THE EARLY DEVELOPMENTAL CONTEXT AND COURSE OF FIRST-EPISODE PSYCHOSIS

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ABSTRACT

While there is a wealth of knowledge concerning premorbid risk factors for first-episode episode psychosis (FEP), premorbid development can also account for some of the heterogeneity in clinical features of FEP associated with poor post-onset outcome. The current study was therefore designed to evaluate the following hypotheses: 1) low cognitive reserve would confer greater vulnerability to cognitive decline in FEP, 2) more "difficult" premorbid temperamental styles would increase susceptibility to substance abuse in FEP, and 3) FEP onset would lead to increasing dependence on family members to meet attachment needs. Fifty-four individuals with FEP and their parents provided consent for collection of data pertaining to early central nervous system development, premorbid temperament, premorbid and post-onset attachment networks, as well as clinical status and cognition through the early phase of psychosis. Our results indicate that, first, individuals with low and normal cognitive reserve experienced cognitive declines of similar magnitude early in psychosis. Second, more "difficult" permorbid temperamental styles were associated with significantly increased odds for substance abuse at presentation. Finally, increasing emotional dependence on family members was not universally reported; instead, only those without romantic partners showed consolidation of attachment networks into a few family relationships. Longer duration of illness predicted intensified dependence on family members, and more severe negative symptoms were associated with difficulties forming new peer attachments. These results suggest that risk factors from the developmental literature can account for some of the heterogeneity in particular clinical features of FEP. Some aspects of

premorbid development, such as temperament, are especially useful predictors of specific difficulties early in FEP.

DEDICATION

For my Aunt Steph.

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CHAPTER 1: INTRODUCTION

First-episode psychosis (FEP; Abrams & Nathanson, 1966; Johnstone, Crow & Johnson, 1986) refers to the initial presentation of clinical psychotic symptoms. The cardinal symptom of psychoses is loss of touch with reality, reflected by delusional beliefs, hallucinations, and / or thought disorder (American Psychiatric Association, 2000; Haahr et al., 2008). Associated clinical features such as negative symptoms (e.g., blunted affect, apathy, and withdrawal), cognitive impairments, behaviour problems, and social dysfunction can precede or follow the onset of psychotic symptoms (Davidson et al., 1999; Larsen et al., 2004; Melle et al., 2005; Yung, Stanford, Cosgrave & McGorry, 2006). A wide range of pre-existing difficulties has been noted in the early developmental histories of those with FEP, and extensive research has evaluated premorbid developmental anomalies as predictors of risk for psychosis.

Early abnormalities in central nervous system (CNS) maturation in children at high genetic risk for psychosis have long been recognized as constituting an additional vulnerability for the condition (e.g. Fish, 1987). Prospective studies of children born to mothers with chronic psychosis suggested that those children who developed psychoses themselves had early neuromotor problems (Fish, Marcus, Hans, Auerbach & Perdue, 1992; Marcus et al., 1987). Poor muscle tone, atypical physical growth, and delayed or disorganized

acquisition of motor skills predicted future susceptibility to psychosis (Fish, 1977; Marcus et al., 1987). Individuals who suffered the most severe forms of psychotic illness also had histories of obstetrical complications and evidence of prenatal growth retardation (Fish et al., 1992). Pandysmaturation (Fish & Kendler, 2005; Fish, 1987; Fish, 1977) refers to the cluster of anomalies in early central nervous system (CNS) development that can increase the risk for psychosis in those already genetically vulnerable to the disorder.

Birth cohort and clinical studies found that markers of early CNS insults such as exposure to certain obstetrical complications (Cannon et al., 2002; Geddes et al., 1999), and markers of atypical development such as craniofacial abnormalities (Lane et al., 1997) and delayed motor skills modestly increased the risk for psychosis in the general population as well (Cannon et al., 2000; Vourdas, Pipe, Corrigal & Frangou, 2003). Premorbid abnormalities in brain structure and function are also interpreted as evidence of atypical CNS development in FEP (Ananth et al., 2002; Borgwardt et al., 2007; Meisenzahl et al., 2008; Riley et al., 2000; Simon et al., 2007). Neurodevelopmental models of psychosis posit that early abnormalities in CNS maturation and other aspects of development (e.g. affective and behavioural functions; see Mirsky & Duncan, 1986) correspond to increased vulnerability for psychosis in some individuals (Kunugi, Nanko & Murray, 2001; Murray, 1994).

Much research in FEP thus evaluates early developmental anomalies as predictors of risk for psychosis. However, individuals with psychosis have greatly variable early life courses (e.g., Weinberger, 1987) and some individuals have no

known developmental anomalies preceding psychosis (van Os, Linscott, Myin-Germeys, Delespaul & Krabbendam, 2009). Developmental anomalies are evident for other individuals with FEP, and there is some evidence that such difficulties predict clinical features of psychosis such as negative symptoms (Ruiz-Veguilla et al., 2008). The current study was therefore designed to evaluate the relationship between specific aspects of premorbid development and the course of selected clinical features early in psychosis, as outlined below.

1.1 Premorbid development in FEP

Numerous early risk factors are physical or behavioural indicators of unspecified anomalies in CNS development predating the onset of psychosis (Marenco & Weinberger, 2000; Murray, Lappin & Di Forti, 2008). Late acquisition of developmental milestones and poor motor coordination are considered physical markers of atypical CNS development and risk for psychosis (Ballon, Dean & Cadenhead, 2008; Cannon et al., 2002; Isohanni et al., 2000; Lloyd et al., 2008; Pantelis et al., 2005; Salokangas & McGlashan, 2008). Difficulties with motor control and coordination can present early in development in those with psychosis (e.g. Fish et al., 1992), and have also been documented in pre-psychotic school-age children. For instance, Walker and colleagues (1994) examined home movies of children who later developed psychoses and found that, relative to their unaffected siblings, they showed odd posturing and poor motor coordination well before psychiatric symptoms emerged (see also Browne et al., 2000; Emsley, Turner, Oosthuizen & Carr, 2005).

In addition to early neuromotor problems, difficulties with academics later in childhood appear to increase the risk for psychosis (Maki et al., 2005). Premorbid academic achievement of individuals who develop FEP tends to be lower than that of the normal population in both birth cohort studies and clinical samples (Cannon et al., 2000; Fuller et al., 2002; Isohanni et al., 2000; van Oel, Sitskoorn, Cremer & Kahn, 2002). Individuals who convert to psychosis also have lower premorbid intellectual abilities than their age peers (Woodberry, Guiliano & Seidman, 2008). Thus, markers for atypical CNS development in childhood and adolescence are more common in individuals with FEP than in the general population.

Similarly, affective and behavioural problems in childhood and adolescence predate psychotic symptoms in some individuals with FEP (Owens & Johnstone, 2006). Individuals with FEP can have premorbid difficulties with anxiety and depression (Olin et al., 1998) and nonspecific issues such as hyperactive, oppositional, or aggressive behaviour (Keshavan et al., 2003; Marcus, Hans, Auerbach & Auerbach, 1993). Childhood externalizing or antisocial behaviours often precede the onset of psychotic symptoms (Tarbox & Pogue-Geile, 2008) but are considered nonspecific indicators of risk for psychosis as they can predate other psychiatric illnesses (Keshavan et al., 2008).

Premorbid social withdrawal and isolation are also commonly reported prior to the onset of psychosis (Addington, Penn, Woods, Addington & Perkins, 2008; Davidson et al., 1999; van Kampen, 2005). Social withdrawal or

internalizing difficulties present relatively frequently in later childhood and adolescence in those who convert to psychosis, but are also reported in children who develop other forms of psychopathology (Tarbox & Pogue-Geile, 2008). Childhood social problems are not specific to psychosis, but they can be early markers for psychosis-related social issues. For instance, premorbid interpersonal difficulties and social withdrawal predict the severity of negative symptoms following psychosis onset (Jeppesen et al., 2008; Monte, Goulding & Compton, 2008).

The aforementioned premorbid difficulties are evident in some individuals who convert to psychosis (Isohanni, Murray, Jokelainen,Croudace & Jones, 2004; Maki et al., 2005; Marenco & Weinberger, 2000) but can be very difficult to disentangle from the early clinical manifestations of psychosis. Conversion to FEP is often preceded by a prodromal period involving changes in an individual's thought patterns, affective responses, cognition, or interpersonal skills (e.g., Addington, van Mastrigt & Addington, 2003b; Møller & Husby, 2000). Mild delusions or hallucinations, cognitive difficulties, anxiety, mood symptoms, somatic complaints, and social passivity or withdrawal may present during the prodromal period (Corcoran et al., 2007; Miller et al., 1999; Yung & McGorry, 1996).

The severity and nature of prodromal symptoms varies and the onset of clinical psychotic symptoms can be insidious (Beiser, Erickson, Fleming & Iacono, 1993; Platz et al., 2006). Longer prodromal periods and a more subtle onset of psychotic symptoms may lead to longer durations of untreated

psychosis (DUP), which in turn can predict worse clinical prognosis (Harris et al., 2005; Jeppesen et al., 2008; Klosterkotter, Schultze-Lutter & Ruhrmann, 2008; Schimmelman et al., 2008). Negative symptoms can also emerge in the prodrome, frequently escape detection or are attributed to normative adolescent changes, and can be highly resistant to treatment after psychotic symptoms develop (Corcoran et al., 2007; Davidson & McGlashan, 1997). The adverse effects of intractable symptoms could be mitigated by reducing DUP (Crumlish et al., 2009), which highlights the importance of understanding premorbid trajectories into psychosis.

A simple common developmental pathway to psychosis is unlikely and most studies suggest that there are numerous premorbid trajectories leading to the onset of psychotic symptoms (Addington et al., 2003b; Larsen et al., 2004; Rabinowitz, Harvey, Eerdekens & Davidson, 2006; Rabinowitz, De Smedt, Harvey & Davidson, 2002). For example, some individuals who develop FEP show stable, positive premorbid functioning, while others experience deterioration of social and academic abilities prior to psychosis onset (Addington et al., 2003b; Larsen et al, 2004). Still others show stable, poor adjustment throughout childhood and adolescence (Rabinowitz et al., 2002). There is considerable heterogeneity in patterns of premorbid development in FEP, as well as in the duration and severity of prodromal symptoms (van Kampen, 2005).

1.2   Heterogeneity of clinical features

Individuals with FEP often differ markedly in symptom manifestation at onset and throughout the illness course (McGrath et al., 2004; Mohr et al., 2004;

Salvatore et al., 2007). Heterogeneity is also evident in three associated clinical features of psychosis that are particularly important to prognosis. Firstly, in some individuals with FEP, cognitive deficits appear before or very early in the course of psychosis, and are associated with refractory symptoms and adjustment difficulties in the early phase of illness (Bodnar, Malla, Joober & Lepage, 2008; Holthausen et al., 2007; Leeson, Barnes, Hutton, Ron & Joyce, 2009). There is substantial unexplained variance in the severity of psychosis-related cognitive impairments (Riley et al., 2000; Rodriguez-Sanchez, Crespo-Facorro, Gonzalez-Blanch, Perez-Iglesias & Vazquez-Barquero, 2007). It is unclear whether aspects of premorbid development (such as atypical CNS maturation) could predict the severity of psychosis-related cognitive decline.

Secondly, abuse of substances such as cannabis may precipitate FEP (Wade et al., 2006) by lowering the threshold for conversion to psychosis (Arsenault et al., 2002; Corcoran et al. 2008; Hambrecht & Hafner, 2000; Haroun, Dunn, Haroun & Cadenhead, 2006). Substance abuse is also related to an earlier age of FEP onset (e.g., Barnes, Mutsatsa, Hutton, Watt & Joyce, 2006; Barnett et al., 2007; Gonzalez-Pinto et al., 2008; Ongur, Lin & Cohen, 2009), increased risk for suicide attempts (Robinson et al., 2009), and poor prognosis (Conus et al., 2006; Grech, van Os, Jones, Lewis & Murray, 2005; Isohanni et al., 2000; Pencer, Addington & Addington, 2005). Premorbid predictors of substance abuse have received little attention, though they have the potential to improve our understanding of risk for substance abuse in FEP (Larsen et al., 2006).

Lastly, individuals who exhibit social withdrawal and isolation at the time of their first episode (Harris, Brennan & Anderson, 2005) have difficulties maintaining relationships (Ballon, Kaur, Marks & Cadenhead, 2007; Goodwin et al., 2003; Hjern, Wicks & Dalman, 2004). Premorbid social maladjustment predicts the severity of treatment resistant aspects of psychosis such as negative symptoms (Jeppesen et al., 2008; Monte, Goulding & Compton, 2008). Though social dysfunction is widely recognized in individuals with FEP, the trajectory of social withdrawal early in psychosis has not been systematically evaluated (Harris et al., 2005).

The purpose of the current study was to clarify the course of cognitive impairment, substance abuse, and social isolation during the first episode of psychosis. I investigated whether markers of atypical brain maturation through infancy, childhood, and adolescence predicted the severity of cognitive impairment during the first episode of illness. Secondly, I assessed whether premorbid temperament predicted substance abuse early in FEP. Lastly, I evaluated whether social withdrawal in FEP involved increasing dependence on family members to meet emotional needs, and whether the severity of post-onset negative symptoms interfered with the capacity to form new peer attachments.

1.3   PART 1 – Cognition

1.3.1   Markers for atypical brain maturation: Delayed milestone acquisition and academic difficulties

Some features of early development suggestive of atypical CNS maturation appear to be associated with increased risk for FEP and may

negatively affect the course of illness (Cannon et al., 2000; Karlsgodt et al., 2008). The following section reviews the FEP literature that addresses delays in developmental milestone acquisition and low academic achievement. Both of these factors are considered markers for atypical CNS functioning.

As the CNS matures, infants attain milestones such as the ability to crawl, stand, walk, and talk in a sequential pattern. Milestone acquisition is therefore considered a measure of CNS development (Hallett & Proctor, 1996) and a predictor of language and other cognitive skills (Halberda & Feigenson, 2008; Mundy, Card & Fox, 2000). There has been considerable interest in describing the acquisition of developmental milestones in children who subsequently convert to FEP to establish whether these anomalies in CNS maturation are observable at an early age. Late milestone achievement is related to increased risk for FEP (Isohanni et al., 2000; Isohanni et al., 2001; Isohanni et al., 2004). Late milestones are also associated with delays in receptive language and intellectual development in children at high genetic risk for psychosis who subsequently convert to FEP (Cannon et al., 2000).

The association between delayed early milestones and cognitive skills in childhood suggests that a stable trajectory of atypical CNS maturation is associated with increased risk for psychosis. Significant problems with academic achievement are evident in childhood and adolescence in some individuals who develop FEP, reflecting ongoing difficulties meeting cognitive challenges (Cannon et al., 2000; Fuller et al., 2002; van Oel et al., 2002). These findings indicate that individuals who fall behind peers in milestone acquisition and

academic achievement are more likely to develop psychosis than individuals whose development proceeds normally. From this perspective, early difficulties with CNS maturation are associated with increased risk for psychosis (Isohanni et al., 2004; Maki et al., 2005).

Atypical CNS development (e.g., Karslgodt et al., 2008) likely underlies psychosis-related cognitive difficulties, which can emerge before psychotic symptoms. Abnormalities in CNS development are associated with premorbid cognitive impairments in some, but not all, individuals who subsequently convert to FEP (Cannon et al., 2003; Pantelis, Yucel, Wood, McGorry & Velakoulis, 2003). Premorbid cognitive impairments can worsen at psychosis onset, and typically persist during the early course of illness (Hoff, Svetina, Shields, Stewart & DeLisi, 2005; Hoff et al., 1999; Rund et al., 2007; Rund et al., 2004; Simon et al., 2007). However, the cognitive deficits presenting early in psychosis are heterogeneous in their severity (Mesholam-Gately, Giuliano, Goff, Faraone & Seidman, 2009), differentially affecting some individuals with FEP. It may be that those individuals with premorbid markers of atypical CNS maturation also experience more severe FEP-related cognitive deficits than individuals without such premorbid markers. Prospective neuroimaging studies indicate that psychosis-related gray matter loss is superimposed upon pre-existing structural anomalies in some individuals with FEP (Pantelis et al., 2007; Pantelis et al., 2005). This pattern of early and late anomalies in CNS development preferentially affecting a subgroup of individuals with FEP has not been

examined using early behavioural measures of CNS functioning (e.g., milestone acquisition, academic achievement).

Studies of early behavioural measure of CNS functioning tend to include either measures of early neuromotor development (Ruiz-Veguilla et al., 2008) or premorbid academic achievement as predictors of the severity of psychiatric symptoms in FEP (e.g., Crespo-Facorro et al., 2007; Jeppesen et al., 2008; Malla & Payne, 2005; Monte et al., 2008; Petersen et al., 2008). Premorbid neuromotor development and academic achievement have not been systematically evaluated as predictors of cognition in FEP. The paucity of research in this area is surprising, as premorbid neuromotor and cognitive difficulties should lower the threshold for subsequent cognitive deficits in psychosis (Niendam et al., 2007; Rodriguez-Sanchez et al., 2008). Academic difficulties predict impaired verbal abilities early in psychosis (Gonzalez-Blanch et al., 2008a; Rund et al., 2007), a relatively intuitive finding. It is unclear whether similar relationships exist between cognition and earlier markers of atypical CNS development such as milestone acquisition. A novel approach would use both delayed milestones and academic difficulties as evidence of compromised CNS development from a very early age. Early and persistent CNS difficulties may be a particularly useful marker of susceptibility to psychosis-related cognitive deterioration. Cognitive reserve theory provides a plausible model for the relationship between early CNS development and susceptibility to psychosis-related cognitive impairments.

1.3.2 Cognitive reserve

Cognitive reserve theory suggests that individual differences in brain structure and function partly explain variability in normal cognition and the cognitive effects of neural pathology (Richards & Deary, 2005). Individual differences in cognition are attributed to both passive and active components of cognitive reserve (Stern, 2002). Passive reserve implies that natural variation in brain morphology is an important determinant of cognitive abilities and the threshold for clinical deficits caused by brain pathology. For example, larger brain size protects against age-related cognitive decline (Anstey et al., 2007; Cummings, Vinters, Cole & Khachaturian, 1998; Fotenos, Mintun, Snyder, Morris & Buckner, 2008) and cognitive impairment following acquired brain injury (Kesler, Adams, Blasey & Bigler, 2003). Greater redundancy of neurons or synaptic connections increases cognitive efficiency and mitigates cognitive deterioration following injury or degenerative processes (e.g., Tisserand, Bosma, Van Boxtel & Jolles, 2001).

The efficiency of the neural networks underlying cognition is considered an active component of cognitive reserve that facilitates recruitment of cortical resources to meet task demands and to compensate for neuronal insult or degeneration (Stern et al., 2005; Stern, 2002). Greater efficiency of neural processing and flexible recruitment of brain regions during cognitive tasks support better cognition in healthy individuals (Stern et al., 2003) and diminish cognitive impairments related to neural pathology (Stern, 2002). Efficient cortical functioning, as indicated by intelligence, education, and cognitive activity level buffers age and dementia-related cognitive declines (Acevedo & Loewenstein,

2007; Coffey, Saxton, Ratcliff, Bryan & Lucke, 1999; Fritsch et al., 2007; Habeck, Hilton, Zarahn, Flynn, Moeller, & Stern, 2003; Staff, Murray, Deary & Whalley, 2004; Valenzuela & Sachdev, 2009; Valenzuela, Breakspear & Sachdev, 2007). Education and cognitive challenges bolster cognitive abilities across the lifespan, highlighting the importance of active components to cognitive reserve (see Fratiglioni & Wang, 2007 for a review).

Passive and active components of cognitive reserve also interact in complex ways to determine cognitive abilities or compensation for neural pathology. Cortical morphology appears to be an important rate-limiting factor of cognitive reserve whereby the extent of structural redundancy sets the parameters for neural efficiency (Bartréz-Fas et al., 2009; Mortimer, Snowdon & Markesbery, 2003; Park & Reuter-Lorenz, 2009; Solé-Padullés et al., 2009). Cortical volume is inversely related to neural activation in healthy young adults with the strongest cognitive abilities, indicating that greater redundancy corresponds to restricted cortical recruitment (i.e. greater neural efficiency; Craik, 2006).

However, the relationship between brain structure and function varies with age. For instance, pruning of surplus neurons and synaptic connections in childhood and adolescence is considered an important developmental precursor of neural efficiency (Foster et al., 1999; Van Petten et al., 2004) and cortical volume loss is correlated with increasingly efficient activation. Neural loss in adulthood or old age, in contrast, can be a precursor of dementia – and so is related to decreasing neural efficiency (Tisserand & Jolles, 2003). Developmental

stage also affects the interpretation of correlations between cortical activation and cognition. Strong cognitive performance in both children and the elderly is associated with wider cortical recruitment than in healthy young adults for different reasons (Cabeza, 2002; Li, Brehmer, Shing, Werkle-Bergner & Lindenberger, 2006). While children are starting to lay the foundations for increasing neural efficiency with broad recruitment, elderly adults are most likely compensating for decreasing neural efficiency through wider cortical activation (Craik, 2006). Cognitive reserve is an important determinant of cognitive abilities across the lifespan, with shifting relationships between passive and active components.

Cognitive reserve in adulthood is routinely assessed using education level or estimated premorbid IQ, which reflect the contributions of both passive and active components to cognitive reserve (Valenzuela & Sachdev, 2006). However, childhood cognitive abilities predict susceptibility to age-related cognitive decline more strongly than contemporaneous measures of education or occupation (Deary et al., 2006; Richards & Sacker, 2003). Childhood CNS development may be the best predictor of individual differences in cognitive reserve (e.g. Bloss, Delis, Salmon & Bondi, 2008). Hence, individual differences in CNS development can explain some of the variability in normal cognition and cognitive decline related to neural pathology.

1.3.3   Cognitive reserve and psychiatric disorders

In contrast to the literature on aging, studies have only recently suggested that individual differences in cognitive reserve may be relevant to psychiatric

problems. Low cognitive reserve may increase the likelihood of conversion to psychiatric conditions (Koenen et al., 2009; MacCabe et al., 2008) and may also affect symptom manifestation and clinical outcomes (Barnett, Salmond, Jones & Sahakian, 2006). In psychosis, weaker cognitive abilities reduce the capacity to rationalize odd thoughts or perceptions, which in turn may foster delusional interpretations of unusual perceptual experiences (Krabbendam, Myin-Germeys, Hanssen & van Os, 2005). Archival estimates of childhood IQ have also been found to predict long-term clinical outcomes in individuals with schizophrenia-spectrum psychoses (Munro, Russell, Murray, Kerwin & Jones, 2002).

