

THE PRODROMAL COURSE

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Schizophrenia and other psychotic disorders are often preceded by prodromal changes, lasting for periods ranging from several days to several years, which foreshadow the onset of illness. The prodromal phase is potentially important in defining markers of risk for progression to psychotic illness and investigating novel biological and psychological treatments to prevent a transition to psychosis (Heinssen et al., 2001).

This chapter characterizes the prodromal phase of schizophrenia and other psychotic disorders, reviews and compares prodrome rating scales, and explores age-specific characteristics of the prodrome and the transition to psychosis. Empirical aspects are drawn from studies conducted in the Personal Assistance and Crisis Evaluation (PACE) Clinic in Melbourne, Australia. PACE is a service for the treatment and research of adolescents and young adults aged 15-29 years who experience perceptual or cognitive changes, unusual thoughts or behaviors, or significant deterioration in role functioning (McGorry et al., 2002).

Characteristics of the Prodrome

'Prodrome' refers to the early symptoms of an illness which precede the manifestation of the fully developed disorder, or a period of disturbance which represents a deviation from a person's previous experience and behavior (Yung & McGorry, 1996a). Prodromal symptoms such as

perceptual distortions, short transient hallucinations or mild paranoia are common in schizophrenia and can be thought as the earliest form of emergent psychosis. However, these symptoms are far more prevalent in the general population than clinical cases of psychotic disorders (McGorry et al., 1995; van Os et al., 2001) and not all individuals who experience psychotic symptoms develop a psychotic illness. Accordingly, disturbances in individuals who have not yet experienced a psychotic episode can be viewed as indicators of a risk of becoming psychotic, rather than signs inevitably associated with progression to a psychotic disorder. The term 'at-risk-mental-state' has been used to describe such symptoms. 'At-risk mental state' can be applied prospectively, in contrast to a 'prodrome' which can only be defined retrospectively once a disorder has been diagnosed (McGorry & Singh, 1995).

Most research on the prodrome in psychosis has been conducted in individuals with schizophrenia. Research techniques include retrospective reconstruction of symptoms and events through interviews with patients while they are acutely psychotic or after their symptoms have remitted. Other techniques include interviews with other informants such as parents, siblings and teachers, and, to much lesser extent, prospective observation of individuals during the development of psychosis.

Retrospective reconstruction has been used by clinicians to characterize the prodrome of schizophrenia since the illness concept was first defined (e.g., Bleuler, 1911). In this tradition Yung and McGorry (1996b) studied 21 first-

episode patients (14 male, 7 female; mean age 23.1 years, SD 4.9 years) who were referred to the Early Psychosis Prevention Intervention Centre (EPPIC) in Melbourne, a specialized service for 15-29 year olds with recent onset psychosis. A prodromal phase was detected in all cases, ranging in duration from 3 days to 6 years. The most frequently-reported symptoms were sleep disturbance, anxiety, and irritability, occurring in 100%, 86%, and 86% of individuals, respectively. Other common symptoms were deterioration in role functioning (76%), depressed mood (76%), social withdrawal (71%), poor concentration (71%), suspiciousness (71%), loss of motivation (68%), perceptual disturbances (62%), motor changes (62%) and weight loss (57%). A sense of confusion, perplexity and bewilderment was described in 50% of individuals as a late phenomenon, occurring just prior to frank psychosis. Obsessive-compulsive symptoms occurred in 19%. Suicidal thoughts and self harm were reported by 24% and 15% respectively. Half the patients identified specific events as 'triggers' which precipitated prodromal changes.

The broad range of symptoms observed in the sample was consistent with previous descriptions (e.g., Klosterkötter, 1988; Ebel et al., 1989). The range also highlights the restrictive nature of the DSM-III-R conceptualization of the schizophrenia prodrome which focused on behavioral features (American Psychiatric Association, 1987). The most detailed list of symptoms and signs which have been found to herald psychosis has been provided by Yung et al. (1996a; Table 2).

