptoms are categorized as having "positive schizophrenia." Similarly, patients with predominantly negative symptoms are categorized as having "negative

schizophrenia.” Patients that fit into both of these categories were diagnosed with mixed schizophrenia. Dividing patients into these groups yielded differences in various domains of functioning (Andreason & Olsen, 1982). Patients classified as having negative schizophrenia tended to have a longer length of hospitalization, have a lower score on the Mini Mental Examination, and a larger ventricle to brain ration (indicating general brain deterioration). (Although caution must be used with this last finding as it was not replicated in a later study (Andreason, Flaum, Swayze, Tyrell, & Arndt, 1990)).

While Andreason’s theory proved to be a useful early conceptualization of negative symptoms, a fundamental flaw quickly emerged. The mixed schizophrenia group was so large that the utility of this system came into serious question. What’s more, the temporal stability of the system was low as patients often switched between diagnostic groups (Andreason, et al., 1994). Although this early approach to categorizing positive and negative symptoms has been largely abandoned, the introduction of the SANS and SAPS scales has helped to move the field forward and led to further developments in the understanding of the structure of schizophrenic symptomatology.

Instead of merely describing the structure of negative symptoms, Crow (1980) suggested that positive and negative symptoms arose from different underlying neuropathologies. While maintaining that the fundamental liability for schizophrenia was the same across all subtypes (Crow, 1985), he believed that negative symptoms primarily arose from structural changes (arising from cell death) in the brain. These changes resulted in a syndrome with poor prognosis and poor drug response. Positive

symptoms, however, resulted from an increase in dopamine receptors, a claim supported by the effectiveness of antipsychotic medications in their treatment. Negative symptoms do not respond to these medications because antipsychotics do not affect their underlying cause. Because these two sets of symptoms are independent of one another, it is possible for them to co-occur.

Section 2: The Structure of Negative Symptoms in Schizophrenia

While these theories can be tested empirically, their development was based on clinical judgment and not necessarily on the empirically-determined structure of schizophrenic symptomatology. This complaint has also been made of the DSM (for a discussion see chapter two of Schmidt, Kotov, and Joiner, 2004). One of the tools for the statistical investigation of the relationship between positive and negative symptoms is factor analysis. If positive and negative factors emerge as separate factors, this bolsters the claim that these symptoms are, in fact independent; this then provides an indication that negative symptoms are not merely secondary to other symptoms.

In the factor analytic studies that have been conducted on the symptoms of schizophrenia, there is often great disagreement on the number of factors identified. Some of the first studies on the nature of schizophrenic symptoms found there to be two factors: positive and negative symptoms (Lewine, Fogg, & Meltzer, 1983; Kay, Opler, & Fiszbein, 1986). Subsequent models have identified three factors: positive, negative, and disorganized (which typically encompasses symptoms of formal thought disorder and bizarre behavior) (Palacios-Arus, Herran, Sandoya, Gonzalez de la Huebra, & Diez-Manrique, 1995; Grube, Bilder, & Goldman, 1998). Others have found two and three factor models to be inadequate and have instead proposed five

factor models encompassing positive, negative, relational or emotional disorder, disorganized, and excitement symptoms (Nakaya, Suwa, & Ohmori, 1999). However, as pointed out by Blanchard and Cohen (2006), while the number of factors does vary, negative symptoms consistently emerge as a separate factor. Thus, the results of factor analytic studies consistently indicate that negative symptoms represent a dimension that is separate from psychotic and affective symptoms and not merely secondary to them.

Given the above findings, the question then becomes whether individual differences in negative symptoms lie along a continuum or whether individual differences are best represented as categorical distinctions. Several theories have been outlined to describe categorical difference in the negative symptoms of schizophrenia; foremost among them is the deficit syndrome. This concept was introduced in 1988 by Carpenter, Heinrichs, and Wagman. Patients with the deficit syndrome are characterized as having “primary and enduring” negative symptoms. The distinction between primary and secondary symptoms (which was previously discussed) is made based on whether the negative symptoms are endogenous to the illness (primary) or due to some external factor: such as medication, depression, or neurocognitive dysfunction (secondary). The “enduring” requirement (12 months and/or present during periods of stability) is made to ensure that the symptoms designated as primary truly represent endogenous features. If a symptom persists over time, then the clinician can be reasonably assured that this symptom is, in fact, not due to secondary source. Symptoms sufficient for a diagnosis of the deficit syndrome include restricted affect, diminished emotional range, poverty of speech, curbing of interests,

diminished sense of purpose, and diminished social drive (Kirkpatrick, Buchanan, McKenney, Alphas, & Carpenter, 1980). Several lines of evidence exist to support the categorical model of negative symptoms. Specifically, negative symptoms have been found to be informative in regards to course, prognosis, and other aspects of the schizophrenia illness.

Section 3: Course and Symptom Correlates

Several different important outcomes have been found to be associated with negative symptoms. One clinically relevant correlate of negative symptoms is the patient's current level of functioning. In a study of seven measures of negative symptoms, Fenton and McGlashan (1992) found that all of these measures yielded findings indicating that the more severe the patient's negative symptomatology the worse the long-term outcome. However, as pointed out by Palacios-Arus, et al. (1995), care must be taken because one of the most commonly used measures of negative symptoms (the SANS) may share item content with certain outcome measures. However, when item content is controlled, there remain many studies that find correlations between negative symptoms and functional outcome measures. Several such studies have found that patients with pronounced negative symptoms have a reduced ability to care for themselves and live independently once released from the hospital (Dickerson, Ringel, & Parente, 1999; Moller, Bottlender, Wegner, Wittmann, & Straub, 2000). In addition, ability to work (specifically competence, ability to be supervised, and motivation to work) has also been found to be impaired in these patients (Suslow, Schonauer, Ohrmann, Eikelmann, & Reker, 2000). Negative symptoms have also been found to correlate with worse social functioning

(Horan & Blanchard, 2003; Blanchard, Horan, & Collins, 2005; Milev, Ho, Arndt, & Andreason, 2005).

While impairment from negative symptoms is apparent after the onset of illness, other results suggest that this impairment is a part of a more enduring profile of the illness. Premorbid adjustment has been found to be worse in patients with elevated negative symptoms (McGlashan & Fenton, 1992; for a review, see Walker and Lewine, 1988). Studies have found that negative symptoms identified after the onset of the illness are associated with a premorbid pattern of gradual withdrawal from interests and peer relationships (Garver, Nair, & Christensen, 1991) which is evident in early childhood (Horan & Blanchard, 2003; Buchanan, Kirkpatrick, Heinrichs, & Carpenter, 1990). Such a history of impairment is indicative of an insidious onset and is evidence that negative symptoms are enduring characteristics of the illness (Andreason, Flaum, Swayze, Tyrell, & Arndt, 1990).

Given the clinical significance of negative symptoms, the concern then becomes how best to treat these symptoms. Current antipsychotics are largely ineffective in treating negative symptoms (Buchanan, Breier, Kirkpatrick, Ball, & Carpenter, 1998; Malaspina, Goetz, Yale, Berman, Friedman, Tremeau, et al, 2000; Filbey, Holcomb, Nair, Christensen, & Garver, 1999). Studies that report improvement in negative symptoms typically find that there are improvements in secondary negative symptoms (symptoms that are not endogenous to the illness but are instead due to other factors such as drugs, psychosis, or depression) but the core set of negative symptoms remain unaffected (Garver, Holcomb, & Christensen, 2000). Concern over the ineffectiveness of current antipsychotic therapies has

culminated in a call to action by the NIMH, FDA, and the drug industry. In 2006, an NIMH consensus workshop was held to examine the problem of enduring negative symptoms (Kirkpatrick, Fenton, Carpenter, & Marder, 2006). Experts at this meeting concluded that negative symptoms represent a currently unmet therapeutic need and that further study into the nature of negative symptoms and a continued search for potential treatments represent important goals for the scientific community.