Cognitive reserve may predict broad clinical outcomes in FEP, but overlap between markers of cognitive reserve, premorbid psychosis-related problems, and markers of other developmental anomalies can make such relationships difficult to interpret (Barnett et al., 2006). However, cognitive reserve theory generates specific predictions concerning susceptibility to psychosis-related cognitive impairment. Those with low reserve should be more vulnerable to cognitive deficits following psychosis onset, while those with high reserve should show greater cognitive resiliency.

These predictions have received some support in recent research linking indicators of higher cognitive reserve to cognitive resiliency. Sparing of cognitive abilities was related to learning in animal models of psychosis (Naimark et al., 2008) and to level of education in cognitively normal patients with first-episode schizophrenia (Holthausen et al., 2002), Conversely, low cognitive reserve, suggested by obstetrical complications and low premorbid IQ, predicted post-

onset cognitive deterioration in patients with first-episode bipolar affective disorder (Martino et al., 2008). Contrary to what would be predicted in a cognitive reserve model, individuals with higher premorbid IQ showed greater psychosis-related declines in intellectual functions than those with lower premorbid IQ (van Winkel et al., 2006).

Early developmental markers of low cognitive reserve such as late milestone acquisition and attenuated academic achievement have not been investigated as specific risk factors for global cognitive deficits in FEP, despite their potential to account for individual differences in the severity of these deficits. If cognitive reserve theory predicts cognitive functioning in psychosis, a subgroup of individuals with FEP with low cognitive reserve should be especially vulnerable to the deleterious cognitive effects of psychosis. Those with normal reserve, in contrast, should have greater resilience against such impairments. In summary, individuals with low cognitive reserve, defined by late milestone acquisition and academic difficulties should have lower estimated premorbid intellectual abilities, attenuated educational attainment, and should also be more susceptible to cognitive impairment than individuals with normal cognitive reserve.

1.3.4   Hypothesis 1:

Relative to a pattern of normal cognitive reserve, low cognitive reserve, as defined by late milestones, premorbid academic problems, and reduced premorbid intellectual abilities and educational achievement will be associated with greater cognitive decline during the early course of illness (see Figure 1.1).
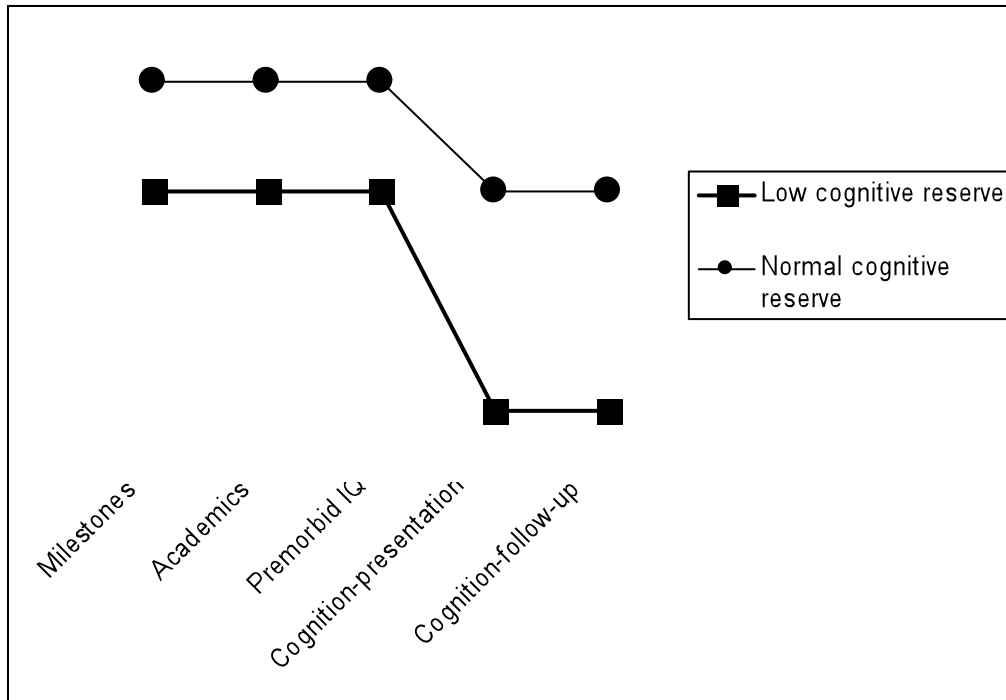
Figure 1.1   Schematic diagram of hypothesis 1.

1.4   PART 2 – Temperament

1.4.1   Markers for substance abuse risk: temperamental styles

Temperament refers to the characteristic ways of responding to the

external environment that underlie our ability to respond flexibly and adaptively in

times of stress (Bijttebier & Roeyers, 2009). Thomas and Chess (1977) initially

defined temperament as particular styles of behaviour that were observed to

persist from infancy to adulthood (see also Windle 1989a). Other models of

temperament assess behaviours putatively controlled by specific

neurotransmitter systems (Etter, Pelissolo, Pomerleau & De Sainte-Hilaire, 2003;

Mardaga & Hansenne, 2007), or generalize adult personality or temperament

measures to childhood or infancy (Lyoo et al., 2004). Temperamental styles as defined by Thomas and Chess (1977) were derived from observational studies of infant behaviour and as such have unique and well-established age continuity (Windle & Windle, 2006).

Research using Thomas and Chess's (1977) model of temperament (Windle & Lerner, 1986) characterizes an individual's behavioural style as a stable determinant of his or her ability to cope with stress during development (e.g. Blackson, Tarter & Mezzich, 1996; Dixon, Smith & Clements, 2006; Kagan, 1982; Lerner, Lerner & Zabski, 1985; Rothbart, 2004; Thomas, Chess & Korn, 1982). Ratings of an individual's behavioural style can be organized into higher-order dimensions of temperament (adaptability / positive affect, general rhythmicity, and attentional focus), with lower scores on each dimension reflecting more "difficult" or maladaptive temperamental styles (Revised Dimensions of Temperament Survey, DOTS-R; Windle & Lerner, 1986; see Appendices 4B and 4C; see also Windle, 1992; Windle 1989a; Windle 1989b).

Individuals with "difficult" temperamental styles tend to show less positive affect in daily situations (e.g. smiling or laughing), are less regular in their biological functions, and are less capable of sustained attention (Windle & Lerner, 1986; Windle, 1992). "Difficult" temperamental styles have long been associated with intense and negative reactions to neutral events, withdrawal from new situations, and difficulty adapting to change (Henderson & Wachs, 2007; Prior, 1992; Thomas & Chess, 1977). "Difficult" temperamental styles increase the risk for maladaptive reactions to environmental challenges and are

associated with the development of a wide range of psychopathology (Nigg, 2006; Poustka, Parzer, Brunner & Resch, 2007; Saudino, 2005; Wills, DuHamel & Vaccaro, 1995). Substance abuse is a potentially maladaptive way of coping with stress and is predicted by "difficult" temperamental styles in young people with (Ohannessian & Hesselbrock, 2008) or without familial histories of substance abuse problems (Giancola, 2004; Giancola & Mezzich, 2003; Stice, Kirz & Borbely, 2002; Tubman & Windle, 1994; Windle & Windle, 2006).

Some researchers use the terms temperament and personality interchangeably (e.g., Mufson, Nomura & Warner, 2002), although there is evidence that they are separate constructs and that temperament may foster personality development (Rothbart, 2007). Temperamental styles in the tradition of Thomas and Chess (1977) are considered especially potent predictors of substance use problems because they describe affective and behavioural repertoires with a strong biological basis that present consistently across situations (Hulbert, Jackson & McGorry, 1996; Loken, 2004). Personality theories often make claims about cognition and motivation in describing the spectrum of normal functioning and psychopathology (e.g., Copeland, Landry, Stanger & Hudziak, 2004; Guillem, Bicu, Semkovska & Debruille, 2002; Maher & Maher, 1994; Nigg, 2006). Hence temperamental styles may present more consistently across situations that some personality traits. Phenomenological similarities between personality traits and psychiatric symptoms can also make predictive relationships between personality and psychopathology difficult to assess (e.g., Horan, Subotnik, Reise, Ventura & Nuechterlein, 2005). The distinction between

temperament and personality may be relatively insignificant if the aim is simply to describe an individual's general disposition. However, statements about a style of behaviour that is presumed to be consistent across the lifespan and comparable between individuals require descriptors that can be used reliably for infants, young children, and adults (Windle, 1992; Windle, 1989a; Windle, Iwawaki & Lerner, 1988). Temperamental styles are therefore particularly useful early indicators of risk for substance abuse because of their age stability.

1.4.2   Substance abuse in first-episode psychosis

Patients with FEP are more likely to use substances than individuals in the general population (Larsen et al., 2006). Concomitant substance abuse frequently interferes with the effective treatment of psychotic symptoms and is considered a significant clinical problem in FEP (Malla et al., 2008; van Mastrigt, Addington & Addington, 2004). The relationship between psychotic symptoms and substance use is complex. Substance use predates psychotic symptoms in some individuals (Wade et al., 2006) but cannot be isolated as a cause of psychosis (e.g. Degenhardt, Hall & Lynskey, 2003). A number of longitudinal studies report that heavy cannabis use substantially increases the risk for subsequent onset of psychosis (Ferdinand et al., 2005; Henquet et al., 2005, van Os et al., 2002). Some researchers suggest that substance use, particularly cannabis, may lower the threshold for conversion to psychosis in some individuals (e.g., Corcoran et al., 2008). Interestingly, psychotic symptoms also increase the risk for cannabis use in those who previously abstained, raising the

possibility that some individuals with FEP use substances to manage their symptoms (Henquet et al., 2005).

It is unclear whether substance abuse precedes or follows the onset of psychosis (Dervaux et al., 2001; Goswami, Mattoo, Basu & Singh, 2004; see Gregg, Barrowclough & Haddock, 2007 for a review; Khantzian, 1997; Schaub, Fanghaenel, & Stohler, 2008; Scheller-Gilkey, Moynes, Cooper, Kant & Miller, 2004; Talamo et al., 2006). Uncertainty as to whether psychotic symptoms cause or are caused by substance abuse, or whether both disorders arise from the same common factor (Compton, Whicker & Hochman, 2007; Weiser & Noy, 2005) make it difficult to elucidate the pathways into substance abuse in FEP. Premorbid identification of individuals at risk for substance abuse would benefit both our understanding of the precipitating factors for substance abuse and our treatment of the problem (Gregg et al., 2007).

Premorbid attributes may increase the risk for substance abuse in psychosis. Some correlates of lifetime history of substance abuse such as male gender and younger age of psychosis onset are consistently noted in the FEP literature (Addington & Addington, 2007; Gonzalez-Pinto et al., 2008; Thorup et al., 2007). Substance abuse in chronically ill psychotic patients is associated with sensation seeking traits, or the need for new and varied sources of stimulation (Bizzarri et al., 2009; Kim, Kim, Park, Lee & Chung, 2007), as well as the tendency to exaggerate the rewarding properties of substances (Krystal et al., 2006). No research has extended this work to assess developmental predictors of substance abuse in FEP. Temperament, as a known risk factor for substance

abuse, could explain why some individuals grapple with substance abuse early in

FEP.

1.4.3   Temperament and premorbid substance abuse in FEP

Temperament has yet to be evaluated as a risk factor for substance abuse

in FEP. Most research has explored stable, internal personality characteristics

such as novelty seeking and inhibition only as risk factors for psychotic

symptoms in normal adolescents (Cloninger, Przybeck & Svrakic, 1993;

Cloninger, 1986; Daneluzzo, Stratta & Rossi, 2005) and clinical samples with

mixed results (Guillem, Pampoulova, Rinaldi & Stip, 2008; Poustka et al., 2007).

"Difficult" temperamental styles may or may not increase the risk for psychosis.

However, there are clear and well-established relationships between "difficult"

temperamental styles and substance abuse that merit further exploration

(Giancola & Mezzich, 2003; Ohannessian & Hesselbrock, 2008).

Researchers have yet to investigate the possibility that risk factors evident

in normal development, such as temperament, may explain why some individuals

with FEP have substance abuse problems while others do not. If temperament

plays a stable and important role in determining the likelihood of substance

abuse for individuals with FEP, it will have implications for early detection and

prevention of substance abuse in this population.

1.4.4   Hypothesis 2:
More "difficult" temperamental styles as measured by lower scores on

premorbid temperamental dimensions of adaptability, general rhythmicity, and

attentional focus will increase the risk for substance abuse early in the course of FEP.

1.5   PART 3 – Attachment

1.5.1   Markers for social isolation: Attachment networks

Social difficulties are not unique to psychosis, but are often present premorbidly in those who develop psychosis (Tarbox & Pogue-Geile, 2008). Social withdrawal can occur during the prodrome, when other clinical features such as negative symptoms may also appear (Iyer et al., 2008). Psychotic symptoms typically emerge during adolescence or young adulthood, when individuals are shifting towards greater reliance on peers than parents for emotional support (Thorup et al., 2006). Developing psychotic illnesses can profoundly alter the ability to relate to others and to use relationships as a source of support during periods of stress (Bentall & Fernyhough, 2008; Berry, Barrowclough & Wearden, 2007; Jeppesen et al., 2008; see Crespi & Badcock, 2008 for a review of social development).

Attachment historically referred to the nature and quality of the bond between an infant or child and parents, particularly under conditions of stress (e.g., Bowlby, 1979). Others have described adolescent and adult relationships in terms of attachment bonds (Hazan & Zeifman, 1994). According to Trinke and Bartholomew (1997), the following critical components define a person as an attachment figure: being able to count on the person for understanding, for love, the presence of a strong emotional connection with the person (whether positive, negative, or ambivalent), wanting to spend time with the person, and mourning

the hypothetical loss of the person. These internalized dimensions of important

relationships, with a foundation in infancy and childhood experiences (Collins &

Read, 1990; Meyer & Pilkonis, 2001), are best conceptualized as buffering the

effects of stress or psychopathology (Cozzarelli, Karafa, Collins & Tagler, 2003;

Cicchetti, Toth & Lynch, 1995; Dieperink, Leskela, Thuras & Engdahl, 2001; Eng,

Heimberg, Hart, Schneider & Liebowitz, 2001; Hoermann, Clarkin, Hull &

Fertuck, 2004).

Some theorists suggest that children and adults maintain true attachment

bonds with only one figure (parent and romantic partner, respectively; Hazan &

Zeifman, 1994). However, others describe networks containing multiple

attachments as better satisfying a person's emotional needs in different

situations, and as being more realistic than considering attachments in terms of a

single relationship (Bretherton, 1985; Oppenheim, Sagi & Lamb, 1988; Trinke &

Bartholomew, 1997). Trinke and Bartholomew (1997) found that young adults

tended to rely primarily on romantic partners to meet attachment needs, followed

by mothers, fathers, best friends, and siblings. This is consistent with other

research findings suggesting that the transition to adulthood results in a

normative shift towards increasing reliance on peer relationships to fulfil

attachment needs (Benson, McWey & Ross, 2006; Doherty & Feeney, 2004;

Friedlmeier & Granqvist, 2006).

1.5.2 Developmental shifts in attachments

Early attachments to caregivers provide emotional security to infants and

children, whereas peer attachments in adolescence tend to be more egalitarian

and reciprocal in nature (Giordano, 2003). This reciprocity is considered critical to the development of emotion-regulation abilities (Campa, Hazan & Wolfe, 2009; Fraley & Davis, 1997), which in turn foster pro-social behaviour (Dykas, Ziv & Cassidy, 2008; Feeney, Cassidy & Ramos-Marcuse, 2008; Laible, 2007). Adolescents rely more heavily on romantic attachments as they grow older (Adams, Laursen & Wilder, 2001; Meeus, Branje, van der Valk & de Wied, 2007; Nieder & Seiffge-Krenke, 2001) although parents can still retain their importance as attachment figures (Freeman & Brown, 2001; Markiewicz, Lawford, Doyle & Haggart, 2006). Increasing emotional reliance on peers facilitates the developmental shift towards greater insight into relationships and into internal emotional states (Allen, Moore, Kuperminc & Bell, 1998).

Normative changes in attachments thus correspond to developmental shifts in emotional maturity. As such, attachment bonds tend to be more stable over shorter time spans (test-retest correlation coefficient = 0.27 for an 18 year span as compared with 0.67 for a 5 year period; Fraley, 2002). The importance of attachment figures relative to each other may change over time, although it is possible to lose attachment relationships (Cozarelli et al., 2003). Attachment bonds can also change substantially in response to major life events, especially when those events are stressful (Allen, McElhaney, Kuperminc & Jodl, 2004; Charuvastra & Cloitre, 2008).

Stress can challenge attachment bonds, increase conflict with attachment figures, and reduce the emotional comfort and safety that can be derived from those relationships (Conger, Ge, Elder, Lorenz & Simons, 1994; Daley &

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Hammen, 2002). High levels of stress in adolescence and young adulthood can strain attachment networks and thus undermine the foundations for developing emotional maturity (Allen et al., 2004). As conversion to FEP is a major stressor it would be expected to correspond to significant shifts in attachments. Research has yet to evaluate shifts in attachments during the first episode of psychosis, and whether certain features of psychosis such as negative symptoms affect the course of changes in attachment.

1.5.3 Attachments in psychosis

There have been concerns that fluctuating symptoms of mental illnesses may reduce the reliability of self-reported attachments (Berry et al., 2007b). However, the temporal stability in self-ratings of attachment in those with psychosis tends to be similar to that reported in samples without mental disorders (Favaretto, Torresani & Zimmerman, 2001; Willinger, Heiden, Meszaros, Formann & Aschauer, 2002). Some clinical aspects of FEP are especially likely to affect interpersonal relationships. For instance, more severe negative symptoms early in psychosis are associated with reduced daily contact with friends (Thorup et al., 2006). This does not reflect attachment bonds per se, but the findings suggest that negative symptoms such as amotivation and passive social avoidance interfere with the daily activities that are used to maintain friendships (Hansen, Torgalsboen, Melle & Bell, 2009). The relative intractability of negative symptoms is considered a risk factor for ongoing social difficulties in FEP (Barnes et al., 2008).

People with psychosis tend to categorize their attachments as disproportionately insecure relative to controls and they often feel they cannot count on attachment figures to fulfil their emotional needs (Berry, Wearden & Barrowclough, 2007; Berry et al., 2007b; Couture, Lecomte & Leclerc, 2007). They also tend to have negative perceptions of parental attachments independent of the severity of their psychotic symptoms (Rankin, Bentall, Hill & Kinderman, 2005). High levels of parental criticism (e.g., negative or derogatory feedback in response to a child's behaviour), emotional enmeshment, and poor communication are often evident in families that include a child with FEP (Kuipers et al., 2006; McFarlane & Cook, 2007; Patterson, Birchwood & Cochrane, 2005; Tienari et al., 2004). These features of family relationships can increase the likelihood that a child with FEP will have poor clinical outcomes (Pourmand, Kavanagh & Vaughan, 2005).

Premorbid social difficulties are often evident in FEP (Tarbox & Pogue-Geile, 2008) and there is increasing evidence that the onset of psychotic symptoms affects close relationships. Some research suggests that longer duration of untreated psychosis (DUP) increases the risk for more severe psychiatric symptoms and for social withdrawal after onset (Iyer et al., 2008). Greater family involvement in seeking treatment was related to shorter DUP in some studies, suggesting that those with stronger family relationships are most likely to access treatment in a timely manner (Morgan et al., 2006). Others note that families with strong relationships often assume considerable responsibility for managing early psychotic symptoms, resulting in longer periods of untreated

illness (Compton, Chien, Leiner, Goulding & Weiss, 2008). Family members appear to be heavily involved in the treatment process, either managing the difficulties themselves or encouraging individuals with FEP to seek treatment. It is not clear whether peer attachments are lost, de-emphasized, or can be an additional source of emotional support early in psychosis.

The development of FEP is presumed to lead to increased emotional dependence on family members (Addington, Coldham, Jones, Ko & Addington, 2003), particularly in severe cases of illness. These assumptions have not been directly assessed using attachment measures. Researchers have not evaluated whether individuals become more dependent on family members in the early phase of FEP, and whether this is intensified by a longer duration of illness. Studies also have yet to evaluate whether romantic relationships reduce reliance on family attachments, as is the case in typically developing adolescents and young adults (Doherty & Feeney, 2004; Trinke & Bartholomew, 1997). Negative symptoms reduce the frequency of contact with friends though no studies have evaluated whether negative symptoms compromise the ability to use such peer relationships to meet fundamental attachment needs early in psychosis.

There are three outstanding questions with respect to attachment networks in psychosis. First, it is unclear whether attachment networks become restricted to family relationships during conversion to psychosis. Second, it is unclear whether duration of illness intensifies emotional reliance on family members after psychosis onset, and whether the availability of other attachment figures such as a romantic partner might mitigate the dependence on family

members. Third, it is unknown whether the severity of negative symptoms affects the ability to form peer attachments early in the course of psychosis, as opposed to simply reducing the frequency of contact in existing friendships.

1.5.4   Hypothesis 3A:

Relative to premorbid attachment networks, individuals with FEP will report increased dependence on family members to fulfil attachment needs in the post-onset period. A longer duration of illness will predict greater emotional dependence on family members and having a romantic relationship post-onset will reduce dependence on family members.

1.5.5   Hypothesis 3B:

The severity of negative symptoms, but not psychotic symptoms, will be associated with difficulties forming new peer attachments early in psychosis. As a group, individuals who fail to form new peer attachments would be likely to have more severe negative symptoms than individuals who form new peer attachments.

CHAPTER 2: METHODS

2.1 Participant recruitment

Participants for the current study were recruited from a large catchment area sample of adolescents and young adults enrolled in the "Early Psychosis Identification and Intervention" (EPII) Program. EPII operated from 2000-2006 within the Fraser Health Authority. All adolescents and young adults suspected of having symptoms of a first episode of psychosis (N = 439) were referred to the EPI Program by family physicians and / or treating psychiatrists. The EPII Program provided specialized clinical assessment and treatment from psychiatrists, psychologists, psychiatric nurses, and ancillary therapists.

One hundred and thirty-one EPII Program participants were recruited into a large, multi-year (2001-2006) research project entitled "Interactions of development, early life experience, and genetic predisposition to schizophrenia" (hereafter the "Interactions" study; see Appendix 1 for a list of Principle and Co-Investigators). Participants in the "Interactions" study underwent intensive examination in a number of domains at enrolment in the study, after 6 months of treatment, and at 9-12 months after enrolment (see Appendix 1 for a brief description). A subset of 54 participants from the "Interactions" study was recruited into the current study from 2005 to 2008.

The methods of the current study were approved by the Research Ethics Boards of Simon Fraser University and the Fraser Health Authority. Both ethics

bodies follow the Tri-Council Policy Statement concerning ethical research with human subjects. Questionnaires administered in the current study were carefully selected to minimize invasiveness. To safeguard confidentiality, data were purged of identifying information. Paper versions of questionnaires were retained in a locked filing cabinet and electronic spreadsheets were maintained on a password-protected system. Participants understood that their eligibility for clinical treatment was not contingent upon completing the current study.