Prodrome Criteria/ Assessment Scales

Psychosis usually develops gradually and it may be difficult to define the point when a person can be defined as psychotic. The boundary between 'different but not psychotic' ('pre-psychotic') and 'frankly psychotic' is often blurred (Yung & McGorry, 1996a). However, a detailed characterization of typical signs and symptoms is necessary to assist classification and to guide early intervention. Research on the prodrome has a long tradition in Germany but most of this research has been retrospective (Huber et al., 1980; Klosterkötter, 1988; Häfner et al., 1999). Prospective assessment of developing psychosis is important because patients, their families and other informants tend to distort retrospective accounts.

BSABS

The Bonn Scale for the Assessment of Basic Symptoms (BSABS) was the first instrument in which operational definitions of pre-psychotic experiences were listed, along with typical statements of patients and examples of questions to allow assessment in a semi-structured interview (Gross et al., 1987). The BSABS measures disturbances of thought, language, perception, bodily perception, stress tolerance, affect, energy, concentration, memory, emotional reactivity, social contacts and non-verbal expressions.

Klosterkötter and colleagues (2001) prospectively investigated 160 individuals of which 110 met the description of prodromal state according to BSABS criteria. At follow-up after a mean of 9.6 years, 49% (79 of 160) had developed DSM-IV schizophrenia (American Psychiatric Association, 1994). Of those, 98% (77 of 79) met BSABS prodromal criteria at the first

assessment. Only 2 of 50 individuals who were not considered prodromal at baseline developed schizophrenia. The absence of prodromal symptoms excluded subsequent schizophrenia with a probability of 96% (sensitivity: 0.98; false-negative predictions: 1.3%). Presence of prodromal symptoms predicted schizophrenia with a probability of 70% (specificity: 0.59; false-positive predictions: 20%). Among the 66 BSABS symptoms, those most predictive of schizophrenia were thought interference, disturbances of receptive language and visual distortions. Transition to psychosis was observed after a mean of 6.7 years in males and 4.3 years in females following onset of the prodrome.

CAARMS

Based on studies conducted in the PACE Clinic in Melbourne, Australia, Yung and colleagues examined prodromal criteria to identify individuals at risk of developing psychosis in the near future using the Comprehensive Assessment of At-Risk Mental States (CAARMS; Yung et al., 1998). CAARMS defines three prodromal subgroups characterized by a recent functional decline plus genetic risk, the recent onset of subthreshold psychotic symptoms or the onset of brief transient psychotic symptoms (Table 1). Between 30% and 40% of individuals who fulfilled the 'at-risk' criteria developed psychosis within 6-12 months (Yung et al., 1998; Phillips et al., 2000).

Insert Table 1 about here

About 31% of individuals registered at PACE between 1996 and 1999 fulfilled the criteria for more than one prodromal subgroup (McGorry et al., 2002). Diagnoses of the 'Attenuated Group' and the 'BLIP Group' are based on the experience of positive symptoms as rated on a checklist including disorders of thought content, perceptual abnormalities and disorganized speech. Each item is rated by severity, frequency and duration. Additional ratings record the relation of symptoms to stressful experience and/or substance use. In contrast to the BSABS, the CAARMS assesses symptom severity, frequency and duration of prodromal experiences. This is an important advance from approaches which focused solely on the quality of symptoms. The complete CAARMS is more detailed than the intake criteria (see Table 1) and rates seven groups of symptoms: Positive Symptoms, Cognitive Change, Emotional Disturbance, Negative Symptoms, Behavioral Change, Motor/Physical Change, and General Psychopathology. CAARMS aims not just to determine if an individual meets the PACE intake criteria of 'at-risk mental state', but also to rule out or confirm acute psychosis and to map a range of psychopathology and functioning over time.

