THE EFFECTS OF PERSONALITY DISORDER TRAITS ON INDIVIDUAL THERAPY OUTCOMES IN INDIVIDUALS AT CLINICAL HIGH RISK FOR SCHIZOPHRENIA

by

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Abstract

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Despite a high prevalence of comorbid personality disorder traits in those considered to be high risk (or prodromal) for schizophrenia (Woods et al., 2009), and the known negative effects of personality disorders on treatment in schizophrenia (e.g., Tyrer et al., 2000), little is known regarding the effect of personality disorder traits on the treatment of prodromal individuals. Using a ten-year sample from the Recognition and Prevention (RAP) Program at Zucker Hillside Hospital in New York, this dissertation used retrospective, naturalistic methods to investigate personality disorder traits and the ways in which these traits affected both the assessment and the treatment of prodromal symptoms. Results did not support that personality disorder traits moderated treatment outcomes, but did support that particular treatment techniques were used more often with certain personality traits (e.g., borderline personality disorder) or symptom severities. In addition, it was found that, overall, particular treatment techniques were associated with reductions in negative symptoms, but not with positive symptom or global functioning changes. Results also indicated that aspects of the suspiciousness and hallucinations scales from the Structured Interview for Prodromal Syndromes (SIPS) were associated with personality traits and not predictive of transition to psychosis. These results suggest that treatment planning could use symptom presentation on intake to determine the most effective treatment techniques.

Further research is required to further the diagnostic and predictive ability of assessment measures, including the important determination of whether currently considered prodromal symptoms may be better accounted for by personality traits.

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CHAPTER I

INTRODUCTION

According to a California-based study, the estimated cost of schizophrenia in the United States in 2002 was $62.7 billion, including direct health care, non-direct heath care, and other indirect costs (Wu, Birnbaum, Shi, Ball, Kessler, Moulis, et al., 2005). Beyond the economic ramifications, the debilitating effects of poorly managed schizophrenia symptoms on an individual's quality of life are well known. Moreover, the treatment of this illness is not always successful. Despite recent advances in both medication and psychotherapeutic interventions for schizophrenia, the enormous costs and debilitating effects associated with this disorder have led many researchers to focus on prevention.

Trends in healthcare during the early 1990s brought the concept of "indicated prevention" of disorders to the forefront of medical, and later behavioral health, research. As an intervention, indicated prevention describes the implementation of preventative measures to those showing "high risk" signs or symptoms in the hopes of either delaying or completely preventing the full progression of an illness. Researchers during this period were investigating the efficacy of indicated prevention for disorders such as Type II diabetes (Tuomilehto, Schwarz, & Lindstrom, 2011) and obesity (Gill, 1997). The interest in indicated prevention soon made a noteworthy impression on schizophrenia clinicians and researchers for the many potential benefits of preventing, or at least delaying, the onset of psychosis.

Indicated prevention, therefore, brought focus to what has been termed the "prodromal" phase of schizophrenia, or the period of time when symptoms first emerge, but have not yet

reached a level sufficient to diagnose schizophrenia. The focus on the prodrome stemmed from the assumption that this period of time was optimal for both identification of those at risk and implementation of preventative intervention strategies. Some twenty years after the renewed interest in the "prodrome," research suggests that there are effective ways to treat symptoms experienced during the prodrome, primarily attenuated psychotic symptoms (Preti & Cella, 2010; Olsen & Rosenbaum, 2006). However, indicated prevention for schizophrenia has proven to be extremely complicated for many reasons. First, symptoms of the "prodrome" were not shown to be specific to the manifestation of psychotic disorders, producing theoretical and methodological concerns about false positives. Second, in addition to those symptoms considered to be "prodromal" in nature, help-seeking individuals present with a variety of other Axis I and Axis II symptoms (Woods et al., 2009). In fact, when first presenting for treatment, it is often the non-prodromal symptoms that individuals identify as the presenting problem.

When considering treatment (and indicated prevention), clinicians must not only treat those symptoms considered "prodromal" or pre-psychotic, but also be aware of the many other symptoms that are non-psychotic and how these non-psychotic symptoms may affect treatment of the "prodromal" symptoms. One such comorbidity of interest is that of the personality disorders and corresponding traits, which are both prevalent in this population (Woods et al., 2009), and have previously been identified as moderating treatment effectiveness in other Axis I disorders (e.g., Keown, Holloway, & Kuipers, 2009). The following review discusses the potential moderating effects of personality disorder traits on treatment of "prodromal" symptoms and why this is a crucial treatment consideration for this population. The review begins with discussion of the prodrome generally (Part I) and moves to issues of personality disorder

comorbidity (Part II), culminating in the hypotheses, methodology, results and discussion of the dissertation that addressed this important comorbidity (Part III).

CHAPTER II

LITERATURE REVIEW

Part I: The Prodrome

In order to discuss any comorbidity among individuals considered "prodromal," the concept of the prodrome must be discussed in full. Part I of this review, therefore, presents the current conceptualization of the prodrome, symptoms of the prodrome, and the emerging developmental theory behind the prodrome.

Conceptualizing the prodrome. Though there have been many definitions of what characterizes the psychotic "prodrome," each highlight the period of time from when a person experiences a significant change in his or her experience or behavior to the time he or she presents with frankly psychotic symptoms (Yung & McGorry, 1996a). This pre-psychotic, yet symptomatic phase has been both conceptualized and defined in different ways. Most agree, however, that the term "prodrome" is a retrospective medical term. That is, one cannot be "prodromal" unless it is known that the person eventually developed psychosis (Yung & McGorry, 1996a). In this way, the word "prodrome," by strictest definition, coveys pre-psychosis or psychosis in its attenuated, but inevitably emerging form (Yung & McGorry, 1996a). This period of time in which a person experiences the first change from his or her own baseline of experience until frank psychosis appears to have a pattern of symptoms associated with it. However, somewhere between 46-78% of individuals who develop the same set of symptoms, and therefore a change in baseline, do not go on to develop psychosis (McGorry, Yung, & Phillips, 2003). Therefore, they cannot be said to be "prodromal" in the sense of

impending psychosis. This has led some researchers to consider this period a syndrome in and of itself, one that indicates increased vulnerability to psychosis as compared to the "normal" population, but not an inevitable progression towards psychosis (Yung & McGorry, 1996a). Most researchers now consider the term "prodromal" to convey high risk of psychosis rather than inevitability, or choose alternative terms such as "clinical high risk" or "ultra high risk" for psychosis (e.g., Yung & McGorry 1996a & 1996b; McGorry, Yung, & Phillips, 2003).

One of the most difficult aspects of research with the "prodrome," or those at high risk for psychosis, is defining the population. In fact, there have been many different interpretations of a) whether the prodrome is a common or universal experience for those who eventually develop psychosis and b) at what point in both time and symptom presentation the prodrome begins and ends.

In an attempt to determine whether the prodrome is a precursor to psychosis for many or most psychotic individuals, two large studies are cited to support the fact that most individuals do experience a prodromal or symptomatic phase prior to full psychotic symptoms. The first study, the ABC Schizophrenia study, was retrospective and conducted with individuals experiencing their first episode of psychosis; the second study, the Cologne Early Recognition (CER) study was prospective and conducted with prodromal individuals.

One of the most extensive studies of first episode psychosis was the ABC (Age, Beginning, Course) Schizophrenia study conducted in West Germany (Hafner et al., 1993). Individuals were interviewed within the first two weeks of their first inpatient psychiatric admission and retrospectively reported the symptoms that they experienced prior to hospitalization. Individuals were considered "first episode" if their symptoms had never reached

a psychotic level for more than 13 days (prior to the current episode requiring hospitalization). Using the ABC study data, an der Heiden and Hafner (2000) analyzed the self-reported pre-hospitalization data to provide information on symptoms prevalent during the prodrome, or the period from which patients first noticed symptoms until first hospitalization. The authors included 232 first-episode patients in their analyses and found an average prodrome length of 5 years, with 68% of the sample reporting a prodromal phase of over one year. The remainder of the sample split between what they called a sub-acute onset of between a month and a year (15%) and an acute onset of one month or less (18%).

A prospective epidemiological study, the Cologne Early Recognition (CER) study, was also conducted by German researchers. The CER study used the Bonn Scale for the Assessment of Basic Symptoms (BSABS) to determine prodromal criteria and included 160 German adolescents and young adults. Schultze-Lutter, Klosterkötter, Picker, Steinmeyer, Ruhrmann, et al. (2007) used the CER data to analyze the 79 individuals who progressed to psychosis within the first year of the CER study. These authors determined an average prodrome length of 5.6 years and further broke their sample into a short, medium, and long prodrome based on duration of symptoms noted by the authors (any statistical procedures used to make these distinctions were not included in the paper). First, fisher exact tests were used to determine which symptoms were most predictive of the prodrome length (short, medium, long). The short prodrome, experienced by of 12 individuals, lasted less than one year and seemed to be characterized by deficiencies in the coordination or integration of top-down and bottom up processing. The symptoms associated with the integration problem included disturbance of receptive language, changes in the perceived intensity and quality of acoustic stimuli, and derealization. The medium prodrome, experienced by 37 individuals, lasted between 13 and 72 months and was

distinguishable by difficulties in top-down processing only. The top-down processing manifested through symptoms of subjective perception of changes in the face or body of others (false perceptions) as well as hyperdistractibility as a result of environmental stimulus overload. Those in the medium length prodrome also experienced disturbance of receptive language and thought pressure. Finally, 26 individuals experienced a long prodrome, which lasted longer than 72 months, and had problems in both top-down and bottom-up processes. These individuals had processing difficulties such as decreased ability to discriminate between ideas and perception or between fantasy and true memories, hypersenstitivity to light and certain optic stimuli, self-perceived nonexistent changes of their own reflection, and captivation of attention by details of the visual field. The individuals in long prodrome group also experienced thought pressure.

After determining symptom presentation, these three prodrome lengths were entered into a logistical regression model in an attempt to determine the ability of the prodrome lengths and basic symptoms to predict conversion to psychosis (when compared to normal controls). All three prodrome lengths showed significant predictive ability in differentiating those who converted to psychosis and those who did not convert to psychosis, with the short and long durations similarly specific (0.98 and 0.96, respectively) and the long duration having the best sensitivity (0.73).

Based on the large-scale epidemiological studies reported here and reviews of the literature (e.g., Yung, 2007; Yung & McGorry, 1996a), it is believed that the prodrome for psychosis can last anywhere from weeks to years, with an average between a few months to five years. A few studies have indicated that individuals have reported a transition to psychosis without a prodrome, though this appears to be the exception (Yung & McGorry, 1996). Although

the retrospective nature of the ABC study introduced methodological limitations such as participant memory bias, the CER study corrected for this methodological problem. However, the CER study compared "converters" to "non-converters" to report their findings. This dichotomy is problematic when, after only one year of follow-up, many of their "non-converters" may very well have become "converters."

As mentioned previously, the prodrome can refer to varying symptom experiences, in addition to varying degrees of assumed inevitability of progression to psychosis. For the purpose of this review, unless otherwise indicated, the term "prodromal" is used to indicate individuals who experience a constellation of symptoms known to predate psychosis. As a result of these symptoms, these individuals are considered at high risk for psychosis, but psychosis is not considered to be inevitable.

Models of the prodrome. Current attempts to identify and/or predict individuals who are prodromal, or at high risk for psychosis, primarily rely on one of three models of the prodrome: the Basic Symptom Model (Moller & Husby, 2000), the Ultra High Risk Model (Yung et al., 2003; McGorry et al., 2003), or the Clinical High Risk Model (Cornblatt, Lencz, Smith, Correll, Auther, & Nakayama, 2003).

The Basic Symptoms Model was developed by Huber and describes increasingly severe disturbances from baseline experience. Huber describes three levels of basic symptoms, with the latter two levels being specific to psychosis (Schultze-Lutter, 2009). Level I of the basic symptoms describe subtle self-perceived disturbances in drive, affect, concentration, and memory. The first level basic symptoms are not considered to be either specific to or pathognomonic of schizophrenia, but are thought to be of the first symptoms to develop. The

level II symptoms describe alterations in thinking, speech, bodily perception, and motor action. Symptoms of this nature would include thought interference, disturbance of receptive speech (hearing), disturbance in presenting oneself in miming and gesture, and loss of automatic skills (Schultze-Lutter, 2009). Level III symptoms are considered to be frank psychotic symptoms (e.g., first rank symptoms). Huber's theory includes a progression from level I to level III, although he accounts for spontaneous symptom remission, intervention, and other possibilities that may alter this course (Schultze-Lutter, 2009). Though the basic symptom approach has gained popularity in Europe, especially Germany, the basic symptom model will not be discussed in detail, as this model is rarely used in the United States, where the Ultra High Risk Model is preferred.

The Ultra High Risk Model was developed in Australia by Yung and colleagues (Yung et al., 2003; McGorry et al., 2003) and has been used throughout the United States after McGlashen and colleagues developed a structured clinical interview based on this approach (the Scale of Prodromal Syndromes [SOPS]; Miller et al., 1999). These researchers initially sought to adjust the procedure for identifying those individuals "at risk." Prior to the SOPS (and similar measures), the favored research methods involved the extremely inefficient practice of following first-degree relatives of those with psychotic disorders (McGorry, Yung, & Phillips, 2003). Thus, the need was created for a screening strategy that identified higher percentages of individuals who converted to psychosis with a lower false positive rate and expenditure of fewer resources (McGorry et al., 2003). The researchers came to the theoretically-based conclusion that three groups of individuals present elevated risk for psychosis: an attenuated psychosis syndrome group (APS), a brief limited intermittent psychosis syndrome (BLIPS) group, and a genetic risk and deterioration syndrome (GRDS; also called the state and trait risk factor group, Yung, 2007),

each is described in further detail below. This approach has significantly enhanced the ability to predict conversion to psychosis (e.g., Miller et al., 1999).

These three ultra high risk categories were then translated into two measures, the most widely used of the two being the Scale of Prodromal Syndromes (SOPS; Miller et al., 1999). The SOPS is a structured clinical interview with four symptom subsections: positive, negative, disorganized, and general symptoms. All symptoms are rated on a 0-6 point scale, with a 0 indicating an absence of a symptom and a 6 indicating severe and psychotic/extreme. Individuals are considered psychotic (by the SOPS criteria) if any positive symptom is rated at a severe and psychotic level of intensity (6) and has lasted for at least one hour per day and four days a week over the course of one month, or any positive symptom is considered seriously disorganizing or dangerous. Scores in the 3 to 5 range are considered moderate or attenuated symptoms and place the individual within eligibility for the ultra high risk group membership. However, as shown below, it is the positive symptom scale that primarily determines group membership rather than the other three symptom groupings. Each ultra high risk category is described below, along with the corresponding SOPS criteria for inclusion.

For inclusion in the attenuated psychosis syndrome (APS) group, individuals must have experienced positive symptoms at a moderate, but not psychotic level of intensity (Yung et al., 2003). The SOPS specific criteria requires at least one score in the range of 3-5 on the positive symptoms, but receive no positive symptom score of a 6 (all other symptom categories are irrelevant). Positive symptoms include such experiences as suspiciousness, ideas of reference, sub-threshold hallucinatory experiences, or overvalued ideas. In addition, this symptom must have occurred at least once per week at the rated intensity (3-5) and either begun, or increased to

the current level in the past 12 months. The latter criterion is to distinguish these symptoms from a personality disorder, such as schizotypal, in which unusual symptoms occur over a long period of time and are considered stable. To meet the brief limited intermittent psychosis (BLIPS) criteria, an individual must have had a positive symptom that met a psychotic level of intensity, but not duration (Yung et al., 2003). SOPS criteria specify that a positive symptom can be scored at a 6 level, and must have begun within the past three months; however, the symptom did not meet full duration and frequency criteria for a psychotic disorder (see above criteria). Finally, the state and trait risk group, called the genetic risk and deterioration syndrome (GRDS) by the Yale group, must either meet criteria for schizotypal personality disorder or have a first degree relative with schizophrenia *and* have experienced a functional decline in the past year (Yung, 2007; Miller et al., 1999). The SOPS specifies a functional decline as at least a 30% drop in the Global Assessment of Functioning (GAF) score. Of note, the criteria for schizotypal personality disorder require at least one attenuated positive symptom to be present (American Psychological Association, 2000). Therefore, the only way an individual can meet any of the currently held "prodromal" criteria without experiencing a positive symptom is to have a first degree relative with schizophrenia along with a significant decline in functioning (GRDS; state and trait risk). Research suggests that the APS group accounts for the predominant amount of participants, with the BLIPS and state and trait vulnerability cases ranging from 0-40 % of samples (Olsen & Rosenbaum, 2006).

Finally, Cornblatt and colleagues (Cornblatt, Lencz, Smith, Correll, Auther, & Nakayama, 2003) have developed the clinical high risk classification, which is a blend of the basic symptom and ultra high risk criterion. The Clinical High Risk Model, described in detail further in the review, is based on the assumption that prodromal symptoms progress along a

continuum of symptom severity (See Figures 1 & 2). The model posits that early insults affect the developing brain and lead to structural, functional, and biochemical abnormalities. These abnormalities form a biological vulnerability that first presents as non-specific cognitive deficits, affective symptoms, and social isolation/school failure. According to the model, a second trigger (genetic, biological, environmental, or otherwise) causes attenuated positive symptoms to develop, which may progress to full psychotic symptoms (See Figure 1). As such, Cornblatt has developed a classification that consists of three groups of "prodromal" individuals, the clinical high risk, negative (CHR-) group, the clinical high risk positive (CHR+) group, and the schizophrenia like psychosis (SLP) group. Despite a slightly altered model and group classification from the Ultra High Risk Model, the Clinical High Risk groups are also determined by SOPS criteria (for details on the Clinical High Risk criteria, please see Method section).

The Clinical High Risk Negative Group is comprised on the individuals who present with the non-specific cognitive deficits, affective symptoms, and social isolation that Cornblatt and colleagues believe is the earliest sign of the clinical risk. SOPS criteria for this group include a 3-6 on at least one of the negative symptoms, indicating a moderate to severe level of negative symptoms. The CHR- group is similar to the basic symptom approach (level I) in the identification of early non-specific symptoms that pre-date even attenuated positive symptoms. The CHR+ group consists of individuals who experience moderate or attenuated positive symptoms (SOPS scores of 3-5). In some publications, Cornblatt and colleagues have further distinguished this group into a moderate (CHR+ mod) and severe (CHR+ severe) based on positive symptom total score. Cornblatt and colleagues have even provided a psychotic (i.e., not prodromal) category that predates full schizophrenia called "schizophrenia-like psychosis" (SLP) that the authors believe to be an intermediate symptom step between prodrome and

schizophrenia (these individuals would often be diagnosed with psychotic disorder NOS). Cornblatt and colleagues symptom progression model is shown in Figure 2.

Despite three different categorizations of prodromal groups, the three approaches are similar in many ways. The basic symptom and clinical high risk approaches suggest developmental models of symptom progression and incorporate the non-specific (general) and negative symptoms as early signs of the prodrome. The Ultra High Risk and Clinical High Risk approaches have similar, though not identical, criteria for the high risk groups. Differences include the inclusion of clinical high risk, negative (CHR-) and exclusion of both the genetic and deterioration and risk (GRDS) and brief, limited, intermittent psychosis (BLIPS) from "prodromal" criteria on the part of the Cornblatt team. However, the Cornblatt group does use similar criteria for their SLP group as the ultra high risk group's BLIPS. The difference is that Cornblatt and colleagues consider such individuals to be psychotic and no longer prodromal, though they do agree that this group has not fully (and may never) fully progress to schizophrenia.

Currently, most research in the United States, Australia, and areas of Europe use the Ultra High Risk model. Unless otherwise specified, the following studies should be assumed to have used the Ultra High Risk criteria.