Of the 131 individuals who enrolled in the "Interactions" study, 27 withdrew before they could be contacted, and 25 could not be found through their original contact information or comprehensive searches of provincial and national telephone directories (see Figure 2.1). The purpose and methodology of the current study was explained over the telephone to the 79 "Interactions" participants who could be contacted. If prospective participants were interested, questionnaires were either sent to them by courier or given when they attended a clinical appointment at the EPII Program. The median time between enrolment in the "Interactions" study and recruitment for the present study was 28 months, with lag times ranging from 2 months to 50 months.
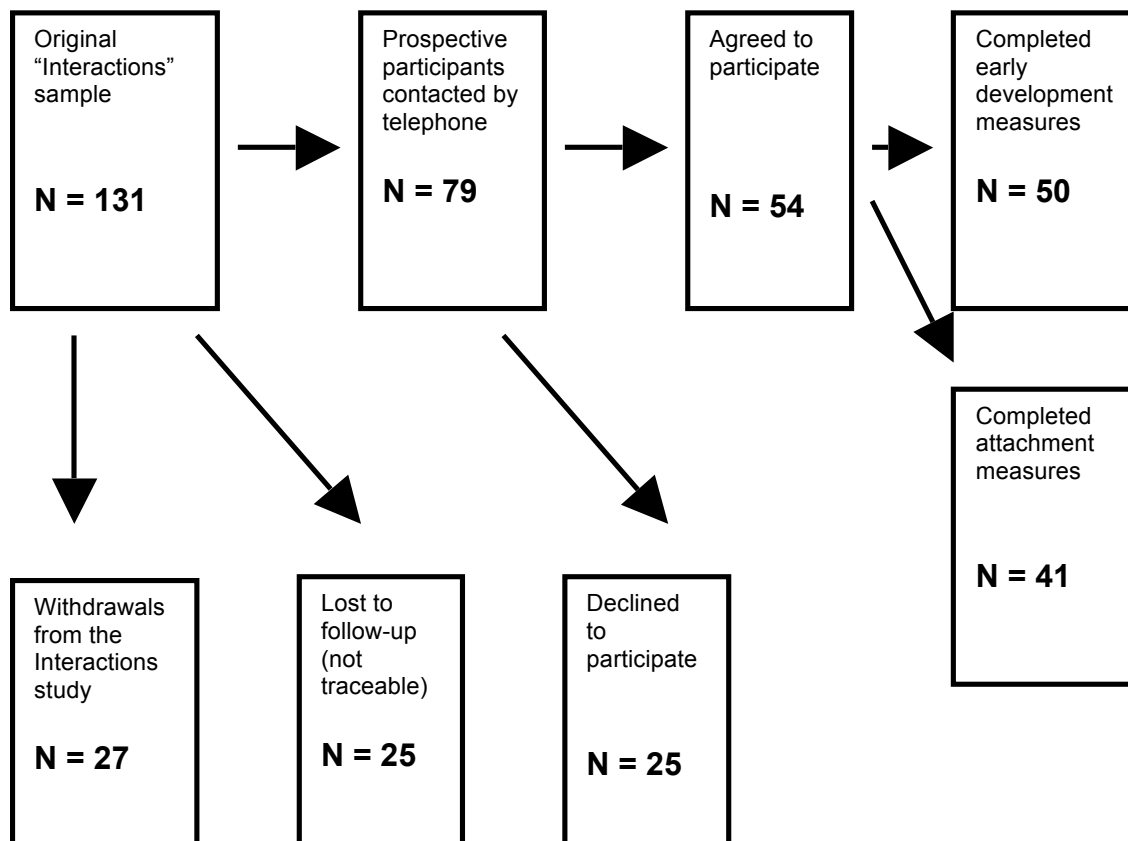
Figure 2.1   Participant recruitment from the "Interactions" study.

Of the 79 patients who could be contacted, 25 declined participation and 54 agreed to complete the current study (see Table 1; Appendix 2 contains demographic information of individuals who withdrew, were lost to follow-up, or declined to participate in the current study). Fifty of 54 participants provided fully informed consent for their parents to report on their early development. Three participants were estranged from their families and one's age (over 50 years) precluded collection of developmental data. Forty-one of 54 participants completed self-report attachment measures (see Figure 2).

Table 1   Demographic and diagnostic characteristics of the current sample (N = 54).

Variables	Mean (SD)	Range	% of sample (N)
Age	25.34 (7.62)	15.30 – 51.30	
Years of education	11.91 (1.80)	7.00 – 17.00	
Gender (% male)			68.52 % (37)
Diagnosis:			
Schizophrenia			42.59 % (23)
Schizoaffective			14.82 % (8)
Bipolar Affective Disorder			16.67 % (9)
PNOS			16.67 % (9)
MDE with psychosis			1.85 % (1)
PANSS Positive Scale Score[a]	16.85 (6.36)	7.00 – 39.00	
PANSS Negative Scale Score [a]	17.21 (5.61)	8.00 – 32.00	
PANSS General Scale Score[a]	37.48 (8.61)	22.00 – 55.00	
PANSS Total Score [a]	71.54 (17.11)	47.00 – 126.00	

Notes: PNOS = Psychosis not otherwise specified; MDE = Major Depressive Episode; PANSS = Positive and Negative Syndrome Scale at "Interactions" enrolment. [a] Available for 52/54 participants

2.2   Measures

Participants and their parents provided fully informed consent for information collected during the "Interactions" study to be used in the current study. Data from the enrolment assessment evaluated functioning at presentation, and data from the 9-12 month assessment reflected functioning at follow-up. Upon recruitment into the current study, participants reported on premorbid and post-onset attachments while their parents rated early developmental milestones and premorbid temperament.

2.3 Assessment of psychopathology:

All participants were assessed by trained raters using the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein & Opler, 1987; Kay, Opler & Lindenmayer, 1989). The PANSS is a 30-item scale (see Appendix 3A) evaluating Positive symptoms (7 items), Negative symptoms (7 items), as well as General psychopathology such as anxiety, depression, and disinhibition (16 items). Symptom severity is scored for each item (0 = absent, 1 = minimal, 2 = mild, 3 = moderate, 4 = moderately severe, 5 = severe, 6 = extreme) and then aggregated into Positive, Negative, and General Scale scores. The test authors (Kay, Opler & Lindenmayer, 1988) reported adequate to good inter-rater reliability (r = 0.83-0.87). Kay et al. (1988) also reported convergent validity (r = 0.52 - 0.77) with the Scale for the Assessment of Positive Symptoms (SAPS), the Scale for the Assessment of Negative Symptoms (Andreasen, 1982), and the Clinical Global Impressions Scale (CGI; Guy, 1976; see also Mortimer, 2007). PANSS ratings from the enrolment assessment were included in the current study as an estimate of the severity of psychopathology at presentation, and ratings from the 9-12 month assessment evaluated the severity of symptoms at follow-up.

Diagnostic information was collected from participants using structured clinical interviews (i.e., SCID) and corroborating information was collected from one or more family members. Consensus diagnoses were established using criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychological Association, 2000). Individuals describing a six-month

period of continuous social or occupational deterioration with active psychotic symptoms for at least one month were diagnosed with schizophrenia. Those who endorsed concurrent major depressive, manic, or mixed episodes and psychotic symptoms received diagnoses of schizoaffective disorder. Participants describing predominant affective instability (manic, mixed, or depressive episodes) and brief episodes of psychosis were diagnosed with Bipolar Disorder with Psychotic Features or Major Depressive Episode with Psychotic Features. Those reporting psychotic symptoms that did not meet any of the above criteria and could not be accounted for by substance abuse were diagnosed with Psychosis Not Otherwise Specified (PNOS).

A structured questionnaire was administered to each participant and at least one parent at enrolment into the "Interactions" study to estimate the duration of untreated psychosis (DUP; see Appendix 3B). Duration of untreated psychosis was calculated as the time, in weeks, from age at first psychotic symptoms to age at enrolment in the "Interactions" study. Medical charts were reviewed for each participant to check that records corroborated parent and participant reports as to when psychotic symptoms first presented.

2.4   Markers of atypical CNS development: milestone acquisition and academic achievement

2.4.1   Milestone acquisition

Mothers (or both parents if fathers were available) completed a retrospective scale of developmental milestone acquisition upon recruitment into

the current study (see Appendix 3A; taken from Cowen, Work, Wyman & Jarrell, 1994; see also Famularo & Fenton, 1994; Gunther, Slavenburg, Feron & van Os, 2003; Rapee & Szollos, 2002; Reich, Todd, Joyner, Neuman & Heath, 2003). The scale allows parents to categorize their child's relative pace (1 = much sooner, 2 = somewhat sooner, 3 = same time, 4 = somewhat later, 5 = much later) of acquisition of 12 specific milestones compared with other children. The test authors did not evaluate test-retest reliability, but reported good internal consistency (Cronbach's α = 0.83) as well as predictive validity for subsequent academic achievement (Cowen et al., 1994; Wyman et al., 1999). Participants whose parents reported late acquisition (score of 4 or 5) of at least three of twelve milestones (including at least one major milestone: crawling, walking, and saying single words or sentences) received a score of "1" indicating delays in early milestone development (see Isohanni et al., 2001 for categorical treatment of developmental milestones). Participants whose parents reported late acquisition of two or fewer milestones, on-time milestones, or early acquisition of milestones received a score of "0" indicating no significant delays in development.

2.4.2 Academic achievement

Parents completed the Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982) at enrolment into the "Interactions" study. The PAS is a widely used semi-structured interview evaluating a child's level of functioning up to 6 months prior to the onset of psychosis (e.g., Addington et al., 2003b; Larsen et al., 2004; Rabinowitz et al., 2002). The PAS has good to excellent internal consistency

(Cronbach's α = 0.81 – 0.93), good inter-rater reliability (*ICC* = 0.79; Rabinowitz, Levine, Brill & Bromet, 2007), and predictive validity for ongoing adjustment problems following conversion to psychosis (Krauss, Marwinski, Held, Rietschel & Freyberger, 1998; van Mastrigt & Addington, 2002). Parent ratings of scholastic performance in the 6-11 and 12-15 year-old age ranges (see Appendix 4B) were used to assess academic achievement during childhood and early adolescence, respectively.

A rating of "0" corresponded to an excellent (i.e. straight A) student, "1" denoted a good student (A and B grades), "2" referred to a solid B student, "3" indicated an average (i.e. B and C grades) student, "4" denoted a fair student (C grades), "5" corresponded to a student who failed some classes, and "6" indicated a student who failed all classes. Children who achieved A grades in special education or learning disabled classes received a rating of "4". These seven-point PAS ratings were dichotomized to reflect whether each participant had achievement problems in childhood or early adolescence. Participants whose parents reported C grades (score of "4") or lower in the 6-11 or 12-15 year-old ranges received scores of "1" for achievement problems in childhood or early adolescence, respectively. Participants whose parents described B and C grades (score of "3") or higher received scores of "0" indicating no achievement problems in the 6-11 or 12-15 year-old ranges.

2.4.3 Developmental markers of low cognitive reserve

Participants were separated into two cognitive reserve groups according to their patterns of premorbid functioning. Participants with a score of "1" for late

developmental milestones and scores of "1" for academic problems in *both* 6-11

and 12-15 year-old age ranges were given a low cognitive reserve score of "1"

(for other examples see Desmarais, Sylvestre, Meyer, Bairati & Rouleau, 2008;

Larsen et al., 2004). A rating of "1" indicated the presence of markers of atypical

CNS development starting in the first year of life and persisting through childhood

and early adolescence, or low cognitive reserve (see Appendices 3A and 3B for

case by case details of milestone acquisition and academic achievement scores).

A rating of "0" indicated no markers of atypical CNS maturation or inconsistent

evidence of atypical maturation (late milestones but no academic problems, or

academic problems but no milestone delays). Scores of "0" denoted normal

cognitive reserve. Further review of clinical data showed that none of the

participants had experienced any neurological events such as head injuries or

seizures that could explain late milestones or academic problems.

2.4.4   Cognitive functioning at Presentation and Follow-up:

Upon enrolment in the "Interactions" study, all participants completed a

series of standardized tests of cognition that, with the exception of tests of

premorbid and current intellectual abilities, were repeated after a 9-12 month

delay. Standard scores reflecting an individual's performance on each test were

calculated to correct for the influence of demographic variables such as age,

gender, and education (see below for details; see also Strauss, Sherman &

Spreen, 2006). Tests were selected for having good to excellent reliability, for

their validity as tests of neuropsychological domains of ability (see Strauss et al.,

2006 for comprehensive validity information), and with the exception of tests of

intellectual ability, as endophenotypes of FEP (e.g., Eastvold, Heaton & Cadenhead, 2007; Green et al., 2004; Larson et al., 2004; Mesholam-Gately et al., 2009).

2.4.5 Premorbid abilities

Participants completed the North American Adult Reading Test (NAART, Blair & Spreen, 1989; see also Uttl, 2002), a test of word reading that is relatively invulnerable to deterioration. The NAART has been used to estimate premorbid ability in first-episode psychosis (e.g., Leeson et al., 2009). Estimates of internal consistency and test-retest reliability are excellent (above 0.90, and 0.98, respectively), and NAART scores tend to predict high proportions of variance in current intellectual functions (Strauss et al., 2006). Participants' age and education-corrected standardized scores (with a mean of 100 and standard deviation of 15) were used to gauge premorbid level of intellectual functioning. Each participant's standard score was converted to a z-score to reflect the deviation from the mean of the standardization sample of each individual's performance.

2.4.6 Intellectual functioning at Presentation

The Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990) was administered to assess verbal and nonverbal reasoning skills. Tests of confrontation naming and vocabulary assessed verbal abilities, while nonverbal abilities were evaluated using a matrices task. The K-BIT has excellent internal consistency and test-retest reliability (both above 0.90; Strauss et al., 2006). The

K-BIT has established concurrent validity as a measure of intellectual functions, showing strong correlations (r = 0.73 - 0.89) with the Wechsler Adult Intelligence Scale and the Wechsler Abbreviated Scale of Intelligence (see Canivez, Neitzel & Martin, 2005 for a review; Hays, Reas & Shaw, 2002; Strauss et al., 2006). Composite IQ scores (with a mean of 100 and standard deviation of 15) correcting for age were used to describe participants' intellectual abilities at the time of enrolment into the "Interactions" study.

2.4.7   Attention and working memory

The Digit Span and Letter-Number Sequencing subtests from the Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III; Wechsler, 1997) were administered as measures of auditory attention and working memory, respectively. Digit span required participants to repeat the number sequences in forward and reverse order. Letter-number sequencing relied on the ability to mentally rearrange auditory sequences of numbers and letters so they could recite the numbers, in order, and then the letters in alphabetical order. The digit span subtest has excellent internal consistency (above 0.90) and high test-retest reliability (above 0.80), while letter-number sequencing has high internal consistency (above 0.80) and adequate test-retest reliability (above 0.70; Strauss et al., 2006). Age, gender, and education-corrected T-scores (with a mean of 50 and a standard deviation of 10) were calculated using data from the standardization sample included in the test manual, and then converted to z-scores using the same mean and standard deviation. For both digit span and

letter-number sequencing, lower z-scores correspond to worse auditory attention and working memory skills.

2.4.8   Processing speed

Participants completed the Digit Symbol Coding subtest from the WAIS-III, which provides an index of psychomotor processing speed. Using a key of 8 digit and symbol pairs, individuals were presented with a long, randomized series of the 8 digits and were asked to write the corresponding symbol in a blank space under each digit. The digit-symbol subtest has high (above 0.80) test-retest reliability (Strauss et al., 2006). Lower z-scores, calculated from age, gender, and education-corrected T-scores using the method described above, indicate worse (i.e. slower) performance.

2.4.9   Memory

The California Verbal Learning Test, 2nd Edition (CVLT – II; Delis, Kramer, Kaplan & Ober, 2000) was used to assess immediate and delayed memory. The CVLT comprises a 16-item word list presented for five learning trials. After each presentation, participants were asked to recall as many items as they could, in any order. Following the final learning trial, an interference list of 16 new words was presented for one learning trial. Immediately following participants' recall of the interference list, they were asked to recall the initial list. After this recall trial, participants completed a cued recall trial where they were given superordinate category labels to facilitate recall. Following a delay of 20 minutes, there were again given free and cued recall trials followed by a recognition memory test. The

total number of words recalled across all five learning trials (converted to an age, education, and gender corrected T-score, with a mean of 50 and standard deviation of 10) was selected as the most reliable measure of verbal learning and memory (test-retest coefficient above 0.80; Strauss et al.) and converted to a z-score. Lower z-scores, or number of words learned and recalled, indicate worse verbal learning and memory.

2.4.10 Global estimates of cognition

Participants' z-scores on the WAIS-III digit span, letter-number sequencing, and digit symbol tasks, as well as the CVLT were summed and then divided by the number of tests to yield an estimate of global cognitive functioning at presentation (e.g. Arvanitikas, Wilson, Li, Aggarwal & Bennett, 2006; see also Strauss et al., 2006). Cognitive data from the 9-12 month assessment session were calculated relative to baseline age to accurately reflect changes in cognition. Enrolment and 9-12 month assessment scores reflect the overall severity of cognitive deficits, in terms of average deviations from standardization samples, at presentation and follow-up. A difference score between presentation and follow-up cognition was calculated to evaluate the change (deterioration, stability, or recovery) in cognition during the early course of psychosis.

2.5 Substance abuse at presentation

Participants were asked about their history of alcohol and drug use using a structured interview (Appendix 5) upon enrolment in the "Interactions" study. Participants described their use of alcohol, tobacco, cannabis or other drugs prior

to presentation. Participants were also screened for substance abuse using the DSM-IV diagnostic criteria if they reported use of any substances at presentation (American Psychiatric Association, 2000; see also Appendix 5). Participants who reported substance use for at least one month before presentation and whose pattern of use also met diagnostic criteria for substance abuse were given a score of "1". Participants who described abstaining from substances or who used substances but did not meet the diagnostic criteria for substance abuse were given a score of "0". A score of "1" therefore denotes substance abuse at presentation.

2.6   Premorbid temperament

Parents completed the Revised Dimensions of Temperament Survey upon recruitment into the current study (DOTS-R, Appendix 6A; Windle 1992, Windle 1989, Windle & Lerner, 1986; see also Appendices 6B & 6C). This questionnaire was used to assess typical behavioural style up until three to four years before receiving a psychiatric diagnosis (see Ong, Wickramaratne, Tang & Weissman, 2006 for a similar methodology). Parents rated 54 temperament descriptors on a Likert-type scale (A = false, B = somewhat false, C = somewhat true, D = very true). Test developers report high internal stability (above 0.80; Windle & Lerner, 1986) and subsequent studies have reported adequate test-retest reliability (0.70-0.80) and good predictive validity for psychosocial adjustment problems (Windle & Windle, 2006). Responses were aggregated into three summary scores for the distinct temperamental dimensions of adaptability/positive affect, general rhythmicity, and attentional focus. Adaptability / positive affect indexed

their child's tendency to move towards new situations or people, ability to adapt to changes in the environment, and expression of positive affect. General rhythmicity assessed the regularity of sleep, eating, and bodily functions. Attentional focus assessed their child's ability to persist with activities and to resist distractions and external stimuli. Lower scores on each dimension are generally considered to reflect temperamental styles that confer greater risk for substance abuse.

2.7   Attachment Networks

Participants completed the Attachment Networks Questionnaire upon recruitment into the current study (ANQ; Trinke & Bartholomew, 1997, see Appendix 7) to describe their relationships before and after psychosis onset. The ANQ evaluates the number and quality of attachment bonds maintained by young adults. Internal consistency estimates calculated by type of attachment ranged from moderate (0.70 for best friends) to high (0.90 for romantic partners; Trinke & Bartholomew, 1997). Test-retest reliability was high (0.82) for total number of attachments over a 1 month follow-up period (Trinke & Bartholomew, 1997). In the current study, participants were asked to report on attachment networks for the period up to 3 or 4 years prior to receiving a diagnosis and then for the period since receiving a psychiatric diagnosis (see Appendix 7 for precise instructions; see also Irons, Gilbert, Baldwin, Baccus & Palmer, 2006; Kelley et al., 2005; McLaren, Kuh, Hardy & Mishra, 2007 for similar approaches to retrospective recall of relationships).

The rank order of attachment figures who satisfied emotional needs was used to describe the strength of family attachments and the size of the attachment network. Strength of family attachments was measured using the proportion of attachment roles filled by family members. The size of attachment networks was quantified by the number of attachment figures that participants reported using to meet their attachment needs. Strength of family attachments and network size were calculated for both premorbid and post-onset periods. Increased strength of family attachments and decreased network size from premorbid to post-onset periods would indicate restriction of attachment to family members after onset.

Duration of illness was calculated by adding months of untreated psychosis to months since enrolment in the "Interactions" study and participants were categorized according to whether they had romantic attachments post-onset to evaluate the effects of untreated illness and intimate relationships on attachment networks. Participant reports of new peer attachments in the post onset period were also included to assess whether negative symptoms adversely affect the formation of such attachments.

CHAPTER 3: RESULTS

3.1   General approach to statistical analyses

Data were checked systematically to ensure they met the distributional

assumptions for statistical techniques (e.g., Erceg-Hurn & Mirosevich, 2008).

Each variable was screened for outliers. Outlying values were evident in duration

of untreated psychosis (DUP; N = 4), cognitive tests (N = 2), and temperament

ratings (N = 2). None of the outliers resulted from entry or scoring errors. Outlying

cognitive data resulted from poor language proficiency and severe symptoms at

testing, while temperament outliers reflected invalid responses to items.

Cognitive and temperament outliers were eliminated from the analyses as noted

in the sections below.

The statistical analyses of the current study will be presented in three

discrete sections. First, I will evaluate the hypotheses that individuals with late

milestones and academic problems, or low cognitive reserve, will experience

sharper cognitive decline through the early phase of the illness than individuals

without such a history. Second, I will assess whether lower scores on premorbid

temperamental dimensions of adaptability, general rhythmicity, and attentional

focus increase the risk for substance abuse at presentation. Finally, I will explore

whether individuals with psychosis rely more heavily on family members to meet

attachment needs following illness onset, and whether negative symptoms

interfere with the ability to form new peer attachments post-onset.

3.2 Participant characteristics for each analysis

As outlined in the Methods section, retrospective measures of premorbid CNS development and temperament were available for 50 participants and attachment measures were completed by 41 participants. Thirty-seven individuals had both premorbid development and attachment measures, 13 had only premorbid development measures, and 4 had only attachment measures (see Table 2). Complete demographic and diagnostic information was available for all participants. Five individuals lacked estimates of duration of untreated psychosis (DUP), four lacked estimates of age at psychosis onset, and two were missing symptom ratings at presentation. The four individuals who completed only attachment measures were significantly older than other participants (F (2, 51) = 6.42, p < .05). There were no other differences in demographics or psychosis features according to availability of measures.