SIPS, SOPS, COPS

The Structured Interview for Prodromal Symptoms (SIPS, a diagnostic semi-structured interview), and the Scale of Prodromal Symptoms (SOPS, a severity scale) are closely modeled on the CAARMS. McGlashan and colleagues at the Yale University PRIME Research Clinic (Prevention through Risk Identification, Management, and Education) used these instruments to define, diagnose and measure psychopathological

symptoms in individuals who may be in a pre-psychotic state (Miller et al., 1999). Prodrome classification using SIPS and SOPS yielded acceptable inter-rater reliability ($\kappa= 0.81$) (Miller et al., 2002). Diagnosis is accomplished using the Criteria for Prodromal States (COPS), modeled after the PACE intake criteria. The cutoff point to confirm or rule out psychosis in the COPS is more conservative compared to the CAARMS, allowing less subthreshold psychotic experiences. Nevertheless, 7 of the 13 at-risk patients (54%) had converted to psychosis within 12 months (Miller et al., 2002).

Defining Prodromal State with the PANSS

A relatively high transition rate of at-risk individuals has also been noted by researchers in the United Kingdom (Morrison et al., 2002). In accordance with the PACE criteria, being at-risk was defined by the presence of transient psychotic symptoms, attenuated (subclinical) psychotic symptoms or family history plus functional decline. The study used the Positive and Negative Syndromes of Schizophrenia Scale (PANSS; Kay et al., 1987) to define the duration and severity of subthreshold psychotic symptoms. Transient psychosis was defined by symptoms that scored 4 or more for hallucinations, 4 or more for delusions, or 5 or more for conceptual disorganizations, lasted less than one week and resolved without antipsychotic medication.

Attenuated symptoms were defined by the presence of symptoms that scored 3 for delusions, 2-3 for hallucinations, 3-4 for suspiciousness or 3-4 for on conceptual disorganisation. They observed transition to psychosis in 5 of 23 of individuals (22%) at 6 months.

Predictors for Psychosis in Individuals with Prodromal Symptoms

Characteristics of 49 PACE clients were evaluated monthly to assess the predictive validity of clinical risk indicators of schizophrenia (McGorry et al., 2001a). The assessments included a comprehensive rating of psychopathological variables such as presence of psychotic symptoms, depressive features, manic features, Huber's basic symptoms (Klosterkötter et al., 2001), anxiety symptoms, drug and alcohol use and general functioning. Twenty of 49 subjects (40.8%) developed a psychotic disorder within 12 months. Highly significant clinical predictors of psychosis at intake were: long duration of prodromal symptoms (>900 days), poor functioning (GAF score <51) (Global Assessment of Functioning; American Psychiatric Association, 1994), low grade psychotic symptoms (BPRS total score >15; BPRS psychotic subscale score >2) (Brief Psychiatric Rating Scale; Overall & Gorham, 1962), depression (HRSD score >18) (Hamilton Rating Scale for Depression; Hamilton, 1960) and disorganization (SANS attention score >1) (Scale for Assessment of Negative Symptoms; Andreasen, 1983), and cannabis dependence. A recent analysis combining some predictive clinical variables in this sample yielded a strategy for psychosis prediction with good sensitivity (86%), specificity (91%), positive predictive value (80%), and negative predictive value (94%) within 6 months (Yung et al., in press).

The PACE Clinic also investigated neuroimaging, neurocognitive and neurodevelopmental variables as potential predictors of psychosis.

Individuals who met PACE inclusion criteria had reduced left hippocampal

volumes similar to first-episode psychosis patients when compared with normal controls (Velakoulis et al., 1999). However, contrary to our hypothesis, smaller hippocampal volumes predicted a lower rather than a higher risk of transition to psychosis (Phillips et al., in press). Neurocognitive functions were impaired in the total sample but did not predict transition, nor did developmental milestones, perinatal complications or childhood behavioral disturbance.

The incidence of schizophrenia and other psychotic disorders, as well as symptomatic expression in schizophrenia, vary with age and gender. In a study on 391 individuals aged from 14 to 74 years with schizophrenia spectrum diagnoses, there were significantly fewer positive and disorganized symptoms in older subjects (Schultz et al., 1997). Older age was associated with fewer hallucinations, delusions, bizarre behavior and inappropriate affect. There was no age effect for formal thought disorder or negative symptoms. Consistent with these findings, another survey in individuals with no history of psychiatric disorder reported a negative association between psychotic experiences and age (Verdoux et al., 1998). The authors concluded that normal neuronal developmental processes (e.g., Weinberger, 1987) may underlie the influence of age on delusion formation and psychosis.