The fact that antipsychotics are ineffective in treating negative symptoms gives evidence to theories such as Crow's (1980, 1985) which state that positive and negative symptoms arise from different biological processes. Because negative symptoms are not responsive to medication that is effective in treating positive symptoms, it is likely that they are arising from different underlying neurotransmitter processes. As shown below, further evidence for separate pathophysiological pathways can be found in neurocognitive functioning, differences in eyetracking patterns, and in genetic liability to the disease.

Neurocognitive functioning is considered to be generally impaired amongst people with schizophrenia (for a review, see Bowie & Harvey, 2005). However, studies have shown that these cognitive deficits are more profound among patients with elevated negative symptoms (Buchanan, Strauss, Kirkpatrick, Holstein, Breier, & Carpenter, 1994). Studies have found that negative symptoms are correlated with worse performance on measures of frontal lobe functioning (Horan & Blanchard, 2003; Brazo, Delamillieure, Morello, Halbecq, Marie, & Dollfus, 2005), sensory integration (Arango, Kirkpatrick, & Buchanan, 2000), and attention (Buchanan, Strauss, Breier, Kirkpatrick, & Carpenter, 1997). This pattern of neurocognitive

deficits continues to be evident in elderly patients with prominent negative symptoms (Harvey, Lombardi, Leibman, White, Parrella, Powchik, & Davidson, 1996). Despite the significant relationship between neurocognitive deficits and negative symptoms, negative symptoms are not merely secondary to neurocognitive deficits (Kirkpatrick, Fenton, Carpenter, & Marder, 2006). Studies have found that changes in cognition do not translate into changes in negative symptoms beyond the impact of antipsychotic treatment (Bark, Revheim, Huq, Khalderov, Ganz, & Medalia, 2003). Similarly, changes in negative symptoms do not lead to changes in neurocognitive deficits (Bell & Mishara, 2006; Hughes, Kumari, Soni, Das, Binneman, Drozd, et al., 2002).

In addition to cognitive impairments, negative symptoms are associated with other indicators of neuropathology. Elevations in negative symptoms have been correlated with progressively enlarging ventricles (Garver, Nair, Christensen, Holcomb, Ramberg, & Kingsbury, 1992); however, further research has suggested that ventricular size is unstable and varies between periods of psychosis and remission (for a review, Garver, Holcomb, & Christensen, 2000). Negative symptoms have also been associated with reduced cerebral blood flow in the frontal lobes (Liddle, Friston, Frith, Hirsch, Jones, & Frackowiak, 1992) which may be related to neurocognitive dysfunction. Finally, it has been postulated that negative symptoms are associated with abnormal smooth pursuit eye movements (Ross, Thaker, Buchanan, Kirkpatrick, Lahti, Medoff, et al., 1997) and evidence has been found to support this (Ross, 2000). These studies indicate that there is a great deal of generalized brain dysfunction associated with negative symptoms in schizophrenia.

Findings that the genetic underpinnings associated with negative symptoms

are different from those associated with other aspects of schizophrenia provide some of the best evidence for different disease etiologies. Some studies have found that patients with a family history of schizophrenia were more likely to display elevated negative symptoms (Malaspina et al., 2000). More commonly, studies find that when patients with prominent negative symptoms have affected family members, these family members show a similar pattern elevated negative symptoms (Filbey, et al., 1999; Garver, et al., 2000). Other studies have found that social withdrawal in relatives of patients with schizophrenia is a good predictor of negative symptomatology in the proband (Kirkpatrick, Ross, Walsh, Karkowski, & Kendler, 2000). These studies suggest that negative symptoms can be, at least in part, inherited and that this heritability is distinct from that of other types of schizophrenic symptomatology.

Section 4: Criticisms of the Current Conceptualization

As can be garnered from the lines of research presented, negative symptoms are an important feature of the illness of schizophrenia. Additionally, evidence is available to support the concept of a categorically distinct subgroup of individuals with schizophrenia who show elevated levels of negative symptoms, as represented by the deficit syndrome. However, the concept of the deficit syndrome suffers from a major weakness, namely that it is based on arbitrary criteria. For instance, in the Schedule for the Deficit Syndrome (SDS; Kirkpatrick, Buchanan, Alphas, McKinney, and Carpenter, 1989) the first criteria required for a diagnosis of deficit schizophrenia is two or more negative symptoms; which, while based on clinical judgment, represents an arbitrary choice. In addition, to meet the second criterion, these

symptoms must have been expressed for at least the past year. The authors' intention is to ensure that these symptoms are stable and trait-like; however, the time frame of twelve months is, again, purely arbitrary. Instead, it is important that criterion such as duration of illness or number of negative symptoms be identified empirically.

In addition to the criteria of the deficit syndrome representing arbitrary cutoffs, there is also difficulty in the claim that the authors make about the categorical nature of this grouping of symptoms. The deficit syndrome is explicitly conceived of and assessed as categorical (Carpenter, et al., 1988). However, the observable structure of a phenomenon is dependent, in great part, on the tools which are used to measure it (Ruscio & Ruscio, 2004a). It is possible that the deficit syndrome criteria identify a group of individuals that receive extreme scores on the SDS. When compared to individuals that receive low scores, this group gives the appearance of being categorical. Such issues are not trivial and affect the way that disease models are tested (Haslam, 2003a). In order to reduce the heterogeneity of schizophrenia and uncover the divergent etiologies of the illness, valid subtypes of the illness must be identified. Using faulty divisions hampers our understanding of the illness and retards progress. Therefore, it is important to uncover true latent classes within the illness of schizophrenia in a systematic and scientific way.

Taxometrics are a group of statistical techniques that allow for the quantitative determination of whether the underlying structure of a phenomenon is continuous or categorical (taxonic). These analyses were developed and advocated for by Paul Meehl (Meehl, 1995). They allow for the uncovering of statistical relationships between variables that indicate natural boundaries between groups (Waller & Meehl,

1998). Taxometric methods have been shown to be superior to other forms of classification procedures (Waller & Meehl, 1998) and have been found to be more sensitive to taxonic results than other methods (Cleland, Rothschild, & Haslam, 2000).

These methods have been successfully used to investigate the taxonic nature of various psychopathologies. They have been applied to the investigation of narcissistic personality disorder (Foster & Campbell, 2007), borderline personality disorder (Clifton & Pilkonis, 2007), and antisocial personality disorder (Buchholz, Hesselbrock, Heath, Kramer, & Schuckit, 2000); as well as a variety of other personality disorders (Haslam, 2003b). These methods have also been applied to Axis I disorders such as depression (Baldwin & Shean, 2007) and anxiety (Bernstein, Zvolensky, Norton, Schmidt, Taylor, Forsyth, et al., 2007). Recently, they have also been applied to the investigation of negative symptoms.

In a 2005 study, Blanchard, Horan, and Collins investigated the latent structure of negative symptoms within a group of 238 patients with a diagnosis of schizophrenia, schizoaffective disorder, or schizophreniform disorder. The authors predicted that approximately 25-30% of the patients with schizophrenia in this group would be classified in the negative symptom taxon, which is in line with previous predictions for the deficit syndrome (Kirkpatrick, et al., 2001). In addition, it was predicted that proportionately more males would be found within the taxonic group and that individuals in this group would evidence worse social functioning. These investigators found that there was a latent class, and that it represented about 28-36% of the sample. In addition, as predicted, individuals identified as taxonic were more

likely to be male and exhibited worse psychosocial functioning; however, the two groups did not differ in terms of psychotic symptoms.