Table 2   Availability of measures collected in the current study.

Variable	Premorbid development only Mean (SD)	Both Mean (SD)	Attachment only Mean (SD)
Demographics:	N = 13	N = 37	N = 4
Age	25.92 (6.35)	23.96 (5.98)	36.37 (12.39)*
Years of education	12.31 (1.44)	11.73 (1.91)	12.50 (2.38)
Gender (% male)	69.23% (N=9)	70.27% (N=26)	50.00% (N=2)
Psychosis features:			
Median duration untreated psychosis (DUP in weeks) [a]	23.50 (106.18) N = 10	35.00 (134.70) N = 35	102.50 (483.21) N = 4
Age at psychosis onset	22.62 (7.83) N = 11	18.81 (5.44) N = 35	16.60 (4.04) N = 3
PANSS Positive Scale Score	18.07 (7.34) N = 13	18.71 (5.48) N = 35	21.00 (7.19) N = 4
PANSS Negative Scale Score	19.15 (7.94) N = 13	18.09 (6.60) N = 35	16.75 (6.85) N = 4
PANSS General Scale Score	37.08 (10.46) N = 13	38.11 (7.72) N = 35	40.50 (13.03) N = 4
PANSS Total Scale Score	76.39 (22.92) N = 13	77.43 (16.87) N = 35	78.25 (23.96) N = 4
Proportion with schizophrenia / schizoaffective disorder	69.23% (N=9)	64.86% (N=24)	50.00% (N=2)[b]

Notes: PANSS = Positive and Negative Syndrome Scale; [a] = Median reported as measure of central tendency; [b] = one individual was diagnosed with Major Depressive Episode with Psychotic Features; * = $p < .05$, 2-tailed.

3.3   Cognitive reserve and cognition early in psychosis

Just over 20% (N = 11) of the 50 individuals with premorbid developmental data had late milestones as well as academic difficulties in elementary and middle school years and were classified as having low cognitive reserve. Normal and low cognitive reserve groups did not differ in age or gender. Four individuals from the normal cognitive reserve group were missing information about the age

of psychosis onset and five were missing estimates of duration of untreated

psychosis (DUP). The remainder of the normal cognitive reserve group (N = 34)

did not differ from those with low cognitive reserve in age of psychosis onset or

DUP. Table 3 shows that approximately 91% of individuals in the low cognitive

reserve group and 62% of those in the normal cognitive reserve group received

schizophrenia / schizoaffective diagnoses (relative to bipolar affective disorder or

psychosis not otherwise specified). These proportions were not significantly

different from one another (χ^2 (1, N = 50) = 3.40, p = 0.065).

Table 3   Characteristics of individuals with low and normal cognitive reserve.

Variable	Low Reserve Mean (SD)	Normal reserve Mean (SD)	Effect size (Hedge's $\hat{g}$)
Demographics:	N = 11	N = 39	
Age	22.98 (5.15)	24.88 (6.31)	- 0.31
Years of education	10.91 (1.64)	12.15 (1.77)	- 0.72 *
Gender (% male)	81 % (N = 9)	66 % (N = 29)	
Psychosis features:			
Median duration untreated psychosis (DUP in weeks) [a]	32.00 (79.75)	29.00 (140.71) N = 34	
Age at psychosis onset	19.31 (5.44)	19.85 (6.51) N = 35	- 0.09
Proportion with schizophrenia / schizoaffective disorder	90.90% (N=10)	61.54% (N=24)	

Notes: Hedge's $\hat{g} = \hat{\mu}_1 - \hat{\mu}_2 / \hat{\sigma}$, where $\hat{\sigma} = \sqrt{[\sigma_1^2(n_1 - 1) + \sigma_2^2(n_2 - 1) / n_1 + n_2 - 2]}$; [a] = Median reported as measure of central tendency; * = p < .05, 2-tailed.

At presentation, one individual (normal reserve group) was missing an

estimate of intellectual functions, and two (normal reserve group) did not have

symptom ratings at presentation or follow-up. Before calculating z-score

averages to reflect global cognition, data were evaluated to ensure that participants' test scores accurately reflected their abilities. It was evident that one individual's language proficiency (normal reserve group) and another individual's level of psychiatric symptoms (low reserve group) invalidated tests of their cognitive abilities. Hence, valid global cognitive data at presentation were available for 48 individuals. One individual from the low cognitive reserve group and seven individuals from the normal cognitive reserve group left the "Interactions" study before follow-up assessment. Individuals lost to attrition did not differ from remaining participants in the severity of their cognitive deficits or psychiatric symptoms (ps = ns) and attrition did not differentially affect either reserve group.

Averaged z-score summaries of performance on tests of attention, working memory, processing speed, and long-term memory (see Table 4) were calculated to reflect global cognition at presentation and follow-up of individuals with low and normal cognitive reserve. Averaged z-scores permitted inclusion of one participant missing a digit symbol test at initial assessment, and two participants missing letter-number sequencing scores at 9-12 month assessment (average z-scores were based on three tests). Estimates of global cognition were available for 48 individuals at presentation and 40 individuals at follow-up (see Table 4).

Table 4 Presentation and follow-up cognition of individuals with low and normal cognitive reserve.

Variable	Low Reserve Mean (<u>SD</u>)	Normal Reserve Mean (<u>SD</u>)	Effect size (Hedge's $\hat{g}$)
Functioning at presentation:	*N = 10*	*N = 38*	
Premorbid IQ (NAART FSIQ)	99.80 (<u>8.73</u>)	103.08 (<u>7.78</u>)	- 0.39
K-BIT Composite IQ	94.80 (<u>12.16</u>)	97.24 (<u>10.38</u>)	- 0.22
		N = 37	
Global cognition (average z-score)	- 0.85 (<u>0.60</u>)	- 0.41 (<u>0.68</u>)	- 0.68
PANSS Positive Scale score	21.00 (<u>7.80</u>)	17.78 (<u>5.44</u>)	0.48
		N = 36	
PANSS Negative Scale score	21.30 (<u>7.85</u>)	17.14 (<u>6.33</u>)	0.57
		N = 36	
PANSS General Scale score	40.40 (<u>10.87</u>)	36.36 (<u>7.08</u>)	0.43
		N = 36	
PANSS Total Scale score	84.90 (<u>26.74</u>)	73.86 (<u>14.79</u>)	0.50
		N = 36	
Functioning at follow-up:	*N = 9*	*N = 31*	
Global cognition (average z-score)	- 1.02 (<u>0.40</u>)	- 0.30 (<u>0.84</u>)	- 1.07 *
PANSS Positive Scale score	10.56 (<u>2.83</u>)	10.55 (<u>3.55</u>)	0.003
		N = 29	
PANSS Negative Scale score	18.56 (<u>5.32</u>)	13.79 (<u>5.05</u>)	0.91
		N = 29	
PANSS General Scale score	29.56 (<u>5.13</u>)	29.45 (<u>8.86</u>)	0.02
		N = 29	
PANSS Total Scale score	58.67 (<u>10.64</u>)	53.79 (<u>15.31</u>)	0.36
		N = 29	

Notes: NAART = North American Adult Reading Test; FSIQ = Full Scale Intelligence Quotient; K-BIT = Kaufman Brief Intelligence Test; Potential range of average z-scores = [-4.90 – 4.90]; PANSS = Positive and Negative Syndrome Scale; Premorbid to presentation change in cognition = [Presentation global cognition – NAART z-score]; Premorbid to follow-up change in cognition = [Follow-up global cognition – NAART z-score]; Hedge's $\hat{g} = \hat{\mu}_1 - \hat{\mu}_2 / \hat{\sigma}$, where $\hat{\sigma} = \sqrt{[\sigma_1{}^2(n_1 - 1) + \sigma_2{}^2(n_2 - 1) / n_1 + n_2 - 2]}$.

Though I expected that attenuated premorbid abilities would be evident in those with low cognitive reserve, the low cognitive reserve group did not show significantly lower premorbid intellectual abilities (NAART; see Table 4) than

individuals with normal cognitive reserve (F (1, 48) = 1.40, p > .05). However, those with low cognitive reserve did complete significantly fewer years of formal education than those with normal cognitive reserve (F (1, 48) = 4.37, p < .05).

The first analysis was used to evaluate the hypothesis that individuals with low cognitive reserve would show intensified cognitive decline from presentation to follow-up relative to individuals with normal cognitive reserve. Average z-score summaries were used to reflect the magnitude of global cognitive deficits at presentation and follow-up. If individuals with low cognitive reserve are more susceptible than those with normal cognitive reserve to the deleterious cognitive effects of psychosis onset, an interaction between group and assessment session should be evident. In this case, cognitive deficits should intensify from presentation to follow-up. Linear mixed modelling was used to evaluate this hypothesis, as the technique allows for missing data due to attrition (from presentation to follow-up) and permits specification of covariance structure. The reserve group variable was entered first as a fixed factor, session as a repeated measure, and presentation and follow-up global cognition were entered as the dependent variate to examine the fit of different covariance structures.

The suitability of covariance structures was evaluated by comparing measures of log likelihood model fit (-2RLL) of alternate covariance structures relative to that of a compound symmetrical matrix. Evaluating the change in chi-square value (-2RLL change) relative to changes in the number of parameters estimated (df change) reveals whether an alternate covariance structure offers a statistically significant improvement in fit. Table 5 shows that unstructured and

variance components covariance structures did not provide significant

incremental improvements in chi-square estimates of model fit relative to a

compound symmetrical covariance structure.

Table 5   **Fit indices for compound symmetry, unstructured, and identity covariance matrices in a group x session linear mixed model.**

Model	AIC	-2RLL	df + 1	-2RLL change	df change	p-value
Compound symmetry	177.18	173.18	6			
Unstructured	177.88	171.88	7	1.30	1	0.254
Variance components	195.28	191.28	6	-18.10	0	NA

Notes: AIC = Akaike Information Criterion; -2RLL = -2 Restricted Log Likelihood; df + 1 = number of parameters estimated; -2RLL change = [-2RLL compound symmetry - -2RLL alternate structure]; df change = [parameters compound symmetry – parameters alternate structure].

A compound symmetry covariance matrix was therefore used to model the

relationship between cognitive reserve grouping as a fixed effect and global

cognition as a repeated measure at presentation and follow-up. Across sessions,

the low cognitive reserve group had significantly worse cognition than the normal

cognitive reserve group (F (1, 45.55) = 5.68, $p < .05$). There was no main effect

for session (F (1, 40.26) = 0.01, $p > .05$), suggesting that for the entire sample

global cognition was stable from presentation to follow-up. There was no

evidence for an interaction of group and session, indicating that the low cognitive

reserve group did not experience more severe cognitive decline than the normal

cognitive reserve group (F (1, 40.26) = 0.91, $p > .05$).[1]

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[1] Individuals with low cognitive reserve exhibited the same magnitude of cognitive deficits relative to a diagnostically matched normal reserve control sample, suggesting that these results are not an artefact of differences in the prevalence of schizophrenia-spectrum diagnoses between low and normal cognitive reserve groups. See Appendix 8 for matched groups and analyses.

Differences in premorbid abilities were not statistically significant but could account for some of the variation in global cognition between low and normal reserve groups. Global cognition reflects the extent of cognitive deficits relative to standardization samples but does not account for the possibility of differential decline relative to premorbid ability level in cognitive reserve groups. For instance, one reserve group may decline more steeply relative to their baseline (premorbid) ability levels than the other. To clarify the relationship between reserve grouping and psychosis-related cognitive deficits, a measure of decline from premorbid abilities was calculated for each participant. Z-score summaries of presentation and follow-up global cognition were subtracted from estimated premorbid abilities (NAART z-scores) to quantify the decline in cognition, relative to premorbid abilities, experienced by each cognitive reserve group at each session. Table 6 indicates that small to medium group differences were evident in premorbid abilities, as well as declines from premorbid abilities at presentation and follow-up. While the severity of presentation and follow-up declines from premorbid abilities appeared to be stable in the low cognitive reserve group, this should be viewed in light of the limited power due to the small group size.

Table 6   Presentation and follow-up decline from premorbid abilities of individuals with low and normal cognitive reserve.

Variable	Low Reserve Mean (<u>SD</u>)	Normal Reserve Mean (<u>SD</u>)	Effect size (Hedge's $\hat{g}$)
NAART z-score	- 0.01 (<u>0.58</u>) *N = 10*	0.21 (<u>0.51</u>) *N = 38*	- 0.39
Decline from premorbid abilities to presentation	- 0.83 (<u>0.63</u>) *N = 10*	- 0.62 (<u>0.61</u>) *N = 38*	- 0.33
Decline from premorbid abilities to follow-up	- 0.89 (<u>0.64</u>) *N = 9*	- 0.49 (<u>0.84</u>) *N = 31*	- 0.53
Change from presentation to follow-up	-0.06 (<u>0.32</u>) *N = 9*	0.13 (<u>0.68</u>) *N = 31*	- 0.35

Notes: NAART = North American Adult Reading Test; Decline from premorbid abilities to presentation = [Global cognition at presentation – NAART z-score]; Decline from premorbid abilities to follow-up = [Global cognition at follow-up – NAART z-score]; Change from presentation to follow-up = [Decline at follow-up – Decline at presentation]; Hedge's $\hat{g} = \hat{\mu}_1 - \hat{\mu}_2 / \hat{\sigma}$, where $\hat{\sigma} = \sqrt{[\sigma_1{}^2(n_1 - 1) + \sigma_2{}^2(n_2 - 1) / n_1 + n_2 - 2]}$.

Linear mixed modelling was used to evaluate whether the low cognitive reserve group showed greater declines from premorbid abilities at presentation and follow-up than the normal cognitive reserve group. First, reserve group was entered as a fixed factor, session as a repeated measure, and presentation and follow-up declines from premorbid abilities were entered as the dependent variate to examine the fit of different covariance structures. When measures of model fit were compared, the significant incremental improvement in the chi square value of log likelihood model fit (-2RLL change) indicated that an unstructured covariance matrix offered the best fit for the data (see Table 7). Relative to a compound symmetry structure, an unstructured matrix permits greater heterogeneity of variance-covariance estimates.

Table 7 **Fit indices for compound symmetry, unstructured, and variance components covariance matrices in a group x session linear mixed model.**

Model	AIC	-2RLL	df + 1	-2RLL change	df change	p-value
Compound symmetry	174.78	170.78	6			
Unstructured	172.44	166.44	7	4.34	1	0.037
Variance components	191.98	187.98	6	- 17.20	0	NA

Notes: AIC = Akaike Information Criterion; -2RLL = -2 Restricted Log Likelihood; df + 1 = number of parameters estimated; -2RLL change = [-2RLL compound symmetry - -2RLL alternate structure]; df change = [parameters compound symmetry – parameters alternate structure].

An unstructured covariance matrix was therefore used to model the relationship between cognitive reserve grouping as a fixed effect and decline from premorbid abilities as a repeated measure at presentation and follow-up. Once premorbid abilities were accounted for, the magnitude of decline from premorbid abilities did not differ by reserve group (F (1, 46.62) = 1.87, $p > .05$), and deficits were stable across sessions (F (1, 38.55) = 0.08, $p > .05$). There was likewise no interaction between reserve group and assessment session, suggesting that the same pattern of deficits from presentation to follow-up was evident for both low and normal reserve groups (F (1, 44.85) = 0.66, $p > .05$). Thus, presentation and follow-up declines from premorbid abilities in the normal reserve group were similar in magnitude to those of the low reserve group (see Figure 3.1).
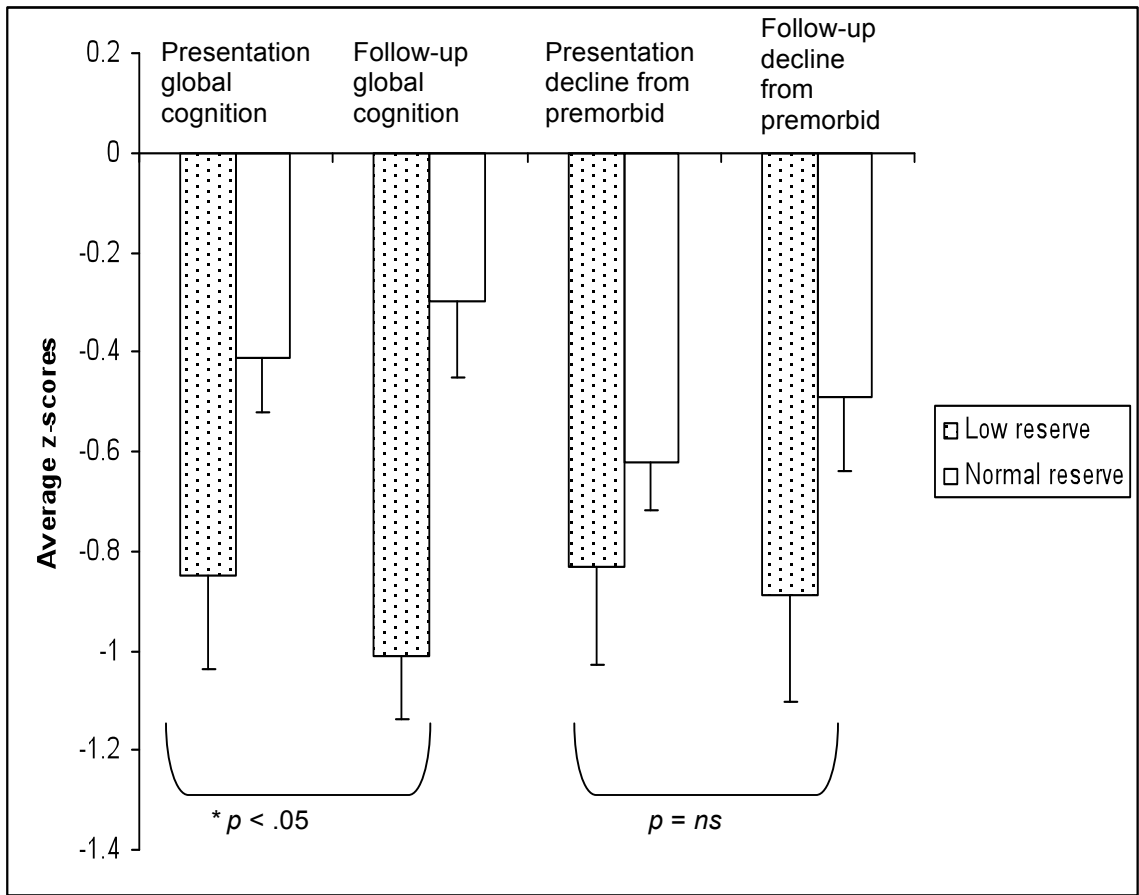
Figure 3.1   Global cognition and decline from premorbid abilities in low and normal cognitive reserve groups.

3.3   Premorbid temperament and substance abuse at presentation

Two individuals were missing information pertaining to substance abuse and PANSS symptoms at presentation. Fifty-four percent of the 48 remaining participants (N = 25) reported substance abuse at presentation, while 46 % (N = 23) denied substance abuse. In addition to the two participants without

substance abuse data, four individuals lacked information pertaining to age of

psychosis onset, and another participant lacked details regarding DUP. For

comparisons of current age, age of onset, and DUP between substance abuse

groups, the sample sizes were 48, 44, and 43, respectively. Table 8 includes

demographic and symptom information for those with and without substance

abuse at presentation. Individuals reporting substance abuse were significantly

older (F (1, 46) = 8.33, p < .05), but had significantly shorter durations of

untreated psychosis (*Welch's F* (1, 32.35) = 12.35, p < .05)[2] than those who

denied substance abuse. Substance abuse groups were similar in terms of

education level, gender proportions, severity of psychiatric symptoms, and

diagnostic category.

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[2] Four individuals who denied premorbid substance abuse had DUPs of more than 280 weeks. To prevent these outlying values from unduly influencing subsequent analyses, their values were transformed to the next highest non-outlying value (Tabachnick & Fidell, 2001). In the resulting analysis, Welch's F statistic was reported to correct for inflation of the probability of Type I error due to inequality of error variances between groups.

Table 8   Characteristics of substance abuse groups at presentation.

Variable	Substance abuse at presentation:	
	Yes (N = 25) *Mean (SD)*	No (N = 23) *Mean (SD)*
Demographics:		
Age	27.11 (6.78)	22.34 (4.61)*
Gender (% male)	74 % (N = 17)	68 % (N = 17)
Years education	12.26 (1.71)	11.64 (1.89)
Symptoms:		
Median duration of untreated psychosis (DUP in weeks) [a]	10.50 (46.7) *(N = 23)*	109.00 (156.71)* *(N = 20)*
Age at psychosis onset	22.12 (6.81) *(N = 21)*	17.81 (5.17) *(N = 23)*
PANSS Positive Scale score	19.30 (7.05)	17.84 (4.79)
PANSS Negative Scale score	17.30 (6.19)	19.36 (7.51)
PANSS General Scale score	39.30 (9.62)	41.08 (8.46)
PANSS Total Scale score	78.28 (18.43)	75.91 (18.81)
Diagnosis (% SCHZ psychosis)	60.00 % (N = 15)	73.91 % (N = 17)
Premorbid temperament ratings:		
Adaptability / positive affect	59.45 (10.37)	62.68 (6.92)
General rhythmicity	49.59 (7.88)	48.59 (11.20)
Attentional focus	19.09 (4.11)	22.32 (6.40)

Notes: PANSS = Positive and Negative Syndrome Scale; SCHZ = schizophrenia-spectrum; Possible range for raw temperament scores – Adaptability / positive affect [43 - 52], General rhythmicity [22 - 58], Attentional focus [11 - 29]; [a] = Median reported as measure of central tendency; * = $p < .05$.

Next, temperament ratings were evaluated to ensure that they were valid. Two parents felt that they were unable to accurately recall their child's disposition prior to psychosis. The response patterns of another two parents were uniformly low (i.e. all responses rated as "never") and invalid. Forty-six individuals had valid ratings of premorbid temperament, and forty-four had valid temperament ratings as well as information regarding substance abuse and PANSS ratings at presentation.

To first address the possibility that temperament ratings might be conflated with psychosis symptoms or diagnostic category, parent ratings were correlated with Total PANSS scores (as an estimate of general psychopathology). The correlations between PANSS Total Score and adaptability / positive affect (r (44) = - . 14, p > .05), general rhythmicity (r (44) = - . 02, p > .05), and attentional focus (r (44) = - . 17, p > .05) were not statistically significant. No significant differences were evident across diagnostic categories (schizophrenia / schizoaffective disorder vs. other psychoses) in premorbid ratings of adaptability / positive affect (F (1, 44) = 0.57, p > .05) or attentional focus (*Welch's F* (1, 40.91) = 0.67, p > .05). Those with schizophrenia or schizoaffective disorder had lower general rhythmicity (M = 47.47, <u>SD</u> = 10.44) than those with other diagnoses (M = 52.69, <u>SD</u> = 6.14). The difference in general rhythmicity between groups (*Hedge's ĝ* = - 0.60) fell short of statistical significance (F (1, 44) = 3.36, p = .08) and on further inspection proved attributable to four outlying values in the schizophrenia / schizoaffective group.[3] Thus, premorbid temperament ratings do not appear to vary systematically as a function of illness severity or diagnostic category.