Prompted by these observations, the role of age and gender on transition to psychosis in 92 PACE clients (48 male, 44 female; mean age 20.0 years, SD 3.7 years) who were participating in a randomised controlled intervention

study (McGorry et al., 2002). Cox regression analysis revealed that after adjustment for the effects of different treatments (low dose neuroleptics, standard treatment, treatment refusal), younger age and female gender were significant predictors of psychosis. Among 14-19 year olds, there were 19 of 42 individuals (45%) who developed psychosis during follow-up, compared to a transition rate of 17% in both 20-24 year old and 25-29 year old groups. These findings emphasize that adolescents, particularly females, with prodromal symptoms have the highest risk of developing a psychosis.

Age-Specific Characteristics of the Prodromal Phase of Schizophrenia

To our knowledge there have been no studies on age-specific characteristics of the prodrome in schizophrenia or other psychosis. In the sample of 92 individuals in the PACE study described above, there were no differences in global functioning, quality of life, negative symptoms, positive symptoms, manic symptoms, depressive symptoms and anxiety between age groups (14-19 years, 20-24 years, 25-29 years). Structured Clinical Interview for DSM-IV (SCID) Axis I section (First et al., 1996) at entry revealed a substantial proportion of comorbid DSM-IV disorders beside the prodromal symptomatology. Proportions of individuals with a DSM-IV disorder at baseline were 71%, 76%, and 83% in the three age groups (no significant difference). Affective and anxiety disorders were the most prevalent Axis I disorders (Leicester et al., 2002).

A wide-ranging neuropsychological test battery was used to compare 71 PACE participants, 32 young people with a first episode of psychosis and 51

matched normal controls (Francey et al., 2002). In general, the PACE group performed at a level between the two comparison groups on almost all of the tests administered. However, the PACE group was distinguished by particular impairments in verbal memory and attentional or executive functioning compared to the controls. Performance improved with age on tests of verbal memory and selected tests of attentional or executive function. It was hypothesized that neuropsychological impairment in the prodromal phase is likely to reflect neurodevelopmental compromise, and this may be more severe in those experiencing prodromal symptoms at an earlier age.

Intervention in the Prodromal Phase

Clinical Management

Given the broad variety of non-specific symptoms which occur in the prodromal phase and their relatively high prevalence in the general population the risk of 'false positives' is crucial for planning intervention strategies in individuals considered at immediate risk for psychosis. Until more knowledge about the nature of transition has been gathered preventative interventions remain limited. Nevertheless, there are approaches that can be recommended despite the current lack of knowledge. Early recognition, easy access to care and close follow-up are key elements of intervention in the prodromal phase (Edwards & McGorry, 2002). Young people with prodromal symptoms often seek help. They need to be engaged, offered regular assessment and support, and offered treatment for syndromes such as depression, anxiety or substance use. Family education

and support are often needed. If young people with prodromal symptoms are not seeking help, then regular contact with family members can be an appropriate strategy. Families should be provided with information in a flexible, careful and clear way about the risks for psychosis and other mental disorders as well as about existing syndromes and problems.

Despite psychosocial treatment and active treatment of syndromes such as depression and anxiety, the transition rate to psychosis is high in this group. Until the 1990s it was considered clinically and ethically correct to delay psychosis-specific treatments until a definite diagnosis of psychosis was made (McGlashan, 2001). Over the last decade a growing body of evidence has suggested that early intervention might not just be palliative but might also affect the natural course of psychotic disorders. Support for early intervention has been strengthened by the advent of new 'atypical' neuroleptic agents which have fewer serious side effects (e.g., tardive dyskinesia, neuroleptic malignant syndrome) and equal or better efficacy than traditional neuroleptic drugs. However, as part of the routine clinical management, antipsychotic medication should be only considered when suicidal behavior or hostility is present.