Results from this study are encouraging, but as the authors note, there are several limitations that must be addressed. First, the sample size of 238 is small, and towards the lower end of what is recommended for these analyses. Typically, in order to conduct a latent class analysis, a sample size of at least 300 is recommended (Meehl, 1995). In addition, the nature of taxometric analysis requires replication before confidence can be had in the results (Waller & Meehl, 1998), something the authors readily acknowledge. In addition, the sample in this paper was nonrepresentative.

Patients in this study were chronically ill and stable on antipsychotic medications. Other samples must be investigated to verify the generalizability of the sample. Finally, if the expectation is that the negative syndrome is due to biological underpinnings of the disease, then it should be demonstrable in an international study and not only evident in a single country.

Chapter 3: Rationale for the Current Study

The purpose of this study is to investigate the latent structure of negative symptoms in large representative sample of individuals with schizophrenia. The World Health Organization study, the Determinants of Outcome of Severe Mental Disorders was an extensive study of 1,379 patients seeking first-time treatment for severe mental illness in ten different countries. Data from this study will be subjected to taxometric methods in an attempt to examine the following hypotheses: 1) that a negative symptom taxon does exist; 2) that this subtype represents approximately 25-35% of the sample; 3) in agreement with the deficit syndrome, that patients in this taxon will have lower rates of depression and be more likely to be male; and 4) that there will be no difference in the severity of psychotic symptoms between patients in the taxon and those that are not.

Chapter 4: Method

Section 1: The WHO Ten-Country Study of Schizophrenia

From 1978-1984, the World Health Organization began an extensive epidemiological study of schizophrenia. This study was known as the Determinants of Outcome of Severe Mental Disorders. The investigation took place at twelve different sites in ten different countries. Participants were recruited from India, Colombia, the United States, Denmark, Japan, the United Kingdom, Ireland, the Czech Republic, Nigeria, and Russia. After initial screening, 1,379 individuals were included in the study. Follow-ups were conducted at two and ten years after the beginning of the study.

The objective of the study was to describe first-episode patients (or, at least patients who had never sought treatment before). Subjects were included in the study if they were between the ages of 15-54 years of age and had shown at least a) one definitive symptom of psychosis (i.e.-hallucinations, delusions, or bizarre behavior) or b) at least two symptoms that indicated probable psychosis (i.e.-significant social withdrawal). Participants were recruited from local area treatment centers (including local healers at some sites). Participants were excluded if there was evidence of organic brain dysfunction. Further, because this was a study of first episode patients, if the subject had ever previously sought treatment for the presenting complaint, they were not included in the study.

Section 2: Measures

Screening and clinical assessment was conducted only by extensively trained

psychiatrists or other qualified investigators (i.e.-a clinical psychologist or social worker). Tapes were exchanged between sites to ensure reliability and consistency (Jablensky, 1987).

Current psychopathology was assessed using the 9th edition of the Present State Exam (PSE) (Wing, Cooper, & Sartorius, 1974). This is a semi-structured interview that is designed to be administered by a trained psychiatrist (Cooper, Copeland, Brown, Harris, & Gourlay, 1977). The reliability of this instrument has been found to be acceptable (Wing, Nixon, & Mann, Leff, 1977; Luria, & McHugh, 1974), however it has been found to be reliant to a great degree on the training of the person administering the interview (Jablensky, 2002). For the WHO study, only trained psychiatrists were permitted to administer this interview. Again, reliability between interviewers was constantly assessed via reliability training and tape exchange between the sites (Jablensky, 1987).

Section 3: Statistical Method

Taxometric analysis is dependent upon the number of independent factors identified in the data; therefore, determination of the taxometric method to be used will be made after the number of independent factors in the WHO study have been identified. These factors will be identified via factor analysis. Likely candidates for this include: social withdrawal, blunted/flattened affect, and avolition.

MAMBAC

MAMBAC (mean above minus below a cut) only requires two factors. In this procedure one factor is used as an input variable and the other as the output. A cut is placed on the input variable. The mean on the other variable for all people who scored

at or above this point is created. A mean is also calculated for the people who score below this cut. Differences between the means are plotted. Like MAXCOV, MAMBAC provides a base rate estimate for taxon members.

The results are graphed. If the graph is U-shaped, this is an indication of a non-taxometric result. However, an inverted U-shaped graph represents a taxon. The idea being that a “bulge” or “peak” will result wherever there is a large difference between the two groups. If the bulges occur on the extreme ends of the graph (creating a U-shaped curve) then this means that there is a big difference between scores on either extreme of the curve and the rest of the group. However, if a true concave curve is found, then this is a taxon. It is expected that there will be a large difference between members of the taxon and people who are not in the taxon. (Using the example from before, people who score high on social withdrawal are expected to also score high on affective blunting.)

MAXCOV

Maximum covariance is a method that is designed to find the points of maximum correlation between at least three factors. One of the three factors will serve as an input variable. The covariance between this factor and the other factors are examined along their ranges. If a latent class exists, then the correlations will not be homogenous along the continuum of the anchor factor. Instead, a peak of maximum covariance will appear when there is an equal mix of the taxon and nontaxonic groups. When graphically represented, a clear peak will be visible. If no peak exists, then differences between the two groups are likely dimensional. Calculations of a base rate for the taxon group can be made based on where the peak is identified.

Chapter 5: Results

Section 1: Factor Analysis

In order to determine the number of independent factors to be used in the taxometric analyses, items from the Present State Exam were first analyzed using factor analysis (Table 1). Items measuring negative symptoms were culled from the PSE. These items were then submitted to a principle-components analysis using oblim rotation which yielded an eigenvalue scree plot with two independent factors.

To examine the stability of this two-factor solution, split-halves comparability coefficients were computed for the factor scores (Everett & Entekin, 1980). For this, the data set was randomly split into two groups (using the random split procedure in SPSS). Using the two-factor score coefficients from each matrix, factor scores were computed. The correlations between the two sets of factor scores were computed for the entire sample in order to examine the stability of this solution. Results indicated high split-half comparability coefficients which supported the two-factor solution (see Table 2).

Table 1
PSE Items Related to Negative Symptoms

Item Number	Title	Description
22	Recent loss of Interest	<i>There is a definite recent diminution in the subject's interests, either some interests have been dropped, or the intensity of interest has decreased. 'Recent loss of interest' means 'within the present episode of illness.'</i>
28	Social Withdrawal	<i>In the less intense form of the symptom, the subject does not seek company but does not refuse it when offered. In the more intense form, the subject actively withdraws and refuses company even when it is offered.</i>
36	Subjective Anergia and Retardation	<i>The subject feels that he has been slowed down in movement and/or has been markedly lacking in energy, compared to his usual condition. The symptoms may have lasted since the onset of the episode of illness but it is rated only on the past month.</i>
54	Loss of Affect	<i>The subject complains that he has lost the ability to feel and/or to express emotions. He can remember a time when he did have this capacity (though it might have been months or years ago) and is quite clear about losing it. The symptom may be associated with depression (particularly chronic depressive apathy) and other affects.</i>
108	Self Neglect	<i>Consider subject's degree of cleanliness, state of hair, make-up and clothes, whether shaven or not, etc. Only rate self-neglect if there is marked lack of attention to at least one of these aspects of personal appearance.</i>
110	Slowness and Underactivity	<i>The subject sits abnormally still or walks abnormally slowly or takes a long time to initiate movement. The symptom has to be fairly marked and unusual for the subject.</i>
128	Blunted Affect	<i>This term includes flatness of affect, emotional indifference and apathy. Essentially, the symptom involves a diminution or emotional response. The subject's face and voice are expressionless, he does not become involved with the interview or respond emotionally to changing topics of conversation, he seems indifferent when apparently distressing matters are discussed (whether or not delusional). There is a very limited range of emotional expression.</i>
130	Slowness of Speech	<i>There are long pauses before the subject answers and each word follows very slowly after the one before. Often the subject stops answering altogether and has to be reminded before starting again. The interview may be impossible to complete because the subject is so slow and cannot be hurried.</i>
134	Restricted Quantity of Speech	<i>The subject repeatedly fails to answer, questions have to be repeated, answers are restricted to the minimum often one word, or telegraphic style.</i>

Items which loaded onto factor 1 included self-neglect, slowness and underactivity, blunted affect, slow speech, and restricted quantity of speech. These items were interpreted to reflect behaviors which could be observed by the interviewer and are consistent with the symptoms of flat and blunted affect. Items with loaded onto factor 2 included loss of interest, subjective anergia and retardation, social withdrawal, and lost emotions. These items were thus interpreted to reflect

subjective experiences that had to be reported by the subject and are consistent with the symptoms of anhedonia and asociality.