Rates of transition to psychosis. The rate of transition to psychosis is a difficult statistic to estimate, as different studies use one of the three characterizations of the prodrome mentioned above (basic symptoms, ultra high risk, or clinical high risk). In a review of 22 prospective studies of the prodrome, Olsen and Rosenbaum (2006) reported a wide range of transition rates. Of the studies using the ultra high risk criteria, studies reported transition rates between 9% and

54%. Studies using the basic symptoms criteria have less available information, though some report transition rates as high as 70%. The review included only one study that utilized clinical high risk criteria, of which the transition rate was 26.5% of CHR+ groups and 0% of CHR- groups at 6 month follow-up.

Most recently, studies have reported transition rates around 30% using the ultra-high risk criteria. A NAPLS study, conducted by Cannon et al. (2008) reported a 35.3% transition rate at two and half year follow-up, using one of the largest samples to date (*n*= 291). Fusar-Poli et al. (2012) conducted a meta-analysis of studies reported transition rates of participants at clinical high-risk for psychosis through 2011. These authors found transition rates of 18% at 6 months, 22% at 1 year, 29% at 2 years, and 36% at 3-year follow-up.

Converging evidence suggests that approximately 30% of clinical high risk individuals transition to psychosis between one and two years post follow-up, largely based on individuals fitting the ultra high risk categorization (Yung et al., 2003; Olsen & Rosenbaum, 2006; Yung, 2007; Fusar-Poli et al., 2012). If accurate, these individuals in the ultra high risk groups are at a risk for psychosis that is several thousand fold that of the normal population (Yung, 2007). Promising though this breakthrough may be, even the ultra high risk researchers have acknowledged that the sample being collected is very likely of those individuals in the late stages of the prodrome (Olsen & Rosenbaum, 2006) Moreover, the ultra-high risk model does not encompass individuals experiencing solely negative symptoms, despite these researchers' endorsement of a theoretical approach that includes a developmental progression from negative to positive symptoms and finally to psychosis (Yung & McGorry, 1996a; Salokangas & McGlashan, 2008).

Symptoms characterizing the prodrome. Preliminary research indicates that negative and non-specific symptoms are the symptoms most *frequently* reported during the prodrome, albeit retrospectively (Yung & McGorry, 1996a). In fact, of the 10 most frequently cited symptoms in a literature review of prodromal studies up to 1996, three symptoms were negative, three were non-specific or general, one was positive, and one was disorganized (Yung & McGorry, 1996).

Similarly, current research indicates that negative or non-specific (general) symptoms are the symptoms most frequently cited by psychotic individuals as the *first* symptom to develop. In the retrospective ABC first-episode schizophrenia study described previously, 73 % (n = 232) retrospectively reported first experiencing non-specific or negative symptoms, whereas only 7% reported initial positive symptoms (Hafner & an der Heiden, 1999). The remaining 20% reported an initial onset of both positive and negative or positive and non-specific symptoms. On a much smaller scale, Yung and McGorry (1996b) also interviewed first-episode individuals from their first-episode research clinic (exact criteria for "first-episode" were not given). These authors found that 19 of their 21 first-episode psychosis patients presented with what they termed "neurotic-type" initial symptoms, which included symptoms of anxiety, anger/irritability, and obsessive-compulsive features (all termed "classical neurotic symptoms") and depression. The other two presented with positive symptoms, one with perceptual disturbances and the other with preoccupation with overvalued ideas.

Although there appears to be a consensus in the literature with regard to which symptoms are most often present during the prodrome, there are conceptual and methodological limitations that must be mentioned. First, considerable literature suggests that many individuals with

psychotic disorders lack awareness, or insight, into their symptoms (e.g., Amador, Flaum, Andreasen, Strauss, Yale, Clark, & Gorman, 1994). Lack of insight may limit the ability of participants to accurately report their symptoms in both retrospective and prospective studies. Moreover, the retrospective nature of most of the studies, combined with interesting discrepancies associated with subtype of psychosis (Gourzis, Katrivanou, & Beratis, 2002) and with symptom intensity (Moller & Husby, 2000) make it necessary to more closely examine specific symptoms in light of contextual factors. For clarity, the symptoms will be presented in the order of presentation in the most widely used prodromal assessment measure in North America, the Scale of Prodromal Syndromes (SOPS; Miller et al., 1999). The SOPS measure divides the symptoms of the prodrome into positive, negative, disorganization, and general (or non-specific) symptom groupings, all of which are discussed in the following sections. However, within each grouping, only the symptoms with significant discussion in the literature will be discussed in detail.

Positive symptoms. Positive symptoms are termed "positive" because they are considered excesses or distortions of normal experiences (American Psychological Association, 2000). The positive symptoms included on the Scale of Prodromal Syndromes (SOPS) include unusual thought content/delusional ideas, suspiciousness/persecutory ideas, grandiose ideas, perceptual abnormalities/hallucinations, and disorganized communication (Miller et al., 1999); all but one of these (grandiose ideas) will be discussed further.

Unusual thought content/delusional ideas. On the SOPS, the unusual thought content and delusional ideas category is broken down into several categories: perplexity or delusional mood,

first rank symptoms (thought withdrawal, insertion, or control), over-valued beliefs, and other delusional content (Miller et al., 1999). The first and third symptoms are discussed further.

Perplexity or delusional mood. The symptom of perplexity or delusional mood involves the patients' sense that something profound and unexplainable is occurring or an uncertainty in what is happening to them and around them (Miller et al., 1999). Sometimes this will include perceiving time as unnaturally slower or faster, familiar surroundings as strange, or present events as having occurred before (Miller et al., 1999). For example, Yung and McGorry (1996b) found that 60% of their 21 first-episode psychotic patients experienced either a change in the sense of self, others, or the world, and 66% experienced perplexity or confusion related to the feeling that they didn't know what was going on both around and within them. Moller and Husby's (2000) conducted a similar retrospective study to Yung and McGorry (1996b), interviewing 19 first-episode individuals about symptoms prior to psychosis onset. Moller and Husby's participants met study criteria by experiencing a first-episode of schizophrenia (no further criteria were given) that was also less than two years following the initiation of "adequate" treatment. The individuals in this sample also reported a feeling or fear of losing inner control, difficulties controlling thoughts, and an inner chaos.

The delusional mood symptom seems to be an underrepresented and undervalued prodromal symptom. In one of the few studies to investigate the symptom, Moller and Husby (2000) found that it was not only a frequent occurrence, but also one of the first symptoms to develop in their patients. Despite this finding, an endorsement of delusional mood on the SOPS (without additional symptoms) will score in the "questionably present" or "mild positive

symptom" range, one that is insufficient in intensity on its own to meet the prodromal threshold required in most prodromal studies (Yung, Phillips, Yuen, et al., 2003; Miller et al., 1999).

Overvalued beliefs. Overvalued beliefs are unusual beliefs that are held at an intensity level just short of delusional conviction (Miller et al., 1999). These beliefs can be unusual either in content (bizarre), in degree of importance (preoccupation), or in the influence on behavior (leading to withdrawal or bizarre behavior; Miller et al., 1999). An aspect of this particular symptom, termed "odd beliefs or magical thinking," which also involves bizarre thought content and typically influences behavior, was a symptom of the psychotic prodrome in the third edition of the diagnostic manual (DSM-III-R; American Psychological Association, 1987). The preoccupation with such ideas can often lead to withdrawal, which was reported by Moller and Husby's (2000) patients. Fourteen of their 19 (74%) first-episode schizophrenia patients retrospectively reported an extreme preoccupation with and withdrawal to overvalued ideas. In a larger study, Gourzis, Katrivanou, and Beratis (2002) conducted interviews with 100 individuals currently hospitalized for schizophrenia in Greece. Seventy-four of these individuals were considered to be in their first episode, with no participant experiencing greater than 3 episodes (including the current episode). Gourzis et al. (2002) found that 18% of their total sample of 100 schizophrenic patients experienced odd beliefs or magical thinking and 8% had overvalued ideas. However, when broken down into schizophrenia subtype, the paranoid subtype experienced both of these phenomena more frequently, at 28% and 14% respectively. Importantly, this symptom has been documented not only retrospectively, but prospectively as well. In a prospective sample, Cannon et al. (2008) found that unusual thought content was associated with transition to psychosis within two and a half years follow up.

Non-persecutory ideas of reference. Non-persecutory ideas of reference denote patient perceptions that events or attention has special meaning or focus for them, which is not paranoid or persecutory in nature (Miller et al., 1999). Such ideas of reference are rarely discussed in the prodromal literature as frequent symptoms, but Gourzis et al. (2002) found that these ideas were most common in the prodrome reported by paranoid schizophrenic patients (50%), followed by the undifferentiated (35%) and disorganized (8%) schizophrenics.

As the first symptom to develop, Gourzis et al. (2002) reported that ideas of reference were the fourth most commonly reported initial symptom of individuals with paranoid schizophrenia. This symptom appeared to be subtype-specific, as the individuals with the disorganized, undifferentiated, or catatonic subtypes did not report it as an initial symptom.

Suspiciousness and persecutory ideas. Other distorted thought content, such as suspiciousness and persecutory ideas, have also been reported as a relatively frequent positive symptom the prodromal literature. Suspiciousness was reported as the seventh most commonly reported symptom (and only positive symptom) in Yung and McGorry's (1996a) review of the prodromal literature. Consistent with this finding, the same authors also found that suspiciousness was reported as a prodromal symptom in two-thirds of their sample of first episode schizophrenics in a separate study (Yung & McGorry, 1996b). Suspiciousness is also frequently reported retrospectively by psychotic patients' significant others. Hambrecht, Hafner, and Loffler (1994), using the ABC schizophrenia study data, analyzed the informant reports of their significant other's symptom onset. These researchers found that withdrawal and suspicion, as a combined symptom, was reported by 17.5% of patient's significant others, the second most common informant reported symptom. Suspiciousness may be partially accounted for by specific

types of psychotic patients. Investigating the effect of schizophrenia subtype, Gourzis et al. (2002) reported that 34% of patients reported suspiciousness during their prodrome, but (not surprisingly) paranoid schizophrenia patients, of whom 64% reported suspiciousness, primarily accounted for this number.

Persecutory ideas have been one of the few positive symptoms to be mentioned in the literature as one of the initial (as opposed to frequent) symptoms to develop during the prodrome. The ABC schizophrenia study indicated that persecutory delusions were the eighth most frequently reported initial sign of illness as reported retrospectively by schizophrenic patients (Hambrecht et al., 1994). The term "delusion", however, implies full transition to psychosis, so it is unclear if these were attenuated delusions (i.e., persecutory ideas) or whether the first noticeable sign for the patient was full psychosis. The patients' informants also reported the persecutory delusions, ranking as the tenth most frequently informant-reported first signs of illness (Hambrecht et al., 1994).

Beyond being an initial symptom to develop, suspiciousness or paranoia has also been documented as one of the few predictive positive symptoms. In a prospective study of prodromal symptoms, Cannon et al. (2008) noted that paranoia, along with unusual thought content, was predictive of transition to psychosis at two and half year follow-up. Though positive symptoms generally have been linked to transition (e.g., Ruhrmann et al., 2010; Yung et al., 2003), suspiciousness and unusual thought content have been the first of these symptoms to be discussed as predictive as stand alone symptoms (Cannon et al., 2008).

Unusual perceptual experiences. Unusual perceptual experiences have also been reported often enough to have been a symptom of prodromal psychosis in the DSM-III-R (American

Psychological Association, 1987). These experiences are most often an attenuated hallucinatory experience, either a misperceived, intensified, or changed perception of an actual external stimulus or a vague, infrequent perception of a stimulus in the absence of one (American Psychological Association, 1987; Miller et al., 1999).

Yung and McGorry (1996b) found that perceptual changes, in general, were described by over half of their sample of first-episode patients during their prodrome, including either an increase or decrease in the intensity of sensory perceptions. Similarly, Moller and Husby (2000) reported that 6 out of 19 patients experienced some change in simple perception. These disturbances included the intensity of sensory perception as well as distorted perception of the body and vague attenuated hallucinations (ringing sounds, thunderclaps, foggy vision). Broken down by subtype, Gourzis et al. (2002) found that 60% of undifferentiated schizophrenic patients reported unusual perceptual experiences during the prodrome, whereas 31% of the disorganized and 28% of the paranoid schizophrenia patients reported such an experience.

Disorganized communication. Disorganized communication, the symptom attempting to capture the construct of thought disorder, primarily measures a disruption in goal-directed thought on the SOPS (Miller et al., 1999). This is seen in the degree of so-called "loosening of associations" during conversation, measured by a person going off track (circumstantiality) or never getting to the point (tangentiality; Miller et al., 1999; American Psychological Association, 2000). Clinicians are also told to include other evidence of thought disorder such as deficiencies in content (poverty of content) or sheer volume of speech (poverty of speech) or being unable to complete a thought (thought blocking).

The DSM-III-R considered the "digressive, vague, over-elaborate, or circumstantial speech; poverty of speech; or poverty of content of speech" to be a symptom of the psychotic prodrome (American Psychological Association, 1987). Yung and McGorry (1996b) found that one half of their sample reported experiencing abnormal speech patterns during the prodromal phase. Gourzis et al. (2002) found that 36% of their sample experienced poverty of speech and 20% experienced poverty in content of speech. Both symptoms were most common in the disorganized subtype of schizophrenia, occurring in 62% and 58% of the disorganized patients, respectively. Other symptoms of thought disorder, such as thought blocking, appear to be much less common. Yung and McGorry (1996b), the only authors to mention this symptom during the prodrome, found that four (19%) of their first-episode patients retrospectively reported this phenomenon.

The only disorganized communication symptom to appear in the literature as a primary initial symptom was poverty of speech. Gourzis et al. (2002) found that individuals in the paranoid schizophrenia subtype were the only ones to report poverty of speech as one of the first noticed symptoms. They found that poverty of speech was the third most frequently cited first symptom among those individuals in the paranoid subtype.

Negative Symptoms. Negative symptoms are termed "negative" to reflect a loss or lack of normal experiences or expressions (American Psychological Association, 2000). The SOPS assessment measure includes social anhedonia, avolition, and decreases in expression of emotion, experience of emotions and self, ideational richness, and occupational functioning as negative symptoms of the psychotic prodrome. The emotional expression, experience of

emotions and self, and ideational richness will not be discussed due to the lack of research on these particular symptoms.

Social anhedonia, social isolation, and/or withdrawal. Social anhedonia, social isolation, and/or withdrawal have been among the most frequently cited prodromal symptoms in the literature, often considered one of the hallmark characteristics of the phase. Marked social isolation or withdrawal was considered a symptom in the DSM-III-R (American Psychological Association, 1987) and was the sixth most frequently reported prodromal symptom in Yung and McGorry's (1996a) review. Yung and McGorry (1996b) noted that social withdrawal was reported in two thirds of their patient sample, whereas Moller and Husby (2000) noted that withdrawal was described by 14 of 19 patients and isolation by 10 of 19 patients. The social isolation symptom is so prevalent in the literature that Cornblatt et al. (2003) list it as one of their four core vulnerability symptoms (all negative symptoms) for schizophrenia and a hallmark of the clinical high risk, negative (CHR-) group (along with school failure). Interestingly, Gourzis et al. (2002) found that though patients with paranoid schizophrenia were more likely to experience marked isolation (92%), patients with disorganized schizophrenia were more likely to report marked withdrawal (69%). The differentiation between the two symptoms was not entirely clear, but the former implies more physical removal, or seclusion, whereas the latter implies a retreat either physically or in the quality or quantity of interpersonal interaction.

In terms of symptom progression, social withdrawal and isolation have also commonly been reported as the first noticed symptoms by significant others that are different from the patient's normal baseline. The German ABC schizophrenia study with first-episode patients indicated that this symptom ranks somewhere between the sixth and ninth most frequently

reported first symptom (Hambrecht et al., 1994; Hafner & an der Heiden, 1999). Withdrawal and suspicion, when combined, is reported by approximately 10% of patients as an initial symptom (Hambrecht et al., 1994; Hafner & an der Heiden, 1999). However 10% also report social withdrawal by a lack of communication (Hafner & an der Heiden, 1999). Informants also report social withdrawal as a preliminary symptom of illness, the second most frequently reported initial symptom by patients' significant others (17.5%; Hambrecht, Hafner, & Loffler, 1994).

Withdrawal or isolation seems to vary as a function of schizophrenia subtype. Marked isolation was the most frequently reported initial symptom of paranoid schizophrenics who retrospectively described their prodromal experience (Gourzis et al., 2002). In the disorganized and undifferentiated subtypes, withdrawal was the third most frequently reported initial symptom. Neither withdrawal nor isolation was one of the most frequent symptoms reported by catatonic schizophrenics.

Social deficits as a global symptom has been found to be predictive of transition to psychosis in a prodromal sample at two year follow-up (Cannon et al., 2008). It could not be determined by the data presented in the study whether these deficits were associated with or driven by social withdrawal, anhedonia, or avolition.

Avolition. According to Yung and McGorry (1996a), avolition was the second most frequently reported prodromal symptom across multiple studies reviewed. This reduction in drive, motivation, or energy, once considered a DSM-III-R symptom of the psychotic prodrome, has been reported in over two thirds of some samples of psychotic patients (American Psychological Association, 1987; Yung & McGorry, 1996b; Moller & Husby, 2000). More specifically, Yung and McGorry (1996b) found that approximately two thirds of their sample

reported loss of drive and fatigue or loss of energy, and half of the sample reported a loss in interests. Gourzis et al. (2002) also found a high overall rate of lack of initiative, interests, or energy (43%), with most reports stemming from patients with either the disorganized (92%) or undifferentiated (65%) subtypes of schizophrenia.

Lack of energy or slowness ranked as the seventh most frequently reported first symptom to develop in the German ABC sample, experienced as an initial prodromal symptom by 12% of patients (Hafner & an der Heiden, 1999; Hambrecht et al., 1994). Avolition was also reported by significant others; eleven percent of informants reported lack of energy as the patients' initial symptom, placing it as the sixth most frequent symptom among informants (Hambrecht et al., 1994). Interestingly, individuals classified in the disorganized subtype reported this symptom as the first to appear (Gourzis et al., 2002). Marked lack of initiative, interests, or energy was the most frequently reported primary symptom by this subgroup but not by the paranoid, undifferentiated, or catatonic subtypes.

Occupational functioning. Another similar and often reported symptom is a decrease in occupational, school, or other role functioning. This symptom, which was also considered a DSM-III-R prodromal symptom, was the eighth most frequently reported prodromal symptom across studies in the Yung and McGorry literature review (1996a; American Psychological Association, 1987). Yung and McGorry, in their 1996b sample, reported that two thirds of patients experienced such a decline in role functioning. Even more frequently, the Moller and Husby (2000) sample reported near universal experience of role decline, with 17 of 19 reporting the symptom. Gourzis et al. (2002) found evidence of impairment of role functioning in 59% of their schizophrenic sample, with the frequencies ranging from 92% in the disorganized and 80%

in the undifferentiated to 30% in the paranoid subtype. The prevalence of this symptom has led Cornblatt et al. (2003) to define this symptom as another core vulnerability dimension for schizophrenia.

Although not frequently reported by significant others, poor work performance was reported by 11% of patients (rank of 8) in the ABC schizophrenia first-episode sample as one of the first three symptoms to occur in their illness (Hafner & an der Heiden, 1999; Hambrecht et al., 1994). Although this symptom is often thought to be a result of other prodromal symptoms, for both the undifferentiated and catatonic subtypes, this symptom was the most frequently reported *first* symptom reported during the prodrome (Gourzis et al., 2002). The disorganized subtype reported the impairment in role functioning as the fourth most frequently reported first symptom, whereas this symptom did not appear as a first symptom frequently for the paranoid subtype (Gourzis et al., 2002).