Treatment Studies

Based on findings in established psychotic disorders, neuroleptics and cognitive behavior therapy (CBT) have been considered as potentially helpful during the prodromal state. Several clinical trials have been launched to investigate these approaches in comparison to standard care such as

antidepressants, anxiolytics and mood stabilisers. The first intervention study conducted in PACE examined the efficacy of atypical neuroleptics plus CBT compared to standard treatment in 33 individuals. In the following 12 months, 35.7% of those receiving standard care developed psychosis compared to only 9.7% of those who received atypical neuroleptics and CBT (the difference was statistically significant). In 2 years after ceasing treatment, only 2 more individuals from the specific treatment group developed psychosis. The mean dose of risperidone in the PACE intervention study was 1.3 mg (range 0.5-2.0 mg). Treatment was initiated with 0.5 mg daily and increased by 0.5 mg weekly to 2.0 mg per day if well tolerated. Usually the medication was administered at night. The most common side effects were akathisia, sedation and weight gain (McGorry et al., 2002).

Novel Approaches

There is clinical and ethical controversy regarding neuroleptic treatment during the prodromal phase. The main ethical criticism is that only about one-third of individuals with prodromal symptoms develop psychosis, so the majority of individuals are exposed to potentially harmful medication for no reason. The effects of antipsychotics on the developing brain are unknown. Although atypical antipsychotics are associated with fewer extrapyramidal side effects, other side effects such as weight gain and changes in lipids and glucose metabolism are not uncommon (Meyer, 2002). Therefore, novel pharmacological strategies which might be helpful in the phase of emerging psychosis need to be pursued.

Dysfunction of glutamatergic neurotransmission seems important in the pathophysiology of schizophrenia and is a promising target for drug development (Goff & Coyle, 2001). The N-methyl-D-aspartic acid (NMDA) subtype of the glutamate receptor may be particularly important, as blockade by substances such as phencyclidine (PCP) or ketamine causes schizophrenia-like psychosis in humans and increases dopamine release in the mesolimbic system. Agents that indirectly enhance NMDA receptor function can reduce negative symptoms and improve cognitive functioning in individuals with schizophrenia (Javitt, 1999). It has been suggested that reduced function of the NMDA receptor might be linked with glutamate-mediated neurotoxicity involving calcium release from nerve cells and subsequent release of neurotoxic nucleases and proteases. Nitrous oxide and probably hydrogen dioxide are also released, which might lead to excessive pruning of cells in the central nervous system (Farber et al., 2002). Substances which influence the process of neurodegeneration and cell death may be therapeutic or curative in the onset phase of psychosis, even those substances are not helpful in later stages of the disorder. Lithium and Lamotrigine which have been shown to be neuroprotective in animal models are also candidates for further investigation in prodromal schizophrenia and other psychosis.

Lipids might play an important role in schizophrenia. By weight, the human dry brain is 50-60% lipid. A major proportion of these lipids consist of bioactive lipids such as arachidonic acid (AA) and its metabolites, also referred to as “derived essential fatty acids” (EFA). In the brain EFA are

mainly bound to glycerophospholipids (GPL). Due to their unique chemical structure, GPL spontaneously form bi-layers and are the basic molecules of all cell membranes. Bioactive lipids are released through direct and indirect enzymatic pathways (e.g., phospholipases) from membrane GPL. AA is one of the main bioactive lipids in the brain released through phospholipase action. AA is the precursor of eicosanoids such as prostaglandins, thromboxanes, leukotrienes and prostacyclins. Preclinical studies have demonstrated that EFA deficiency and EFA supplementation influenced nearly every receptor system in the CNS. Of particular interest, in the context of schizophrenia, was the finding that dopamine D₂ receptors in the nucleus accumbens of EFA deficient rats was increased by 35% compared to rats fed with a standard diet. Animal studies and preliminary studies in humans have shown an association between bioactive lipid metabolism, behaviour and cognition (Zimmer et al., 2000).