Table 2
Factor Loading of the PSE Negative Symptom Items

Item	Factor 1	Factor 2
Item 22-Slow speech	.84	.33
Item 28-Slowness and underactivity	.71	.39
Item 36-Restricted quantity of speech	.66	.21
Item 54-Blunted affect	.39	.18
Item 108-Self-neglect	.25	-.01
Item 110-Loss of interest	.17	.69
Item 128-Subjective anergia and retardation	.16	.62
Item 130-Social withdrawal	.16	.52
Item 134-Lost emotions	.22	.45

Subscales were then calculated from these factors. Items receiving eigenvalues of .30 or higher were summed on the respective factor. Self neglect only received a loading of .25, but was placed on factor 1 in order to increase the number of items. Internal consistency reliabilities (Cronbach's alphas) were calculated for each of the factors. The alpha score for factor 1 was .69 and for factor 2 the alpha was .66.

Section 2: Mean Above Minus Below A Cut

The taxometric procedure MAMBAC (mean above minus below a cut) only requires two input variables. For this procedure, one variable serves as an input variable and the other as the output variable. Cuts are made along the input variable and the means on the other variable are calculated above and below that cut. The difference is then taken between those two means and plotted.

In order to conduct base rate analyses, a cut point was chosen to ensure that at least twenty individuals were present above and below each cut. This same criterion

was used on all MAMBAC analyses.

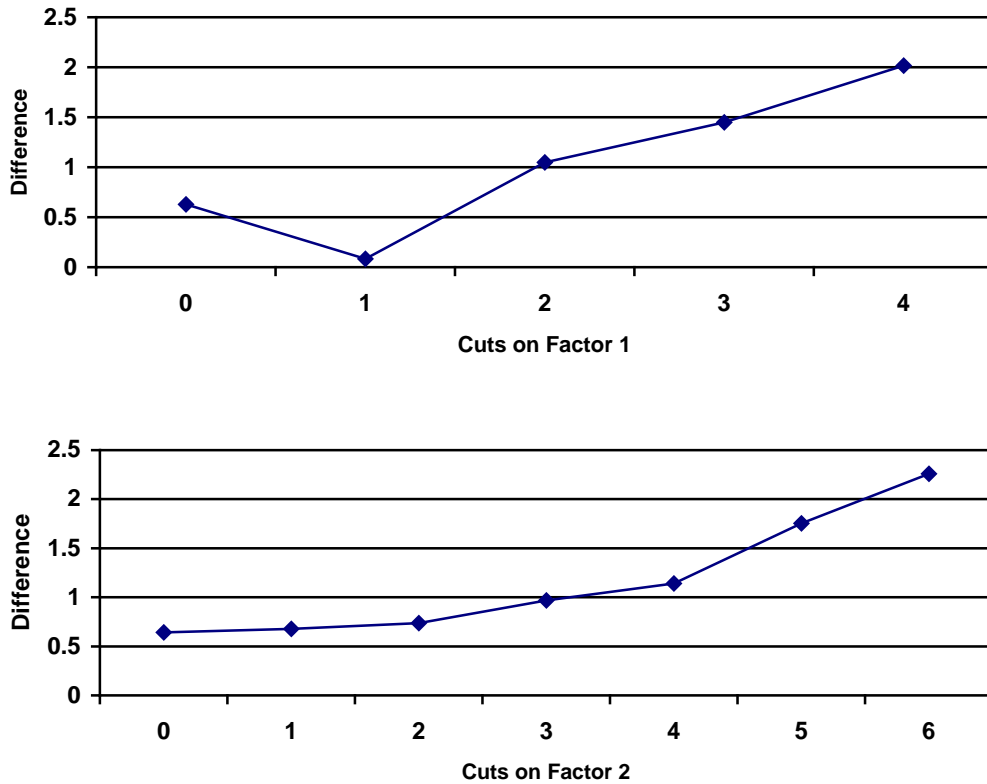


Figure 1: MAMBAC (mean above minus below a cut) curves for factors 1 and 2

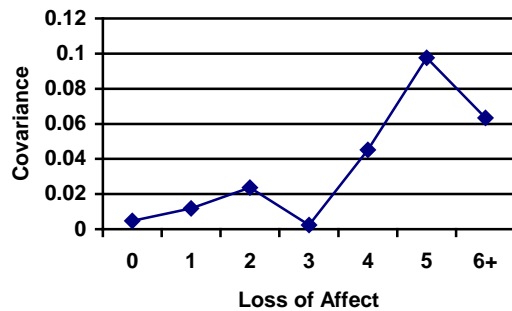
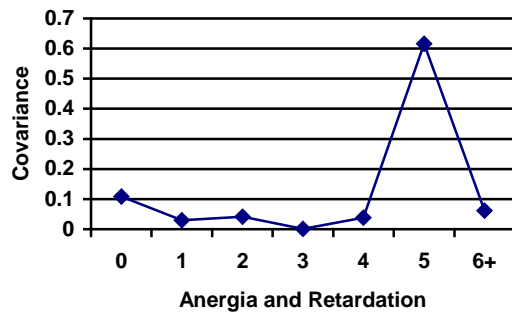
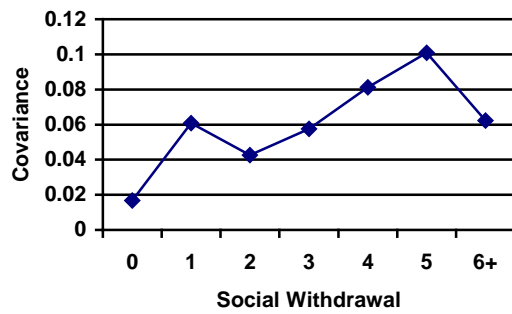
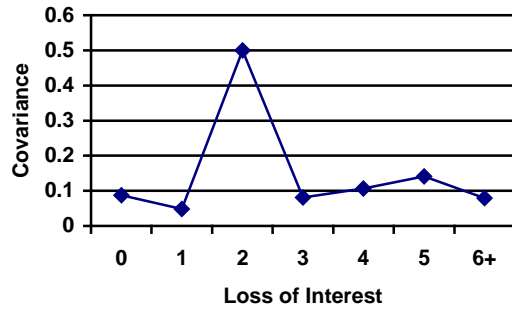
Plots from the MAMBAC analyses were consistent with a taxon (figure 1). Typically, dish-shaped plots are characteristic of taxonic results; however, up-ward sloping MAMBAC plots can also be indicative of taxa with low base-rates (Meehl & Yonce, 1994). Base rates for the taxon group were calculated using the method outlined by Meehl (Meehl & Yonce, 1994). This procedure yielded a base-rate of .13 for Factor 1 and .15 for Factor 2, yielding an average base rate of .14 for the negative symptom taxon group.