Disorganization Symptoms. The disorganization symptoms are a category of disorganized thought and behavior patterns that characterize the prodrome and later psychotic phase. The SOPS includes the following symptoms: odd behavior or appearance, bizarre thinking, difficulties in focus or attention, and impairment in personal hygiene (Miller et al., 1999). Because only one symptom of this type, deficiencies in concentration and attention, has been discussed at any length in the literature, it will be the one presented here.

Concentration and attention. Not only is marked difficulty in concentration and attention the most discussed disorganization symptom, but it is also the most frequently reported prodromal symptom in the literature, according to Yung and McGorry's (1996a) review. Supportive of this finding, concentration difficulties were reported by two thirds of the Yung and

McGorry (1996b) sample, and Moller and Husby (2000) reported that approximately the same percentage of their sample experienced disturbances in formal thought, in which they included difficulties in concentration. Not only do patients notice difficulties in concentration, informants report observing this symptom in their prodromal significant others, though at a much lower rate (Hambrecht et al., 1994). Other similar symptoms include distractibility and difficulties with memory function (Yung & McGorry, 1996b). This cluster of symptoms has led Cornblatt et al. (2003) to label "cognitive deficits" another of their underlying vulnerability factors for schizophrenia.

Of the disorganized symptoms, difficulties with concentration and attention have also received the most support as a potential initial prodromal symptom. The German ABC schizophrenia study, depending on the definition of other symptoms, ranked the deficits in thinking and concentration as either the fourth (16%) or fifth (12%) most commonly reported first prodromal symptom by patients (Hafner & an der Heiden, 1999; Hambrecht et al., 1994). Informants also indicate these two symptoms may be one of the first they notice, with 8% of informants ranking it among the first to develop (ranked 9th; Hambrecht et al., 1994). These cognitive symptoms may be particularly prognostic for the disorganized schizophrenia subtype. Gourzis et al. (2002) found that among their sample of individuals with disorganized schizophrenia, these symptoms were the second most frequently reported initial symptom. Individuals with other subtypes did not frequently report the cognitive symptoms as primary initial symptoms.

General or Non-Specific Symptoms. The general symptoms, also called non-specific symptoms, are symptoms considered not to be specific or uniquely pathognomonic to the psychotic

spectrum of disorders. Therefore, though frequently reported during the prodrome, these symptoms are often difficult to identify as "prodromal" symptoms in the absence of other, more specific symptoms. Symptoms grouped in this cluster in the SOPS are sleep disturbance, dysphoric mood, motor disturbance, and impaired tolerance to normal stress (Miller et al., 1999). The two symptoms that have received the most attention in the literature, and will be discussed further, are sleep disturbances and dysphoric mood.

Sleep disturbance. Sleep disturbance can refer to an increase or decrease in hours of sleep or a shift in the timing of the sleep/wake cycle (night/day reversal; Miller et al., 1999). Any form of sleep disturbance was ranked ninth overall in most frequently reported prodromal symptom according to the Yung and McGorry (1996a) literature review. Even more prevalent, Yung and McGorry's (1996b) descriptive account of the prodrome indicated that 100% of their patients' reported experiencing some form of sleep disturbance.

Changes in sleep, when combined with changes in appetite, ranked as the fourth most frequently reported initial symptom according to the ABC schizophrenia study patients (Hambrecht et al., 1994). One of the more observable symptoms, change in sleep pattern was the second most often informant-reported initial symptom (Hambrecht et al., 1994). Ruhrmann et al. (2010) even reported sleep disturbance as *predictive* of transition to psychosis in their prospective analysis of the prodrome.

Dysphoric mood. Dysphoric, depressed, irritable, or anxious mood encompasses several of the most commonly reported prodromal symptoms. Yung and McGorry (1996a) indicate that depressed mood is the third most frequently reported prodromal symptom, whereas anxiety and irritability are the fifth and ninth, respectively. In the 21 first-episode individuals interviewed by

Yung and McGorry (1996b), two thirds experienced anxiety, irritability, and depressed mood during their prodrome. Corresponding with the anxiety and depression symptoms, these researchers also found that over 20% had suicidal ideation, 40% had mood swings, 20% had obsessive-compulsive features, and 50% had aggressive or disruptive behavior (Yung & McGorry, 1996b). Moller and Husby (2000) also found two thirds of their sample experienced what they termed neurotic-like disturbances, which included depression, suicidal ideation, anxiety, unstable mood, restlessness, anger, and irritability. These affective disturbances, as Cornblatt et al. (2003) have termed them, are also one of the core vulnerability dimensions for schizophrenia according to these researchers.

The triad of depression, anxiety, and either restlessness or irritability may be both the most frequent symptoms across the prodrome and the earliest reported to emerge. The ABC schizophrenia study ranked depression, anxiety, and restlessness as the top three most frequently reported first symptoms, reported by 17-19%, 18%, and 19%, respectively (Hafner & an der Heiden, 1999; Hambrecht et al., 1994). These patients' informants also reported depression as the most frequent first symptom (18%), restlessness as the fourth most frequent (14%), and anxiety as the fifth most frequent (12%). Irritability was reported by 10% (ranked 7th) of the informants as one of the most frequent symptoms, whereas only 4% (ranked 16th) of the patients' reported it (Hambrecht et al., 1994).

When taking subtype into account, irritability was a commonly reported first symptom for those with paranoid schizophrenia (Gourzis et al., 2002). This was the second most frequently reported first symptom for the paranoid schizophrenic individuals, though no other subtype mentioned it as frequently. One prospective study has identified depression as a

predictor of psychosis in the prodromal population. Yung et al. (2003) determined that depression was associated with transition to psychosis in a prodromal sample within a six month follow-up period.

Conclusion. Despite multiple studies describing the initial and frequent symptoms of the prodrome, most have been conducted retrospectively and without comparison to a control group (normal control or clinical control). These methodological limitations can only definitively state that these symptoms are characteristic of individuals prior to development of schizophrenia, not whether these symptoms can predict subsequent schizophrenia. In fact, research is clear that many individuals who experience these symptoms do not go on to develop schizophrenia (McGorry, Yung, & Phillips, 2003).

Recent prospective studies (e.g., Cannon et al., 2008; Yung et al., 2003; Ruhrmann et al., 2010) provide some insight into the positive (unusual thought content, paranoia) and negative or general symptoms (sleep, depression, social impairments) that may be predictive of psychosis. Large-scale longitudinal research projects are currently in progress that further attempt to use these symptoms as prospective and predictive tools (e.g., Woods et al., 2009, Piskulic et al., 2012).

With these limitations in mind, much can be said about the symptoms that are frequent prior to psychosis. When picturing the development of psychosis, many people would describe positive symptoms. However, the negative and non-specific or general symptoms that are reported by patients to be both the most prevalent and the first symptoms to emerge. Three of the negative symptoms (social anhedonia, avolition, and occupational functioning) ranked in the top ten most frequently reported symptoms during the prodrome in a review of studies spanning the

past 100 years (Yung & McGorry, 1996a). Studies frequently report these three symptoms as being experienced by between one half to two thirds of psychotic patients during the prodromal phase (Moller & Husby, 2000; Yung & McGorry, 1996b; Gourzis et al., 2002). The non-specific symptoms of dysphoric mood, or more generally, depressed mood, anxiety, and irritability, are the third, fifth, and ninth, most reported symptoms and are experienced by two thirds of patients (Yung & McGorry, 1996a; Moller & Husby, 2000; Yung & McGorry, 1996b). The disorganized symptom of difficulties with concentration and attention is also quite prevalent. Yung and McGorry's (1996a) literature review found that this symptom was the most frequently retrospectively reported prodromal symptom, and other empirical studies found at least two thirds of prodromal patients experienced these difficulties (Moller & Husby, 2000; Yung & McGorry, 1996b).

Developmentally speaking, the negative and non-specific symptoms are the most frequently retrospectively reported as the first emerging noticeable sign of change. Social anhedonia, avolition, and occupational functioning are cited as the sixth, seventh, and eighth most frequently reported initial symptoms (Hafner & an der Heiden, 1999). Social anhedonia or withdrawal ranks even higher on the frequency of informant-reported symptoms as the second most common symptom reported (Hambrecht et al., 1994). The general symptoms of depression, anxiety, and restlessness were the top three most frequently reported first symptoms by patients and were also very frequent among informant reports (Hafner & an der Heiden, 1999; Hambrecht et al., 1994). Concentration and attention problems, the most common disorganized symptom to be reported as an initial symptom, also ranked in the top five in prevalence of all initial symptoms reported (Hafner & an der Heiden, 1999; Hambrecht et al., 1994).

In comparison to the other symptom types, positive symptoms were rarely reported. These symptoms were less frequently reported overall, with only one symptom (suspiciousness) reaching Yung & McGorry's (1996a) top ten most frequently reported symptoms. These postitive symptoms were reported even less frequently as initial symptoms, with the seeming exception of individuals who developed paranoid schizophrenia (Gourzis et al., 2002). The exception may be the prodromal symptom of attenuated delusional mood, which has continued to be discussed infrequently yet compellingly in qualitative studies (e.g. Moller & Husby, 2000, 16/19 patients; Yung & McGorry, 1996b, 14/21 patients). This symptom has failed to reach the attention of most researchers, with current classification systems designating this symptom to be insufficient in and of itself to qualify as a positive prodromal symptom. Despite the low frequency of reports of attenuated positive symptoms, especially as initial symptoms, attenuated positive symptoms are often the primary diagnostic threshold used to make both predictive and treatment decisions. As a result, some researchers are considering a developmental trajectory of the prodrome that explains the progression of different prodromal symptoms, as well as the development of subsequent psychosis.

A developmental perspective of the prodrome. Cornblatt and colleagues' Recognition and Prevention (RAP) program is one of the first known groups to develop and subsequently test a developmental model of the prodrome for psychosis (the other being Huber and the basic symptom group). According to Cornblatt and colleagues (Figure 1), individuals who become psychotic have an underlying biological vulnerability to the disorder, the cause of which has speculated to be such factors as genes or environmental toxins that impact the development of the brain (Cornblatt et al., 2003). This biological vulnerability begins to present itself in childhood as behavioral deficits and cognitive deviations (Maier, Cornblatt, & Merikangas,

2003). Transitioning into adolescence, prodromal individuals begin to experience non-specific and negative symptoms that are also expressions of the same underlying vulnerability (Maier et al., 2003). These disturbances, according to their theory, tend to take the form of affective disturbances, school failure, and finally social isolation and characterize the CHR- prodromal group as defined by these researchers (Cornblatt et al., 2003). The Cornblatt theory posits that as a result, these adolescents likely acquire affective or anxiety diagnostic labels if/when interacting with the mental health system (Maier et al., 2003). As these adolescents move into the late prodromal phase and develop attenuated or pre-psychotic positive symptoms at an increasing rate (the CHR+ group), they are likely to be brought to the attention of mental health professionals, often adding schizotypal, schizoid, paranoid, or other personality disorders to their diagnostic charts (Maier et al., 2003). Until recently, it wasn't until the adolescent or young adult developed fully psychotic symptoms that he or she would be flagged as at risk for psychosis (Maier et al., 2003).

The neurodevelopmental perspective (Cornblatt et al., 2003; Maier et al., 2003), as these researchers have termed it, is parsimonious with the retrospective literature on the psychotic prodrome to date. They proposed that the underlying genetic component for schizophrenia is expressed along four core vulnerability dimensions, or CASIS (Cornblatt et al., 2003). CASIS refers to the cognitive deficits, affective disturbances, social isolation, and school failure that are reported frequently (and discussed in detail above) by psychotic patients during their prodromes. The presence of the vulnerability, however, does not inevitably produce psychosis (Cornblatt et al., 2003). The vulnerability must be combined with environmental or biological trigger, or series of triggers, which then produces increasingly severe attenuated positive symptoms, usually

occurring in mid to late-adolescence (Cornblatt et al., 2003). These increasing positive symptoms are likely to eventually transition into psychosis (Cornblatt et al., 2003).

Researchers have noted, however, that even individuals with positive symptoms do not always progress to full psychosis (Yung et al., 2003). The RAP neurodeveopmental model accounts for this by explaining that positive symptoms may present in certain individuals in the absence of the aforementioned biological vulnerability (Cornblatt et al., 2003). There can be various reasons why attenuated positive symptoms may occur in individuals without schizophrenia; these reasons include stress, certain Axis I and Axis II disorders (borderline personality disorder, post-traumatic stress disorder, obsessive compulsive disorder, depression, bipolar disorder), medical disorders (epilepsy, brain tumor), or substance use (marijuana, hallucinogens, stimulants). Likewise, it is possible for an individual to have the biological vulnerability and not develop schizophrenia, likely developing schizotypal personality disorder or even no noticeable symptoms. Therefore, according to these researchers, both the vulnerability expressed as negative and non-specific symptoms (CASIS) and attenuated positive symptoms brought on by a trigger are necessary to produce schizophrenia (Cornblatt et al., 2003).

Not only is the neurodevelopmental model the most comprehensive model of the prodrome, it has been empirically supported. In 2003, Cornblatt et al. followed 62 adolescents and young adults that met criteria for either the CHR- or CHR+ groups. These researchers tracked the participants' symptoms over three-years at six, 6-month time-points. When analyzing the data, the researchers noted a bimodal distribution of the CHR+ group and decided to split the CHR+ group into a moderate (CHR+ moderate) and severe (CHR+ severe) positive symptom

group based on total SOPS positive symptom score. Researchers then analyzed the follow-up data for each group after a minimum of six months post-baseline (Cornblatt et al., 2003). Forty-eight participants were available for the follow-up and eleven had made a transition from one group to another (or psychosis). Seven individuals (*n*=15) from the CHR+ severe group made the transition to full psychosis over the six-month period. Two individuals (*n*=19) from the CHR+ moderate group made the psychotic transition, one straight from CHR+ moderate to psychosis and the other transitioning through the CHR+ severe group. None of the individuals (*n*=14) from the CHR- group transitioned to psychosis. However one CHR- individual developed positive symptoms, transitioning into the CHR+ moderate group.

This transitional pattern is consistent with the neurodevelopmental prospective proposed by Cornblatt et al. (2003). Those with attenuated negative symptoms as their only risk factor did not progress to psychosis within 6 months, but one did develop positive symptoms at a moderate level. Those with moderate positive symptoms progressed either to severe positive symptoms or psychosis, the latter of which may indicate an inability to interview the person at the time that he or she progressed through the severe positive symptoms group. Finally, almost half of the participants in the severe positive symptoms group progressed to psychosis during the interval, supporting the notion that this phase is the latest of the prodromal phases.

As revolutionary as the RAP approach is, it leaves several questions unanswered. The first is whether most of the individuals presenting with attenuated negative symptoms are, in fact prodromal, or if they are simply false positives. From the study results, it is unclear whether the remainder of the CHR- individuals would eventually develop positive symptoms because the follow-up period was limited to six months. The other main question is whether negative

symptoms are the *first* symptoms to develop. The CHR- group, though determined by endorsement of negative symptoms, was allowed to have positive symptoms as long as these symptoms did not reach a moderate level (Cornblatt et al., 2003). Therefore, it is possible that the first symptom(s) to develop were low-level negative symptoms, low level positive symptoms, or moderate level negative symptoms, all of which would be lumped into the CHR- group. The possibility of low-level positive symptoms being the initial symptoms to emerge is not a new concept. As reported in Yung and McGorry's (1996a) review, Chapman and colleagues proposed the emergence of low-level positive and negative symptoms as initial symptoms, with the non-specific or general symptoms as a reaction to these changes. Moller and Husby (2000), in their previously reported retrospective first episode study, also noted that the first symptoms reported by their patients were the disturbance in the perception of the self, noted by 16 of the 19 individuals. What these authors describe parallels delusional mood, providing descriptions of "something totally wrong" or "pervasively changed" (Moller & Husby, 2000, pgs 222-223). This vague, yet clearly disturbing, perception in the prodromal patients provides a reasonable explanation for many of the negative symptoms such as social isolation or withdrawal, as well as many of the non-specific or general symptoms like depression, anxiety, or irritability.

Additionally, the Cornblatt et al. (2003) study has several methodological limitations. First, the researchers either did not assess or account for treatment during the phase of follow-up. The article did include an informal discussion of medication targeting stage of prodrome (CHR- vs. CHR+), but transition data analyses did not control for medication or psychotherapeutic intervention effects. Moreover, the small sample size and lack of a comparison group (normal controls or clinical controls) limits confidence in the information provided. Without a comparison group, it is unclear whether those that would not fall under the CHR- or CHR+

categorizations would also transition to psychosis (false negatives) or whether the proposed screening methodology improves upon chance in identifying those at high risk for schizophrenia. This may be especially true for the CHR- group, whose symptoms are non-specific and run a high risk of mis-categorization and limited utility. However, the data on transition from the CHR- to CHR+ groups suggests that this group should, at the very least, be studied further.

A full developmental model of the prodrome is, therefore, still being researched. Currently, however, the RAP model has been the only one to be tested empirically (with the exception of some research on the basic symptoms model), and was largely supported.

Axis I comorbidity and the prodrome. Individuals thought to be prodromal for psychosis (or "clinical high risk") do not currently meet criteria for a psychotic diagnosis, with one exception. The BLIPS group (or SLPs in the Clinical High Risk model) could technically be diagnosed as Psychotic Disorder Not Otherwise Specified. Though treatment seeking, these individuals were not necessarily seeking treatment for psychotic-like symptoms, specifically. Therefore, upon entry to a research study or clinic, these individuals present with a variety of other Axis I and Axis II disorders.

The largest North American study to date, Woods et al. (2009) combined data from 8 sites across North America as part of the North American Prodrome Longitudinal Study (NAPLS). Together, the sites collected 860 participants, meeting criteria for one of the ultra-high risk groups (APS, GRDS, or BLIPS), normal controls, or help-seeking controls (referred as potentially meeting prodromal criteria, but subsequently did not meet ultra high risk criteria). The NAPLS study is a retrospective pooling of prospective data and followed the eligible individuals' prodromal symptom development from 1998-2005 for the data presented (the

NAPLS study is currently ongoing). The authors reported general demographics of the sample, along with clinical characteristics. Among the various statistics reported were high rates of comorbid diagnoses in the prodrome. Of those individuals meeting criteria for the prodrome (*n*=377), 69% met criteria for at least one mood or anxiety disorder (See Table 1 for each disorder). This finding is consistent with multiple single site studies (included in the NAPLS analyses) that have previously reported mood and anxiety disorders as the most common Axis I diagnosis among prodromal patients (e.g., Lencz, Smith, Auther, Correll, & Cornblatt, 2004). In the Woods et al. (2009) study, 25% of prodromal participants met criteria for a substance abuse or dependence disorder and 44% met for at least one personality disorder (Table 2). This indicates that beyond attenuated psychotic symptoms, individuals considered prodromal for psychosis present with a wide variety of other symptoms in need of treatment. It is unclear whether these additional non-psychotic symptoms are part of the prodrome itself (especially the mood and anxiety disorders), are secondary to developing psychotic symptoms, or are independent of the prodrome entirely. Regardless of the etiology of such symptoms, these symptoms will clearly impact treatment of the attenuated psychotic symptoms as well as require separate treatment targets.

Treatment during the prodrome. Initial investigations into the treatment of the psychotic prodrome have been based on the principle of indicated prevention (Olsen & Rosenbaum, 2006). Individuals considered "high risk" are given medication, psychotherapy, or both to attempt to prevent the transition to psychosis (Preti & Cella, 2010; Olsen & Rosenbaum, 2006). Individual clinical trials and reviews have concluded that both pharmacological and psychological interventions are useful for indicated prevention, although the exact mechanisms

of action are unclear (Preti & Cella, 2010; Olsen & Rosenbaum, 2006). To date, only a few randomized controlled trials have been completed, though each has been promising.