I hypothesized that lower parent ratings on the three dimensions of premorbid temperament would increase the likelihood of substance abuse at presentation, but before evaluating this possibility it was important to establish whether a logistic model would fit the data. To check whether a logistic model was a reasonable fit for the data, substance abuse was entered as a

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[3] Replicating the analysis without outlying values, there were no significant differences in general rhythmicity by diagnostic group (F (1, 40) = 1.04, p > .05).

dichotomous dependent variable (yes / no) and temperament ratings were entered as covariates in binary logistic regression. There was no systematic relationship between standardized residuals and predictors and the conditional mean function of the dependent variable (substance abuse at presentation) was S-shaped. Moreover, the Hosmer & Lemeshow goodness of fit test (χ^2 (8, N = 44) = 7.63, p > .05) suggested that a logistic regression model offered a reasonable fit for the data. Thus, there was no evidence to suggest that the regression function between temperament and substance abuse was not logistic in nature.

An evaluation of the omnibus likelihood ratio test for the logistic model (χ^2 (3, N = 44) = 8.63, p < .05) indicates that premorbid temperament does indeed predict the presence or absence of substance abuse at presentation. For this logistic function, the equation constant corresponds to the Y intercept for the odds (Exp [B]) associated with zero scores for predictors. In other words, Exp [B] was calculated to reflect the odds of having substance abuse if all covariate scores were set at zero (i.e. indicating the most 'difficult' temperament imaginable). If more difficult premorbid temperament is an important predictor of substance abuse at presentation, the odds should be larger than one, indicating a multiplicative increase in the likelihood of substance abuse as temperament ratings approach zero. In the current logistic function, when all three temperamental predictors were held to zero (the "worst possible" temperament), the odds of substance abuse at presentation were significantly greater than one

(OR = 97.40; 95% CI = 96.56 – 98.23). As predicted, a more "difficult" premorbid temperament confers increased risk for substance abuse early in psychosis.

3.4 Attachment networks in psychosis

Self-reported attachment networks were heterogeneous (see Appendix 9 for a full description). During the premorbid period, participants ranked mothers, friends, and romantic partners as fulfilling attachment roles most often, with the exception of conflictual emotion. Fathers and romantic partners were ranked as eliciting the strongest conflictual emotions. In the post-onset period, mothers and romantic partners were ranked most highly with respect to the frequency with which they fulfilled most attachment roles (see Appendix 10 for more details). Attachment rankings were available for all 41 individuals who completed attachment measures. For subsequent analyses, three individuals were missing estimates of duration of untreated psychosis and two lacked ratings of symptom severity at presentation.

I quantified both the strength and the dispersion of attachments as outlined in the Methods section in order to establish whether conversion to psychosis is marked by consolidation of attachment networks into a core of family relationships. The proportion of attachment roles fulfilled by family members reflected the strength of family attachments, while the number of attachment figures described as satisfying attachment needs indicated compactness of attachment networks in both the premorbid and post-onset period (see Table 9).

Table 9   Strength of family attachments and compactness of attachment networks.

Variable	Premorbid period Mean (SD)	Post-onset period Mean (SD)
	N = 41	N = 41
Proportion of attachments to family	0.57 (0.34)	0.64 (0.33)
Number of attachment figures	2.80 (1.03)	2.59 (1.10)

Notes: Proportion of attachments to family = number of attachment roles filled by family members / number of attachment roles filled by peers; Number of attachment figures = total number of attachments reported.

One sample t-tests were used to test the hypotheses that: 1) the difference between premorbid and post-onset strength of family relationships (i.e., proportion of family members in the network) would be significantly greater than zero (positive), reflecting a group tendency to increasing strength of family relationships, and 2) that the difference between premorbid and post-onset network sizes would be significantly less than zero (negative), indicating a decline in network size. Though participants did report that family members fulfilled a larger proportion of attachment functions post-onset than in the premorbid period (M = 0.07, SD = 0.41), the change in strength of family attachments did not differ significantly from zero (t (40) = 1.11, p > .05). Likewise, while participants reported that the number of attachment figures in their networks declined from premorbid to post-onset time points (M = - 0.22, SD = 1.19), the reduction did not differ significantly from zero (t (40) = -1.18, p > .05).

Next, I evaluated the hypothesis (3A) that greater post-onset strength of family attachments would be associated with smaller number of post-onset attachments as the network consolidated into a few family attachments. A partial correlation was calculated between post-onset strength of family attachments

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and number of post-onset attachments holding premorbid strength of family attachments constant. An inverse linear relationship would indicate that, holding the initial strength of family attachments constant, increased strength of family attachments was directly linked to reduced network size. Interestingly, once premorbid family attachment strength was held constant, no linear relationship was evident between post-onset strength of family attachments and number of attachments (*partial r* (38) = -.01, *p* > .05). Thus, it does not appear that increased strength of family attachments was linked to smaller size of attachment networks. Changes in strength of family attachments and the overall number of attachments appear to be independent to one another, and are not statistically significant in their magnitude.

An important caveat to this finding is outlined in hypothesis 3A, where being in a romantic relationship and having a shorter duration of illness could attenuate the consolidation of networks into a few family attachments. To test this possibility, participants were first categorized according to whether they reported having a romantic attachment in the post-onset period. Not surprisingly, the 29 individuals who did not have romantic partners post-onset reported a high proportion of post-onset attachments to family (M = 0.79, <u>SD</u> = 0.21) relative to the 12 participants who did have romantic attachments (M = 0.27, <u>SD</u> = 0.26). Second, duration of illness was calculated for those individuals with available data (N = 38) by adding months of untreated psychosis to months since entry into the "Interactions" study (M = 55.03 months, <u>SD</u> = 41.22 months).

Multiple regression was used to assess whether the independent variables of being in a romantic relationship and having a shorter duration of illness predicted decreased strength of family attachments from premorbid to post-onset periods. Examination of residuals and measures of influence indicated that a linear combination of duration of illness and romantic relationship status (yes/no) could be used to predict changes in the dependent variate of strength of family attachments. Predictors were entered in blocks to evaluate their contributions to the regression model. A dummy coded variable reflecting whether an individual was in a romantic relationship post-onset was entered in Block 1 and duration of illness was entered in Block 2. Block 3 assessed the interaction between romantic relationships and duration of illness. Inspection of beta weights indicated that being in a romantic relationship predicted reduced dependence on family ($\Delta R^2 = 0.22$, $\beta = -0.52$, $p < .05$) in Block 1, while longer duration of illness predicted increased dependence on family ($\Delta R^2 = 0.16$, $\beta = 0.41$, $p < .05$) in Block 2. In Block 3, the interaction of relationship status and illness duration did not predict additional variance in dependence on family members ($\Delta R^2 = 0.004$, $\beta = -0.14$, $p > .05$). The interaction term was therefore dropped from the final regression model (see Table 10).

Table 10   Final model of predictors of dependence on family members.

Variables	R^2	R^2 Change	*F* Change	Std. β
Block 1	0.22	0.22**	9.91**	
Romantic relationship				- 0.47*
Block 2	0.38	0.16**	9.39**	
Romantic relationship				- 0.52*
Duration of illness				0.41*

Notes: N = 38; Statistical details reported for variables entered in each block; Romantic attachment was coded as a dummy variable with 0 = not being in a romantic relationship and 1 = being in a romantic relationship; * p < .05; ** p < .01.

Given that being in a romantic relationship predicts reduced dependence on family members from premorbid to post-onset periods, individuals who were not in a romantic relationship post-onset might be more likely to show the expected pattern of network consolidation into a few family relationships (see Table 11). Those without a romantic partner post-onset increased their dependence (M = 0.19, SD = 0.35), while those who were in a relationship reduced their dependence (M = -0.21, SD = 0.41) on family attachments from premorbid to post-onset periods (t (1, 39) = 3.12, p < .01). Decreased number of attachments were reported by those without romantic partners (M = -0.07, SD = 1.10) and in romantic relationships (M = -0.58, SD = 1.37), with no differences evident between groups (t (1, 39) = 1.26, p > .05). A partial correlation was calculated between post-onset strength of family attachments and number of post-onset attachments holding premorbid strength of family attachments constant for those without (N=29) romantic partners post-onset. For these participants, increased strength of family attachments was correlated with a smaller number of attachments (*partial r* (26) = -0.47, p < .05). Hence, individuals

without romantic attachments show consolidation of their attachment networks into a core of family relationships early in psychosis.

Table 11 Strength of family attachments and compactness of attachment networks by romantic relationship post-onset.

Variable	Premorbid period Mean (SD)	Post-onset period Mean (SD)
Proportion of attachments to family		
No romantic relationship (N = 29)	0.61 (0.31)	0.79 (0.21)
In a romantic relationship (N = 12)	0.48 (0.39)	0.27 (0.26)
Number of attachment figures		
No romantic relationship (N = 29)	2.76 (0.99)	2.69 (1.11)
In a romantic relationship (N = 12)	2.92 (1.17)	2.33 (1.07)

Notes: Proportion of attachments to family = number of attachment roles filled by family members / number of attachment roles filled by peers; Number of attachment figures = total number of attachments reported.

Hypothesis 3B posits that negative symptoms would compromise the formation of new peer attachments following psychosis onset. About one quarter of participants (N = 10) reported being able to form at least one new peer relationship fulfilling important attachment functions during the period since psychosis onset. Ratings of the severity of positive and negative symptoms at presentation were available for 39 individuals. As shown in Table 12, participants who were unable to form such relationships had more severe negative symptoms at illness onset than those who reported new peer attachments (*Welch's F* (1, 34.3) = 9.72, $p < .05$). In contrast, no such pattern was evident for the severity of positive symptoms (F (1, 37) = 0.41, $p > .05$). It appears that more severe

negative symptoms, in particular, are detrimental to the formation of new peer

attachments following the onset of psychosis.

Table 12   Psychiatric symptoms and post-onset peer attachments.

Variable	PANSS Positive Symptoms Mean (_SD_)	PANSS Negative Symptoms Mean (_SD_)
	N = 10	N = 29
New peer attachments post-onset (N=10)	18.62 (5.73)	14.20 (3.08)
No new peer attachments post-onset (N=31)	19.90 (5.37)	19.24 (6.95)

Notes: PANSS = Positive and Negative Syndrome Scale.

CHAPTER 4: DISCUSSION

4.1 Cognitive reserve and cognition early in psychosis

The current study generated three main findings concerning the relationship between cognitive reserve and early course cognition in FEP. First, individuals with low cognitive reserve had significantly worse global cognition at presentation and follow-up than those with normal reserve, when cognition was evaluated relative to demographically matched standardization samples. This statement is qualified by the second major finding that once premorbid differences in cognitive abilities were accounted for, the cognitive decline from premorbid abilities was comparable for low and normal cognitive reserve groups during the early course of illness. Lastly, there was no evidence that individuals with low cognitive reserve showed deterioration through the early phase of psychosis relative to those individuals with normal cognitive reserve.

Overall, it appears that the onset of psychosis has a similarly adverse effect on cognitive functions regardless of whether an individual has low or normal cognitive reserve. In other words, low cognitive reserve is associated with worse cognitive deficits at presentation relative to standardization data but not with intensified decline from premorbid abilities in the early phase of psychosis. Cognitive reserve does not appear to predict the severity of psychosis-related cognitive declines, though it should be noted that the current study was likely

underpowered to detect subtle relationships between cognitive reserve and susceptibility to cognitive decline.

4.1.1 Cognitive deficits associated with psychosis onset

There is a large literature documenting significant cognitive deficits relative to normative samples in individuals with FEP (Bodnar et al., 2008; Gonzalez-Blanch et al., 2008b; Lappin et al., 2007; Rund et al., 2007; Simon et al., 2007). These deficits tend to persist as stable impairments when schizophrenia-spectrum (Heinrichs & Zakzanis, 1998; Lee & Park, 2005; Reichenberg & Harvey, 2007) and bipolar affective (Bora, Yucel & Pantelis, 2009; Robinson et al., 2006; Torres, Boudreau & Yatham, 2007) psychoses become more chronic. Cognitive impairments relative to normative comparison groups can predate the onset of symptoms and are considered by some to be a core feature of psychotic disorders (Caspi et al., 2003; Gheorge, Baloescu & Grigorescu, 2004). Others note that psychosis onset is often associated with declines in cognition that can be superimposed on existing cognitive impairments (e.g., Rund, 2009).

Thus, it is widely accepted that psychosis onset tends to be associated with significant cognitive deficits relative to healthy controls. It is also clear from existing research that these cognitive deficits are heterogeneous and that there is considerable unexplained variance in the severity of psychosis-related cognitive impairments (Heinrichs, 2004; Mesholam-Gately et al., 2009). In the current study, global cognition of individuals with low and normal cognitive reserve differed at presentation because cognitive declines of a similar magnitude were superimposed upon differences in NAART-measured premorbid abilities.

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Specifically, the differences between low and normal cognitive reserve groups in premorbid abilities (Hedge's $\hat{g}$ = -0.39) and cognitive decline at presentation (Hedge's $\hat{g}$ = -0.33) were similar in magnitude. This suggests that some of the heterogeneity in FEP-related cognitive deficits reported in the literature could be attributed to individual differences in NAART-measured premorbid abilities.

There are potential drawbacks to the methodology of the current study, which quantified FEP-associated cognitive decline relative to NAART-measured premorbid abilities. The NAART appear to be a more powerful predictor of premorbid abilities than demographic variables (O'Carroll, 1995) and controls for the half standard deviation difference in premorbid IQ between those with psychosis and healthy controls reliably documented in numerous studies (see Woodberry, Giuliano & Seidman, 2008 for a meta-analysis). The NAART is also considered relatively invulnerable to the cognitive effects of psychosis (Dragovic, Waters & Jablensky, 2008; Hayes & O'Grady, 2003; Joyce, Hutton, Musatsa & Barnes, 2005; Kondel, Mortimer, Leeson, Laws & Hirsch, 2003). However, educational limitations or test anxiety can suppress NAART scores resulting in underestimates of premorbid abilities (O'Carroll, 1995; Strauss et al., 2006). It is important to recognize the potential limitations of the NAART as a measure of premorbid abilities in interpreting the findings of the current study.

4.1.2   An additive model of premorbid abilities and psychosis-related cognitive decline

The hypothesized interaction between cognitive reserve and the cognitive effects of psychosis whereby those with low cognitive reserve would experience

the steepest psychosis-related cognitive declines was not supported in the current study. Low cognitive reserve does not predict increased susceptibility to cognitive decline (see also Alley, Southers & Crimmins, 2007; Bracco et al., 2007; Roselli et al., 2009) and does not appear to provide an adequate explanatory model for the neurocognitive deficits in psychosis. Declines in global cognition from premorbid levels were stable across presentation and follow-up, with no evidence for differential vulnerability to such declines in those with low cognitive reserve. Cognitive declines of similar magnitude in low and normal cognitive reserve groups at presentation suggest an additive model whereby comparable psychosis-related cognitive impairment is superimposed upon individual differences in premorbid abilities.

Other researchers have raised the possibility that cognitive impairments early in psychosis could reflect the additive effects of psychosis-related impairments and differentially compromised premorbid abilities (Goldberg et al., 2009; Linscott, 2005). In addition, higher premorbid abilities have been associated with more severe cognitive decline at psychosis onset (van Winkel et al., 2006), in direct contrast to the predictions of the cognitive reserve hypothesis. Taken together with the current findings, these studies suggest that cognitive reserve does not effectively predict the severity of psychosis-related impairment. Individual differences in premorbid abilities appear to be more salient determinants of the magnitude of cognitive deficits relative to standardization samples early in FEP.

Some investigations have documented lower premorbid abilities in those who convert to FEP relative to controls (e.g. Lencz et al., 2006; Reichenberg et al., 2005). Lower premorbid abilities are thus characterized as markers of the risk for psychosis but few efforts have been made to use premorbid ability level as a baseline for assessments of early course cognition in FEP. The vast majority of research estimates FEP-related cognitive declines using standardization or control samples rather than an individual's own premorbid baseline (see Mesholam-Gately et al., 2009). Failure to account for individual differences in premorbid abilities precludes accurate estimation of the degree of cognitive impairment directly attributable to psychosis onset. The current study demonstrates that what appear to be significant individual differences in cognition at FEP presentation actually represent a combination of divergent premorbid abilities and comparable psychosis-related cognitive impairments. Such additive models of premorbid abilities and psychosis-related cognitive declines could also clarify the course of cognition through the often subtle and insidious onset of psychotic symptoms (e.g., Cornblatt et al., 2003).

4.1.3   Premorbid abilities and psychosis-related cognitive impairment

Although abnormal early CNS development and cognitive deficits during adolescence are often observed in those who convert to psychosis (Ballon, 2008; Cannon et al., 2002; Isohanni et al., 2000; Lloyd et al., 2008; Mason & Beavan-Pearson, 2005), there is variability in the severity of cognitive deficits presenting prior to the onset of psychotic symptoms. Some studies find little or no impairment immediately preceding symptom onset whereas others report stable

and persistent deficits relative to standardization data or healthy controls (Brewer et al., 2006). If we extend the findings of the current study to the prodromal period, it may be that individual differences in premorbid abilities can account for some of the variability in cognitive deficits prior to onset. Individuals with low NAART-measured premorbid abilities would be most likely to show prodromal cognitive impairments relative to standardization data or controls, which could persist over the longer term course of their illnesses.

Hence, there may be a subgroup of individuals with low premorbid abilities who manifest a stable, low level of cognitive functioning over the long-term course of their illnesses. There is some evidence that individual differences in cognitive functioning may be stable across the course of FEP. Some researchers report that those with low premorbid abilities (assessed by tests of confrontation reading) showed stable low intellectual functioning while those with higher premorbid abilities experienced an initial decrement followed by cognitive recovery by 10-year follow-up (van Winkel et al., 2007; van Winkel et al., 2006). Low premorbid abilities, in contrast to what would be predicted for low cognitive reserve, do not appear to confer added vulnerability to cognitive deterioration in psychosis. Low premorbid abilities and early course cognitive deficits appear to persist as stable, long-term cognitive impairments for some individuals with FEP. Future research could further clarify whether controlling for individual differences in premorbid abilities (i.e. accounting for NAART scores) accounts for some of the variability in prodromal and long-term cognition in FEP.

The current study found that cognitive development (i.e., reserve) had little predictive value for FEP-related cognitive decline after accounting for individual differences in premorbid abilities. Future studies could also use a similar approach to clarify the relationship between cognitive deterioration and psychiatric symptoms in FEP. The estimated relationships between the extent of cognitive impairment and symptom severity early in FEP tend to be variable and small in magnitude (see Dominguez, Viechtbauer, Simons, van Os & Krabbendam, 2009 for a review). Failure to consider baseline abilities in such research may obscure strong associations between some features of psychosis such as negative symptoms and the attendant cognitive decline at presentation. Without controlling for differences in premorbid abilities it is possible to erroneously conclude that cognitive declines and clinical features such as negative symptoms are unrelated or weakly associated.

4.2 Premorbid temperament and substance abuse at presentation in FEP

As predicted, the current study found that individuals whose parents rated their premorbid temperament as being more "difficult" (lower adaptability/positive affect, general rhythmicity, and attentional focus) were far more likely to endorse substance abuse at presentation than individuals whose parents described "easier" premorbid temperaments. This finding is significant for the following reasons: 1) it demonstrates that temperament operates in a similar manner in FEP as in typically developing adolescents and young adults (Giancola & Mezzich, 2003; Stice et al., 2002; Wills et al., 1995), and 2) it establishes that

stable aspects of development predict risk for substance abuse early in FEP.

This latter finding could inform future research seeking to disentangle the

complex relationship between premorbid risk factors for substance abuse,

premorbid risk factors for psychosis, and concomitant substance abuse and

psychotic symptoms.

4.2.1   Temperament as a specific risk factor for substance abuse in FEP

Most research evaluates personality traits or temperament as predictors of

conversion to psychosis in order to improve early identification and intervention in

FEP (e.g., McGorry et al., 2005). However, there is equivocal evidence that

temperament and personality traits predict general risk for psychosis (Cloninger

et al., 1993; Cloninger, 1986; Daneluzzo et al., 2005; Guillem et al., 2008;

Poutska et al., 2007). The developmental literature suggests that "difficult"

temperamental styles are especially potent predictors of maladaptive coping in

the face of stress (Nigg, 2006), and substance abuse can be considered a

prototypic example of maladaptive coping (e.g., Anderson, Ramo & Brown, 2006;

Hyman & Sinha, 2009; Lloyd & Turner, 2008). Temperament should therefore be

a much stronger risk factor for substance abuse (coping strategy) in FEP than for

psychosis itself. Indeed, the current study demonstrates that "difficult" premorbid

temperament styles substantially increase the risk for substance abuse early in

psychosis.

Researchers also make a distinction between substance use or

experimentation and substance abuse, where individuals with more "difficult"

temperamental styles appear particularly prone to using substances to the point

where negative consequences occur (Giancola, 2004). Though estimates vary substantially, studies of lifetime substance use in FEP suggest that the prevalence of premorbid drug and alcohol experimentation tends to be higher (Barnes et al., 2006; Harrison et al., 2008) than the prevalence of substance abuse (Larsen et al., 2006; Wade, Harrigan, McGorry, Burgess & Whelan, 2007; Wade et al., 2006). Individuals in the current sample whose premorbid temperamental styles were more "difficult" were far more likely to abuse substances at presentation than those with "easier" temperamental styles. It is not clear whether these findings also apply to experimentation or casual substance use in FEP. Future studies could evaluate if temperamental styles account for why some individuals with FEP abuse substances and why others abstain or use substances at a milder or less impairing level.

4.2.2   Temperament and the course of substance abuse in FEP

The current study evaluated "difficult" temperamental styles as a risk factor for substance abuse at presentation. The temperament literature suggests that this risk should be relatively stable across development (e.g. Windle & Windle, 2006), which has implications for models of substance abuse in FEP. Substance abuse early in FEP has received considerable attention in the literature and is considered to be a risk factor for ongoing substance abuse (Wade et al., 2006; Wade et al., 2005). Ongoing substance abuse tends to be associated with more severe residual symptoms during the early course of the illness (Harrison et al., 2008; Lambert et al., 2005; Wade et al., 2007).