A recent review of 15 published studies confirmed a depletion of bioactive lipids in cell membranes of patients with schizophrenia (Fenton et al., 2000). The most consistent findings were reductions in AA and its precursors, and these were independent of drug treatment (Yao et al., 1996). Reductions in AA and its precursors have also been found in post mortem brains of patients with schizophrenia, relative to normal control brains (Yao et al., 2000). Three randomized controlled treatment studies conducted over 12 weeks found 2g/day ethyl-eicosapentaenoic acid (E-E) significantly more effective than placebo in reducing psychopathological symptoms in individuals with schizophrenia (Peet et al., 2001; Emsley et al., 2002).

Symptom improvements in those studies were both, clinically relevant and statistically significant. On the other hand, Fenton et al. (2002) investigated augmentation of neuroleptics with 3 g/day of E-E on symptoms and cognition in patients with schizophrenia or schizoaffective disorder and reported a negative finding. The patients in Fenton et al.s' study, however, had been ill for two decades and had substantial symptoms, despite treatment with newer neuroleptics, including clozapine. The patients described as benefiting from E-E in the other studies were younger and had a shorter duration of illness.

In all E-E treatment studies, no treatment-related side effects or adverse biochemical or haematological effects have been observed. E-E proved safe to administer to schizophrenic patients as an adjunct therapy and did not cause side effects other than mild gastrointestinal symptoms by itself, nor did it enhance the side effects of existing drugs. Patients found E-E highly tolerable (Peet et al., 2001). Because E-E combines the acceptance of a natural product without significant side effects with a potency potentially similar to neuroleptic drugs, E-E seems an ideal candidate for intervention studies in the prodromal phase.

Psychotherapeutic Interventions in the Prodromal Phase

Developmental changes during adolescence, including neurobiological and neurocognitive changes, may contribute to an individual's vulnerability to psychosis. Environmental stressors such as relationship problems, societal commitments and lifestyle factors appear to increase the vulnerability.

Together, these factors are described in the 'stress-vulnerability model'. Integrated psychotherapy developed in PACE uses cognitive strategies to strengthen the individual's coping resources. Table 2 lists goals of psychotherapeutic intervention in the prodromal phase.

Insert Table 2 about here

Case Vignettes

The following vignettes describe typical adolescents and young adults during initial assessment, treatment and follow-up in the PACE Clinic.

Sarah, 15 Years

Sarah was referred to PACE by her general practitioner and school counselor after she experienced episodes of brief auditory hallucinations, disorientation and panic for about 3 months.

Initial Assessment

Sarah said the changes started occurring at a school camp 3 months ago when she experienced an incident that began with sensations of anxiety and confusion but escalated to disorientation. Extreme panic ensued, accompanied by auditory hallucinations that made derogatory comments toward her and exacerbated the panic and confusion. Sarah noticed a number of subsequent changes including periods of anger and agitation lasting for up to 30 minutes, disorientation and hallucinatory experiences. These occurred 2 or 3 times a week, lasting 20 to 30 minutes each time and leaving her tired and confused.

Sarah's parents said they had noticed she had a very variable mood and irritability, as well as isolation from family and friends and a decline in academic performance. Sarah had previously been an excellent student, an active participant in sports and socially outgoing.

At the initial assessment, Sarah offered minimal insight into her experiences and provided very little information about her mood or level of functioning. She was especially concerned about her mood variation and what she described as 'outbursts' at school. The hallucinations were disturbing, but not a motivating factor in seeking treatment. She was accepted to the clinic on the grounds of attenuated psychotic symptoms.

Family Background

Sarah's father had a history of depression and had been treated with antidepressants. There was family history of psychotic disorder. Conflict between Sarah and father had been a significant stressor for the last 18 months. Sarah's father said her recent difficulties were particularly frustrating and had worsened their strained relationship.

Progress

Sarah attended weekly psychotherapy sessions at PACE for 5 months and maintained regular contact with medical staff. Sessions focused on relationships with family and friends, with particular attention to coping with conflict and adversity. Although she continued to have difficulty

providing information about her episodes of panic, she improved considerably in coping with social, family and personal challenges.