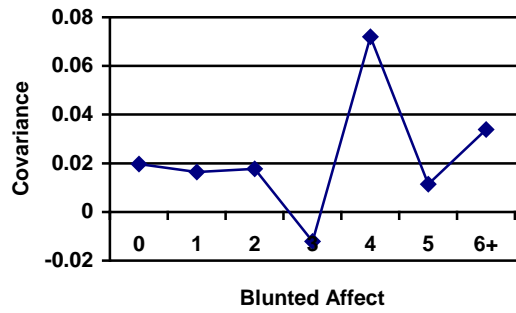
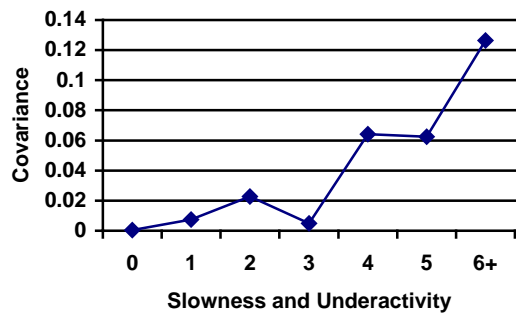
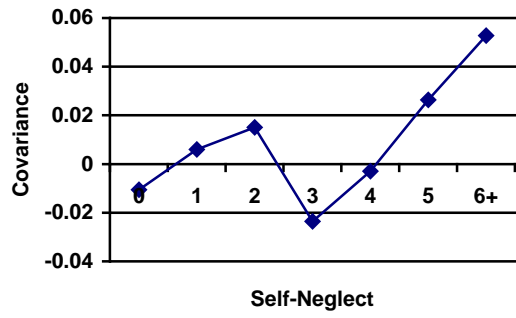
Section 3: Maximum Covariance

The maximum covariance (MAXCOV; Meehl & Yonce, 1996) procedure requires at least three indicator variables. The factor analysis on the PSE conducted for this analysis only yielded two indicator variables. In order to corroborate the results from the MAMBAC analysis, a modified MAXCOV procedure was used (Gangestad & Snyder, 1985). These procedures have been used previously for taxometric analyses (Horan, Blanchard, Gangestad, & Kwapil, 2004; Korfine & Lenzenweger, 1995). In this procedure, two variables are chosen as the output variables. The other seven variables are combined into a summed scale and cuts are made along the range of the scale. Covariances of the two output variables are taken at each of these points. As with the MAMBAC analysis, cut points were chosen so that at least 20 individuals were present at points above and below those cuts. Covariance curves were calculated for each individual item and for the overall mean covariance curve. For these analyses, covariance curves for individual items were based on the median covariance of that item across all pairings with the eight other items selected from the PSE. The mean covariance curve was calculated by averaging across all of the 36 item pairings.

As can be seen in figure 2, results from the MAXCOV analysis were each indicative of a taxon. Similar to the results obtained during the MAMBAC analysis, the graphs resulting from this analysis were upward sloping plots. Base rates for the latent class were calculated. For the MAXCOV procedure, the HITMAX interval is identified. In this interval is defined as the interval with the maximum amount of covariance, which is a result of an approximate equal number of taxon and non-taxon

individuals in this interval. The number of taxon individuals is then calculated for the other intervals.





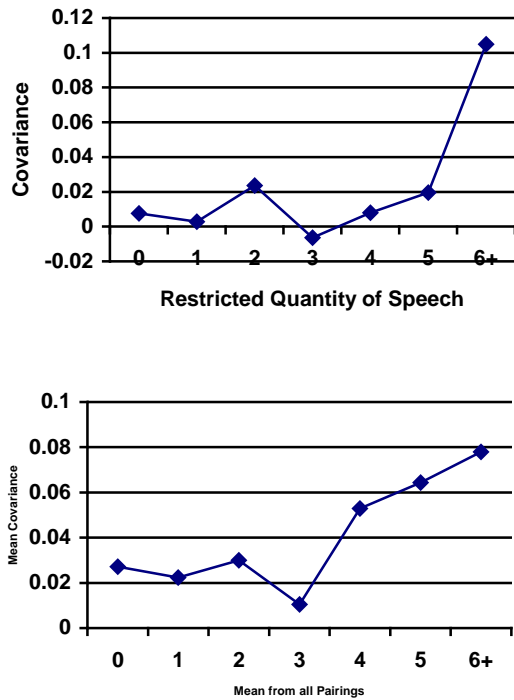


Figure 2: MAXCOV (maximum covariance) curves for each item and for the mean across all pairings

For individual items, base rates are calculated from an average of that item's pairing with all other items (see Table 3). The overall base rate was calculated from the average of all 36 pairings. Results from this analysis yielded a base rate of .16. This base rate is comparable to the base rate calculated in the MAMBAC analysis, which provides additional support for the existence of a taxon.

Table 3

Base Rates Calculated for Individual Curves and for Average of the Curves

Item Content	Base Rate
Item 22-Slow speech	.13
Item 28-Slowness and underactivity	.17
Item 36-Restricted quantity of speech	.05
Item 54-Blunted affect	.10
Item 108-Self-neglect	.08
Item 110-Loss of interest	.10
Item 128-Subjective anergia and retardation	.10
Item 130-Social withdrawal	.09
Item 134-Lost emotions	.09
Mean base rate	.16

Section 4: Group Comparisons

In order to compare the taxon to the non-taxon group, individuals had to be assigned membership basis of each individual's scoring pattern on the nine indicator variables based on the MAXCOV analysis. Bayesian probabilities were calculated for each individual's scoring pattern. Individuals who had a probability of .80 or greater of belonging to the taxon (N = 153) were assigned to the taxon group. All others were assigned to the compliment (nontaxonic) group (N = 539).

In terms of demographic data, chi square tests revealed that the two groups were not significantly different on sex ($\chi^2(1, N = 692) = .29, p = .60$). The two groups were also not significantly different in age ($t(688) = 1.59, p = .15$).

Table 4
Group Comparisons

Group	Age	Sex		Positive Symptoms	Depression
	(years)	Male	Female	(mean)	(mean)
Taxon	26.56	82	71	6.92	5.18**
Compliment	27.87	302	237	6.40	2.67

* $p = .05$, ** $p < .00$

In order to compare the taxon and non-taxon groups on symptomatology, items were culled from the PSE that related to positive symptoms (Table 6) and depression (Table 5). Items related to positive symptoms were combined into a summed scale. The two groups were not significantly different from one another in the severity of positive symptoms ($t(307) = -.55, p = .15$). Items related to depression were also combined into a summed scale and the two groups were compared to one another. It was found that individuals in the high probability taxon group had higher mean levels of depressive symptoms than individuals in the low probability taxon group ($t(491) = -7.93, p < .00$).