There are a number of competing explanatory models of co-occurring substance abuse in FEP, none of which are conclusively supported by empirical work (Gregg et al., 2007; Chambers, Krystal & Self, 2001; Gonzalez, Bradizza, Vincent, Stasiewicz & Paas, 2007). Premorbid substance abuse is considered to trigger the onset of psychotic symptoms by some researchers who note that regular premorbid use of substances (Corcoran et al. 2008; Hambrecht & Hafner, 2000) appears to hasten the onset of psychoses in those at genetically high risk for the disorder (Henquet, Di Forti, Morrison, Kuepper & Murray, 2008). Temperamental styles can be used to improve research models of how substance abuse might hasten conversion to psychosis in some individuals. For example, studies documenting the relationship between cannabis abuse and earlier age of psychosis onset (e.g., Barnett et al., 2007; Gonzalez-Pinto et al., 2008) typically do not consider factors that might predispose some individuals to cannabis abuse. Individuals with "difficult" temperamental styles may be far more likely to use cannabis heavily and at earlier ages than those with "easier" temperamental styles, which may in turn increase their risk for conversion to psychosis. "Difficult" temperamental styles may reduce the threshold for psychosis onset through increasing the risk for substance abuse.

Others note that it can be difficult to distinguish the negative clinical outcomes related to substance abuse from adverse consequences associated with an underlying predisposition for substance abuse in FEP (Mata et al., 2008). Temperament, as a stable risk factor for substance abuse, could clarify the association between substance abuse and emerging psychotic symptoms. For

instance, longitudinal studies could evaluate the predictive value of temperament for premorbid substance abuse, substance abuse early in FEP, and associated clinical difficulties early in FEP. Such studies could also assess whether "difficult" temperamental styles are associated with premorbid or prodromal behavioural problems and clinical features that independently increase the likelihood of substance abuse in FEP.

If, in addition to substance abuse at presentation, "difficult" temperamental styles lead to increased risk for substance abuse premorbidly and post-onset, it would suggest differential vulnerability to substance abuse and its adverse clinical consequences for "difficult" and "easier" temperamental styles. There may be an early divergence in substance abuse risk associated with "difficult" and "easier" temperamental styles that remains stable through the illness course. Temperament may thus provide the foundation for both substance abuse and the associated clinical difficulties in FEP (e.g., Rothbart, 2007). Alternatively, temperament may predict substance abuse exclusively at presentation, suggesting that temperamental style selectively increases the risk for substance abuse as a coping mechanism at times of extreme stress (such as conversion to psychosis), or that temperament interacts with psychotic symptoms to determine the risk for substance abuse.

It is also possible that other aspects of premorbid development mediate the risk between temperamental styles and substance abuse in FEP. Recent research indicates that more "difficult" temperamental styles increase the risk for childhood hyperactive or disruptive behaviours, which in turn increase the risk for

substance abuse in adolescence (Martel et al., 2009). Similar processes may be evident in the premorbid or prodromal period in FEP. For example, those with "difficult" temperamental styles may also be more vulnerable to nonspecific premorbid difficulties with hyperactivity and disruptive behaviours, which could lead to substance abuse in the prodrome or at onset. There may be a specific constellation of problems associated with "difficult" temperamental styles that culminates in substance abuse at presentation. These individuals may also be more likely than those with "easier" temperaments to continue abusing substances after psychosis onset.

The lack of consensus as to whether substance abuse is a cause, effect, or correlate of psychotic symptoms suggests that the relationship between substance abuse and psychosis is complex. This underscores the importance of improving our understanding of how substance abuse and conversion to psychosis might be predicted by relatively stable aspects of premorbid development. The current study is significant because it is the first to indicate that "difficult" temperamental styles significantly increase the likelihood of substance abuse at FEP presentation. "Difficult" temperament can be considered a stable developmental risk factor for substance abuse in FEP where few such risk factors have been established (Addington & Addington, 2007; Gregg et al., 2007; Larsen et al., 2006). The findings of the current study can be used by future researchers as an impetus to substantively clarify our understanding of substance abuse before, during, and after psychosis onset.

4.3 Changes in attachments with conversion to psychosis

The current study failed to find any statistically significant changes in either the strength of family attachments or in the size of attachment networks over the early course of psychosis. Interestingly, while the entire sample did not become more reliant on family members in the early phase of psychosis, those who did not have a romantic partner post-onset showed consolidation of attachment networks to primarily family members as psychotic symptoms emerged. Being in a romantic relationship post-onset predicted reduced emotional dependence on family members, while longer duration of illness predicted increased dependence on family from premorbid to post-onset periods. Thus, general developmental consideration such as the availability of non-familial attachment figures (Trinke & Bartholomew, 1997) as well as psychosis-specific factors such as duration of illness predicted changes in emotional dependence on family members. Additionally, individuals who were able to form new peer attachments post-onset had milder negative symptoms than those who were not able to do so. While active social avoidance or suspicion are recognized as detrimental to the quality of relationships (Berry et al., 2007a; Berry et al., 2007b), this is the first indication that passive social withdrawal also affects the ability to rely on peers to meet major attachment needs.

4.3.1 Consolidation of attachment networks early in psychosis

Individuals with romantic partners tended not to rely heavily on family members to meet attachment needs, as expected for young adults in such intimate relationships (e.g., Doherty & Feeney, 2004). Less than a third of

participants in the current study reported an intimate relationship post-onset.

Despite the low frequency of such attachments, having a romantic relationship

appeared to buffer the increased emotional dependence on family that often

follows psychosis onset (Addington et al., 2003a). There are a number of

potential explanations for the relatively high proportion of the current sample who

were not in romantic relationships and depended more heavily on family

attachments after psychosis onset.

Those without romantic partners might have lost the capacity to form such

attachments with psychosis onset (Lencz, Smith, Auther, Correll & Cornblatt,

2004), or failed to acquire relationship skills earlier in development (Iyer et al.,

2008). The stigma (Compton & Esterberg, 2005) and attendant social discomfort

(Birchwood et al., 2007) associated with psychosis onset could also affect peer

relationships. Side effects of pharmacological treatment on sexual desire and

functioning (e.g. Fortier, Mottard, Trudel & Even, 2003) could further interfere

with the formation or maintenance of intimate relationships. Poor social skills and

antisocial or disruptive behaviours are often evident in the premorbid period, so it

may be that some individuals with psychosis have longstanding problems with

peer relationships that continue after onset (Niemi, Suvisaari, Haukka &

Lonnqvist, 2005; Olin et al., 1998; Tarbox & Pogue-Geile, 2008).

It is also possible that romantic relationships are not, in and of themselves,

protective against restriction of attachment networks to family members. It may

be that the ability to form and maintain romantic relationships is actually a marker

for broader social capabilities that reduce withdrawal and isolation from peers in

some individuals with FEP. In other words, capacities such as empathy and perspective taking, which typically foster the development of romantic relationships may also buffer against the adverse effects of psychosis on attachment networks (e.g., O'Brien et al., 2009; Thorup et al., 2007). Those individuals with romantic partners post-onset may have stronger social skills than those who find they must turn to family members to meet their emotional needs.

Consistent with our observations, the capacity to sustain intimate relationships may diminish over the longer-term course of illness (e.g., Norman et al., 2005). While individuals with chronic psychoses report normative levels of interest in sexual exploration and relationships, they have far lower perceptions of their own sexual abilities and lower sexual satisfaction than healthy controls (Fan et al., 2007; Peitl, Rubesa, Peitl, Ljubicic & Pavlovic, 2009). Some participants in the current study reported having romantic relationships that met attachment needs, but more chronic forms of the illness are associated with lack of self-confidence and satisfaction in the psychosexual realm. The current study indicates that longer duration of illness independently predicts increased dependence on family relationships to meet emotional needs. Such findings do not augur well for the formation of new intimate relationships, or the continuation of existing relationships as the illness progresses.

Longer illness duration may correspond with more intense exposure to stereotypes concerning mental illness, which consistently include overestimations of the severity of social impairments (Crisp, Gelder, Rix, Meltzer & Rowlands, 2000). Such stigmatization could cause individuals to withdraw from

relationships, particularly with peers, which in turn may lead to a mutually reinforcing cycle of social isolation and lack of peer support during the difficult process of seeking and engaging in treatment (Castelein et al., 2008; Drake, Haley, Akhtar & Lewis, 2000). Both factors could explain withdrawal from peer relationships, which may partially account for the pattern of intensified emotional dependence on family members in those with longer duration of illness.

4.3.2   Methodology and self-reported attachments

In contrast to other research focusing on peer or parent attachments in psychosis (Berry et al., 2007a; Berry et al., 2007b), the current study allowed participants to simultaneously report on the quality of both family and peer relationships on the Attachment Networks Questionnaire (ANQ; Trinke & Bartholomew, 1997). Typically, studies have reported that individuals with chronic psychosis tend to rate themselves as being highly avoidant and insecure, which can be difficult to distinguish from illness-related social withdrawal and paranoia (Berry, Barrowclough & Wearden, 2008; Berry et al., 2007a; Pickering, Simpson & Bentall, 2008). Rather than asking about an individual's perceptions of his or her attractiveness as a relationship partner, the trustworthiness of others, and so forth, the ANQ is more behaviourally oriented. The ANQ allows participants to report on whether they could actually count on people to meet their emotional needs, regardless of their self-perceptions.

Individuals with psychosis may not trust that others will meet their emotional needs and may see themselves as undesirable relationship partners (Couture et al., 2007; Patterson et al., 2005; Pourmand et al., 2005). However,

the current study suggests that those with FEP feel that their basic attachment needs are being met on a daily basis (i.e. all participants reported that they were able to go to someone for love and support when needed). From a therapeutic perspective, such behavioural evidence that others can be counted on for love and understanding from day to day could be used to challenge negative perceptions about one's attractiveness as a relationship partner (Berry et al., 2007a; Berry et al., 2007b).

All participants in the current study were enrolled in an early-detection community program. Many prior studies recruited patients at first hospitalization, which often corresponds to longer durations of untreated psychosis (DUP) and more severe symptoms (Hafner et al., 2004; Harris et al., 2005). Early detection and specialized treatment increase the likelihood that relationships are successfully maintained over the early course of the illness (Berry et al., 2007b; McGorry et al., 2005). As such, individuals in the current sample may show levels of relationship functioning that are better than is typical of FEP. Other researchers have suggested that attachment problems can be circumvented if parents or families receive assistance that helps them to cope with the real and imagined losses associated with an emerging psychosis (Patterson et al., 2005). Individuals in the current sample and their families may be in the midst of this process and the effects of protracted psychotic symptoms on attachments may not yet be evident (e.g., Howard, Leese & Thornicroft, 2000). Future research could use a longer follow-up period to explore this possibility.

4.3.3   Peer attachments and negative symptoms

Social dysfunction is a widely recognized issue in FEP (e.g., Cornblatt et al., 2003; Møller & Husby, 2000; Reininghaus et al., 2008; Shim et al., 2008; Wiersma et al., 2000) although the effects of psychotic symptoms on peer attachments have received very little attention. The current study is the first to extend previous research documenting associations between more severe negative symptoms and difficulties sustaining the types of day-to-day activities needed to maintain friendships (Barnes et al., 2008; Thorup et al., 2006) by examining attachment networks. The present findings indicate that individuals who established new peer relationships of an intensity and quality that satisfied major emotional needs had less severe negative symptoms than individuals who did not form such relationships.

This finding is notable because peer attachments become especially important for emotional development during young adulthood (Benson, McWey & Ross, 2006; Doherty & Feeney, 2004; Friedlmeier & Granqvist, 2006). Hence, negative symptoms may cause problems with peer attachments and reduce opportunities to practice and master emotional regulation within such relationships. Alternatively, peer relationship problems could simply be another facet of the negative symptom complex, of which asocial behaviour is a major component (e.g., Thorup et al., 2006). Though the current study cannot address whether negative symptoms are an independent predictor of peer attachment problems, the findings do describe the real-world changes in peer relationships during the early course of illness. Difficulties with peer attachments are a tangible example of the adverse social effects of negative symptoms.

While negative symptoms may affect the capacity for peer attachments, there is a lack of consensus in the literature regarding the association between more global social impairment and negative symptoms. Some investigators characterize premorbid social withdrawal as an early manifestation of the profound disengagement from the environment that marks negative symptoms, which may precede or follow psychosis onset (Strous et al., 2004; Monte et al., 2008). Others report weaker relationships between social dysfunction and the severity of negative symptoms in both high-risk (Shim et al., 2008) and clinical samples (Iyer et al., 2008).

Though speculative, findings from the present study suggest that negative symptoms may have the most significant effects on emerging interpersonal skills in young adulthood. Newly developing social skills demand the highest levels of motivation, emotional interest, and tolerance for failure and frustration (Campa et al., 2009). Negative symptoms such as passive social withdrawal, amotivation, and blunted affect would undermine the emotional resilience and flexibility needed to form close peer attachments (Hansen et al., 2009). Thus, negative symptoms may not show consistent relationships with general social withdrawal early in psychosis but they are related to significant problems with the quality of peer attachments.

4.4   Clinical implications of the current findings

The findings of the current study suggest that early, identifiable risk factors drawn from the developmental literature explain some of the heterogeneity in early clinical features of FEP. In addition to elucidating the course of cognitive

deficits, substance abuse, and social isolation in FEP, these risk factors also have implications for recovery and rehabilitation in these domains. If we consider the first three to five years of a psychotic illness as the window in which intensive treatment will be optimally successful (McGorry et al., 2005), our findings underscore the importance of considering the inclusion of rehabilitation efforts in broad-based treatment programs.

4.4.1   Effective rehabilitation in FEP

The current findings suggest that psychosis has similarly detrimental cognitive effects regardless of cognitive reserve level. Despite the widespread recognition that cognitive deficits in turn predict poor social functioning and life quality in FEP (Addington et al., 2008; Addington, Saeedi & Addington, 2005), cognitive rehabilitation (Prouteau et al., 2005) has yet to be evaluated as a standard treatment for FEP. Our findings suggest that individuals with milder cognitive deficits may still be grappling with a substantial deterioration from premorbid levels of ability, and could benefit from rehabilitation.

Temperamental risk for substance use problems can be mitigated via targeted interventions such as motivational interviewing and CBT (Hawkins, 2009; Kirisci, Vanyukov & Tarter, 2005). Such interventions have already proven effective in reducing substance misuse in more chronic psychosis (Barrowclough et al., 2001; Castle & Ho, 2003) but they have yet to be evaluated in FEP (see Archie et al., 2007 for effectiveness of psychoeducation in FEP). Finally, our findings suggest that individuals with FEP felt that family members met their emotional needs on a day-to-day basis despite the stress of coping with

psychosis. In a therapeutic context, the strength of family relationships could be used as a starting point for developing and generalizing social skills to peer relationships.

4.5 Limitations

There are a number of significant limitations of the current study that should be considered when interpreting the findings.

4.5.1 Sample size

The most important limitation of the current study is the small number of participants who completed the study measures. Hypotheses and statistical analyses were selected to maximize power in this relatively small group of individuals, but the study was still underpowered to detect small to medium effects. As such, the current findings should be interpreted with the understanding that subtle relationships or small to moderate group differences would not reach statistical significance. A larger sample would have also allowed for comprehensive assessment of the relationships between different aspects of development (cognition, temperament, and attachment), or consideration of developmental trajectories in each area of interest.

Other researchers note that the clinical features of first-episode psychosis frequently reduce participation in clinical research studies, leading to small sample sizes (Furimsky, Cheung, Dewa & Zipursky, 2008; Heinssen, Cuthbert, Breiling, Colpe & Dolan-Sewell, 2003). Accessing participants through an early-detection catchment area study follows some of the recommendations put

forward by Heinssen and colleagues (2003) to minimize these problems. Even so, attrition and withdrawal from the larger "Interactions" study were problematic. On a positive note, those who were contacted participated at a relatively high rate (54/79, or about 68%) in the current study, and those who participated were representative of the catchment area sample in terms of symptoms and diagnoses. Thus, the current sample was small but did not appear to be biased.

Another limitation of the current study is related to missing data. The "Interactions" study involved intensive data collection from patients and their parents over a number of appointments and data were missing for a number of participants due to time constraints, participant fatigue, or lack of availability of a parent. This served to further reduce the sample size in many of the analyses. There were no systematic relationships between participants' level of functioning, symptoms, diagnoses, and missing data. In some cases, participants were unable to accurately recall the information or may have been unable to give adequate effort to a cognitive task.

4.5.2   Retrospective reports

Another major limitation of the current study was the reliance on retrospective self-report data. Retrospective methodologies are typically employed to collect data concerning premorbid adjustment in first-episode psychosis (e.g., Monte, Goulding & Compton, 2008) although recollections of individuals with FEP and their families could be affected by current symptoms. Reconstructive biases have the potential to affect the accuracy of recollections. This is especially likely when judgements are more subjective in nature, as is the

case with attachments (Scharfe & Bartholomew, 1998). This imposes general limits on the interpretability of retrospective self-report data. However, it does not appear that individuals with psychosis are disproportionately susceptible to such distortions (Favaretto et al., 2001; Willinger et al., 2002).

In the current study, this limitation is likely to affect attachment estimates where analyses were based completely on retrospective reports of individuals with FEP. As a result, interpretations of the analyses were more tentative. In contrast, parent reports of premorbid academic achievement were collected with a widely used and validated retrospective measure. This increases the confidence with which such reports can be interpreted. With respect to ratings of temperament, current psychiatric symptoms did not appear to unduly affect parent recollections of their child's premorbid disposition. Furthermore, temperament is by definition considered to be relatively stable over time. If parent recollections were affected by their child's current disposition it is not clear that this would result in inaccurate premorbid ratings.

4.5.3   Measurement of cognitive reserve

The literature distinguishes between passive components of cognitive reserve such as brain size and active reserve components such as brain activation or cognitive activity level (Stern, 2002). The current study found that markers of cognitive reserve reflecting both passive and active components (e.g. academic performance) did not predict cognitive decline in psychosis. However, it may be that passive and active reserve components predict distinct facets of FEP-related cognitive decline. Numerous neuroimaging studies have established

that anomalies in brain structure are evident before (Fornito et al., 2008) and after psychosis onset (e.g., Borgwardt et al., 2008; Sun et al., 2009). Future research could evaluate whether such anomalies (indicating low passive reserve) confer added risk for cognitive decline following psychosis onset. Subsequent studies could also evaluate whether active reserve components such as daily cognitive activity level predict recovery from psychosis-related cognitive declines.

4.6   Summary

The current study drew upon the developmental literature to clarify our understanding of cognitive impairment, substance abuse, and social isolation in FEP. First, differences in premorbid abilities explain some of the variation in the severity of psychosis-related impairment relative to normative samples. Individuals with low and normal cognitive reserve experienced declines from premorbid abilities of a similar magnitude at presentation, which were stable through the early phase of psychosis. Second, more "difficult" premorbid temperamental styles significantly increased the risk for substance abuse at presentation in the current sample. This finding extends a well-established relationship from the developmental literature to FEP. Finally, conversion to psychosis was associated with increasing emotional dependence on family members to meet attachment needs in those without a romantic partner post-onset. While romantic relationships attenuated dependence on family, longer duration of illness intensified emotional reliance on family members. In addition,

more severe negative symptoms adversely affected the ability to form new peer attachments post-onset.

The results of the current study indicate that risk factors drawn from the developmental, schizophrenia, and aging literatures can: 1) explain some of the heterogeneity in early clinical features FEP, 2) clarify the trajectories of these clinical features, and 3) indicate protective factors (such as being able to form romantic relationships). These results improve our understanding of why some individuals with FEP grapple with cognitive deficits, substance abuse, or social isolation while others have less severe difficulties. Future studies with larger, longitudinal samples can improve upon the current findings. For example, researchers could evaluate whether temperamental styles have similar relationships with substance abuse in the premorbid period and in chronic psychosis, and whether emotional dependence on family intensifies as psychoses become chronic. These lines of research would provide insights into how these clinical features develop, and how we can improve prognosis through identification and treatment of specific clinical aspects of FEP.

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APPENDICES

Appendix 1

Primary Investigators and Co-Investigators, "Interactions of development, early life experience, and genetic predisposition to schizophrenia".

Primary Investigator:
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The EPII Program also provides clients with opportunities to participate in research addressing pathways to care, predispositions for psychosis, and treatment response. At enrolment a parent, typically the mother, of each participant completed a developmental interview with "Interactions" researchers. At about the same time, each participant completed a battery of neuropsychological tests to evaluate cognitive status, received an MRI scan, and underwent a psychiatric interview to assess psychopathology and establish an entry diagnosis. Psychiatric symptoms were evaluated again after 6 months of pharmacological and psychotherapeutic treatment. A final neurocognitive assessment session was completed between 9 and 12 months after enrolment, as was a final MRI scan. Finally, participants received a structured psychiatric interview at about the 12 month time-point, which was used to establish a 12 month diagnosis (using DSM-IV diagnostic criteria; American Psychiatric Association, 1997). "Interactions" data included in the current study were collected at enrolment to reflect functioning at presentation, and after 9-12 months to assess functioning at follow-up.

Appendix 2

Sample characteristics

In order to evaluate whether any selection biases might be influencing sample ascertainment, demographic variables and entry diagnoses at the time of enrolment in the Interactions study were compared for individuals who agreed to participate in the current study and those who were either lost to attrition or declined to participate. These data were missing for 2 individuals who dropped out of the "Interactions" study. Participants who participated in the current study (N = 54) were somewhat older when they enrolled in the larger "Interactions" study (M = 23.1, SD = 7.1) than those who declined to participate or were lost to attrition (N = 75; M = 20.6, SD = 5.1). Welch's statistic indicated that the age difference between the groups was statistically significant (F (1, 90.6) = 4.7, p < .05). Those who enrolled in the current study also completed more years of formal education upon entry to the larger study (M = 11.9, SD = 1.8) than those who did not enrol in the current study (M = 10.9, SD = 1.7). Analysis of Variance (ANOVA) indicated that the group difference in education was also statistically significant (F (1, 123) = 9.1, p < .05). Thus, individuals from the larger study who agreed to participate in the current study were both older and better educated on enrolment to the "Interactions" study than those who refused to participate or were lost to attrition.

Table 13   Characteristics of "Interactions" sample who did not participate in the current study.