After 6 months of treatment, episodes had reduced to less than once every 2 months, the auditory hallucinations ceased and her disturbances consisted mainly of dissociation, panic and confusion. The relationship with her father improved considerably, social conflict had diminished and her school performance was improving. Sessions were reduced to once monthly and a pattern of steady improvement continued. Her parents stated that her mood at home was noticeably more 'up beat' and she was more engaged with the family.

Twelve months after commencing treatment, Sarah had not experienced any panic-like incidents for 5 months. At the time of discharge her treating team felt her risk of developing psychosis had reduced considerably.

John, 19 Years

John was referred to PACE by a counselor at a community health center who was concerned about his depressive symptoms, social isolation, auditory hallucinations and poor function.

Initial Assessment

John had experienced a long-standing major depressive disorder characterized by very low self-esteem, sadness and melancholia, lack of interest in activities, minimal social interaction and disturbed sleep patterns.

He said these symptoms had been present in varying degrees since he was 6 years old.

During the initial consultation John described the origins and persistence of his depression in some detail. He had been a victim of bullying throughout primary school because of his poor posture and awkward gait that resulted from a spinal condition. He developed a pattern of isolating himself to avoid further harassment, exacerbating his sense of 'being different'. John continued to be verbally and physically harassed at secondary school, confirming to him that he was unable to interact 'normally' with others.

Since leaving school 2 years ago, John said his self-esteem steadily decreased, exacerbated by unemployment, social isolation and a lack of engagement in regular activity. He was rigid in his beliefs that he felt he would always be different and did not believe he would develop significant relationships. He experienced great discomfort when in public because he thought others perceived him as unusual.

John said that for the last 2 or 3 months he had experienced intermittent derogatory auditory hallucinations, occurring when he was particularly distressed. In the last few weeks he had experienced a scratching sensation behind his rib cage as if something was trying to come out from inside him, again during periods of heightened anxiety and distress.

John was accepted to the PACE Clinic as having attenuated psychotic symptoms. He was keen to overcome his depression and concerned that if he was left without support his functioning would decrease further. Although his unusual perceptual experiences were of some concern, they were not a strong factor in agreeing to attend the clinic.

Family Background

John lived with his biological parents and two younger sisters. Both parents had an extended history of depression, treated with medication. John was emotionally distant from his family and believed they had little understanding of his difficulties.

Progress

John was started on an SSRI antidepressant because of his acute depressive symptoms. With his consent, PACE staff contacted his family to offer information about his presentation and the role of the clinic.

Within 2 weeks John reported a considerable improvement in mood, motivation and self-esteem, and he was no longer experiencing perceptual abnormalities. He progressively developed considerable insight into the onset and course of his distress and displayed substantial improvement at coping with adversity and reducing his patterns of isolation. After seven months of treatment John's functioning had improved considerably. He had engaged well with a number of friends from whom he been isolated for two years, returned to study to complete his final school exams, and fostered

interests that had been dormant for several years such as playing guitar, writing and reading.

At the time of discharge John's depression was in full remission and he was no longer taking SSRI medication. No further perceptual abnormalities had occurred for almost 12 months.

Brian, 24 years

Brian was referred for assessment by a family doctor who was concerned about his social isolation, apparent depression and a family history of psychosis (in one of his brothers).

Initial Assessment

Brian said that his confidence had been steadily decreasing for 12 months, particularly with regard to social interaction. At first this was evident with new people he met, but recently he was increasingly anxious around established friends and acquaintances.

Brian also described panic in environments such as public transport, because he thought people were staring at him. He believed this indicated there was something 'strange' about him, and the beliefs worsened his social anxiety. At the time of assessment Brian was able to question whether he was particularly unusual, but he was often unable to question these thoughts when he was in public.

Brian was accepted to PACE because of a considerable drop in functioning over the past 12 months and a first-degree relative with a history of psychotic illness. His suspicion and paranoid-type thinking were considered as possible attenuated psychotic symptoms. Brian was also thought to be developing social phobia and at considerable risk of developing a depressive illness.