Table 5
PSE Items Related to Depression

Item Number	Title	Description
19	Inefficient Thinking	<i>The subject complains that he is unable to think clearly or efficient or to reach decisions easily even about simple matters. His thoughts are muddled or slow and they tend to go round and round in aimless circles.</i>
20	Poor Concentration	<i>The subject complains that he cannot give his full attention to matters which require it or not for as long as they require. At its most intense, the subject cannot even read a few sentences in a newspaper, cannot watch television and cannot take in a conversation.</i>
23	Depressed Mood	<i>Depressed mood may be expressed in a number of ways – sadness, misery, low spirits, inability to enjoy anything, dejection.</i>
24	Hopelessness	<i>The subject's view of the future is bleak and without comfort.</i>
25	Suicidal Plans or Acts	<i>Does not include a fleeting thought about suicide; include a more deliberate consideration of planning and suicidal attempts that either were or were not intended to end in death.</i>
27	Morning Depression	<i>The subject states unequivocally that depression is worst during the early part of the day and then improves.</i>
29	Self Deprecation	<i>The subject feels inferior to others, even – in the most intensive form of the symptom – worthless. Do not rate delusions here.</i>
34	Loss of Weight	<i>Rate only loss of weight due to poor appetite.</i>
35	Delayed Sleep	<i>Rate delay in getting off to sleep after the subject has gone to bed.</i>

Table 6
PSE Items Related to Positive Symptoms

Item Number	Title	Description
43	Grandiose Ideas and Actions	<i>The subject feels that he is superbly healthy, has exceptionally high intelligence or extraordinary abilities.</i>
55	Thought Insertion	<i>The essence of this symptom is that the subject experiences thoughts which are not his own intruding into his mind. The symptom is not that he has been caused to have unusual thoughts but that the thoughts themselves are not his.</i>
56	Thought Broadcasting or Thought Sharing	<i>Distinguish it from thought reading. 'Thought broadcasting' is only rated when the subject actually experiences his thoughts being shared with others.</i>
58	Thought Block or Thought Withdrawal	<i>The subject feels a sudden stopping of his thoughts, quite unexpectedly, while they are flowing freely, and in the absence of anxiety.</i>
59	Delusions of Thoughts Being Read	<i>Subject feels that others can read his thoughts despite not sharing these thoughts with others</i>
60	Non-verbal Hallucinations	<i>This symptom includes noises, other than words, which have no real origin in the world outside the subject but also no explicable origin in bodily processes, and which the subject regards as separate from his own mental processes.</i>
61	Affective or Non-Specific Verbal Hallucinations	<i>This symptom excludes non-verbal auditory hallucination. The most common form of the symptom is a voice calling the subject's name or simply saying one or two words only.</i>
62	Non-Affective Verbal Hallucinations (About the Subject)	<i>This symptom includes only a voice or voices heard by the subject speaking about him and therefore referring to him in the third person.</i>
63	Non-Affective Verbal Hallucinations (Spoken to the Subject)	<i>This symptom includes only a voice or voices heard by the subject speaking directly to him, and not depressive or grandiose in content or mood</i>
64	'Dissociative' Hallucinations	<i>The subject can hold a conversation (often two-way) with a presence (variously described as a person, ghost, spirit, god, etc.) which may often be sensed in other ways, e.g., visually or by touch or smell.</i>
68	Olfactory Hallucinations or Delusions	<i>Simple olfactory hallucinations, such as a smell of orange peel or perfume, or a smell of 'death' or burning, which other people cannot smell.</i>
69	Delusion that Subject Smells	<i>If the subject thinks that he gives off a smell (though others cannot smell it</i>
70	Other Hallucinations and Delusional Elaborations	<i>If the subject has sensations other than auditory, visual, sexual, or olfactory</i>
71	Delusions of Control	<i>The essence of the symptom is that the subject experiences his will as replaced by that of some other force or agency.</i>
72	Delusions of Reference	<i>What is said by others may have a double meaning, or someone makes a gesture which the subject construes as a deliberate meaning. People may seem to be gossiping about the subject (beyond the bounds of possibility) or he may see references to himself on the television.</i>

73	Delusional Misinterpretations and Misidentifications	<i>Not only do people seem to refer to the subject directly but situations seem to be created which have special meaning. Things seem to be arranged to test him out, objects are arranged so that they have a special significance for him; this may go so far that whole armies of people may seem to be employed simply in order to discover what he is doing.</i>
75	Delusion of Assistance	<i>The subject believes that someone, or some organization, or some force or power, is trying to help him.</i>
76	Delusions of Grandiose Ability	<i>The subject thinks he is chosen by some power, or by destiny, for a special mission or purpose, because of his unusual talents.</i>
77	Delusions of Grandiose Identity	<i>The subject believes he is famous, rich, titled or related to prominent people.</i>
78	Religious Delusions	<i>Both a religious identification on the part of a subject (he is a saint or has special spiritual powers) and an explanation in religious terms of other abnormal experiences (e.g., auditory hallucinations) should be included.</i>
79	Delusional Explanations (Paranormal and Occult)	<i>Include here any delusional explanation or elaboration of other abnormal experiences, such as thought insertion or broadcast or delusions of reference or persecution, in terms of paranormal phenomena.</i>
80	Delusional Explanations (Physical)	<i>Include here any delusional explanations of other abnormal experiences such as thought insertion or broadcast or delusion of reference or persecution or somatic delusions, in terms of physical processes such as electricity, X-rays, television, radio, or machines of various kinds.</i>
81	Delusion of Alien Forces Penetrating or Controlling Mind or Body	<i>This involves an external force which penetrates the subject's mind or body from outside – such as a ray which turns the liver to gold, alien thoughts which pierce the skull or are injected into the mind, or a spirit which speaks with the subject's voice, or a radio transmitter which has been implanted into the brain so that the subject's thoughts are broadcast, etc.</i>
82	Primary Delusions	<i>Primary delusions are based upon sensory experiences (delusional perceptions) in which a patient suddenly becomes convinced that a particular set of events has a special meaning.</i>
83	Subculturality Influenced Delusions	<i>Includes specific idiosyncratic beliefs held with conviction by small subgroups within the community, e.g. sects, tribes or secret societies, but not by the community at large.</i>
85	Delusions of Pregnancy	<i>The subject thinks she is pregnant although the circumstances make it clear that she cannot possibly be.</i>
86	Sexual Delusions and Hallucinations	<i>Any delusion with a sexual content</i>
87	Delusions of Memories, Confabulations, Fantastic a delusion	<i>Delusional memories are experiences of past events which clearly did not occur but which the subject equally clearly remembers, e.g. 'I came down to earth on a silver star in 1964.'</i>
88	Delusions of Guilt	<i>The subject thinks he has brought ruin to his family by being in his present condition or that his symptoms are a punishment for not doing better.</i>
89	Simple Delusions Concerning Appearance	<i>The subject has a strong feeling that something is wrong with his appearance.</i>
90	Delusions of Depersonalizations	<i>The subject has a strong feeling as if he had no brain, a hollow within his skull, no thoughts in his head.</i>
91	Hypochondriacal Delusions	<i>The subject feels that his body is unhealthy, rotten or diseased.</i>
92	Delusions of Catastrophe	<i>The subject feels a sense of impending doom, that something awful will happen, but he doesn't know what</i>

Section 5: Post Hoc Comparisons

A previous taxometric analysis of a United States sample (Blanchard, et al., 2005) did not find a relationship between depression and negative symptoms. This brings into question whether negative symptoms are independent of depression only in samples from the United States.

To investigate the relationship between negative symptoms and depression in the current sample, levels of negative symptoms were first compared across study site. For these analyses, items from the PSE pertaining to negative symptoms were combined to create a summed scale. A one-way analysis of variance test revealed a significant main effect for study site on negative symptoms $F(10, 681) = 5.612, p < .00$. A test of homogeneity of variance was significant, so a Dunnett's T3 post-hoc comparison was used. It was found that the site from the United States (Honolulu) did significantly differ from two other sites (Aarhus, Denmark: $F(10, 681) = 2.89, p < .00$; Nottingham, England: $F(10, 681) = 2.11, p = .04$). Given that the US sample only significantly differed from two of the eleven sites, it cannot be said that the US sample was dramatically different from the overall sample.