Variables	Average	Range	% of sample (N)
"Interactions" sample (N = 77)			
Age	20.63 (5.09)	13.42 – 37.50	
Years of education	10.94 (1.72)	7.00 – 16.00	
Gender (% male)			71.43 % (55)
Diagnosis:			
Schizophrenia or Schizoaffective			62.34 % (48)
Bipolar psychosis			10.39 % (8)
PNOS			18.18 % (14)
MDE with psychosis			5.20 % (4)
PANSS Positive Score [a]	17.84 (5.31)	8.00 – 33.00	
PANSS Negative Score [a]	17.58 (6.13)	8.00 – 43.00	
PANSS General Score [a]	40.22 (8.28)	23.00 – 60.00	

Notes: PNOS = Psychosis not otherwise specified; MDE = Major Depressive Episode; PANSS = Positive and Negative Syndrome Scale at "Interactions" enrolment; [a] Available for 76/77 participants

Sixty-nine percent of those who participated in the current study were male (N = 37), as were 77 % (N = 55) of those who either refused to participate or were lost to attrition. The ratio of males to females did not vary systematically according to whether individuals participated in the current study (χ^2 (1, N = 131) = .06, p > .05). With respect to entry diagnoses, information was missing for 5 of the "Interactions" participants who either dropped out of the study or were lost to attrition. Sixty-seven percent (N = 35) of those who agreed to participate in the current study had entry diagnoses of schizophrenia or schizoaffective disorder. Sixty-five percent (N = 48) of those who refused or left the larger study had entry diagnoses of schizophrenia or schizoaffective disorder. The ratio of those with entry diagnoses of schizophrenia or schizoaffective disorder to those with entry diagnoses of other forms of psychosis (Bipolar Disorder with Psychotic Features, Psychosis Not Otherwise Specified, Major Depressive Episode with Psychosis) was similar between groups (χ^2 (1, N = 131) = .08, p > .05). In terms of entry diagnoses, it did not appear that any diagnostic group was over-represented in the group of individuals who agreed to participate in the current study. There were no statistically significant group differences in the severity of positive (*F* (1, 126) = 0.92, *p* > .05), negative (*F* (1, 126) = 0.12, *p* > .05), or general (*F* (1, 126) = 3.28, *p* = .072) symptoms in those individuals who declined participation in the current study.

Appendix 3A

Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987)

Positive Scale:

P1   Delusions

Beliefs which are unfounded, unrealistic, and idiosyncratic. Basis for rating: Thought content expressed in the interview and its influence on social relations and behaviour.

P2   Conceptual disorganization

Disorganized process of thinking characterized by disruption of goal-directed sequencing, e.g., circumstantiality, tangentiality, loose associations, non sequiturs, gross illogicality, or thought block. Basis for rating: Cognitive-verbal processes observed during the course of the interview.

P3   Hallucinatory behaviour

Verbal report or behaviour indicating perceptions which are not generated by external stimuli. These may occur in the auditory, visual, olfactory, or somatic realms. Basis for rating: Verbal report and physical manifestations during the course of interview as well as reports of behaviour by primary care workers or family.

P4   Excitement

Hyperactivity as reflected in accelerated motor behaviour, heightened responsivity to stimuli, hypervigilance, or excessive mood lability. Basis for rating: Behavioural manifestations during the course of interview as well as reports of behaviour by primary care workers or family.

P5   Grandiosity

Exaggerated self-opinion and unrealistic convictions of superiority, including delusions of extraordinary abilities, wealth, knowledge, fame, power, and moral righteousness. Basis for rating: Thought content expressed in the interview and its influence on behaviour.

P6   Suspiciousness / persecution

Unrealistic and exaggerated ideas of persecution, as reflected in guardedness, a distrustful attitude, suspicious hypervigilance, or frank delusions that others mean one harm. Basis for rating: Thought content expressed in the interview and its influence on behaviour.

P7   Hostility

Verbal and nonverbal expressions of anger and resentment, including sarcasm, passive-aggressive behaviour, verbal abuse, and assaultiveness. Basis for rating: Interpersonal behaviour observed during the interview and reports by primary care workers and family.

Negative Scale:

N1   Blunted affect
        Diminished emotional responsiveness as characterized by a reduction in facial expression, modulation of feelings, and communicative gestures. Basis for rating: Observation of physical manifestations of affective tone and emotional responsiveness during the course of interview.

N2   Emotional withdrawal
        Lack of interest in, involvement with, and affective commitment to life's events. Basis for rating: Reports of functioning from primary care workers or family and observation of interpersonal behaviour during the course of interview.

N3   Poor rapport
        Lack of interpersonal empathy, opennesss in conversation, and sense of closeness, interest, or involvement with the interviewer. This is evidenced by interpersonal distancing and reduced verbal and nonverbal communication. Basis for rating: Interpersonal behaviour during the course of interview.

N4   Passive / apathetic social withdrawal
        Diminished interest and initiative in social interactions due to passivity, apathy, anergy, or avolition. This leads to reduced interpersonal involvements and neglect of daily activities.

N5   Difficulty in abstract thinking
        Impairment in the use of the abstract-symbolic mode of thinking, as evidenced by difficulty in classification, forming generalizations, and proceeding beyond concrete or egocentric thinking in problem-solving tasks. Basis for rating: Responses to questions on similarities and proverb interpretation, and use of concrete vs abstract mode during course of interview.

N6   Lack of spontaneity and flow of conversation
        Reduction in the normal flow of communication associated with apathy, avolition, defensiveness, or cognitive deficit. This is manifested by diminished fluidity and productivity of the verbal-interactional process. Basis for rating: Cognitive-verbal processes observed during the course of interview.

N7   Stereotyped thinking
        Decreased fluidity, spontaneity, and flexibility of thinking, as evidenced in rigid, repetitious, or barren thought content. Basis for rating: Cognitive-verbal processes observed during the course of interview.

General Psychopathology Scale:

G1   Somatic concern
        Physical complaints or beliefs about bodily illness or malfunctions. This may range from a vague sense of ill being to clear-cut delusions or catastrophic physical disease. Basis for rating: Thought content expressed in the interview.

G2   Anxiety

Subjective experience of nervousness, worry, apprehension, or restlessness, ranging from excessive concern about the present or future to feelings of panic. Basis for rating: Verbal report during the course of interview and corresponding physical manifestations.

G3   Guilt feelings

Sense of remorse or self-blame for real or imagined misdeeds in the past. Basis for rating: Verbal report of guilt feelings during the course of interview and the influence on attitudes and thoughts.

G4   Tension

Overt physical manifestations of fear, anxiety, and agitation, such as stiffness, tremor, profuse sweating, and restlessness. Basis for rating: Verbal report attesting to anxiety and, thereupon, the severity of physical manifestations of tension observed during the interview.

G5   Mannerisms and posturing

Unnatural movements or posture as characterized by an awkward, stilted, disorganized, or bizarre appearance. Basis for rating: Observation of physical manifestations during the course of interview as well as reports from primary care workers or family.

G6   Depression

Feelings of sadness, discouragement, helplessness, and pessimism. Basis for rating: Verbal report of depressed mood during the course of interview and its observed influence on attitude and behaviour.

G7   Motor retardation

Reduction in motor activity as reflected in slowing or lessening of movements and speech, diminished responsiveness to stimuli, and reduced body tone. Basis for rating: Manifestations during the course of interview as well as reports by primary care workers or family.

G8   Uncooperativeness

Active refusal to comply with the will of significant others, including the interviewer, hospital staff, or family, which may be associated with distrust, defensiveness, stubbornness, negativism, rejection of authority, hostility, or belligerence. Basis for rating: Interpersonal behaviour observed during the course of interview as well as reports by primary care workers or family.

G9   Unusual thought content

Thinking characterized by strange, fantastic, or bizarre ideas, ranging from those which are remote or atypical to those which are distorted, illogical, and patently absurd. Basis for rating: Thought content expressed during the course of interview.

G10   Disorientation

Lack of awareness of one's relationship to the milieu, including persons, place, and time, which may be due to confusion or withdrawal. Basis for rating: Responses to interview questions on orientation.

G11   Poor attention

Failure in focused alertness manifested by poor concentration, distractibility from internal and external stimuli, and difficulty in harnessing, sustaining, or shifting focus to new stimuli. Basis for rating: Manifestations during the course of interview.

G12   Lack of judgment and insight

Impaired awareness or understanding of one's own psychiatric condition and life situation. This is evidenced by failure to recognize past or present psychiatric illness or symptoms, denial of need for psychiatric hospitalization or treatment, decisions characterized by poor anticipation of consequences, and unrealistic short-term and long-range planning. Basis for rating: Thought content expressed during interview.

G13   Disturbance of volition

Disturbance in the wilful initiation, sustenance, and control of one's thoughts, behaviour, movements, and speech. Basis for rating: thought content and behaviour manifested in the course of interview.

G14   Poor impulse control

Disordered regulation and control of action on inner urges, resulting in sudden, unmodulated, arbitrary, or misdirected discharge or tension and emotions without concern about consequences. Basis for rating: Behaviour during the course of interview and reported by primary care workers or family.

G15   Preoccupation

Absorption with internally generated thoughts and feelings and with autistic experiences to the detriment or reality orientation and adaptive behaviour. Basis for rating: Interpersonal behaviour observed during the course of interview.

G16   Active social avoidance

Diminished social involvement associated with unwarranted fear, hostility, or distrust. Basis for rating: Reports of social functioning by primary care workers or family.

Appendix 3B

Assessment of Duration of Untreated Psychosis (DUP)

I would like to ask you some questions about the events around the time of the onset of illness.

1. Before the first treatment, did ….. believe others were talking about him/her, or trying to harm him/her, and/or have odd thoughts?
   ☐ Yes ☐ No ☐ Unknown

   (If Yes) When did that begin?
   Month _____ Year _____

   How long did it last at the time?
   ☐ Days
   ☐ Over several weeks
   ☐ Over several months
   ☐ Continued to present time

2. Before the first treatment, did ….. believe he/she had special abilities or powers or was a special person?
   ☐ Yes ☐ No ☐ Unknown

   (If Yes) When did that begin?
   Month _____ Year _____

   How long did it last at the time?
   ☐ Days
   ☐ Over several weeks
   ☐ Over several months
   ☐ Continued to present time

3. Before the first treatment, did ….. seem to hear voices when there was nobody there?
   ☐ Yes ☐ No ☐ Unknown

   (If Yes) When did that begin?
   Month _____ Year _____

   How long did it last at the time?
   ☐ Days
   ☐ Over several weeks
   ☐ Over several months
   ☐ Continued to present time

4. Before the first treatment, did ….. believe thoughts were being put into or taken out of his/her head, that others could read or hear his/her thoughts, or he/she was under the control of some force or power?

☐ Yes   ☐ No   ☐ Unknown

(If Yes) When did that begin?
Month _____   Year _____

How long did it last at the time?
☐   Days
☐   Over several weeks
☐ Over several months
☐ Continued to present time

Based on items #1 – 4:

What was the date of onset of first positive symptoms? _____/_____/_____ (d/m/y)

What was the patient's age at onset of first positive symptoms? Age _____

Appendix 4A

Developmental Milestones Questionnaire.

Please indicate at approximately how many months your child:

1) Slept through the night? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

2) Smiled to an adult? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

3) Sat without help? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

4) Crawled? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

5) Walked? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

6) Said words? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

7) Fed self? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

8) Said sentences? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

9) Amused self when alone? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

10) Dressed self? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

11) Was toilet trained? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

12) Said numbers and letters? _____ (months). Relative to other children I knew, this was

1	2	3	4	5
much sooner	somewhat sooner	same time	somewhat later	much later

Appendix 4B

Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982).

Scholastic Performance Scale – administered separately for 6-11 year and 12-15 year age ranges:

I'd like to ask you some questions about school from the age of _____.

1. What was the name of your child's school?
   Was it a public school, religious school, or another type of school?
   Did your child go to a special needs school?
   (Special school = school for children with severe learning or emotional difficulties. If participant attended special school, highest possible rating for item = 4)
   If attended regular school: Did your child attend regular classes with most other kids or did your child go to a special class in a regular school?

2. Some kids find school very difficult. How hard were your child's subjects for him / her?
3. What subject did (s)he do the best in? What was the best grade (s)he ever got?
4. What subjects did (s)he have the hardest time in? What was the worst grade (s)he ever got?
5. Compared to other kids, how did (s)he do in school at this age?
6. Thinking about all his / her subjects, how did (s)he do overall: excellent, good, average, fair, or failing student?
7. Did (s)he repeat any years of schooling?
8. Would his / her exam marks have been good enough for him / her to get into any school?

Scoring criteria:
0 = excellent (straight A) student, likely to attend post-secondary institution
1 = A and B student, likely to pursue post-secondary studies
2 = Good student (B grades), could pursue post-secondary studies
3 = Average student (B and C grades)
4 = Fair student (C grades)
5 = Failing some classes (some D grades)
6 = Failing all classes (all D or F grades)

Appendix 4C

Categorical classification of low and normal reserve individuals

The chart below contains individual item ratings for each participant on all 12 milestones, with numerical scores corresponding to the categories above. Major milestones of crawling, walking, saying words, sentences, and numbers are letters are highlighted (m4, m5, m6, m8, and m12, respectively). Appendix 3B also contains rankings of premorbid academic adjustment on the Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982). PAS1 denotes Premorbid Academic functioning from ages 6-11 years, while PAS2 indicates Premorbid Academic functioning from ages 12-15 years. The chart also indicates cognitive reserve grouping where 1 = low cognitive reserve and 0 = normal cognitive reserve.

Case	m1	m2	m3	m4	m5	m6	m7	m8	m9	m10	m11	m12	PAS1	PAS2	Group
1	2	3	3	3	3	3	3	5	3	4	4	5	4	4	1
2	1	3	3	3	3	2	3	2	3	3	3	3	1	1	0
3	2	3	3	3	4	4	3	3	3	3	3	4	5	5	1
4	4	2	5	5	5	3	4	4	3	4	3	3	1	1	0
5	3	3	3	3	4	4	3	3	3	3	4	3	4	4	1
6	3	2	2	2	2	3	2	3	3	2	2	2	1	1	0
7	3	3	3	3	4	4	3	4	4	4	4	4	2	3	0
8	3	3	3	3	3	3	3	3	3	3	3	3	2	2	0
9	3	3	3	4	4	3	3	3	3	3	4	4	4	4	1
10	2	3	3	3	3	3	3	2	2	3	3	3	1	1	0
11	3	3	3	3	3	3	3	3	3	3	3	3	2	2	0
12	3	3	3	4	4	3	3	4	3	3	3	2	3	3	0
13	3	3	3	2	1	3	3	3	3	3	3	3	3	3	0
14	1	3	3	3	3	3	3	3	2	3	5	1	3	5	0
15	3	3	2	2	2	1	3	2	2	3	3	2	1	3	0
16	3	3	5	5	4	4	4	5	3	3	5	5	5	5	1
17	1	3	5	4	3	3	4	3	3	3	3	3	3	1	0
18	4	3	2	3	3	5	2	5	3	2	3	5	3	3	0
19	3	3	3	3	3	3	3	3	3	3	3	3	2	2	0
20	4	3	2	1	1	2	2	2	3	3	3	3	3	5	0
21	1	4	4	5	5	4	2	4	3	2	4	3	3	3	0
22	4	3	3	3	3	4	3	4	3	3	3	3	1	1	0
23	1	3	3	3	3	3	3	3	3	3	3	3	1	1	0
24	3	3	3	3	3	3	3	3	3	3	3	3	1	1	0
25	2	3	3	3	4	4	4	4	3	4	4	4	3	5	0
26	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
27	3	2	2	2	2	3	3	3	3	3	2	3	1	2	0
28	3	3	4	5	5	3	3	3	3	3	1	4	3	2	0
29	4	3	3	3	3	3	3	3	3	3	2	3	2	3	0
30	1	3	3	3	4	3	3	3	2	3	3	2	3	3	0
31	4	3	3	3	3	4	3	3	3	3	3	3	1	3	0
32	2	4	3	4	3	3	4	3	3	3	3	3	1	3	0
33	3	3	3	3	3	3	3	2	3	2	2	2	1	1	0
34	2	3	3	3	3	3	3	3	3	3	3	3	4	4	0
35	2	3	4	2	1	1	3	1	3	3	2	5	1	1	0
36	3	3	3	3	3	3	3	3	3	3	3	3	4	4	0
37	2	3	3	4	4	2	3	2	2	4	2	2	3	3	0
38	3	3	4	3	3	5	3	5	3	4	4	5	4	4	1
39	4	3	3	3	3	3	3	3	3	3	4	4	4	4	1
40	3	3	3	3	3	3	3	3	3	3	3	3	4	4	0
41	3	2	3	2	2	1	2	1	3	3	3	3	3	3	0
42	3	3	3	3	3	3	3	2	3	3	3	3	1	1	0
43	3	3	3	3	3	3	3	3	3	3	3	3	4	4	0
44	4	3	3	3	3	3	3	3	3	4	3	4	4	5	1
45	3	3	3	3	4	3	3	4	3	4	3	4	4	5	1
46	3	4	3	4	4	4	3	5	3	3	4	5	4	4	1
47	3	3	3	2	2	3	3	3	3	3	3	3	1	1	0
48	3	3	4	4	4	5	4	4	3	3	3	5	1	1	0
49	3	3	3	3	4	3	3	3	2	3	3	2	1	1	0
50	3	4	3	4	4	3	3	3	3	3	3	3	4	5	1

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Appendix 5:

Structured interview for assessment of substance abuse at presentation.

Source of information: ☐ Patient ☐ Mother ☐ Father ☐ Other _____.

Have you ever used…	Past Month	Past Year	Lifetime
Alcohol? (If answer is **"Yes"** complete section A)	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Marijuana? (If answer is **"Yes"** complete section B)	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Other street drugs? (If answer is **"Yes"** complete section C)	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
Cigarettes? (If answer is **"Yes"** complete section D)	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No

A. Alcohol Use

1. How old were you when you first started using alcohol?	_____ age
How long did that period last?	_____ days _____ months _____ currently still drinking
2. During that time … • € Did you have 5 or more drinks (beer, wine, or alcohol) on one occasion? • € Were you intoxicated or hung over while you were doing something important, like being at school or work, or taking care of children? • € Did you ever miss something important like staying away from school or work, miss an important appointment because you were intoxicated or very hung over?	☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No
3. Did you ever drink in a situation in which it might have been dangerous to drink at all (driving, operating machinery)?	☐ Yes ☐ No
4. Did your drinking get you into trouble with the law? If **"Yes"** what kind of trouble?	☐ Yes ☐ No
5. Has your drinking caused problems with other people such as friends, co-workers, or family members? If **"Yes"** did you keep on drinking anyway? ☐ Yes ☐ No	☐ Yes ☐ No

6. What are your current drinking habits like?	☐ Never ☐ Almost never ☐ Occasionally ☐ Several times/week ☐ Daily

B. Marijuana Use

1. How old were you when you first started smoking marijuana?	_____ age
2. How long did that period last?	_____ days _____ months _____ currently still smoking
3. During that time … • ∈ Did you ever get high while you were doing something important, like being at school or work, or taking care of children? • ∈ Did you ever miss something important like staying away from school or work, miss an important appointment because you were high?	☐ Yes ☐ No ☐ Yes ☐ No
4. Were you ever high during a situation in which it might have been dangerous to smoke at all (driving, operating machinery)?	☐ Yes ☐ No
5. Has smoking marijuana ever gotten you into trouble with the law? If **"Yes"** what kind of trouble?	☐ Yes ☐ No
6. Has smoking marijuana ever caused problems with other people such as friends, co-workers, or family members? If **"Yes"** did you keep on smoking anyway? 　　☐ Yes ☐ No	☐ Yes ☐ No
7. What is your current marijuana smoking habits like?	☐ Never ☐ Almost never ☐ Occasionally ☐ Several times/week ☐ Daily

C. Street Drug Use

1. How old were you when you first started using street drugs?	_____ age

2. How long did that period last?	_____ days _____ months _____ currently still taking

3. During that period, what drugs were you using?

4. During that time…

- Did you ever consume street drugs while you were doing something important, like being at school or work, or taking care of children?

-

Did you ever miss something important like staying away from school or work, missing an appointment because you had consumed street drugs?

☐☐ Yes ☐ No

☐ Yes ☐ No

5. For each of the following, describe your overall history of use?	

	Never	Have tried	Occasionally	Several times/wk	Daily
Stimulants: Amphetamine, "speed", crystal meth, dexadrine, Ritalin, "ice", or other _____.	1	2	3	4	5
Opioids: Heroin, morphine, opium, methadone, darvon, codeine, percodan, demerol, dilaudid, unspecified or other _____.	1	2	3	4	5
Cocaine: Snorting, IV, freebase, crack, "speedball", unspecified or other _____.	1	2	3	4	5
Hallucinogens / PCP: LSD, mescaline, peyote, psilocybin, STP, mushrooms, PCP (angel dust), ecstasy, MDMA, or other _____.	1	2	3	4	5

	Never	Have tried	Occasionally	Several times/wk	Daily
Other: Steroids, "glue", paint, inhalants, nitrous oxide "laughing gas", amyl or butyl nitrate "poppers", nonprescription sleep or diet pills, unknown or other _____.	1	2	3	4	5

6. Did you ever consume street drugs during a situation in which it might have been dangerous to consume drugs at all (driving, operating machinery)?	☐ Yes ☐ No
7. Has consuming street drugs gotten you into trouble with the law? If **"Yes"** what kind of trouble?	☐ Yes ☐ No
8. Has consuming street drugs caused problems with other people such as friends, co-workers, or family members? If **"Yes"** did you keep consuming street drugs anyway? ☐ Yes ☐ No	☐ Yes ☐ No

D. Cigarette Use

1	How old were you when you first started smoking cigarettes?	_____ Age
2	How soon after you wake up do you smoke your first cigarette?	❑ Within 5 minutes ❑ 6-30 minutes ❑ 31-60 minutes ❑ after 60 minutes
3	Do you find it difficult to refrain from smoking in places where it is forbidden e.g. in church, at the library, at the cinema, etc?	❑ Yes ❑ No
4	Which cigarette would you hate most to give up?	❑ The first one in the morning ❑ All others
5	How many cigarettes do you smoke in a day?	❑ 10 or less ❑ 11-20 ❑ 21-30 ❑ 31 or more
6	Do you smoke more frequently during the first hours after waking than during the rest of the day?	❑ Yes ❑ No
7	Do you smoke if you are so ill that you are in bed most of the day?	❑ Yes ❑ No

Appendix 6A

Dimensions of Temperament Survey – Revised (DOTS-R).

HOW TO ANSWER: On the following pages are some statements about how people like your child may behave. We are interested in what your child's typical behavior was like up to 3 or 4 years before he or she received a psychiatric diagnosis. Some of these statements may be true of your child's behavior and others may not apply. For each statement we would like you to indicate if the statement was usually true of your child, was more true than false of your child, was more false than true of your child, or was usually false of your child. There are no "right" or "wrong" answers because all people behave in different ways. All you have to do is answer what was true for <u>your child</u>.

Here is an example of how to fill out this questionnaire. Suppose a statement said:

"My child eats about the same things for breakfast every day."

If the statement were usually false for your child, you would respond:

"A," usually FALSE.

If the statement were more false than true for your child, you would respond:

"B," more FALSE than true.

If the statement were more true than false for your child, you would respond:

"C," more TRUE than false.

If the statement were usually true for your child, you would respond:

"D," usually TRUE.