Family Background

Brian was the youngest of four siblings and one of his brothers was diagnosed with a psychotic disorder at a similar age. Brian's father had been living in the family's country of origin for several years and had no intention of returning to the family.

Progress

Brian commenced antipsychotic medication and attended weekly psychotherapy sessions after consenting to participate in a clinical trial. He engaged well and was very compliant with therapy. He felt that his social anxiety had reduced and he had stayed in contact with a small group of friends with whom he was able to discuss his difficulties and concerns.

After 6 months of treatment he requested that his appointments be reduced to once monthly, with telephone support if needed, because of his considerable improvement. His concerns about others in public and paranoid beliefs were minimal, and he recognised that his background levels of anxiety and self-doubt contributed to his paranoia.

After 8 months, Brian had found a job. He was functioning well, presenting with minimal concerns and stable mood during clinical sessions. However, he missed several appointments and did not return telephone messages for several weeks. He was seen again after 2 months and it was clear his functioning had deteriorated significantly as he was agitated, disheveled and thought-disordered. He had left his job because he believed other employees were judging him, and had remained isolated ever since. He believed his friends were controlling his cognitive processes and had confronted them, accusing them of conspiring against him. The treating team considered Brian had progressed to acute psychosis and he was immediately transferred to a first-episode psychosis team.

Conclusion

Studies in PACE have provided encouraging preliminary information on treatments to reduce the risk of transition to psychosis. However, more data are needed and the risk:benefit ratio of various interventions must be determined. At present there is no general indication for treatments aimed specifically at reducing the risk of developing psychosis, and antipsychotic medications are not usually indicated unless the person meets criteria for a DSM-IV/ICD-10 psychotic disorder. Some exceptions should be considered: for example, when rapid deterioration is occurring, where the risk of suicide is very high and treatment of any depression had proved ineffective, and when aggression or hostility is increasing and poses a risk to others. If antipsychotics are considered, then low doses of atypical medications are

preferred and should be regarded as a 'therapeutic trial' for a limited period. If there is benefit and resolution of symptoms after 6 weeks, the medication may be continued with the patient's consent for a further 6 months to 2 years, following an explanation of the risks and benefits. After this period, gradual withdrawal of the medication should be attempted if the patient agrees and there has been a good recovery. If the patient has not responded to one atypical antipsychotic, another may be tried if still indicated.

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Table 1: Definition of At-Risk-Mental-State (ARMS; Yung et al, 1998)

- **State and trait risk factors**

1. First degree relative with any history of psychotic disorder or bipolar disorder or schizotypal personality disorder.
2. Reduction on GAF* scale of 30% or more points from premorbid level

- **Attenuated psychotic symptoms**

1. At least one of ideas of reference, odd beliefs or magical thinking, perceptual disturbance, digressive speech or thought, odd behaviour or appearance.
2. The symptom occurs at least several times per week.
3. The change in mental state has been present for at least one week

- **Transient psychotic symptoms**

At least one of: Perceptual disturbance or hallucinations, ideas of reference, magical thinking or delusions, digressive speech, or formal thought disorder, odd behaviour or appearance.

Duration of each is less than one week and resolves spontaneously.

* Global Assessment of Functioning; American Psychiatric Association, 1994

Table 2: Goals of psychotherapeutic intervention in the prodromal phase

- To proactively engage the client, extending therapeutic alliance to accommodate the individual needs and possibly reluctance of the client.
- To accurately assess and develop an understanding of the reasons and cause for presentation to the clinic. A core component of the PACE therapy is the development of an explanatory model for the precipitation and manifestation of presenting symptomatology. This formulation is developed collaboratively between the client and therapist and used as a basis for ongoing therapeutic treatment planning and review.
- To develop adaptive ways of enhancing coping behaviors and to advocate health awareness.
- To recognize and challenge factors which potentially damage or erode self esteem.
- To assist the client in understanding and managing subthreshold psychotic symptomatology with the aim of preventing or reducing the impact of their development.