In the most recent review, and only meta-analysis, of randomized controlled prodromal treatment studies, Preti & Cella (2010) investigated the effects reported by five independent RCTs. Each RCT investigated a different intervention for the prodrome (medication, psychotherapy, supplement), though all but one used the ultra high risk criteria for study entry (one study consisted of schizotypal personality disorder only). Of these, only two were psychotherapy studies for prodromal individuals (the third "intensive family intervention" only included schizotypal participants), of which one combined psychotherapy with medication (risperidone). The meta-analysis indicated that, taken together, the various interventions across the five RCTs were able to significantly reduce the number of participants transitioning to psychosis immediately following treatment, with effectiveness reducing over time. Despite describing this finding as "robust," the analysis provided little information about the effectiveness of the specific type of intervention beyond the single studies. The two psychotherapy studies are therefore discussed here.

McGorry, Yung, Phillips, Yuen, Francey, Cosgrave, et al. (2002), using the ultra high risk prodromal criteria, conducted a randomized, 6 month controlled trial comparing a needs based, supportive psychotherapy to cognitive behavioral therapy (CBT) with antipsychotic medication (daily 1-2 mg risperidone). Results of this trial indicated that at six month follow-up (or the end of the intervention) a significantly fewer percentage of prodromal individuals converted to psychosis in the CBT and antipsychotic group than in the supportive therapy group. However, this difference did not remain six months post-intervention (one year from baseline).

Unfortunately, the active intervention combined psychotherapy and medication, making it impossible to determine the effects of either intervention independently.

Similarly, Morrison, French, Walford, Lewis, Kilcommons, Green, et al. (2004) also used the ultra high risk prodromal criteria and conducted a randomized 6 month controlled trial comparing cognitive therapy versus a monitoring only condition. Over the six-month period (immediately post-intervention), they found that the cognitive therapy group made significantly fewer transitions to psychosis. These researchers found that effects held over a six-month follow-up (one year post-baseline), using the dependent measure as number of positive symptoms rather than transition to psychosis (Morrison et al., 2004). Morrison, French, Parker, Roberts, Stevens, Bentall, and Lewis (2007) have since published follow up data on the same sample that indicates that cognitive therapy benefits may even reduce the likelihood of transition to psychosis up to three years beyond treatment.

Many of the methodological limitations for the two studies described above are similar and common to treatment studies in prodromal research. The sample sizes (n=59 in McGorry et al., 2002; n=58 in Morrison et al., 2002, 2004, 2007), though small, are typical for studies in the prodromal area as a result of a low base-rate for individuals considered prodromal by any criteria. However, the small sample sizes did not limit the ability to detect significant effects. It should be noted, however, that Morison et al. (2004) excluded two participants post-hoc, determining that the participants were psychotic upon entry (based on information gathered post-baseline). Importantly, had these two individuals been included, the differences between the intervention groups would not have been significant. This result illustrates the very precarious group differences with sample sizes as small as 58. Though both studies attempted to blind

raters, participants often un-blinded them by mentioning medication or therapists during assessments. This limitation, though not ideal, is unlikely to account for the transition rate differences since the diagnoses were also confirmed by psychiatrist diagnosis (independent psychiatrist in Morrison et al., one of the authors in McGorry et al.). Finally, because there were no measures of treatment adherence to any therapeutic intervention, it is possible (though perhaps not probable) that effects are due to non-specific effects of directive contact with a mental health professional, rather than specific to cognitive therapy (Morison et al., 2004). In both cases, the comparison groups provided professional contact, but in an as-needed supportive (McGorry et al.) or monitoring (Morrison et al.) capacities. The number of patient contacts and type of contact (directive vs. non-directive) were not consistent when comparing active and comparison interventions.

Despite the encouraging results of multiple other preliminary clinical trials and the above RCTs (Olsen & Rosenbaum, 2006), the effects of cognitive and cognitive behavioral therapy appear to target transition to psychosis specifically, and may neglect other problems for these individuals. In the Morrison et al. (2004) study, data suggested that neither general functioning nor distress improved over time for either intervention. McGorry et al. (2002) had similar findings, indicating that symptoms improved but functioning levels did not. This has led to symptom-specific interventions, such as Bechdolf, Wagner, Veith, Ruhrmann, Pukrop, Brockhaus-Dumke, et al. (2007) whose adapted CBT model included cognitive remediation and a focus on negative symptoms. Bechdolf et al. randomized 113 participants, who met the basic symptom criteria for the prodrome, to receive either the adapted cognitive behavior therapy or supportive counseling for 12 months. Despite the adaptation specific to social adjustment, Bechdolf et al. found no differences between the cognitive and supportive therapy groups in the

"work," "social," and "global" domains. Both therapeutic techniques resulted in improvement in one or more areas, but there were no significant differences between the two. However, improvement in these symptom domains had previously been problematic in other RCTs. Limitations of this study were similar to the prior two RCTs, including non-blind assessment, no adherence ratings for the interventions, no control for amount of contacts, and the use of an adjustment measure for individuals with schizophrenia rather than prodromal symptoms. Moreover, a large amount of missing follow-up data (final n=67) may have biased the results towards those who were most successful in treatment.

Despite emerging evidence to suggest that therapies such as CBT are effective in delaying transition to psychosis, little is known about the treatment of other symptoms with which this population presents. Large sample studies such as the NAPLS study (Woods et al., 2009) show that the prodromal population has a wide range of Axis I and Axis II comorbidities. These symptoms could be direct targets in treatment or moderate the effectiveness of targeting prodromal symptoms. Because the current standard is to refer out individuals who present with primary diagnostic needs other than prodromal symptoms (e.g., substance dependence, high risk of harm to self or others), the most likely way that comorbid symptoms affect treatment is by moderating the effectiveness of treatments for prodromal symptoms (including the "general" symptoms such as depressive mood). Of clear interest in this respect are the personality disorders, which have been shown to be both prevalent in the prodromal population (Woods et al., 2009), and are known to moderate treatment effectiveness in patients with schizophrenia (Keown, Holloway, & Kuipers, 2005). Therefore, the focus of Part II of this review is Axis II involvement in the prodrome.

Part II: Axis II Comorbidity and the Prodrome

Although the area of prodromal treatment is making headway, consideration of the influence of personality disorders or corresponding traits remains unstudied. As mentioned above, treatment approaches are currently being developed and adapted, with multiple treatment manuals being published. These manuals do not make specific treatment considerations for individuals with Axis II diagnoses or involvement, despite high prevalence rates (discussed below) reported in the literature. Rates of personality disorders in the prodrome are similar if not higher than those seen in schizophrenia and other psychotic disorders. In the following sections, the comorbidity of the prodrome and personality disorders is discussed, taking into consideration the prevalence, effects, and treatment considerations for those dually diagnosed. Because this area is so limited, research from the psychotic disorders is drawn upon in each section to provide further information were the person to fully develop psychosis.

Prevalence of personality disorders.

Comorbidity with psychotic disorders. The prevalence rates of co-occurring personality disorders and schizophrenia are relatively unclear. Currently, estimates of comorbidity are made from multiple small-scale studies that vary widely in ranges reported. For example, in a meta-analysis conducted in 2008, Newton-Howes, Tyrer, North, and Yang indicated that twenty different studies reported between 4.5 to 100% comorbidity between psychosis and any personality disorder. Overall, these authors cited a 39.5% median comorbity rate, but did not break down the personality disorder diagnoses.

In a 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), investigators assessed seven personality disorders (paranoid, histrionic, schizoid, antisocial, avoidant, dependant, and obsessive-compulsive) and obtained self-reported diagnoses of psychosis (McMillan, Enns, Cox, & Sareen, 2009). These researchers found that each of the personality disorders were found at a higher rate in community members that reported current or previous psychotic diagnoses (60.1%) than those community members who reported no such psychotic diagnosis (14.8%). In fact, those with psychotic diagnoses were 3.28 times more likely to have at least one personality disorder than those without a psychotic diagnosis. The largest odds ratios were found for dependant (35.24) and avoidant personality disorders (16.35), with all other personality disorders ranging from 7.75 to 4.67. Unfortunately, this study did not assess for several key personality disorders, such as borderline, narcissistic, or schizotypal, and also did not assess for psychosis, relying instead on participant self-report of diagnosis.

Keshavan, Duggal, Veeragandham, McLaughlin, Montrose, Haas, and Schooler (2005) conducted structured clinical interviews to obtain personality disorder diagnoses of individuals with first episode schizophrenia, non-schizophrenia psychosis, and healthy controls. These researchers found higher levels of each cluster among individuals with both types of psychotic disorders as compared to healthy controls, with specific clusters associated with specific types of psychoses. Cluster A and Cluster C personality disorders were significantly higher in individuals with schizophrenia, whereas Cluster B and Cluster C were significantly higher in individuals with non-schizophrenia psychoses (bipolar and depressive disorders) as compared to healthy controls. More specifically, within the three clusters, schizotypal (Cluster A) and avoidant (Cluster C) were diagnosed significantly more often in individuals with schizophrenia, whereas

borderline (Cluster B) was diagnosed significantly more often in those with non-schizophrenia psychoses as compared to healthy controls.

It is clear from these epidemiological and smaller scale studies that there is likely a higher rate of personality disorders in individuals with a diagnosis of a psychotic disorder than those without such diagnoses. The reasons for the vastly different reported comorbidities remain unclear. It is possible that some studies do not properly assess for personality disorders and allow symptoms alone to dictate diagnoses, rather than properly adjusting for whether the symptoms are better accounted for an Axis I (psychotic) diagnosis. This might explain the rates of Cluster A diagnoses, which many consider to be along the schizophrenia continuum. In addition, according to the Newton-Howes et al. (2008) meta-analysis, both method and setting accounted for much of the disparity in findings. For example, lower rates were found in RCTs as compared to observational studies, presumably due to the more rigorous assessment present in RCTs. The meta-analysis also found that primary care patients were less likely to be diagnosed than inpatients or outpatients. This may be an artifact of either a) the type of individuals seen in this setting (i.e., higher functioning in primary care) *or* b) rater bias based on setting (i.e., the assumption that behaviors or symptoms are also personality disordered due to hospitalized setting).

Despite disparities, it is likely that the "accurate" comorbidity rates are somewhere in the middle, indicating a somewhat elevated prevalence of such personality traits in those with schizophrenia (either as part of or separate from the psychotic syndrome). For treatment implications, it is more important that the traits exist rather than their etiology. However, researchers will want to determine whether these are true comorbidities or the double coding of

symptoms as personality symptoms and psychotic symptoms in order to calculate prevalence rates and to inform the developmental perspective of these disorders.

Personality disorders in the prodrome. Within the prodromal literature, personality disorder comorbidity data has been reported infrequently, but what has been reported has been consistent. Most prodromal clinics reporting such data have compared individuals considered prodromal to those who were referred to the prodromal clinic, but screened out for various reasons as inappropriate. This comparison group is not a healthy control, or even a clinical control, as these individuals were considered potentially "prodromal" by someone (usually an outside clinician, school counselor, or parent) in order to be initially referred. This can be considered a unique population in and of itself, a sample of those reporting seemingly prodromal symptoms that are not, in fact, considered prodromal. Therefore, the comparison group should be considered with caution.

The first report of comorbidity was by the PRIME prodromal clinic in 2006 (Rosen, Miller, D'Andrea, McGlashan, & Woods, 2006). According to the PRIME clinic, which uses the ultra high risk prodromal criteria, 48% of their sample (n=14) met criteria for at least one personality disorder in addition to meeting the ultra high risk criteria. By cluster, 28% met for a Cluster A disorder, 24% for a Cluster B disorder, and 14% for a Cluster C disorder. The two most frequent diagnoses were schizotypal and borderline personality disorders. However, these comorbidities were not significantly different than the comparison group of inappropriate prodromal referrals to the clinic.

The largest scale report of personality disorders in the prodrome was reported by Woods et al. (2009) in the NAPLS report. These researchers reported a 44% comorbidity rate between

prodromal symptoms and personality disorders across the eight North American sites. These rates were similar to the help-seeking controls that were screened out of the clinic (with the exception of schizotypal personality disorder), but much higher than the normal controls. The percentages per personality disorder are shown in Table 2.

One concern when reporting personality disorder comorbidities with the prodromal samples is the overlap between the Cluster A disorders and prodromal symptoms (also a concern in schizophrenia). The Cluster A disorders are often considered as existing on the "schizophrenia spectrum" and share many symptoms with prodromal criteria. With the exception of the ultra high risk GRDS group, which allows schizotypal personality disorder (plus GAF drop), a Cluster A diagnosis is not sufficient for, and is often irrelevant to, eligibility for prodromal groups. As a result, an individual can meet for a Cluster A disorder and not meet for the prodrome or meet for the prodrome and not meet for a Cluster A disorder. This is primarily accomplished by the SOPS requirement regarding symptom timeline, and, for the ultra high risk group, an additional drop in GAF score for the schizotypal group (part of GRDS).

Theoretically speaking, the symptoms that are shared by both the Cluster A personality disorders and the various prodromal criteria should be distinguished by whether the symptoms are long-standing, indicating a personality disorder, or emerging, indicating the prodrome. Despite the fact that this may seem like a fine distinction, the theory behind the prodrome, and schizophrenia, is that symptoms begin that mark a departure from baseline and deterioration in functioning. Therefore, were an individual to have long-standing unusual symptoms that have minimal impact on functioning, he or she may have schizotypal personality disorder, but is unlikely to be prodromal (at least at the time). However, it is possible to have schizotypal (or

schizoid) personality disorder and then begin to show a more severe level of symptoms, making him or her eligible for the prodrome as well (analogous to the diagnosis of premorbid schizotypal personality disorder in schizophrenia). This progression to the prodrome, however, looks quite different from the individual who showed no (or few) noticeable symptoms until the past year. Though the validity of schizotypal personality disorder as an independent disorder has long been in question, it is clear that many continue with this diagnosis without ever progressing to an Axis I psychotic diagnosis. Therefore, it is possible for the Cluster A diagnoses to moderate treatment, as these diagnoses are not part prodrome. However, because many of the symptoms overlap with the prodrome (as compared to Clusters B and C), they may moderate treatment in a different way that the other clusters.

Effects of comorbidity.

Negative effects in psychosis. Despite the somewhat unclear prevalence rate of the comorbidity between personality disorders and psychosis, there is some evidence to support that this comorbidity has high-risk negative outcomes such as hospitalization, relapse, and symptom exacerbation. In addition, though personality disorders and psychotic disorders are thought to have increased independent risks of both suicide (borderline personality disorder and schizophrenia; Reynolds et al., 2007) and violence (antisocial personality disorder and schizophrenia; Widiger & Trull, 1994; Swanson, 1994), the effects of the comorbid disorders on these risks have yet to be reported in the literature.

A personality disorder diagnosis, when combined with a psychotic diagnosis, has been linked to poorer outcomes compared to psychotic individuals without the comorbid personality disorder (Tyrer, Manley, Van Horn, Leddy, & Ukoumunne, 2000; Tyrer & Simmonds, 2003;

Keown, Holloway, & Kuipers, 2005). Tyrer et al. (2000) conducted a study comparing intensive and standard case management with 201 patients with psychosis. These authors found that psychotic participants with personality disorder diagnoses (not broken down by specific disorder) spent more days in the hospital than those without personality disorders. Keown, Holloway, and Kuipers (2005) followed individuals involved with community mental health in order to find predictors of inpatient psychiatric bed use. These researchers found that psychosis and personality disorders have large, independent effects on the length of time spent on inpatient units.

With regard to specific personality disorders, most of the research has been focused on borderline and antisocial personality disorders. As part of the MacArthur Violence Risk Assessment Study, Bahorik and Eack (2010) assessed individuals on an inpatient psychiatric unit for comorbid personality disorders. They reported that individuals with comorbid psychosis and borderline personality disorder showed significantly less improvement on a one-year follow up assessment post inpatient hospitalization than those without borderline personality disorder (Bahorik & Eack, 2010). The individuals with this comorbidity expressed higher levels of hostility and suspiciousness, as well as lower levels of overall functioning and were more likely to be rehospitalized.

Mueser, Drake, Ackerson, Alterman, Miles, and Noordsy (1997) conducted a study with 158 adolescents diagnosed with schizophrenia or schizoaffective disorder that were currently receiving case management in the community. These authors assessed the adolescents on measures of antisocial and conduct disorder in an attempt to determine antisocial-based subtypes of schizophrenia. The authors found that individuals with antisocial and conduct disorder traits

had higher rates of substance abuse, aggressive and antisocial behavior, and severe symptoms and hospitalizations than those without these traits. Similarly, in a multi-site study, Moran and Hodgins (2004) assessed 232 psychotic individuals recently discharged from inpatient hospitals or forensic units for various antisocial traits and correlates (e.g., substance abuse, criminal behavior). In an attempt to determine antisocial correlates among this sample, the authors found that psychotic individuals with comorbid antisocial personality disorder presented with higher levels of substance abuse, attention and concentration difficulties, and non-violent criminal histories. These authors did not link the comorbidity to symptoms or symptom course, however. Dingemans, Lenoir, and Linszen (1998) sought to assess the ability of personality traits to predict relapse of schizophrenia in 93 adolescent patients. The authors found that comorbid antisocial personality traits were associated with higher rates of psychotic relapse with no corresponding differences in medication adherence.

(Lack of) Research on effects in the prodrome. The symptom and functioning outcome data during the prodrome has been predominately focused on transition to psychosis, with some limited emphasis on negative and nonspecific symptoms (e.g., Lencz et al., 2004). Though the presence of comorbid personality disorders has been reported (e.g., Woods et al., 2009), any potential effects of personality disorders or significant personality disordered traits on symptom severity, hospitalization, medication adherence, and other outcomes has either not yet been investigated or not yet been reported. Given the effects of personality disorders on psychotic symptoms, other Axis I disorders, and general functioning, it is likely that similar negative effects would be found in the attenuated psychotic symptoms and general functioning of the prodromal population. Perhaps of most concern may be the higher risk symptoms and behaviors (i.e., self-injury, suicide, violence) often associated with particular personality disorders, such as

borderline personality disorder (Reynolds et al., 2007; Widiger & Trull, 1994). Though there is no research to date that has investigated whether prodromal symptoms, when combined with borderline personality traits, would increase risks to self or others, theoretically this is a valid concern based on research on these behaviors in schizophrenia and borderline personality disorder (Reynolds et al., 2007; Widiger & Trull, 1994).

Personality disorders and treatment. The effects of personality disorders on treatment of non-psychotic disorders are well known. Research suggests that a personality disorder diagnosis negatively impacts the treatment of depression, panic disorder, obsessive-compulsive disorder, and substance abuse (Reich & Green, 1991; Reich & Vasile, 1993; Reich 2005). Though there is some debate regarding exactly what the effects are and whether the effects are universally negative, it is generally supported that personality disorders reduce the effectiveness of standard treatments (i.e., those treatments not tailored to personality disorders; Reich, 2005). One reduction of effectiveness appears to be in the higher treatment dropout rate for those with personality disorders as compared to those without (Reich, 2005). Moreover, personality disorder traits also appear to have the same negative impact as a full personality disorder on treatment, which would support a dimensional rather than categorical approach to assessment (Reich & Vasile, 1993). This phenomenon has been less researched in the psychotic disorders, and is not discussed at all in the prodromal treatment literature.

Treatment of psychotic disorders. To date, no comprehensive studies have established differential effects of treatment of psychotic disorders as moderated by personality disorders (Newton-Howes, Tyrer, Moore, & Nur, 2007). However, treatments have been developed for particular personality disorders to target individuals who have not responded to treatment as

usual. The most illustrative of these cases is borderline personality disorder (Reynolds et al., 2007).