Next, the relationship between negative symptoms and depression was investigated across study sites. Pearson's product-moment correlations were calculated between the depression summed scale and the negative symptom summed scale across the different sites. Significant correlations (Table 7) were found in the Cali, Colombia sample ($r(77) = .38, p < .00$), the Moscow, Russia sample ($r(19) = .72, p < .00$), the Honolulu, USA sample ($r(35) = .61, p < .00$), the Prague, Czechoslovakia sample ($r(86) = .53, p < .00$), the Chandigarh, India sample ($r(94) =$

.35, $p < .00$), the Nagasaki, Japan sample ($r(67) = .63$, $p < .00$), the Nottingham, England sample ($r(17) = .59$, $p < .00$), and the Dublin, Ireland sample ($r(45) = .52$, $p < .00$). Non-significant correlations were found in the samples from Aarhus, Denmark ($r(13) = .02$, $p = .95$), Arga, India ($r(4) = .33$, $p = .53$), and Ibadan, Nigeria ($r(16) = .34$, $p = .23$). These results show that, on the whole, depression was related to negative symptoms in the sample as a whole. Additionally, the relationship between depression and negative symptoms that was observed in the entire sample was also significant in the sample from the United States. These findings, then, contradict those found in the Blanchard, et al. (2005) study.

Table 7
Correlation between depression and negative symptoms across sites

Country	Aarhus	Arga	Cali	Ibadan	Moscow	Hon.	Prague	Cah.	Nag.	Nott.	Dublin
r.	.02	.33	.38**`	.34	.72***`	.61**`	.53**`	.35**`	.63**	.59**	.52**

* $p = .05$; ** $p < .01$

Next, correlations between the depression summed scale and individual negative symptom variables were calculated in order to further explore the nature of this relationship. First, the broad negative symptom factors were examined. Significant correlations were found between depression and factor 1 ($r(491) = .13$, $p < .00$), and factor 2 ($r(491) = .58$, $p < .00$). Given the large discrepancy between these two correlations, it was decided to test whether factor 2 was significantly more correlated with depression than factor 1. Using the procedure outlined by Meng, Rosenthal, and Rubin (equation 1; 1992) it was determined that the two correlations were significantly different ($Z(693) = -9.86$, $p < .00$), which indicates that factor 2 is more correlated with depression than factor 1.

Since each of the two factors showed significant correlations with the

depression summed scale, individual negative symptoms were then entered into a Person's product-moment correlation with the depression summed scale. Significant correlations were found between depression and loss of interest ($r(491) = .49, p < .00$), social withdrawal ($r(491) = .46, p < .00$), subjective anergia and retardation ($r(491) = .48, p < .00$), lost emotions ($r(491) = .33, p < .00$), slowness and underactivity ($r(491) = .23, p < .00$), slow speech ($r(491) = .17, p < .00$), and restricted quantity of speech ($r(491) = .09, p < .00$). Nonsignificant correlations were found between depression and blunted affect ($r(491) = -.05, p = .29$) and self-neglect ($r(491) r = .07, p = .12$).

Table 8
Correlation between negative symptoms and depression: Individual items

Depression SS x Negative Symptom SS	
Factor 1- Observed	.13**
Self- Neglect	.07
Slowness and Underactivity	.23**
Blunted Affect	-.05
Slow Speech	.17**
Restricted Quantity of Speech	.09**
Factor 2- Subjective	.58**
Loss of Interest	.49**
Subjective Anergia and Retardation	.48**
Social Withdrawal	.46**
Lost Emotions	.33**

* $p = .05$; ** $p < .01$

Next, because depression and positive symptoms have been found to be associated in other samples of individuals with schizophrenia, (Lindenmayer, Grochowski, & Kay, 1991; Sax, Strakowski, Keck, & Upadhyaya, 1996) a Pearson's product-moment correlation was calculated using the positive symptom summed scale and the depression summed scale. The relationship between these two types of

symptoms was not significant ($r(461) = .11, p = .09$).

Finally, because of the well-known association between depression and sex (Nolen-Hoeksema, 1995), it was decided to check for a sex by group interaction. A univariate ANOVA revealed a nonsignificant sex by taxon interaction ($F(1, 487) = 2.59, p = .11$).

Chapter 6: Discussion

The purpose of this study was to investigate the structure of negative symptoms in a large, representative sample of individuals with schizophrenia. It was hypothesized 1) that a negative symptom taxon would exist; 2) that this subtype would represent approximately 25-35% of the sample; 3) that individuals in the taxonic group would be more likely to be male, and have lower rates of depression; and finally, that there would be no difference in severity of psychotic symptoms between the two groups.

This study replicated the results of Blanchard, et al. (2005). That study found that the structure of negative symptoms in a sample of patients with schizophrenia was taxonic. In the current study, taxometric analyses of the PSE resulted in evidence for a high negative symptom latent taxon across both MAMBAC and MAXCOV procedures. These results, in combination with the results of the Blanchard, et al. (2005) study provide support for the concept of a latent class of individuals with schizophrenia with a high level of negative symptoms.

Base rates from these taxometric analyses ranged from .14 to .16. These estimates were consistent across both the MAMBAC and MAXCOV taxometric procedures. These base rates are lower than those estimated in a previous taxometric analysis (Blanchard, et al, 2005), which found an estimated base rate of .28-.36. In addition, these rates are lower than those of the deficit syndrome, which is generally estimated at approximately .30 (Kirkpatrick, et al., 2006). The base rate estimations in this study, however, have been reported in a study of the deficit syndrome in Spanish patients (Peralta & Cuesta, 2004) which found a prevalence rate of between .14 and

.32. In addition, previous research has found that early age of onset is not associated with the deficit syndrome (Kirkpatrick, Castle, Murray, & Carpenter, 2000) and that first-episode schizophrenia may be associated with lower rates of the deficit syndrome (Mayerhoff, Loebel, Alvir, & Szymanski, 1994). The low base rates found in this study, then, do not contradict previous findings.

Prior research suggests that negative symptoms are not associated with depression, or positive symptoms, but are associated with the male sex. Comparisons were made in this sample between the taxon and compliment groups in order to determine the relationship between negative symptoms and these other variables. Comparisons of the two groups revealed that they did not differ in terms of age or sex. Previous research has not found an association between age and negative symptoms (Kirkpatrick and Buchanan, 1990); therefore, this finding was not unexpected. More surprising, however, was the finding that there were no significant sex differences between the two groups. The previous taxometric analysis by Blanchard, et al. (2005) study found that there were more males in the latent class taxon than females. Additionally, a meta-analysis of research on the deficit syndrome has found an association between deficit syndrome schizophrenia and the male sex (Roy, Maziade, Labbe, and Merette, 2001). At this time, sex differences in negative symptoms have not been sufficiently investigated in international samples. Given that the results from this study contradict previous findings, no firm conclusions can be drawn at this time. Further research is warranted.

The high and low probability taxon groups also did not differ in terms of positive symptoms. This finding is consistent with pervious work that has found

positive and negative symptoms to be largely independent of one another (Lewine, et al., 1983; Palacious-Arus, et al., 1995; & Nakaya, et al., 1999), so this finding was also expected.

Perhaps the most surprising finding in this analysis was the strong association between depression and negative symptoms. When individuals from the high and low probability taxon groups were compared with one another, the mean level of depression was significantly higher in the high negative symptom taxon ($t(491) = -9.61, p < .00$). It was also found that negative symptoms were correlated with depression across some, but not all, of the research sites.

In order to further investigate the relationship between negative symptoms and depression, Pearson's product-moment correlations were calculated between each of the two factors and depression and each of the individual negative symptoms and depression. It was found that depression was significantly correlated with both factor 1 and factor 2; however, it was also found that factor 2 had a significantly higher correlation with depression than did factor 1. Factor 1 was considered to be the subjective report of negative symptoms. This factor included items that could be considered to be more associated with depression than the factor 1 items, which was related to the observed manifestation of negative symptoms.

The individual items were also found to be associated with depression. Loss of interest, social withdrawal, subjective anergia and retardation, lost emotions, slowness and under-activity, slow speech, and restricted quantity of speech were all found to be significantly correlated with the depression summed scale. The only two negative symptom items that were not significantly correlated with depression were

blunted affect and self-neglect.