On the line to the left of each statement write an <u>A</u> if the statement is <u>usually false</u> for your child, write a <u>B</u> if the statement is <u>more false than true</u> for your child, write a <u>C</u> if the statement is <u>more true than false</u> for your child, or write a <u>D</u> if the statement is <u>usually true</u> for your child.

PLEASE KEEP THESE FOUR THINGS IN MIND AS YOU ANSWER:

1.   Give only answers that are true or false for your child. It is best to say what you really think.

2.   Don't spend too much time thinking over each question. <u>Give the first, natural answer as it comes to you</u>. Of course, the statements are too short to give <u>all</u> the information you might like, but give the best answer you can under the circumstances. Some statements may seem similar to each other because they ask about the same situation. However, each one looks at a different area of your child's behavior. Therefore, your answers may be different in each case.

3.   Answer <u>every</u> question one way or another. Don't skip any.

4.   Remember,   A = usually FALSE
                            B = more FALSE than true
                            C = more TRUE than false
                            D = usually TRUE

<u>THANK YOU FOR YOUR COOPERATION</u>

A = usually FALSE   C = more TRUE than false

B = more FALSE than true   D = usually TRUE

1. ___   It took my child a long time to get used to a new thing in the home.

2. ___   My child couldn't stay still for long.

3. ___   My child laughed and smiled at a lot of things.

4. ___   My child woke up at different times.

5. ___   Once my child was involved in a task, nothing could distract him / her from it.

6. ___   My child persisted at a task until it was finished.

7. ___   My child moved around a lot.

8. ___   My child could make him or herself at home anywhere.

9. ___   My child could always be distracted by something else, no matter what my child was doing.

10. ___   My child stayed with an activity for a long time.

11. ___   If my child had to stay in one place for a long time, my child got very restless.

12. ___   My child usually moved towards new objects shown to him or her.

13. ___   It took my child a long time to adjust to new schedules.

14. ___   My child did not laugh or smile at many things.

15. ___   If my child was doing one thing, something else occurring wouldn't get him or her to stop.

16. ___   My child ate about the same amount for dinner whether he or she was home, visiting someone, or traveling.

17. ___   My child's first reaction was to reject something new or unfamiliar to him or her.

18. ___   Changes in plans made my child restless.

A = usually FALSE   C = more TRUE than false

B = more FALSE than true   D = usually TRUE

19. ___   My child often stayed still for long periods of time.

20. ___   Things going on around my child could <u>not</u> take him or her away from what he or she was doing.

21. ___   My child took a nap, rest, or break at the same time every day.

22. ___   Once my child took something up, he or she stayed with it.

23. ___   Even when my child was supposed to be still, he or she got very fidgety after a few minutes.

24. ___   My child was hard to distract.

25. ___   My child usually got the same amount of sleep each night.

26. ___   On meeting a new person my child tended to move towards him or her.

27. ___   My child got hungry about the same time each day.

28. ___   My child smiled often.

29. ___   My child never seemed to stop moving.

30. ___   It took my child no time at all to get used to new people.

31. ___   My child usually ate the same amount each day.

32. ___   My child moved a great deal in his or her sleep.

33. ___   My child seemed to get sleepy just about the same time every night.

34. ___   My child did not laugh often.

35. ___   My child moved towards new situations.

36. ___   When my child was away from home, my child still woke up at the same time each morning.

A = usually FALSE   C = more TRUE than false

B = more FALSE than true   D = usually TRUE

37. ___   My child ate about the same amount at breakfast from day to day.

38. ___   My child moved a lot in bed.

39. ___   My child felt full of pep and energy at the same time each day.

40. ___   My child had bowel movements at about the same time each day.

41. ___   No matter when my child went to sleep, my child woke up at the same time the next morning.

42. ___   In the morning, my child was still in the same place as he or she was when he or she fell asleep.

43. ___   My child ate about the same amount at supper from day to day.

44. ___   When things were out of place, it took my child a long time to get used to it.

45. ___   My child woke up at the same time on weekends and holidays as on other days of the week.

46. ___   My child didn't move around much at all in his or her sleep.

47. ___   My child's appetite seemed to stay the same day after day.

48. ___   My child's mood was generally cheerful.

49. ___   My child resisted changes in routine.

50. ___   My child laughed several times a day.

51. ___   My child's first response to anything new was to move his or her head toward it.

52. ___   Generally, my child was happy.

53. ___   The number of times my child had a bowel movement on any day varied from day to day.

54. ___   My child never seemed to be in the same place for long.

Appendix 6B

Description of the temperamental factors from the Revised Dimensions of Temperament Survey (DOTS-R, Windle & Lerner, 1986).

	Description	
Temperamental attribute	*High Score*	*Low Score*
Activity Level – General	High characteristic level of energy, vigor, and overt motor activity.	Low characteristic level of energy, vigor, and overt motor activity.
Activity Level – Sleep	High characteristic motor activity (e.g. tossing and turning) during sleep.	Low characteristic motor activity during sleep.
Approach – Withdrawal	Tendency to approach / move towards new persons, objects, situations, events.	Tendency to withdraw / move away from new persons, objects, situations, events.
Flexibility / Rigidity	Tendency to respond flexibly to changes in the environment.	Tendency to respond inflexibly or rigidly to changes in the environment.
Mood	High characteristic manifestation of positive affect (e.g. smiling, cheerful).	Low characteristic manifestation of positive affect (e.g. infrequent smiling, not cheerful).
Rhythmicity – Sleep	Tendency for timing of daily sleep-wake cycle to be highly regular (varying little from day to day).	Tendency for timing of daily sleep-wake cycle to be highly irregular (varying considerably from day to day)
Rhythmicity – Eating	High characteristic regularity of eating habits pertinent to appetite and quantity consumed.	High characteristic irregularity of eating habits pertinent to appetite and quantity consumed.
Rhythmicity – Daily habits	Tendency to be highly regular in the timing of diurnal activities such as toileting, peak period of energy, taking a rest/break.	Tendency to be highly irregular in the timing of diurnal activities such as toileting, peak period of energy, taking a rest/break.
Distractibiliy	Tendency to be able to concentrate and maintain perceptual focus despite extraneous stimuli.	Tendency to lose concentration easily when potentially distracting stimuli are present.
Persistence	Tendency to stay with, or continue steadily in, an activity for a relatively long period of time.	Tendency to have difficulty staying with, or continuing steadily in, an activity for a relatively long period of time.

From Windle (1989a).

Appendix 6C

Congruence between samples of preschool (N = 114), sixth grade (N = 224), and college students (N = 300) for DOTS-R (Windle & Lerner, 1986) item loadings on factors (as identified through maximum likelihood analysis).

	Congruence coefficients between groups		
Temperamental attribute	Preschool / Elementary	Preschool / Adult	Elementary / Adult
Activity Level – General	.89	.93	.94
Activity Level – Sleep	.95	.97	.94
Adaptability/Positive affect			
Approach – Withdrawal	.78	.80	.81
Flexibility / Rigidity	.70	.75	.84
Mood	.95	.80	.92
General Rhythmicity			
Rhythmicity – Sleep	.68	.84	.65
Rhythmicity – Eating	.92	.87	.91
Rhythmicity – Daily habits	.61	.60	.57
*Attentional focus**			
Distractibility / Persistence	.81	NC	NC

*often loads with activity level.

Appendix 7

Attachment Networks Questionnaire

The statements below concern the relationships you think were MOST important to you from the time up until 3 or 4 years before you received a psychiatric diagnosis (these relationships can include boyfriends / girlfriends, parents, friends, siblings, or other people you feel close to). We would like you to list all the significant people in your life from that time, those people that felt a strong emotional tie to (positive, negative, or mixed emotional tie) in the spaces below (labeled A to J):

A. _____

B. _____

C. _____

D. _____

E. _____

F. _____

G. _____

H. _____

I. _____

J. _____

Now, please fill in the letter (A-J) corresponding to the person from your list to whom you would go in the following situations. We would like you to include ALL the people you feel are relevant for each question. For example, for the next item you might go to a best friend (Person "C" from the list) first, your mother (Person "A" from the list) second, your brother (Person "F" from the list) third, and so on.

Whom do you *want* to go to, to help you feel better when something bad happens to you or you feel upset, *whether or not you actually go to them*?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom do you *actually* to go to, to help you feel better when something bad happens to you or you feel upset?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom would you *like* to be able to count on to always be there for you and care about you no matter what?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom do you feel you can *actually* count on to always be there for you and care about you no matter what?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom is it important for you to see and talk to regularly?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whose death would have the greatest impact or effect on you, regardless of what the effect may be?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom can make you feel upset? (Remember that these are people with whom you have a personal relationship).										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Please rank order ALL OF THE PEOPLE ON YOUR LIST in terms of whom you feel most emotionally connected to, regardless of whether that connection is positive, negative, or mixed.										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

The statements below concern the relationships you think are MOST important to you for the time since you received a psychiatric diagnosis (these relationships can include boyfriends / girlfriends, parents, friends, siblings, or other people you feel close to). We would like you to list all the significant people in your life from that time, those people that you feel a strong emotional tie to (positive, negative, or mixed emotional tie) in the spaces below (labeled A to J):

A. _____

B. _____

C. _____

D. _____

E. _____

F. _____

G. _____

H. _____

I. _____

J. _____

Now, please fill in the letter (A-J) corresponding to the person from your list to whom you would go in the following situations. We would like you to include ALL the people you feel are relevant for each question. For example, for the next item you might go to a best friend (Person "C" from the list) first, your mother (Person "A" from the list) second, your brother (Person "F" from the list) third, and so on.

Whom do you *want* to go to, to help you feel better when something bad happens to you or you feel upset, *whether or not you actually go to them*?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom do you *actually* to go to, to help you feel better when something bad happens to you or you feel upset?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom would you *like* to be able to count on to always be there for you and care about you no matter what?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom do you feel you can *actually* count on to always be there for you and care about you no matter what?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom is it important for you to see and talk to regularly?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whose death would have the greatest impact or effect on you, regardless of what the effect may be?										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Whom can make you feel upset? (Remember that these are people with whom you have a personal relationship).										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Please rank order ALL OF THE PEOPLE ON YOUR LIST in terms of whom you feel most emotionally connected to, regardless of whether that connection is positive, negative, or mixed.										
First	Second	Third	Fourth	Fifth	Sixth	Seventh	Eighth	Ninth	Tenth	Eleventh

Appendix 8

Low cognitive reserve and diagnostically matched normal cognitive reserve control group.

| Cases	Age	Diagnosis	PANSS Total	DUP (weeks)
Low 1	24.65	SCHZ	73.00	14
Match 1	24.24	SCHZAFF	76.00	29
Low 2	27.16	SCHZ	62.00	190
Match 2	25.64	SCHZ	51.00	NA
Low 3	23.60	SCHZ	67.00	133
Match 3	23.79	SCHZ	68.00	114
Low 4	27.37	SCHZAFF	125.00	10
Match 4	28.09	SCHZAFF	119.00	NA
Low 5	17.70	SCHZAFF	82.00	56
Match 5	17.79	SCHZ	62.00	55
Low 6	24.17	SCHZ	116.00	3
Match 6	27.14	SCHZ	97.00	3
Low 7	15.51	SCHZ	116.00	9
Match 7	18.51	SCHZ	64.00	43
Low 8	33.10	SCHZAFF	66.00	18
Match 8	36.55	SCHZ	69.00	4
Low 9	19.27	SCHZ	95.00	115
Match 9	19.40	SCHZAFF	78.00	201
Low 10	22.11	PNOS	47.00	32
Match 10	25.70	PNOS	66.00	4
Low Mean (SD)	23.46 (5.16)		84.90 (26.74)	58.00 (65.19)
Match Mean (SD)	24.69 (5.53)		75.00 (19.61)	56.63 (69.18)

Notes: PANSS = Positive and Negative Syndrome Scale; DUP = Duration of untreated psychosis; SCHZ = Schizophrenia, SCHZAFF = Schizoaffective Disorder; PNOS = Psychosis Not Otherwise Specified.

As would be expected, individuals with low cognitive reserve did not differ from diagnostically matched normal cognitive reserve controls in age (F (1, 18) = 0.26, p > .05), overall symptom severity (F (1, 18) = 0.89, p > .05), or DUP (F (1, 18) = 0.002, p > .05). The small size of the low cognitive reserve and matched normal cognitive reserve groups precluded replication of linear mixed model analyses. Table 11 indicates that global cognition of the diagnostically matched normal control group was comparable to that of unmatched controls at presentation (t (1, 36) = -0.60, p > .05) and follow-up (t (1, 28) = 0.52, p > .05). Follow-up global cognition of individuals with low cognitive reserve was marginally worse than that of matched normal reserve controls (t (1, 9.97) = -2.12, p = .06), suggesting a similar pattern of lower global cognition (relative to standardization data) in the low cognitive reserve group as compared to those with normal cognitive reserve (see Figure 4).

Table 14   Global cognition relative to standardization samples in low cognitive reserve, matched, and unmatched normal cognitive reserve groups.

Time	Low cognitive reserve Mean (SD)	Matched cognitive reserve Mean (SD)	Unmatched cognitive reserve Mean (SD)
Presentation	- 0.85 (0.60)	- 0.52 (0.90)	- 0.37 (0.59)
Follow-up	- 1.01 (0.38)	- 0.20 (1.07)	- 0.37 (0.74)

Figure 4.1   Global cognition in low cognitive reserve, normal cognitive reserve, and diagnostically matched normal cognitive reserve groups.
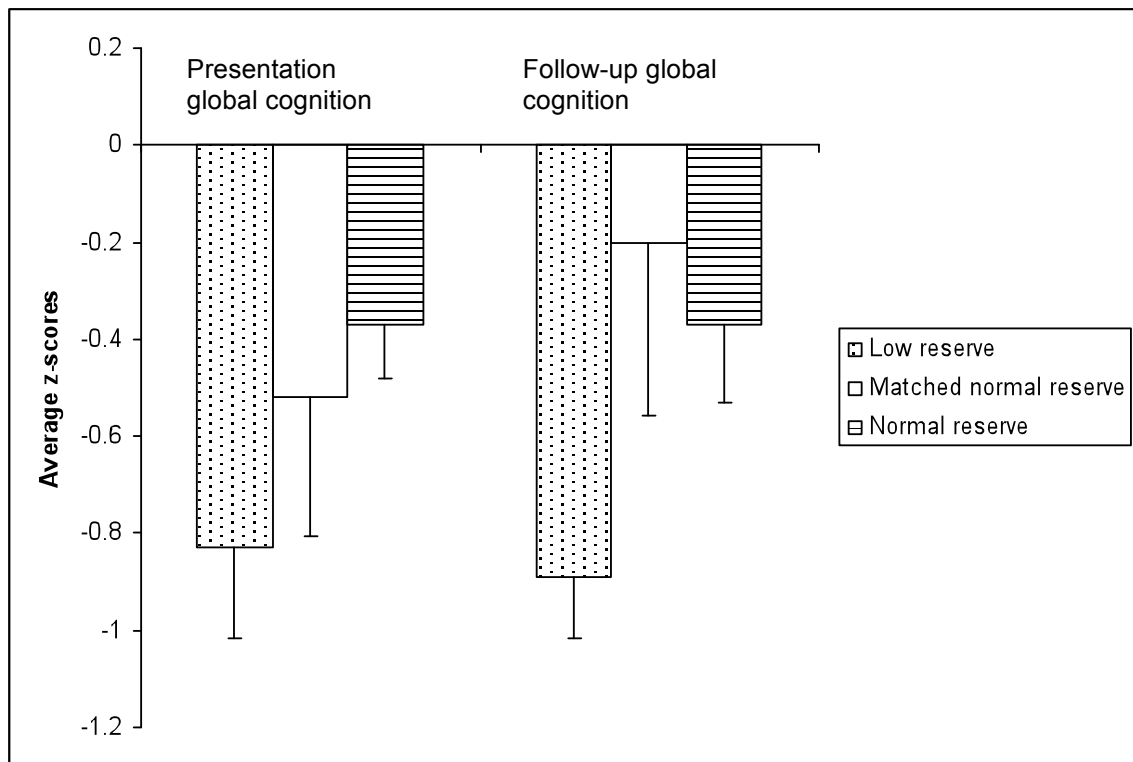
Appendix 9

Specific details of attachment networks in the sample.

According to their self-reported family structures, 22 % (N = 9) of the 41 participants completing the ANQ came from families where parents had either separated or divorced. Three of these participants reported having a stepfather and one had a stepmother as well. Another participant described his family of origin as being intact, but noted that he had been placed with a foster family well before the onset of psychosis. Although a majority of participants reported a two-parent family of origin, ten described having either a single parent or more than two parental attachment figures. As a further complication, five participants reported being emotionally estranged from their parents. In addition, two participants were old enough to have their own children, who they reported as important attachment figures.

With respect to siblings, only 3 participants (7 %) reported that they were only children. Thirty-seven percent (N=15) of the sample had one other sibling, 34 % (N = 14) had two siblings, and 22 % (N = 9) had three or more siblings. Of those participants with siblings, 44 % (N = 18) were first born, 22 % (N = 9) were second born, 12 % (N = 5) were third born, and 7 % (N = 3) were fourth born. So, while most participants came from families with one or two siblings, a substantial proportion (30 %) of the sample was either an only child or had more than two siblings. Together with information regarding parental relationships, this indicates considerable variability in family structures amongst participants, which would translate to differences in the availability of familial attachment figures.

Peer relationships, both in the form of romantic attachments and friendships, are also an important dimension of attachment networks. Fifteen participants reported having at least one romantic relationship, and of those, eleven reported being in such a relationship that also satisfied an attachment role prior to the onset of psychosis. Six of the eleven participants who were in a romantic relationship prior to the onset of psychosis were no longer with that partner in the post-onset period. In addition to the five participants who maintained their relationship through the onset of psychosis, seven more participants entered romantic relationships during the post-onset period. In total, 29 % (N = 12) of the sample reported being in a romantic relationship after the onset of psychosis. Just under 25 % (N = 10) of the sample reported having a best friend in the adolescent years before the emergence of psychosis symptoms. With respect to platonic peer relationships, seven of the ten participants who described having a best friend prior to illness onset were able to maintain that friendship through the early course of psychosis. In the post-onset period, 27 % (N = 11) of the sample described losing some important friendships and establishing others over the early course of their illness.

Including best friends (if identified), participants reported an average of 2.9 (SD = 1.9) friendships fulfilling attachment roles in the premorbid period, and a slightly smaller group of peer attachments post-onset (mean = 2.5, SD = 1.5). When both family and peer attachment hierarchies are considered, the average size of participants' premorbid attachment network (mean = 7.4 people, SD = 2.3) was comparable to the average size of the post-onset attachment networks (mean = 7.1 people, SD = 2.4). Of greater significance are participant rankings of the relative importance of attachment figures. Participants ranked the importance of each attachment figure to each ANQ attachment role, with "1" denoting highest importance. Thus, lower rankings indicate greater reliance on an attachment figure to meet a specific attachment need (see Appendix 10 for average rankings of attachment figures in premorbid and post-onset periods). To allow for

comparisons across the sample, only those attachment figures ranked as "1" for each attachment role were used to assess the strength and number of family and peer relationships.

Further to the analyses in the Results section, I explored the possibility that developmental stage could affect the premorbid strength of family attachments. Relative to young adults in their 20s, adolescents might be more apt to rely heavily on family attachments in the premorbid period if they have not shifted their attachments towards peers. Differences in the strength of family attachments related to developmental stage could obscure any changes in emotional dependence on family members associated with psychosis. Premorbid strength of family attachments was comparable (F (1, 39) = 0.003, p > .05) for participants who were younger than 20 years of age (M = 0.58, $\underline{SD}$ = 0.35, N = 10) and those who were 20 or older (M = 0.57, $\underline{SD}$ = 0.34, N = 31). This suggests that younger participants did not rely more heavily on family than peers in the premorbid period.

Appendix 10

Hierarchical rankings of attachment figures.

Hierarchical rankings of premorbid attachment figures on the Attachment Networks Questionnaire (ANQ; Trinke & Bartholomew, 1997).

Attachment role	Attachment figures most often satisfying attachment role Mean (SD)				
	Mother	Father	Other family	Friend	Romantic partner *
Safe haven desired use	2.36 (2.14)	3.72 (1.93)	3.28 (1.79)	2.51 (1.42)	2.83 (2.72)
Safe haven actual use	2.31 (1.60)	3.95 (2.04)	2.96 (1.88)	2.56 (1.44)	2.09 (2.07)
Secure base desired use	2.40 (2.00)	2.75 (1.69)	3.41 (1.45)	2.53 (1.68)	2.86 (2.14)
Secure base actual use	1.63 (0.94)	3.00 (1.41)	2.97 (1.63)	2.45 (1.39)	4.11 (2.67)
Proximity seeking	2.94 (1.90)	3.30 (1.84)	3.63 (1.79)	1.87 (1.36)	2.67 (2.40)
Impact of death	1.43 (0.78)	2.50 (1.24)	2.81 (1.17)	3.38 (1.60)	3.22 (2.64)
Conflictual emotion	2.87 (2.35)	2.09 (1.24)	3.68 (2.12)	2.76 (1.73)	2.10 (1.91)
Emotional connection	2.47 (2.05)	3.76 (2.36)	3.53 (2.00)	2.72 (1.57)	3.25 (2.63)

* Eleven participants rated their current romantic partners, one rated a former romantic partner

Hierarchical rankings of post-onset attachment figures on the Attachment Networks Questionnaire (ANQ; Trinke & Bartholomew, 1997).

Attachment role	Attachment figures most often satisfying attachment role				
	Mother	Father	Other family	Friend	Romantic partner *
Safe haven desired use	2.72 (1.96)	4.22 (2.03)	4.34 (2.31)	2.03 (1.14)	1.67 (1.11)
Safe haven actual use	2.34 (1.55)	4.12 (2.09)	3.83 (2.19)	2.47 (1.71)	2.46 (2.60)
Secure base desired use	1.95 (1.21)	2.68 (1.63)	3.68 (2.04)	3.41 (1.74)	1.93 (1.39)
Secure base actual use	1.85 (1.33)	3.11 (2.03)	3.34 (1.45)	3.12 (1.93)	2.92 (2.58)
Proximity seeking	1.86 (1.15)	3.22 (1.85)	3.48 (1.65)	3.03 (1.93)	2.39 (2.50)
Impact of death	1.76 (1.52)	2.89 (1.97)	2.97 (1.49)	3.59 (1.60)	2.29 (1.59)
Conflictual emotion	2.42 (1.87)	2.44 (1.55)	2.97 (1.78)	3.07 (1.49)	2.15 (1.57)
Emotional connection	1.73 (1.06)	3.48 (1.92)	3.20 (1.59)	3.28 (1.56)	1.93 (1.39)

* Twelve participants rated their current romantic partners, three rated a former romantic partner