Recently, at least three naturalistic treatment studies have been published investigating the effects of combination of DBT and one of the known treatments for severe mental illness (or its outcomes) with individuals with co-occurring borderline personality disorder and, for the most part, psychosis. Koons, Chapman, Betts, O'Rourke, Morse, and Robbins (2006) investigated the effects of a DBT adaptation for Vocational Rehabilitation with individuals dually diagnosed with a severe mental illness (33.3% psychosis) and a personality disorder (58.3% borderline personality disorder) that previous caseworkers were unable to place or maintain in employment. These researchers found that within the DBT adaptation, the eight treatment completers showed significant improvements in both psychopathology (depression, hopelessness, anger) and employment (satisfaction, hours worked) at six-month follow-up.

An adaptation of the Assertive Community Treatment (ACT) team has also been investigated in individuals with severe mental illness (primarily psychosis) with comorbid borderline personality disorder. Preliminary small sample, uncontrolled naturalistic treatment studies have shown that implementing DBT within an ACT team reduces hospitalizations, improves employment, and includes high client satisfaction with treatment and low clinician burnout (Reynolds, Wolbert, Abney-Cunningham, & Patterson, 2007). There is also evidence to suggest that DBT within an ACT team reduces suicidal ideation and improves global severity of psychopathology, including specific symptoms such as obsessive-compulsive, interpersonal sensitivity, depressive, phobic anxiety, and psychotic symptoms (Ben-Porath, Peterson, & Smee, 2004).

(Lack of) Research on treatment in the prodrome. Even uncontrolled, small sample studies such as the ones mentioned above have not yet been conducted in the area of prodromal psychosis. One would assume that given the similar rates of personality disorders in the prodrome as in psychotic disorders, as well as the well-known effects of such disorders and traits on treatment in other comorbid disorders known to be prevalent during the prodrome (e.g., depression), targeting such traits in treatment directly would only enhance treatment. However, this continues to be clinical speculation until research is conducted to examine this question.

Conclusion. In order to attempt to answer the important question of whether personality disorders (or traits) moderate treatment effectiveness during the psychotic prodrome, inferences must be made from the current literature pertaining to the prodrome, schizophrenia, and other Axis I diagnoses. There is little available data to answer to this question within the prodromal literature, and the question of treatment in general has only begun to be addressed. However, the literature in the other areas, as shown above, discussed three important points. First, personality disorders, and the corresponding traits, clearly and negatively impact the treatment and treatment outcomes of groups of Axis I disorders such as depression, obsessive-compulsive disorder, substance abuse, and panic disorder (Reich & Vasile, 1993). Importantly, during the prodrome, the most common Axis I diagnoses are mood and anxiety disorders (Woods et al., 1999), making this finding particularly relevant to those dually diagnosed prodromal and personality disordered individuals. Second, in psychotic disorders, there are clear negative effects on symptom outcome (including psychotic symptoms and relapse) and hospitalization for those with comorbid personality disorders, though the link to treatment moderation specifically has not been made (Tyrer, et al., 2000; Tyrer & Simmonds, 2003; Keown et al., 2005). Individuals during the prodrome are, for the most part, being treated for attenuated psychotic symptoms. It is a valid

hypothesis, therefore, that attenuated psychotic symptoms would interact similarly with personality disorder symptoms (e.g., negative effects on attenuated psychotic symptoms, increased hospitalization) as full psychotic symptoms. Third, and importantly, it seems that almost half (44.1%) of prodromal individuals are being diagnosed with a personality disorder, with only 26.4% being accounted for by schizotypal personality disorder (arguably a "prodromal symptom personality"). The prevalence rate of personality disorder traits has not yet been reported in the literature, but would certainly be even higher. Clearly this is a relevant treatment consideration, and one with important consequences. Whether targeting the presenting Axis I condition or the attenuated psychotic symptoms, a comorbid personality disorder (or prominent personality disorder traits) increases the risk for poorer treatment outcomes. Research must first be conducted to verify that prominent personality disorder traits (or a full diagnosis) negatively impacts treatment in this population. If substantiated, this finding would be an important starting point for future studies, which could then focus on identification of successful treatment strategies to address the personality disorder symptoms and improve outcomes for such individuals.

CHAPTER III

DISSERTATION

Individuals considered at high risk for schizophrenia, or "prodromal," present with a wide-range of Axis I and Axis II symptoms. Consideration of the various comorbidities is pertinent for effective treatment of "prodromal" symptoms. Of specific interest are personality disorder traits, which have been found to be both prominent in this population (Woods et al., 2009) and to negatively moderate treatment outcomes for various Axis I disorders (Reich & Green, 1991; Reich & Vasile, 1993). This dissertation, therefore, sought to determine the effects of personality disorder traits on the treatment of individuals at clinical high risk for schizophrenia. More specifically, the study investigated the effects of personality disorder traits on prodromal symptom reduction. The study also investigated the effects of personality disorder traits on the assessment of the prodrome, with specific consideration to differential diagnosis.

Method

Participants. One hundred and forty two participants were obtained from the archival data of a study entitled "Characterization of Prodromal Schizophrenia" that was collected at the Recognition and Prevention (RAP) program at the Zucker Hillside Hospital (ZHH), which is part of the North Shore-LIJ Health System, in Glen Oaks, New York. The "Characterization of Prodromal Schizophrenia" study was a National Institute of Mental Health funded study that assessed and prospectively followed individuals considered to be at high risk for schizophrenia and compared these individuals to normal controls on measures of psychiatric symptoms and neurocognitive functioning. For the archival study conducted here, eligible participants included any individual who met the RAP "clinical high risk" (prodromal) or "schizophrenia-like

psychoses" (SLP) eligibility criteria (see below) and signed consent to participate in the research study from the years 2000 to 2006.

"Clinical high risk" eligibility criteria. The "clinical high risk" groups' eligibility criteria for the original study were as follows: 1) the participant must be between the ages of twelve and twenty-two, 2) the individual must meet criteria for one of two risk categories (CHR- or CHR+) or the schizophrenia-like psychosis (SLP) determined by scores on the Scale of Prodromal Symptoms (SOPS; Miller, McGlashan, Woods, et al., 1999), and 3) if under eighteen years of age, the individual must have parental consent to participate.

The SOPS-based risk categories that determined eligibility were the clinical high risk, negative symptoms (CHR-), the clinical high risk, positive symptoms (CHR+), and schizophrenia-like psychosis (SLP). The theoretical model of the prodromal and schizophrenia-like symptom progression as developed by the RAP team is shown in Figure 1. The CHR- group was characterized by attenuated negative and disorganized symptoms only. These individuals had at least one score between a 3 and 6 on the negative symptom items of the SOPS, but they did not have any score that reached a 3 (considered moderate) on the positive symptom items. The CHR+ group received at least one score between a 3 and 5 on the positive symptom items, considered to be moderate but sub-threshold positive psychotic symptoms. The SLP group was characterized by at least one psychotic level symptom that did not meet full criteria for a DSM-IV-TR diagnosis of schizophrenia. The SLP criteria was met in one of three ways, 1) only one symptom met the psychotic threshold (the DSM-IV-TR requires two psychotic-level symptoms for a diagnosis of schizophrenia, with the exception of bizarre delusions and voices conversing), 2) the participant did not have corresponding social or functional decline, or 3) the participant experienced intermittent psychotic-level episodes that did not meet the duration criterion for an

episode of schizophrenia (Lencz, Smith, Auther, Correll, & Cornblatt, 2004). The intermittent psychotic symptoms criterion (#3) was the way that most SLP participants became eligible. Though the RAP program does not consider the SLP group to be prodromal because these individuals are already experiencing psychotic symptoms, these researchers do consider the group to be a phase that is between the prodrome and schizophrenia (See Figure 1), and one that does not inevitably progress to schizophrenia (Lencz et al., 2004). In addition, the "ultra high risk criteria" would consider these individuals to be prodromal, as they would meet for the brief, limited, intermittent psychotic symptoms (BLIPS; Lencz et al., 2004). Because neither group considers the SLPs to be fully transitioned (or in the inevitable transition into) schizophrenia, these individuals are included in analyses.

Participant exclusion criteria included 1) a diagnosis of an Axis I psychotic disorder, such as schizophreniform disorder, schizophrenia, schizoaffective disorder, bipolar disorder, or major depression with psychotic features; 2) a history of neurological, neuroendocrine, or other medical condition known to affect the brain; 3) current substance dependence; 4) an IQ less than 70; 5) moderate to severe risk of harm to self or others (in which case referral was made).

RAP treatment. All participants were offered psychotherapy treatment and medication consultation and monitoring if eligible for the research. Medication was determined on an individual basis by the staff psychiatrists. Individual psychotherapy, conducted by doctoral level RAP psychologists, was supportive and included elements of CBT oriented. However, the therapy was not manualized. Group therapy was also available through the Zucker Hillside hospital if it was deemed clinically appropriate. All treatment was naturalistic and was not part of a manualized clinical trial. Participants were included in the treatment portion of this study if they completed at least four individual psychotherapy sessions.

Measures.

Treatment and treatment covariates. Treatment variables of interest included: number of RAP individual psychotherapy sessions and receipt of psychiatric medication. Participants were considered to be in the RAP treatment condition, and considered for the treatment analyses, if they completed at least four individual psychotherapy sessions with RAP. The number of individual psychotherapy sessions was coded from each participant's chart and included sessions from treatment beginning until the session nearest in date to the two-year follow-up. The psychiatric medication variable was coded as "present" if the participant was prescribed and took any psychotropic medication for at least one month (consecutively) during the two year follow-up period. This variable was coded as "absent" if the participant was never prescribed any psychotropic medication or if he or she was prescribed them but did not take them for longer than one month.

Personality disorder traits. As it was hypothesized that personality disorder traits affected symptom outcomes, personality disorders were measured by the Structured Interview for DSM-IV Personality Disorders (SIDP-IV; Pfohl, Blum, & Zimmerman, 1997). The SIDP-IV is a structured clinical interview intended to determine personality disorders and traits as set forth by the DSM-IV using a four-point scale for each personality disorder trait (0- absent, 1-questionably present, 2-present, 3-strongly present). However, for the purpose of this study, the traits were recoded as present (2 or 3) or absent (0 or 1). This variable was measured as a continuous personality *trait* variable, rather than a dichotomous personality disorder, for several reasons. First, many of the participants are under 18, making a diagnosis of a full personality disorder controversial. Second, research indicates that personality disorders can influence treatment even at the trait level, making the distinction between traits and disorders a less

important one to make (e.g., Reich & Vasile, 1993). The SID-P-IV is generally considered to have adequate inter-reliability for all of the personality disorders (e.g., all above 0.7; Jane, Pagan, Turkheimer, Fiedler, & Oltmanns, 2006). Because the data was collected over ten years, specific reliability data of the multiple raters on the SIDP during this time was not available. However, the RAP program has a standard policy of training all raters, who were PhD-level psychologists, to reliability in accordance with recommended scale standards.

Outcome variables-symptoms. The effects of treatment were defined by three scores from the Scale of Prodromal Symptoms (SOPS; Miller, McGlashan, Woods, et al., 1999): the total positive symptoms SOPS score, the total negative symptoms SOPS score, and the global assessment of functioning (GAF) score. The SOPS has good reliability for each subscale (above 0.75; Miller, McGlashan, Rosen, Cadenhead, Ventura, McFarlane, et al., 2003). Because the data was collected over ten years in a retrospective study, reliability data of the multiple raters on the SOPS during this time was not available. However, the RAP program has a standard policy of training all raters, who were PhD-level psychologists, to reliability in accordance with recommended scale standards.

The SOPS is a structured clinical interview used to determine the presence of prodromal symptoms, rate the current severity of any symptoms, as well as rule out any past or current psychosis. The SOPS divides the prodromal symptoms into four symptom subscales: positive (5 items), negative (6 items), disorganized (4 items), and general (4 items). Across each of the four symptom sets, the SOPS uses a seven point scale to rate the severity and intensity of the symptoms, with anchors slightly different for the symptom sets. For positive symptoms, this scale ranges from absent (0) to severe and psychotic (6). Scores between moderate (3) and severe but not psychotic (5) are considered to be in the "prodromal," or moderate but not psychotic,

range. For the negative, disorganized, or general symptoms, the scale ranges from absent (0) to extreme (6). Again, scores from moderate (3) to severe (5) meet the threshold for the "prodromal" state. When combining across four symptom subscales, total scores can range from 0 to 144.

The SOPS also includes a general assessment of functioning (GAF) score. The GAF ranges from 0 to 100, with higher scores indicating higher levels of general functioning. The scale can be scored in one-level increments, but is also broken down into 10-level increments of functioning (e.g., 0-10, 91-100). For better reliability, the GAF scores will be recoded into the 10-point increments, making the scale a 0-10 (rather than 0-100) scale.

The five SOPS scores (positive, negative, disorganized, general, and GAF) were recorded at baseline and all completed follow-ups. Change scores (follow-up minus baseline) were used as the outcome variables (total SOPS positive and negative score and SOPS GAF score).

The follow-up time period used for outcome was two-years. Because of the inconsistent rate of participant follow-up at each assessment time point, follow-ups were permitted as within the two-year range if the assessment was conducted within one year prior to or one year following the two-year follow-up date (i.e., 1-3 years from baseline). If more than one completed follow-up assessment fell within the 1-3 year time range, the follow-up that was closest to the date and has the least missing data was used.

Outcome variables- psychosis. In the assessment-oriented analyses, the outcome variable was psychosis. Psychosis was either defined one of two ways. The first definition, "full psychosis", only considered a person to be psychotic if he or she met criteria for schizophrenia or schizoaffective disorder. Therefore, a person who was considered a "slip" (the SLP group) by having a level 6 psychotic symptom without meeting full criteria for schizophrenia would not be

considered psychotic in this group. The second definition, "slip psychosis," considered a person to be psychotic if, at any point, he or she was given a 6 (psychotic level) on a positive symptom on the SOPS. Therefore, this second definition categorized both the SLP group and the full psychosis group as being psychotic.

Exploratory Measures.

Therapeutic Techniques. A coding scheme was developed by the authors and includes nine groups of techniques, many with sub-categories (full definitions in Appendix). The nine techniques were as follows: supportive, coping skills, behavioral techniques, case management, psychoeducation, monitoring, symptom assessment, and risk assessment and management. Each technique was coded as present if it was used at least once and absent if never used during the individual psychotherapy session as recorded in the patient's chart. For the analyses, only the techniques (not individual sub-categories) were used due to frequency of use and power requirements.

Assessment- Suspiciousness. Due to a clinical observation that 1) there appeared to be two distinct types of suspiciousness reported by participants and 2) one type seemed to be reported primarily by participants that had comorbid borderline and avoidant personality traits, the SOPS positive symptom of Suspiciousness was recoded post-hoc to examine this observation. Two types of suspiciousness were coded: Interpersonal Suspiciousness and Harm Suspiciousness. Items were recoded as Interpersonal Suspiciousness if the suspiciousness described referred to social criticism, ridicule, or undue attention. Key phrases identifying this type of suspiciousness included: being talked about, being looked at, being laughed at, being made fun of, people watching them, or people judging them. The general theme was one of social mistrust and vague social unease, with a clear absence of physical threat, harm, or a

developed plan to track or pursue on the part of an alleged perpetrator. The other type of suspiciousness, Harm Suspiciousness, by contrast, showed themes of physical harm, plots of social or emotional destruction, and overall persecution. Key phrases in this type of suspiciousness included: physical harm, plotting to be thrown out of school, viruses on computers, stealing/moving belongings, poisoning, tapping/bugging phones, being followed, and "Truman show" experiences. For example, if a participant reported that he thought that people were looking at him, this would be considered Interpersonal Suspiciousness, whereas, if he reported people might be following him, this would be considered Harm Suspiciousness. If a participant reported that people were making fun of her, this would be Interpersonal Suspiciousness; if she reported that people had formed a plot to get her kicked out of school, this would be Harm Suspiciousness.

Items were only recoded if the person would have been scored as prodromal on the original SOPS suspiciousness item (3 or above). The information was obtained from the participants' full report, which described symptoms reported in full.

Assessment- Visual Hallucinations. Similar to suspiciousness, it was noted that the visual hallucinations, especially fully formed hallucinations, seemed to be reported predominately by those with borderline personality disorder or traits. Because visual hallucinations are relatively rare in schizophrenia (Resnick & Knoll, 2008), two types of visual hallucinations were also investigated post-hoc, as was their relation to BPD.

The Visual Hallucinations item on the SOPS was recoded into either 1) Psuedo-hallucinations or 2) Full Hallucinations. Psuedo Hallucinations were considered to be the low-level hallucinations that are often misinterpretations of actual stimuli (illusions) or vague, indistinct true hallucinations. Examples of such hallucinations would be: any illusion, seeing

shadows, seeing ghosts (unformed/vague), and seeing lights/dots/flashes. Full Hallucinations were coded if the participant described fully formed, detailed forms that were not illusions. Examples were: faces, gnomes, people, and animals.

Because Visual Hallucinations is one item and would include all sensory hallucinations, it was not possible to determine what part of a score would be given for the visual aspect and what part would be given for auditory (or other) stimuli. Therefore, all visual hallucinatory experiences reported were recoded. The information was obtained from the participants' full report.

Hypotheses

Hypothesis 1. One aim of the study was to investigate the effects of personality disorder traits on the treatment of "prodromal" symptoms. It was hypothesized that individuals with more personality disorder traits (Structured Interview for DSM-IV Personality Disorders; SIDP-IV) would show fewer reductions in total positive prodromal symptoms (Scale for Prodromal Symptoms; SOPS) [Hypothesis 1a], total negative prodromal symptoms (SOPS) [Hypothesis 1b], and have lower overall functioning (Global Assessment of Functioning; GAF) [Hypothesis 1c] at two-year follow-up than those who have fewer personality disorder traits. Hypothesis 1a, 1b, and 1c were based on the research in Axis I disorders that individuals with higher rates personality disorders and traits have poorer treatment outcomes (Reich & Green, 1991; Reich & Vasile, 1993). Though treatment moderation has not been researched in the prodrome or schizophrenia, researchers have shown various negative outcomes such as higher rates of re-hospitalization for individuals with personality disorders (e.g., Keown et al., 2005).

Hypothesis 2. In addition, therapeutic techniques were explored for those who participated in individual psychotherapy. It was hypothesized that those participants whose

sessions included higher percentages of coping skills and behavioral techniques (see coding technique in Appendix) would show more total positive prodromal symptom improvement (SOPS) [Hypothesis 2a], more total negative prodromal symptom improvement (SOPS) [Hypothesis 2b], greater overall functioning improvement than individuals in sessions without those techniques (GAF; Hypothesis 2c) than those whose sessions had lower percentages of these two techniques. The basis of these hypotheses was the effectiveness of the cognitive behavioral approaches used to date with this population (e.g., Morrison et al., 2004).

Hypothesis 3 (Post-Hoc). Based on clinical observation, the relationship between two types of suspiciousness and borderline and avoidant personality traits were investigated. It was hypothesized that borderline and avoidant personality traits were related to the interpersonal suspiciousness, and not to the harm suspiciousness [Hypothesis 3a]. In addition, it was hypothesized that harm suspiciousness would be more predictive of psychosis (full psychosis), than interpersonal suspiciousness [Hypothesis 3b]. Hypothesis 3a and 3b stemmed from the clinical observations that several symptoms of borderline (e.g. interpersonal suspiciousness, transient paranoia) and avoidant personality (e.g., preoccupation with being criticized) disorder may mimic prodromal suspiciousness, but are distinct in the type (i.e., interpersonal) and ability to predict full psychosis (American Psychiatric Association, 2000). These symptoms are better explained by the personality trait, and, are therefore not part of a pre-psychotic syndrome.