The findings from this investigation are difficult to interpret. Previous research has shown that negative symptoms can be reliably measured independent of depression in schizophrenia (Pouge-Geile & Harrow, 1984; Kuck, Zisook, Moranville, & Heaton, 1992; Kirkpatrick, Buchanan, Breier, & Carpenter, 1994; Malla, Takhar, Norman, Manchanda, Cortese, Haricharan, Verdi, Ahmed, 2002). The fact that the two constructs were so related in this sample causes one to question whether depression, rather than negative symptoms, was being captured in this study. Further complicating this analysis was the fact that positive symptoms and depression were independent of one another in this sample. Previous research has found a correlation between depression and positive symptoms (Lindenmayer, et al., 1991; Sax, et al., 1996). Further research is warranted to further investigate these relationships.

Given the relationship between depression and negative symptoms in this sample, it was decided to examine the subscales in the PSE from which the items identified as negative symptoms came. Items from the PSE were divided up into a variety of syndromes by the authors of the measure. The syndrome associated with each negative symptom item was examined (Table 9). Only one of the items (item 54, lost affect) was considered to be a part of the “special features of depression” syndrome. Given that only one of these items came from a syndrome explicitly designed to assess depressive symptomatology, the high degree of correlation between the individual negative symptoms and depression does not appear to be solely an artifact of item selection.

Table 9
PSE Syndrome Associated with Each Item

Item Number	Description	Associated Syndrome
22	Loss of Interest	Loss of Interest and Concentration
28	Social Withdrawal	Social Unease
36	Subjective Anergia	Lack of Energy
54	Lost Affect	Special Features of Depression
108	Self Neglect	Self-Neglect
110	Slowness and Underactivity	Slowness
128	Blunted Affect	Affective Flattening
130	Slow Speech	Slowness
134	Restricted Quantity of Speech	Slowness

From the findings of this study, one might conclude that negative symptoms and depression are indistinguishable from one another in the schizophrenia population. This would be an inaccurate conclusion. As was mentioned previously, negative symptoms can be reliably measured independently of depression in schizophrenia (Pouge-Geile & Harrow, 1984; Kuck, et al., 1992; Malla, et al, 2002; Kirkpatrick, et al., 1994). Negative symptoms and depression have also been found to have be predictive of different outcomes (Roca, Bellino, Calvarese, Marchiaro, Patria, Rasetti, & Bogetto, 2005). In addition, some may question whether the fact that the results were taxonic implicitly indicates that the two are associated due to a similar biological etiology. This assumption would also be incorrect. Meehl (1999) noted that although genetic and biological reasons can cause latent classes, that “there is nothing about the etiological concept of a taxon, or about the mathematics of detecting one, that says anything so restrictive about substantive causation” (p 168). Therefore, the

finding that depression and negative symptoms were found to associated in this study do not necessarily cast doubt on the concept of negative symptoms as a construct independent of depression.

A few limitations must be noted. First, as mentioned above, the conflation of negative symptoms and depression speaks to the lack of an instrument specific to negative symptoms. The development of measurements specific to negative symptoms did not occur until after this study had been completed. Conceptualizations of negative symptoms have been refined since when the PSE was developed. In particular, as noted above, the publication of Andreason's SANS in 1983 marks an important milestone in this development.

In this study, the PSE appears to conceptualize these items as being state-like, instead of trait-like. As noted above, in Carpenter's conceptualization, negative symptoms should only count towards the diagnosis of the deficit syndrome if they are enduring, or trait-like (Carpenter, et al., 1988). While this study was not designed to be an explicit confirmation of the deficit syndrome, there is general agreement in the field that particular attention should be paid to enduring, trait-like negative symptoms in the study of schizophrenia (Kirkpatrick, et al., 2006). Had an instrument more suited for the identification of negative symptoms been employed, more confidence could have been had in the results.

Given the importance of identifying trait-like and enduring negative symptoms, the question then becomes how best to measure these symptoms. A simple time-delimited cut-off such as the 1-year criterion mandated for the deficit syndrome (Carpenter, et al., 1988) is too simplistic. In addition, as previously noted, the one

year criterion appears to be largely divorced from empirical evidence and based mostly on clinical judgment. Alternatives to this approach, however, have not been forthcoming. In the absence of any empirical data for an appropriate time frame, the concept of persistent negative symptoms as outlined by Buchanan (2007) can provide some guidance for further development. This concept was posed as a relaxed alternative to the deficit syndrome for the purpose of clinical trials. In contrast to the deficit syndrome, secondary negative symptoms can be applied to the diagnosis of persistent negative symptoms, so long as they have been present for at least six months and so long as they have not been responsive to treatment. These relaxed criteria may prove to be easier to diagnose and capture a larger portion of the population than the deficit syndrome; however, more empirical data is needed before it can be applied to large-scale studies.

Additional changes should be made to the PSE in order to improve its ability to capture negative symptoms. As previously mentioned, identifying whether the negative symptoms were primary and endogenous to the illness or secondary to other causes is of critical importance. In this study, it is unclear whether the symptoms that have been identified are actually negative symptoms, depression, or a mix of the two. Taking a cross-sectional measure of negative symptoms makes it difficult to assess whether an individual's symptoms are primary or secondary unless there is a complete absence of any factor which negative symptoms can be secondary to. A long term assessment of the symptomatology is ideal in making this distinction. This is, however, not always possible or practical in a study of this magnitude. Alternatively, it is possible that clinicians with an extensive knowledge of the patient

could make a judgment about whether the negative symptoms are primary or secondary. Again, this approach, while beneficial, could pose a logistical impossibility in a large, international study. Again, the approach outlined by Buchanan (2007) could pose a viable alternative. The criteria for persistent negative symptoms is more relaxed than those for the deficit syndrome and allows for the inclusion of secondary negative symptoms so long as they can be shown to be clinically relevant (see the criteria outlined previously). These criteria would still place a substantial burden on an investigator, however, the inclusion of secondary negative symptoms could allow for the inclusion of clinically relevant symptoms that cannot be definitively ruled as primary.

Finally, consideration must be given to the emerging literature on the difficulties that individuals with schizophrenia appear to have in reporting anhedonic symptoms. For instance, Gard, Kring, Gard, Horan, and Green (2007) found that while individuals with schizophrenia could accurately report pleasure for events they had immediately experienced (consummatory pleasure) they showed deficits in reporting pleasure for events that were in the future (anticipatory pleasure). Similarly, Burbridge and Barch (2007) found that when viewing emotionally evocative pictures, individuals with schizophrenia showed no deficit in reporting their experienced pleasure. They did, however, show a deficit in reporting pleasure on a traditional measure of anhedonia in schizophrenia. This deficit was moderated by deficits in working memory.

Individuals with schizophrenia may need substantial coaching in order to allow them to accurately report their experiences. As noted above, the profound

cognitive impairments that are a feature of this disorder can interfere with their ability to self-report. In the WHO study, the PSE did not allow for the in-depth questioning that may be necessary for individuals with schizophrenia to provide an accurate description. In a similar vein, current measures of negative symptoms (such as the SDS; Kirkpatrick, et al, 1989) do not provide extensive prompting, instead allowing for the subject to provide single word answers with little questioning. Any additional measure of negative symptoms needs to consider this point and provide ample opportunity and prompting for individuals with schizophrenia to report their experiences.

In summary, the findings of this study do support the existence of a negative symptom taxon; however, this taxon group also evidenced high levels of depression. These findings contradict several previous studies that support the independence of negative symptoms and depression in individuals with schizophrenia. It is likely that the measurement used in this study, the PSE, was not well suited for the detection of negative symptoms as they are currently conceptualized. Future studies are warranted, as understanding the structure and nature of negative symptoms is a pressing clinical need.

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