Hypothesis 4 (Post-Hoc). Based on clinical observation, the relationship between two types of visual hallucinations and borderline personality traits were investigated. It was hypothesized that borderline personality traits were associated with full visual hallucinations [Hypothesis 4a]. In addition, it was hypothesized that visual hallucinations would only predict full psychosis if the participant did not have BPD traits [Hypothesis 4b]. Hypotheses 4a and 4b

came from the clinical observation that several symptoms of borderline personality disorder lend themselves to the reporting of full, vivid visual hallucinations, including: intense, vivid dissociative experiences, depersonalization, derealization, a disrupted sense of self, and intense (even hyperbolic) ways of communicating (American Psychiatric Association, 2000).

Procedure

A search of the "Characterization of Prodromal Schizophrenia" study participant database was conducted to determine the number of eligible participants who were in the prodomal (CHR-, CHR+) and SLP groups during the years of 2000-2006. The electronic research database of the RAP program was accessed to obtain the Scale of Prodromal Symptoms (SOPS) scores of all eligible participants. Participant research binders were used to obtain all needed assessment data (i.e., suspiciousness and visual hallucination codes). In addition, a chart request was placed with the chart archives of Zucker Hillside Hospital to determine how many individuals additionally received treatment at the RAP program (n =69), as well as to code individual therapy sessions.

Charts were coded by the author; a second rater independently coded 10% (n =7) of sessions to provide a reliability rating. All data was entered on password-protected computers on a secure database at the RAP program to ensure participant privacy and confidentiality.

Results

Descriptive Analyses. Descriptive statistics were gathered for both the participants' symptoms and the therapeutic techniques. Tables 3-5 provide basic demographic information on the entire sample and the change scores on outcome variables between baseline and follow-up. Thirty-five percent of the sample was considered to be in the CHR- group, which comprised participants with negative symptoms only (Table 4). The CHR+ participants were 53% of the sample and presented with attenuated positive symptoms. Finally, 12% of the sample presented

with at least one psychotic level symptom without meeting criteria for schizophrenia (the SLP group).

Table 5 contains the prevalence rates of the various personality disorders and personality disorder traits of the 142 participants for which there was data (asterisks indicate additional missing cases for Antisocial and Schizotypal Personality Disorders). Participants were eliminated from calculations if their data contained three or more missing items per personality disorder. The most prevalent personality disorders were Avoidant Personality Disorder (27.46%), Schizoid Personality Disorder (24.65%), Paranoid Personality Disorder (9.86%), and Borderline Personality Disorder (7.04%). When considering the trait level (3 or more), the most prevalent traits were similar: Avoidant Personality Disorder (33.80%), Schizoid Personality Disorder (36.62%), Schizotypal Personality Disorder (21.43%), and Borderline Personality Disorder (23.24%).

Figure 3 provides a histogram of the total number of individual psychotherapy sessions for those participants that received 4 or more RAP psychotherapy sessions and for which there was two year follow-up data (n =69) and would therefore be included in later analyses. The mean number of sessions was 27.54, with a standard deviation of 16.80.

Table 6 provides descriptive statistics on the nine psychotherapy techniques coded with the rating scale. Supportive was the most used technique, used in 96% of sessions. Because of the near constant use of this technique, it was excluded from further analyses as a predictive factor. The next most used technique was the assessment of symptoms, which was used in 56% of sessions. Coping skills was the third most used technique at 35%.

Interrater reliability. Interrater reliability statistics (Cohen's kappa) were computed for the eight therapeutic techniques (see Appendix). A total of seven, randomly selected, individual

psychotherapy patient cases (165 total therapy sessions) were rated by the second rater for the purpose of reliability. Though all further analyses used the first rater's ratings, these statistics are used to provide a measure of interrater reliability and validity to the coding scheme. All techniques were coded with moderate to substantial reliability, with the exception of case management: Coping Skills (0.65), Behavioral Techniques (0.61), Psychoeducation (0.66), Monitoring (0.83), Assessment of Symptoms (0.71), Risk Assessment and Management (0.89), and Parent Training (0.69). Case Management was not coded reliably (-.02), and any analyses reported further using Case Management should be considered with extreme caution.

Symptoms and treatment. Three linear regression analyses were conducted to look at the effect of personality disorder traits and treatment outcomes [Hypotheses 1a-1c]. Predictors were total number of personality disorder traits on Cluster A, Cluster B, and Cluster C. Covariates included any psychotropic medications given between baseline and two-year follow-up (0= no meds, 1= any meds). Dependant variables for the three analyses were change in total SOPS positive symptoms score, change in total SOPS negative symptom score, and change in GAF score. No model was significantly significant: the SOPS positive model (F= 0.15, p = 0.98, R^2= 0.13, standard error of the estimate= 5.53) , the SOPS negative model (F= 0.62, p = 0.69, R^2= 0.05, std error= 5.34), or the GAF change model (F= 0.86, p = 0.51, R^2= 0.07, std error=14.45), In addition, no personality trait cluster was found to be significantly related to SOPS positive symptom change, SOPS negative symptom change, or GAF change. Thus, Hypotheses 1a-1c were not supported. However, analyses included only 60 cases (59 for the GAF analysis).

Using the G*Power 3.1 Program, a post-hoc power analysis was run for the three linear multiple regressions, fixed model. The input parameters were as follows: effect sizes f^2 (0.013,

0.05, 0.07,) error probability (0.05), sample size (60), and number of predictors (9). Power was calculated to be 0.14 (postitive symptoms), 0.41 (negative symptoms), and 0.55 (GAF score). Therefore, power is considered a significant limitation to these analyses.

To further look at symptom presentation and the effect on therapy, five post-hoc regressions were conducted to determine the association between symptom presentation on baseline and therapeutic techniques used by therapists. Due to the lack of power, for these analyses, all participants were included if they had *any* RAP individual therapy (n =73). In all three analyses, the predictor variables were the eight therapeutic techniques discussed above.

The first analysis was a logistic regression run to determine the association between those RAP therapy clients with borderline personality traits (dichotomous, 1= 3 or more traits, 0= two or fewer traits) and therapy techniques. The logistic regression model was not significant (X^2= 9.50, p = 0.30, R^2= 0.19), but did indicate that those who presented with borderline personality traits were more likely to have sessions characterized by only one of the eight techniques- risk assessment and management (B=2.41, p=0.08, Exp(B)= 11.78). Those with BPD traits were also less likely to have sessions with psychoeducation (B=-500, p=0.09, Exp(B)= .01). For full results of the therapy techniques, see Table 8.

The remaining four analyses were linear regressions run to determine the association between those RAP therapy clients (n =69) with severe positive (SOPS highest positive score and SOPS total positive score) and negative symptoms on baseline (SOPS highest negative score and SOPS negative score) and therapy techniques.

The first linear regression investigated total positive symptoms. The model was significant (F= 2.16, p = 0.04, R^2= 0.25) with the eight therapy techniques entered as predictors. Results indicated that those participants with more positive symptoms (higher *total* SOPS

positive scores) on baseline were more likely to receive therapy that consisted of Coping Skills (t=2.25, p= .03) and Risk Assessment and Management (t=2.42, p= .02). Looking at it slightly differently, those participants with more severe positive symptoms (highest SOPS positive score) on baseline were more likely to receive therapy that consisted of Coping Skills (t=1.78, p= .08) and Assessment of Symptoms (t=1.74, p= .09). However, the high positive symptom model was not significant (F= 1.45, p = 0.19, R^2= 0.17). These results for positive symptoms are combined for comparison in Table 9.

For those with more (cumulative) negative symptoms (higher *total* SOPS negative scores), therapists were more likely to use Case Management Strategies (t=2.03, p= .05) than those with fewer negative symptoms. However, the full high negative symptom model was not significant (F= 1.14, p = 0.35, R^2= 0.14). Participants with the more severe negative symptoms (highest individual SOPS negative score) did not receive significantly different techniques than those with less severe negative symptoms. The three techniques with the largest t values were Case Management (t=1.67, p= .10), Monitoring (t=-1.44, p= .16), and Risk Assessment and Management (t=-1.36, p= .18). This model was also not statistically significant (F= 0.88, p = 0.55, R^2= 0.11). These results for negative symptoms are combined for comparison in Table 10.

RAP therapy. Three linear regressions were conducted to determine if particular RAP therapy techniques were associated with symptom change [Hypothesis 2a-c]. Participants included the individuals that received at least four RAP individual psychotherapy sessions and for which there was two year follow-up data (n = 69). Predictors in all three analyses included 8 therapy techniques (coping skills, behavioral techniques, case management, psychoeducation, monitoring, assessment of symptoms, risk assessment and management, and parent training).

Supportive was excluded due to the prevalence of its use (see previous explanation above). The covariate was psychotropic medication.

No therapeutic technique was significantly associated with change in GAF score from baseline to two year follow-up and the model was not significant (F= 0.66, p= 0.74; R^2= 0.09; Std Error= 15.49) [Hypothesis 2c]. Similarly, no therapeutic technique was significantly associated with change in SOPS total positive symptom score from baseline to two year follow-up, nor was the model significant (F= 0.65, p= 0.75; R^2= 0.09; Std error= 5.33) [Hypothesis 2a]. Coping Skills (t=1.45, p= .15) and Assessment of Symptoms (t=1.31, p= .19) were the two techniques with the largest t values. However, the negative symptom model approached significance (F= 1.81, p = 0.09, R^2= 0.22; Std error = 4.84). Two techniques were significantly associated with a decrease in SOPS total negative symptoms- Assessment of Symptoms (t=2.65, p= .01) and Parent Training (t=2.28, p= .03) [Hypothesis 2b]. Sessions that included these two techniques were associated with reduced total negative symptoms at two year follow-up (See Table 7). Overall, Hypotheses 2a-c were not supported. However, with more power, it is possible that Hypothesis 2a would have been partially supported and that coping skills would be effective in reducing positive symptoms at follow-up.

Using the G*Power 3.1 Program, post-hoc power analyses were run for the linear multiple regressions, fixed model. The input parameters were as follows: effect sizes (0.09, 0.22, 0.09) error probability (0.05), sample size (69), and number of predictors (9). The power was calculated as 0.16 (positive symptoms), 0.99 (negative symptoms), and 0.16 (GAF score). Therefore, sufficient power was only achieved for the negative symptoms analysis due to the larger effect, which was detected even at the small sample size.

Types of suspiciousness. Three logistic regressions were conducted to look at the differently coded types of suspiciousness (interpersonal and harm) and the relationship between specific personality traits (borderline and avoidant) and psychotic symptoms [Hypotheses 3a & 3b].

The first logistic regression was conducted to determine if borderline and/or avoidant traits were associated with one type of suspiciousness over the other [Hypothesis 3a]. The predictive variable was type of suspiciousness and the criterion variable was 3 or more traits of either borderline or avoidant personality disorder. This model was statistically significant (X^2= 12.25, p = 0.00, R^2= 0.15). The regression indicated that the interpersonal suspiciousness was significantly associated with BPD and APD traits (B =1.48, p=.00), whereas the harm suspiciousness was not (B =0.43, p=.40). Hypothesis 3a was therefore supported.

Two additional logistic regressions were conducted to determine if the two types of suspiciousness were associated with psychosis when defined as either a "slip psychosis" or as "full psychosis." In both analyses, the predictor variables were the types of suspiciousness in step one and traits of borderline or avoidant personality disorder in step two. The criterion variable was psychosis. In a logistic regression with slip psychosis as the criterion ("slip" was considered psychosis) and a criterion variable of type of suspiciousness, the model was statistically significant (X^2= 7.46, p = 0.02, R^2= 0.11). Harm suspiciousness was significantly predictive of psychosis (B =1.75, p=.01), whereas the interpersonal suspiciousness was not (B =0.47, p=.51). The model approached significance with the addition of the personality traits (three or more traits of BPD or APD) into the equation as a dichotomous criterion variable (X^2= 7.47, p = 0.06, R^2= 0.11). Harm suspiciousness continued to be significantly predictive of psychosis (B =1.75, p=.01), whereas the interpersonal suspiciousness was not (B =0.45, p=.54).

In a logistic regression that did not consider a slip as a break ("full psychosis"), the results were the same. Interpersonal suspiciousness was not predictive of psychosis (B =0.69, p=.41) even with personality traits in the equation (B =1.04, p=.24) in a significant model variable, whereas harm suspiciousness was predictive of psychosis without (B =2.08, p=.01) and with (B =2.21, p=.00) the personality traits in the equation. Models were significant without (X^2= 8.15, p = 0.02, R^2= 0.13) and continued with (X^2= 10.34, p = 0.02, R^2= 0.17) BPD and APD traits in the model. Therefore, Hypothesis 3b was fully supported: harm suspiciousness was predictive of psychosis, whereas interpersonal was not.

With the aforementioned results, further analyses were run in order to compare the current assessment of prodromal participants to various other ways to code these participants, using the delineation of suspiciousness. For one set of analyses, participants that initially received a positive code on suspiciousness with the SOPS were recoded to indicate "predictive" suspiciousness (i.e., harm). Non-predictive suspiciousness (i.e., interpersonal suspiciousness) was no longer coded as positive. For another set of analyses, participants that initially received a positive code on suspiciousness with the SOPS were recoded to indicate "non-personality suspiciousness." A participant would receive a positive code on suspiciousness in one of two conditions, 1) if a person did not have borderline or avoidant traits and reported either type of suspiciousness (harm or interpersonal) or 2) if a person *did* have borderline or avoidant traits and reported harm suspiciousness only.

Four logistic regressions were conducted to examine the ability of the current and "predictive" suspiciousness in predicting psychosis when defined two ways. The first analyses defined psychosis as a diagnosis of a psychotic disorder and a slip was not considered a break. Analyses indicated that the predictive suspiciousness recode was significantly predictive of

psychosis (B =1.81, p=.00, R^2= 0.12). Though the current code was also predictive of psychosis (B =1.45, p=.03, R^2= 0.06), less variance was explained. When comparing the predictive suspiciousness recode to the current code, analyses indicated that the predictive suspiciousness recode is predictive over and above the current code (B =1.33, p=.08). The initial model with the current code was significant (X^2= 7.68, p = 0.00, R^2= 0.12) and remained significant with the addition of the current code (X^2= 8.58 p = 0.01, R^2= 0.13). When identical analyses were run with the criterion variable of psychosis coded with a slip as a break, results were the same. Analyses indicated that the predictive suspiciousness recode was significantly predictive of psychosis (B =1.59, p=.01, R^2= 0.10). In addition, the predictive suspiciousness recode is predictive over and above the current code (B =1.22, p=.08). The initial model with the current code was significant (X^2= 7.24, p = 0.01, R^2= 0.10) and remained significant with the addition of the current code (X^2= 7.90 p = 0.02, R^2= 0.11).

Four logistic regressions were also conducted to examine the ability of the current and a "non-personality" suspiciousness recode in predicting psychosis when defined two ways (slip not a break and slip as break). An individual would receive a code on interpersonal suspiciousness in these analyses if he or she *did not* have BPD or APD traits (3 or higher). All individuals who received a harm suspiciousness code would continue to receive the code regardless of personality traits. In the analyses where a slip was not considered a break, the non-personality suspiciousness recode was significantly predictive of psychosis (B =1.52, p=.02, R^2= 0.10). However, this new recode was not found to be predictive over and above the current suspiciousness code (B =0.94, p=.27). The analyses where a slip was considered a break indicated the same. The non-personality suspiciousness was predictive (B =1.19, p=.03), but not over and above the current code (B =0.66, p=.37).

Classification statistics for the current classification and the predictive suspiciousness classification were calculated for further analyses of these two assessments. True negatives were considered participants that were not rated in the "prodromal" range on the suspiciousness item and did not convert to psychosis at two-year follow-up. True positives were considered participants that were rated in the "prodromal" range on the suspiciousness item (score 3-5) and did not convert to psychosis at two-year follow-up. False negatives were considered participants that were not rated in the "prodromal" range on the suspiciousness item and but did convert to psychosis at two-year follow-up. False positives were considered participants that were rated in the "prodromal" range on the suspiciousness item and did not convert to psychosis at two-year follow-up. This is considered an imperfect analysis as the reason for conversion (i.e., paranoid delusions) could not be obtained for all participants and therefore it was transition alone that was used to determine "positive." Psychosis was considered only when a diagnosis of schizophrenia (schizoaffective, delusional disorder) or associated disorder was diagnosed. Table 11 shows the comparison between the current classification and the recode form harm suspiciousness on sensitivity, specificity, true positives, true negatives, false positives, and false negatives. Overall, the recalculation towards harm suspiciousness is more sensitive, specific, and allows for fewer false positives. The new systems does allow for slightly more false negatives (5% compared to 3%), though it is unclear whether these individuals would be detected through other symptoms (e.g., hallucinations, non-persecutory delusions).

Visual hallucinations. Three logistic regressions were conducted to look at visual hallucinations and the relationship between borderline personality traits and psychotic symptoms [Hypotheses 4a & 4b]. Because the pseudo-hallucinations were reported so infrequently, the two hypothesized categories were combined into one "visual hallucinations" category. The first

logistic regression was conducted to determine if borderline traits were associated with visual hallucinations. The regression indicated that visual hallucinations were significantly associated with BPD (B =1.05, p=.04) [Hypothesis 4a]. This finding largely supported Hypothesis 4a, though it was unable to distinguish if BPD was related to one type of hallucination or the other due to low base-rate.

Two additional logistic regressions were conducted to determine if visual hallucinations were associated with psychosis when defined as either a "slip" or a "break" [Hypothesis 4b]. In both analyses, the predictor variables were visual hallucinations in step one and traits of borderline personality disorder in step two. The criterion variable was psychosis. In a logistic regression that considered a "slip" (one symptom reaching the psychotic level) as a break, visual hallucinations were only predictive of psychosis (B =1.45, p=.06) once borderline personality traits were added into the equation at step two. However, no step in the model, nor the final model were significant (X^2= 5.10, p = 0.17, R^2= 0.08). In a logistic regression that did not consider a slip as a break (break required a full diagnosis of a psychotic disorder), the results were the same. Visual hallucinations were only predictive of psychosis (B =1.33, p=.08) once borderline personality traits were in the equation. Again, no step in the model, nor the final model were significant (X^2= 2.87, p = 0.41, R^2= 0.04). This result suggests that visual hallucinations are only predictive of psychosis once borderline personality traits are accounted for, lending some support to Hypothesis 4b.

With the aforementioned results, further analyses were run comparing the current assessment of prodromal participants on visual hallucinations to a new code that took borderline personality traits into account. For this set of analyses, participants that initially received a positive code on hallucinations due to a visual hallucination were recoded to indicate "non-

personality visual hallucinations." A participant would receive a positive code if 1) a person did not have borderline traits, and 2) reported full visual hallucinations.

Four logistic regressions were conducted to examine the ability of the current and "non-personality visual hallucinations" in predicting psychosis when defined two ways. The first analyses defined psychosis as a diagnosis of a psychotic disorder and a slip was not considered a break. Analyses indicated that the non-personality visual hallucinations recode was significantly predictive of psychosis (B =1.90, p=.02, R^2= 0.08), whereas the original code was not (B =0.92, p=.20, R^2= 0.02). When identical analyses were run with the criterion variable of psychosis coded with a slip as a break, results were the same. Analyses indicated that the non-personality visual hallucinations recode was significantly predictive of psychosis (B =1.46, p=.06, R^2= 0.05) whereas the original code was not (B =0.92, p=.20, R^2= 0.02). The recoding lends further support to Hypothesis 4b and the suggestion that visual hallucinations are only predictive of psychosis if the participant does not also have BPD traits.

Discussion

This dissertation allowed an in-depth look at a prodromal sample and the individual psychotherapy they received at the Recognition and Prevention (RAP) Program of ZHH hospital from 2000-2006. In particular, these analyses provided a detailed account of the type of individual psychotherapy individuals received for prodromal symptoms, which of these techniques were effective, and which techniques were used with particular presenting problems. In addition, it described the sample's comorbidity with personality disorders and the possibility that personality disorder symptoms confound the prodromal assessment process.

The "prodrome" and therapy. In their 2007 review of prodromal treatment centers, McGlashen et al. (2007) reported that "most prodromal centers around the world currently offer

psychosocial treatment packages that are mixtures or hybrids of engagement, supportive therapy, case management, stress management, and cognitive behavioral approaches" (p. 721). The descriptive analyses of RAP individual psychotherapy techniques from 2000-2006 were consistent with this finding. RAP therapists used supportive (96%), coping (both cognitive approaches and stress management) skills (35%), and behavioral techniques (14%) in their approach. Strict case management was infrequent (4%), but other techniques often grouped in this category, such as assessment of symptoms (56%) and risk assessment and management (15%) were more frequent. Therefore, these findings indicated that the RAP approach was a mixture of multiple approaches.

Within the RAP approach, analyses showed that particular treatment techniques were found to be effective for particular symptoms for RAP patients. Specifically, when therapists assessed for symptoms (prodromal or other) and gave parents techniques for targeting their children's symptoms, there was a significant reduction in the prodromal level negative symptoms. Assessing symptoms and teaching or reviewing coping skills were not found to be *significant* in the reduction of positive symptoms, but *t* values in these analyses suggest that insufficient power might have impacted the ability of these analyses to detect significant differences. These findings suggest that particular techniques are more effective than others at targeting specific symptoms and that RAP techniques were effective at reducing symptoms. The clinical implications of these analyses suggest a tailored approach to treatment planning may be useful. The study results indicate that symptom presentation on baseline may be useful in selecting maximally effective treatment techniques matched to particular patient needs. This individualization and symptom-focused approach will hopefully maximize treatment effectiveness.

When compared to therapeutic techniques that are most effective, it was interesting to consider which techniques are most used for patients who present as highly symptomatic at baseline. Of interest were those with high emotion dysregulation, high positive symptoms, or high negative symptoms. Perhaps not surprisingly, patients presenting with BPD traits at baseline were more likely to have a higher percentage of sessions that contained risk assessment or management than those without BPD traits. Furthermore, literature on effective treatment of BPD (Linehan, 1993) suggests that implementing several types of techniques, including those techniques targeting suicide risk, during sessions is particularly helpful with patients with BPD traits (McMain et al., 2009). Based on this literature, one would expect sessions with these patients to include a higher rate of coping skills and behavioral techniques than the average at RAP (35% and 14%, respectively). However, the results of this study indicated that patients presenting with BPD traits were no more likely to have sessions with either coping skills or behavioral techniques than those without BPD traits. This study also found that patients with BPD traits were less likely than those without BPD traits to have sessions with psychoeducation, a core component of BPD treatments such as DBT (Linehan, 1993). These results may suggest that therapists treating these patients with BPD traits may have been overwhelmed by the multiple treatment targets and often crisis-generating behaviors that are commonly observed during clinical work with this population. When overwhelmed, therapists may resort to managing the behavior (risk assessment) rather than providing skills to change it (psychoeducation, coping skills, and behavioral techniques). This hypothesis, although consistent with the data and with theory concerning the difficulties of treating BPD (Linehan, 2003), cannot be tested with this dataset and would, in fact, require process notes or interviews from the therapists. Therefore it

will be important for future research to consider whether clinician ability to effectively manage personality traits can impact treatment quality.

Patients who presented with high positive symptoms at baseline, defined either by total positive symptoms or the highest positive symptom score, were more likely to have a larger percentage of sessions that contained coping skills than those who came in with lower level of positive symptoms. This finding was consistent with both the cognitive therapy literature in the prodrome (e.g., Morrison et al., 2004, 2007). These findings implied that RAP therapists, chose to teach and review coping skills with patients who presented with a higher level of positive symptoms. Moreover, analyses indicated that if the patient had several positive symptoms of concern (total positive symptoms), therapists were more likely to have sessions containing risk assessment or management. Additionally, if the patient had a highly rated positive symptom (highest positive symptom), therapists were more likely to use symptom assessment than if the patient had a lower rated positive symptom. The assessment (risk and symptom) by the therapists shows the importance of monitoring the development of all symptoms during the prodromal period in order to properly treat and protect those presenting with high levels of pre-psychotic symptoms.

For the patients who presented with the most negative symptoms (total negative symptoms), the findings are less straight-forward. It seemed that patients who had more negative symptoms on baseline were more likely to receive case management from their therapists than those with fewer negative symptoms on baseline. Although this finding is not inherently problematic, it is likely driven by very few patients, as the mean of this technique across all sessions is 5% (with all patients). In addition, analyses indicated that case management was not effective in reducing negative symptoms on follow-up. The effective techniques were symptom

assessment and parent training. However, case management was the one therapeutic technique that was not reliably coded between the two raters.

A few explanations are plausible for this result. First, the therapists' use of case management may have been driven by very few patients who had severe social and role functioning problems on intake. Case-management may have been necessary with these few patients, despite not being effective in producing long-term symptom change for them (i.e., not significantly reducing negative symptom at 2 year follow-up). Second, this finding may have been attributable to the presentation of those with many patients several moderate or severe negative symptoms. Due to the nature of their symptom presentations, these patients tend to be more difficult to engage clinically, and many other strategies that are typically used (e.g., cognitive) may need to be adapted or pursued over longer periods of time (e.g., behavioral). With such patients, therapists may have been more likely to focus on case-management as concrete strategies that can be used during sessions and often increase the resources available to the patient. This last hypothesis, although consistent with the data and theory concerning treatment of negative symptoms, cannot be tested with this dataset and would, again, need process notes or interviews from the therapists.

The "prodrome," personality disorders, and assessment. The high comorbidity of personality disorders, especially borderline personality disorder (BPD), with prodromal symptoms was initially of concern when considering the *treatment* of the prodrome. However, further investigation during this study indicated that two particular personality disorders, BPD and avoidant personality disorder (APD), may be even more problematic in the *assessment* of the prodrome. The results of this dissertation provided preliminary support for the hypothesis that these two personality disorders (or related traits) may not only have accounted for some of the

positive symptoms reported by participants, but may also have contributed to the percentage of inaccurate categorizations during prodromal assessment. To support this conclusion, it is necessary to consider two symptoms, suspiciousness and visual hallucinations, in further detail.

Suspiciousness is a symptom in the SOPS that is considered to be a precursor to a persecutory delusion. The item is meant to tap beliefs that, though attenuated, are inherently delusional in nature. However, the nature of the questions designed to assess this item makes it capable of tapping what can be considered both paranoid and *anxious* beliefs. For example, consider the following prompts from the SOPS: "Do you ever feel that people around you are thinking about you in a negative way? Have you ever found yourself feeling mistrustful or suspicious of other people?" It is not difficult to imagine that an anxious person, especially to the point of an avoidant person, would respond positively to both. In fact, the anchors themselves allow a score of 3 (considered prodromal) for "Concerns that people are untrustworthy. Sense of unease and need for vigilance (often unfocused). Mistrustful. Recurrent (yet unfounded) sense that people might be thinking or saying negative things about person" (SOPS). This description is surprisingly reminiscent of the description of the avoidant personality disorder symptom criterion 4 "because individuals with this disorder are preoccupied with being criticized or rejected in social situations, they may have a markedly low threshold for detecting such reactions" (American Psychiatric Association, 2000). Those with borderline personality disorder may similarly meet for this anchor based primarily on interpersonal suspiciousness as a result of repeated invalidation, a pattern of chaotic interpersonal relationships, or paranoia-like experiences when emotionally dysregulated (American Psychiatric Association, 2000; Linehan, 1993). Like those with APD, those with BPD are more likely to experience the interpersonal

suspiciousness secondary to the personality disorder, rather than as a pre-psychotic symptom that is unrelated to personality disorder symptoms.

Visual hallucinations are not an independent symptom on the SOPS, but rather part of the Perceptual Abnormalities symptom. There are prompts specific to visual hallucinations, however, and they include questions like "Do you ever think you see people, animals, or things, but then realize they may not really be there?" (SOPS). The item measures both illusions (misinterpretations of actual external stimuli) and pseudo-hallucinations (internal stimuli with intact reality testing). The experience of visual hallucinations may or may not be more prevalent in those with BPD than in those without BPD. However, it is possible that people with BPD are more likely to describe experiences in a way that the evaluator (or the assessment tool) may misinterpret the symptom as being visual hallucinations. Examples of this situation would include an intense, vivid dissociative (depersonalization, derealization) experience, or communication styles that contain hyperbolic, metaphoric, and impressionistic details. Considering the possibility of symptom reporting for secondary gain (e.g., validation, concern, and mental health services) is also relevant for individuals with traits of a Cluster B personality disorder.

The potential for difficult differential diagnoses brings into question the prevalence rates of personality disorders and traits, especially APD and BPD, in the prodrome. In the RAP sample, the two most prevalent non-Cluster A (generally considered to be related to psychosis) personality disorders were APD and BPD. The rate of APD was staggering in this sample, with over 37% meeting full criteria and an additional 34% having three (of the needed four) traits. Seven percent of participants met full criteria for BPD and just over 23% met three (of the needed five) traits. With comorbidity rates this high, it is impossible to ignore the possible

impact this comorbidity may have on the sample, including the possibility that the comorbidity is actually a problem of differential diagnosis.

The results of both the logistic regressions and the classification analyses suggest that, for the suspiciousness item, it is quite possible that difficulties with differential diagnosis contributed to false positives. More specifically, this study identified two types of suspiciousness: Interpersonal Suspiciousness was much less predictive of psychosis at two-year follow-up than Harm Suspiciousness. Moreover, participants with either traits of BPD or APD accounted largely, though not entirely, for Interpersonal Suspiciousness. This pattern of findings suggests that participants with APD and BPD are being classified as prodromal based on the interpersonal suspiciousness that stems from their anxiety (APD) or their dysregulation and interpersonal history (BPD). Clearly the methodological limitations of this study limit firm conclusions. However, there is enough evidence to support the importance of further investigation. Based on these findings, the next steps in this research would include a prospective study with additional assessment questions that would further delineate both types of suspiciousness (interpersonal vs. harm) and the cause of this suspiciousness (anxiety, dysregulation, or pre-psychosis). Suggested questions are included below:

1) Do you ever feel that people around you are thinking about you in a negative way? (original SOPS question)

1a) When do you feel this way? (*must determine if only in social situations*)

1b) Can you describe what was going on before you noticed this? (*determine level of dysregulation*)

1c) Do you know why people are thinking/talking about you? Is there any reason why people would be looking at you or thinking of you negatively? (*interpersonal vs. harm motivation*)

1d) Do you think that these people have any intentions other than thinking about you/talking about you? Will they do anything else? (*harm motivation*)

Rating:

Type of Suspiciousness ___ Interpersonal ___ Harm

Severity 1-6 (anchors altered for interpersonal and harm)

Cause ___ Pre-existing Anxiety ___ Pre-existing Dysregulation

___ General Mistrust due to History/Trauma ____ No clear cause (pre-psychosis)

Similar to suspiciousness, the results of analyses concerning visual hallucinations suggested concerns about differential diagnosis. First, visual hallucinations were reported primarily by those with BPD traits. Second, visual hallucinations alone were not predictive of psychosis, but when borderline personality traits were added to the regression, visual hallucinations became significantly predictive. Again, the post-hoc and archival nature of this study permits only suggestions for future research. As such, future research should investigate the reports of visual hallucinations, especially if those participants also have borderline personality disorder traits. Of particular concern would be SIDP-IV traits of emotion dysregulation and dissociative experiences.

Beyond clear BPD symptoms, it would be important to understand the nature of the experience as well as note the style of communicating exhibited by the participant. It is unusual for individuals with schizophrenia have visual hallucinations other than humans and animals of normal shape, size, and color (Resnick & Knoll, 2008). Reporting of other such visual hallucinations, including visual hallucinations with dramatic presentation, should be assessed for

any variation of malingering, feigning, over-reporting, or unintentional miscommunication. With regard to people with BPD in particular, it is important to consider the potential reinforcers inherent in a treatment evaluation for the prodrome (e.g., parental concern, treatment opportunity, treatment provider concern/attention). Especially in traditionally invalidating environments where crisis escalation has been reinforced, the opportunity to be heard and taken seriously could be worth exaggeration or embellishment for a potential patient. Once that is considered, it is also important to understand the communication techniques that may have been reinforced. Although the patient may not be intentionally malingering or even exaggerating, it is also possible that he or she is describing an experience in a way that is more hyperbole than it is visual hallucination (note: this should be considered with histrionic traits as well). In such a case, it is important for the interviewer to distinguish between visual phenomenon and a communication style that can be metaphorical and somewhat unusual, but not psychotic. These clinical concerns could be investigated in a prospective investigation by tracking the report of visual hallucinatory experiences, along with a malingering inventory and an assessment of communicative style (e.g., "speaks in metaphorical or hyperbolic manner," "speaks with impressionistic, theatrical style," "speech lacks concrete detail").

Limitations. The key limitation of this dissertation was its naturalistic, archival design. With such a design, we are restricted in the conclusions we can draw from our results and the recommendations that can be made. Within such a design, the results are limited by the lack of full reliability data on initial coding, the absence of randomization of participants, and the absence of manualization of therapy techniques. However, even with these limitations, this dissertation was the first study to take such an in-depth look at the psychotherapy techniques of a prodromal clinic during the prodrome that did not occur during a treatment study. As has been

found in a review of prodromal treatment centers, the standardized, manualized treatment that is given during a treatment study does not fully parallel what happens day to day (McGlashen et al., 2007). This study provided a snapshot of exactly what the psychosocial package does look like.

The study was also able to provide new insight into prodromal assessment, personality disorders, and false positives. While prospective studies will be needed to further explore the hypotheses and substantiate what has been found here, these new findings are a first step towards reducing the false positives in the prodromal samples and towards integrated prodromal and personality assessment that will maximize treatment for patients.

An additional limitation isthe exclusion criterion of moderate to severe harm to self. With a study that focused on personality disorders (and traits), this exclusion criterion likely eliminated important individuals from the treatment sample, especially those individuals with Borderline Personality Disorder. When interpreting the results, this sample limitation should be kept in mind.

Sample size, which led to a likely lack of power in several analyses, is also considered a significant limitation. While this is clearly a limitation both statistically and methodologically, the numbers reported here are not drastically different from those reported in similar prodromal studies, especially treatment studies (n =59 in McGorry et al., 2002; n =58 in Morrison et al., 2002, 2004, 2007). This is a result of the low-base rate of the population and the inherent difficulties in obtaining treatment adherence and follow-up data. It emphasizes the importance of research consortiums, such as the North American Prodrome Longitudinal Study (NAPLS), in order to answer import research questions in a reliable and valid manner.

Methodological limitations may explain the small variance accounted for within the models, which included restriction of range and the use of change scores. By nature of selecting

a prodromal population, the scores on the SOPS will be on the higher end of the interval scale (higher scores indicating symptoms). This restriction of range likely limited the amount of variance that could be accounted for by the regression models that relied on this outcome variable. Similarly, by using change scores as outcomes, the reduced number of possible outcomes further restricted the possible variance accounted for.

Despite these limitations, this study not only provided a thorough examination and description of integrative psychotherapy treatment during the "prodrome", the study also provided important new questions into the assessment of comorbid personality traits. The results of this study offer clear direction for future studies and emphasize the importance of a full, thorough differential diagnosis in order to continue to reduce false positives within the clinical high risk research and provide optimal treatment for individuals with a complicated symptom picture.

Appendix:

Individual Therapy Techniques Coding Scheme: A code is given if the technique is used at least once during the session. Each type of technique that is used is coded per session; multiple (unique) codes may be given per individual psychotherapy session.

1- Supportive: Supportive techniques are non-directive techniques that involve validation, empathy, and providing encouragement. This code is also used if the session is primarily used as a way for the patient to "vent" frustrations or difficulties.

2- Coping Skills (8 sub sections a-h): Coping techniques are directive techniques that involve modeling, teaching, or role-playing a coping skill.

2a- Physiological: coping techniques such as relaxation, breathing, or any technique that directly targets physiological symptoms of distress.

2b- Cognitive: coping techniques such as challenging and providing alternative to thoughts.

2c- Pleasant Events: the scheduling of pleasant and enjoyable events as a coping or preventative technique.

2d- Distraction: instruction in various ways to distract oneself from distressing thoughts, emotions, or experiences.

2e- Social Skills: social skills instruction (eye contact, ways to meet others, interpersonal effectiveness).

2f- Emotion Regulation: techniques taught to reduce or cope with intense emotions.

2g- Problem Solving: techniques intended to help solve problems (e.g., pro/cons, thinking of consequences, generating alternative solutions).

2h- Communication: techniques to improve effective communication (active listening, making requests, communicating with family members).

3- Behavioral Techniques (4 sub sections a-d): Techniques that involve the reinforcement or punishment of behaviors.

3a- Rewards: setting up a reward system (reward charts with parents, self rewards).

3b- Self-Monitor: monitoring behavior with charts or other explicitly stated measures.

3c- Goals: explicit discussion of short and long-term goals and progress towards achievement.

3d: Exposure: imaginal or in-vivo exposure.

4- Case Management (5 sub sections a-e): Techniques during session that are primarily case management in nature.

4a- School: session activity directed towards obtaining or changing a school placement or allocation of school resources.

4b- Work: session activity directed towards obtaining volunteer or paid employment.

4c- Housing: session activity directed towards obtaining or changing housing placement.

4d- Financial: session activity directed towards obtaining financial resources (e.g., benefits) or better managing financial resources (e.g., budgeting).

4e- Treatment: session activity directed towards obtaining or changing psychological treatment services.

5- Psychoeducation (6 sub sections a-f): Education provided on various topics.

5a-Psychiatric symptoms: psychoeducation regarding psychiatric symptoms.

5b- Stress: psychoeducation regarding the symptoms and effects of stress.

5c- Psychiatric Treatment and Adherence: psychoeducation regarding psychiatric treatment and treatment adherence.

5d- Healthy Living (Nutrition, Sex, Other): psychoeducation regarding a variety of topics including nutrition, safe sex practices, and other daily living experiences not captured by the other codes.

5e- Sleep: psychoeducation regarding the importance and effects of sleep.

5f- Substances: psychoeducation regarding the effects of psychoactive substances (with the exception of taking medications as prescribed, which would fall under 5c), including illegal drugs.

6- Monitoring: This code is to be used when the therapist was following up on a previously used technique, but did not institute a new technique.

7- Assessment of Symptoms: This code is used when the therapist assess symptom severity or changes in symptoms.

8- Risk (2 sub sections a-b)

8a- Assess: the assessment of risk of harm to self or other.

8b- Manage: the management of risk of harm to self or other (i.e., crisis plan, skills to manage risk, patient taken to hospital).

9- Parent Training: Code to be used when any therapeutic technique is given to a parent (or guardian) of the patient with the purpose of supplementing patient treatment (i.e., training in reinforcing positive behavior, reward charts, communication techniques).

Table 1. Group comparisons on the proportion meeting lifetime criteria for comorbid Axis I psychiatric diagnoses (Edited reprint from Woods et al., 2009)

Dependent Measures	Prodromal	Comparison Group				Overall χ^2
		NC	HSC	FHR	SPD	
	n =297	*n* =142	*n* =162	*n* =2	*n* =41	(p)
Axis I Mood and Anxiety Disorders						
Any Mood/Anxiety	68.4	*0.0*	*49.4*	50.0	*43.9*	231.3 <(0.001)
Any Mood Disorder	55.2	*0.0*	*33.8*	50.0	34.1	173.4 <(0.001)
Any Anxiety Disorder	38.5	*0.0*	31.3	0.0	*14.6*	111.8 <(0.001)
Axis I Substance Abuse or Dependence Disorders						
Any Substance Disorder	25.1	*1.5*	16.8	10.3	15.9	80.4 <(0.001)
Other Axis I Disorders						
Any Eating Disorder	2.6	0.0	0.7	0.0	0.0	7.2 (0.127)
Any Tic Disorder	1.6	0.0	0.0	0.0	9.1	11.9 (0.018)
Attention Deficit	13.6	1.5	24.4	0.0	39.4	44.6 <(0.001)
Learning Disorder	3.6	0.0	5.2	0.0	20.0	11.6 (0.020)
Childhood Behavior D/O	27.8	0.0	33.9	0.0	9.7	41.5 <(0.001)
Conduct disorder	7.6	0.0	15.7	0.0	6.5	16.7 (0.002)
Disruptive	1.3	0.0	0.0	0.0	0.0	3.5 (0.485)
Oppositional	20.3	0.0	20.0	0.0	3.2	26.2 <(0.001)
Adjustment disorders	2.5	1.9	5.2	0.0	20.0	3.2 (0.517)

NC= Normal Control; HSC=Help Seeking Control; FHR=Familial High Risk; SPD=Schizotypal Personality Disorder

Table 2. Group comparisons on the proportion meeting lifetime criteria for comorbid Axis II psychiatric diagnoses (Edited reprint from Woods et al., 2009)

Dependent Measures	Prodromal	Comparison Group				Overall χ^2
		NC	HSC	FHR	SPD	
	n =297	*n* =142	*n* =162	*n* =2	*n* =41	(p)
Axis II Personality Disorders						
Any Axis II Disorder	44.1	0.0	41.4	0.0	100.0	203.8 <(0.001)
Any Cluster A Disorder	40.5	0.0	12.7	0.0	100.0	201.2 <(0.001)
Paranoid	6.5	0.0	2.5	0.0	20.0	31.2 <(0.001)
Schizoid	3.4	0.0	10.2	0.0	30.0	40.4 <(0.001)
SPD	26.4	0.0	0.0	0.0	100.0	246.6 <(0.001)
Any Cluster B Disorder	8.2	0.0	11.5	0.0	10.0	28.3 <(0.001)
Antisocial	1.3	0.0	1.9	0.0	0.0	6.0 (0.197)
Borderline	6.5	0.0	7.0	0.0	7.5	18.2 (0.001)
Histrionic	0.0	0.0	0.0	0.0	2.5	6.6 (0.158)
Narcissistic	0.9	0.0	3.8	0.0	5.0	9.5 (0.049)
Any Cluster C Disorder	14.2	0.0	22.3	0.0	37.5	59.6 <(0.001)
Avoidant	11.2	0.0	19.1	0.0	35.0	54.4 <(0.001)
Dependent	0.9	0.0	0.0	0.0	0.0	3.3 (0.509)
Obsessive-Compulsive	3.4	0.0	3.8	0.0	7.5	9.9 (0.042)
PD NOS	3.0	0.0	2.5	0.0	0.0	7.8 (0.100)

NC= Normal Control; HSC=Help Seeking Control; FHR=Familial High Risk; SPD=Schizotypal Personality Disorder

Table 3. Descriptive Statistics: Sample descriptives

	Mean	Range
Gender	Male (69%)	N/a
Age	15.5	12 to 22
Change in Total Positive Symptoms (2 years)	2.8	-11 to +17
Change in Total Negative Symptoms (2 years)	2.5	-11 to +17
Change in Total GAF score (2 years)	5.8	-38 to +45
Number of RAP therapy sessions	15.5	0-73

Table 4: Descriptive Statistics: Prodromal type.

	Frequency	Percent
Clinical High Risk, Negative (CHR-)	53	35.3
Clinical High Risk, Positive (CHR+)	79	52.7
Schizophrenia Like Psychosis (SLP)	18	12.0
Total	150	100.0

Table 5. Descriptive Statistics: Personality disorders and traits.

Personality Disorder	Full Criteria (Percentage)	3 or More Traits (Percentage)	Number of Participants
Paranoid Personality Disorder	14 (9.86%)	25 (17.61%)	142
Schizoid Personality Disorder	35 (24.65%)	52 (36.62%)	142
Schizotypal Personality Disorder	8 (5.71%)	30 (21.43%)	140*
Antisocial Personality Disorder	5 (3.65%)	-	137*
Borderline Personality Disorder	10 (7.04%)	33 (23.24%)	142
Histrionic Personality Disorder	0 (0%)	5 (3.53%)	142
Narcissistic Personality Disorder	2 (1.41%)	11 (7.75%)	142
Avoidant Personality Disorder	39 (27.46%)	48 (33.80%)	142
Dependant Personality Disorder	2 (1.41%)	17 (11.97%)	142
Obsessive Compulsive Personality Disorder	5 (3.52%)	9 (6.34%)	142

*Missing data resulted in fewer cases
- Cases were not calculated due to three traits needed for full disorder.

Table 6. Descriptive Statistics: Therapy techniques.

Descriptive Statistics					
	n	Min	Max	Mean	SD
Supportive	69	.33	1.00	.96	.10
Coping Skills	69	.00	.78	.35	.19
Behavioral	69	.00	.56	.14	.13
Case Management	69	.00	.50	.05	.08
Psychoeducation	69	.00	.71	.20	.16
Monitoring	69	.00	.55	.11	.14
Assessment of Symptoms	69	.00	1.00	.56	.28
Risk Assess/ Management	69	.00	.86	.15	.21
Parent Training	69	.00	.60	.10	.14
Valid *n* (listwise)	69				

Table 7. Linear regression: Psychotherapy techniques predictive of reduction in negative symptoms at two-year follow-up.

Coefficients						
		Unstandardized Coefficients		Standardized Coefficients		
Model		B	Std. Error	Beta	t	Sig.
1.00	(Constant)	-0.71	2.08		-0.34	0.74
	Coping Skills	-5.15	3.15	-0.20	-1.64	0.11
	Behavioral	-1.24	5.70	-0.03	-0.22	0.83
	Case Management	-2.49	7.53	-0.04	-0.33	0.74
	Psychoeducation	3.13	4.32	0.10	0.72	0.47
	Monitoring	-1.41	4.86	-0.04	-0.29	0.77
	Assessment Sx	6.40	2.44	0.35	2.62	0.01
	Risk Assess/Manage	0.75	2.93	0.03	0.26	0.80
	Parent Training	13.36	5.27	0.36	2.54	0.01
2.00	(Constant)	0.35	2.73		0.13	0.90
	Coping Skills	-5.26	3.17	-0.20	-1.66	0.10
	Behavioral	-1.00	5.75	-0.03	-0.17	0.86
	Case Management	-2.25	7.58	-0.04	-0.30	0.77
	Psychoeducation	3.03	4.35	0.09	0.70	0.49
	Monitoring	-1.35	4.89	-0.04	-0.28	0.78
	Assessment Sx	6.52	2.46	0.35	2.64	0.01
	Risk Assess/Manage	0.71	2.95	0.03	0.24	0.81
	Parent Training	12.49	5.49	0.34	2.27	0.03
	Psychotropic Drugs	-1.16	1.93	-0.07	-0.60	0.55

Table 8. Logistic regression: Psychotherapy techniques associated with borderline personality disorder traits at baseline.

Variables in the Equation						
	B	S.E.	Wald	df	Sig.	Exp(B)
Coping Skills	1.69	1.64	1.07	1.00	0.30	5.45
Behavioral	1.41	2.93	0.23	1.00	0.63	4.10
Case Management	0.25	5.16	0.00	1.00	0.96	1.28
Psychoeducation	-5.01	2.93	2.92	1.00	0.09	0.01
Monitoring	-2.02	3.06	0.44	1.00	0.51	0.13
Assessment Sx	1.09	1.27	0.73	1.00	0.39	2.96
Risk Assess/Manage	2.47	1.37	3.24	1.00	0.07	11.78
Parent Training	0.53	2.51	0.05	1.00	0.83	1.71
Constant	-2.23	1.15	3.73	1.00	0.05	0.11

Table 9. Linear regression: Psychotherapy techniques associated with total positive symptoms at baseline.

Coefficients						
		Unstandardized Coefficients		Standardized Coefficients		
Model		B	Std. Error	Beta	t	Sig.
1.00	(Constant)	2.30	2.12		1.09	0.28
	Coping Skills	6.92	3.08	0.26	2.25	0.03
	Behavioral	-4.74	5.25	-0.12	-0.90	0.37
	Case Management	1.89	7.91	0.03	0.24	0.81
	Psychoeducation	0.46	4.34	0.01	0.11	0.92
	Monitoring	3.58	4.86	0.09	0.74	0.46
	Assessment Sx	2.88	2.42	0.15	1.19	0.24
	Risk Assess/Manage	7.34	3.03	0.28	2.42	0.02
	Parent Training	1.57	4.70	0.04	0.33	0.74

Table 10. Linear regression: Psychotherapy techniques associated with total negative symptoms at baseline.

Coefficients[a]						
		Unstandardized Coefficients		Standardized Coefficients		
Model		B	Std. Error	Beta	t	Sig.
1.00	(Constant)	10.88	2.07		5.26	0.00
	Coping Skills	-3.01	3.01	-0.12	-1.00	0.32
	Behavioral	-6.14	5.13	-0.16	-1.20	0.24
	Case Management	15.71	7.73	0.25	2.03	0.05
	Psychoeducation	0.18	4.24	0.01	0.04	0.97
	Monitoring	-0.98	4.75	-0.03	-0.21	0.84
	Assessment Sx	3.25	2.36	0.18	1.38	0.17
	Risk Assess/Manage	-0.55	2.96	-0.02	-0.18	0.85
	Parent Training	3.31	4.59	0.10	0.72	0.47

Table 11. Classification Statistics: New classification vs. Current classification.

Classification Statistic	New "Harm Only" Classification	Current SOPS Classification
Sensitivity	0.50	0.75
Specificity	0.86	0.59
True Positive	0.25	0.15
True Negative	0.94	0.96
False Positive	0.75	0.85
False Negative	0.05	0.03

Figure 1. Recognition and Prevention (RAP) neurodevelopmental model (Reprinted from Cornblatt et al., 2003).

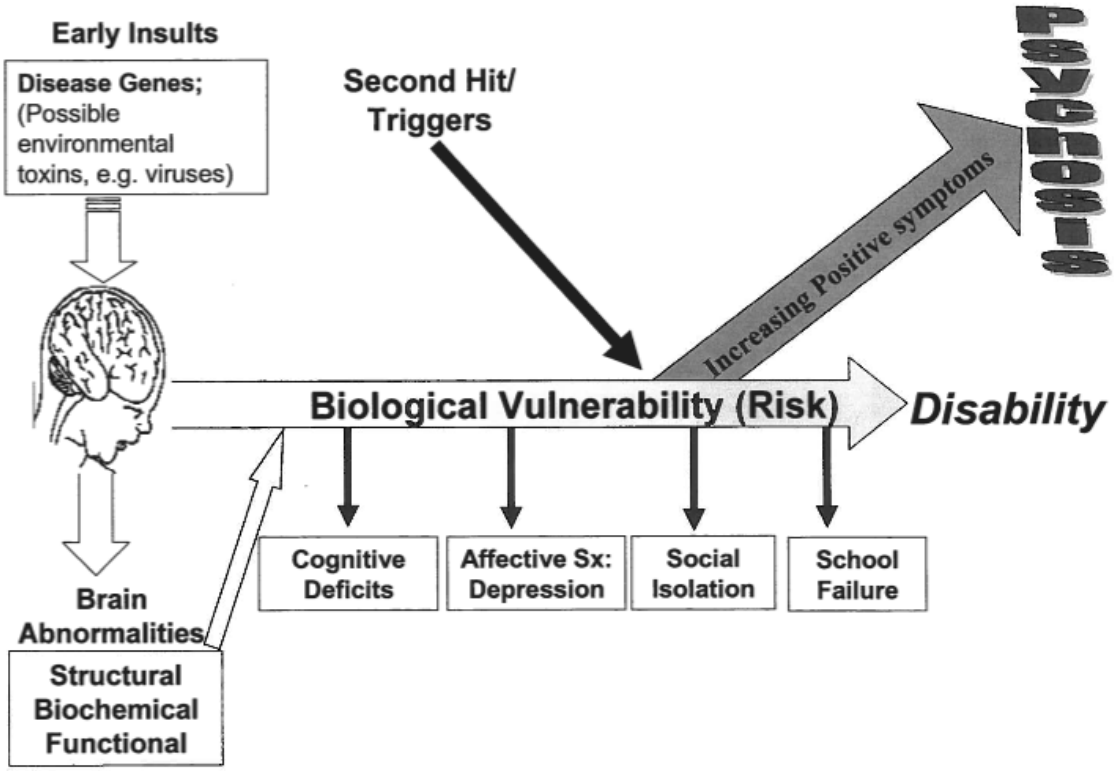


Figure 2. Recognition and Prevention (RAP) model of prodromal symptom progression (Reprinted from Cornblatt et al., 2003).

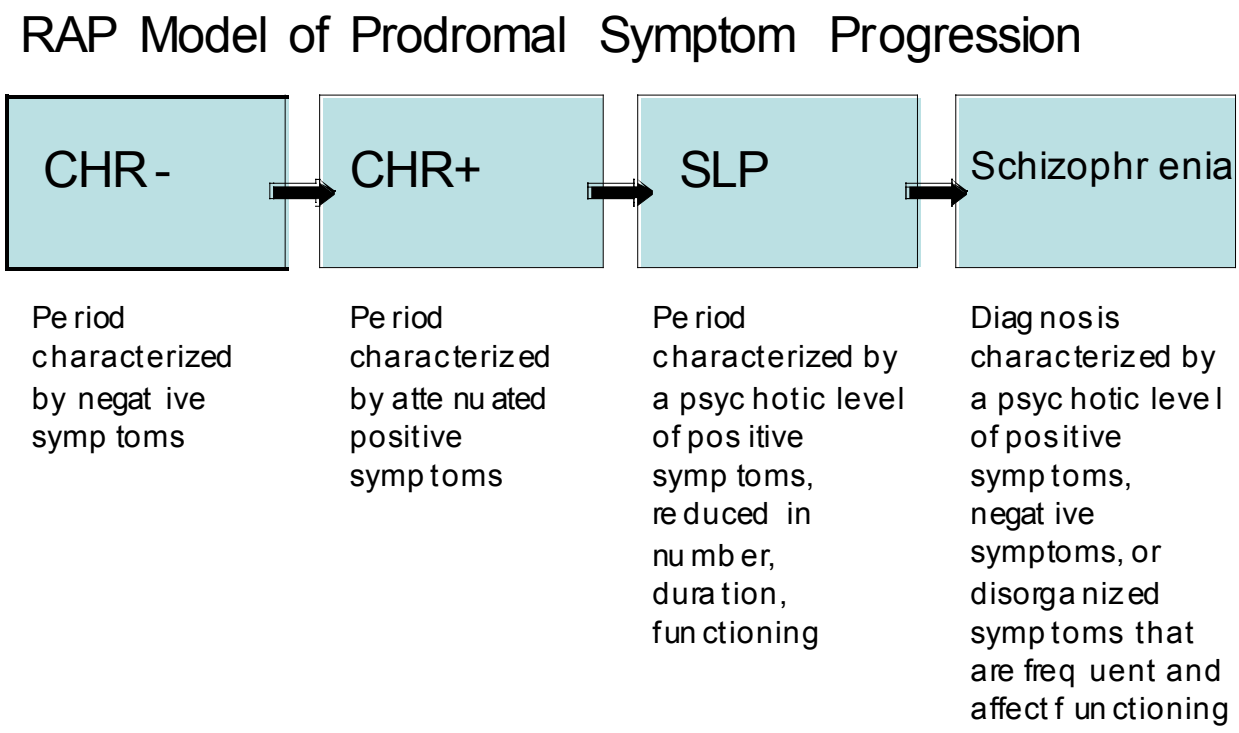
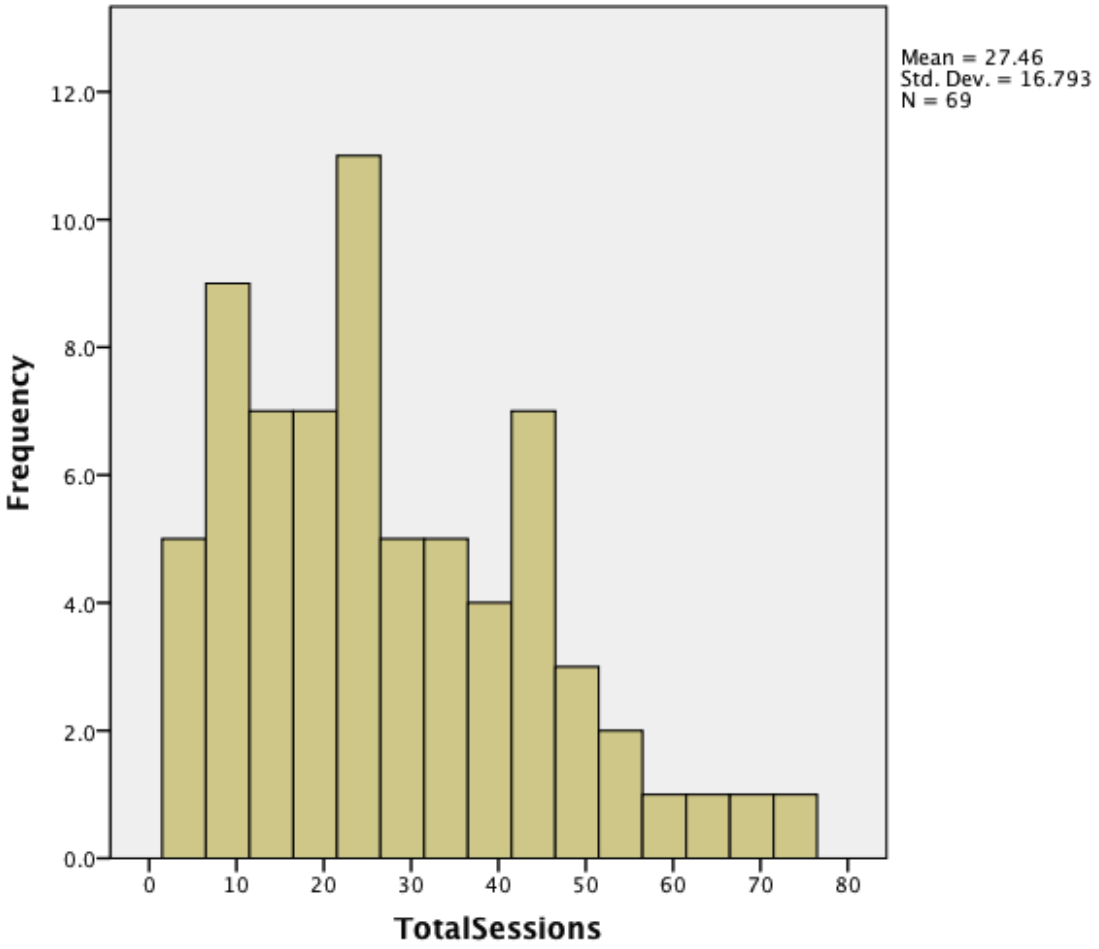


Figure 3. Histogram of total Recognition and Prevention (RAP) individual psychotherapy sessions.



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