Schizophrenia: Early Intervention

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The longitudinal course of a serious mental disorder, such as schizophrenia, may show considerable variation in outcome as reflected by the degree of:

- initial recovery,
- recurrences,
- relapses,
- persistence of symptoms,
- comorbid disorders, and
- deterioration in social functioning.

While variation in the course of illness may reflect innate heterogeneity of the disorder, it may also be influenced by factors that are more amenable to change, such as timing and content of treatment. This has resulted in the recent increased interest in the concept of early intervention in schizophrenia.

Why early intervention?

The rationale for early intervention in schizophrenia draws on several factors, beginning with a fundamental need to substantially modify the widespread presumption of chronicity and disability as a natural consequence of schizophrenia. It has been suggested that a psychotic illness, such as schizophrenia, may have toxic effects on the brain which could result in an incomplete recovery, greater vulnerability to future episodes of psychosis, treatment resistance, and/or more compromised functioning.[1] Central to this postulate is the unexpected, and frequently lengthy, delay between the onset of psychosis and initiation of adequate treatment. Recently, this duration of untreated psychosis (DUP) has attracted much attention due to its possible relationship to treatment outcome and its implications at secondary prevention of chronicity. Estimating DUP is not always easy, given the potential challenges involved

John's odd behaviour

John, 22, was hospitalized after breaking furniture. He has spent the last few months writing poetry and stories which are difficult to comprehend, and he coins new words. He has also been feeding fruit juices to plants. John is single and has a two-year history of withdrawal, irritability, and occasional blank stares. There has been substance abuse since he was 15.

Initially, John was uncooperative upon hospitalization. Gradually, however, he engaged in treatment, which included a low-dose atypical neuroleptic, case management, and psychosocial intervention aimed at engagement and education. Three months after treatment began, John's symptoms were in remission. He suffered a relapse during the fourth year of treatment, due to non-compliance with his medications. At a five-year followup, John is noted to be in remission and taking his medications. He was employed full time during the first three years after his initial treatment. Since then, he has been working off and on. He admits that he is still in the habit of smoking marijuana.

Table 1
Challenges in assessing duration of untreated psychosis

- Define psychosis
- Identify onset of psychosis
- Establish when the "odd" become pathologic
- Understand the difficulties in retrospective reports
- Understand the intermittent nature of psychosis
- Identify onset of treatment
- Differentiate between treatment and adequate treatment
- Adhere to treatment
- Differentiate between "untreated" psychosis and psychosis
- Establish intensity of symptoms

Table 2
Prepsychotic or prodromal symptoms

Symptoms last for 2 to 5 years

Non-specific symptoms

- Anxiety
- Irritability
- Fatigue
- Depressed mood

Negative symptoms

- No drive
- Anergia
- Social withdrawal
- Inability to concentrate

(Table 1). A recent review suggests most studies show a significant relationship between lower DUP and faster or a better level of recovery from positive symptoms in the first year of treatment.[2] Consistent with this finding, the Prevention and Early Intervention Program for Psychoses (PEPP) in London, Ontario, cites higher rates of remission were observed among patients who entered treatment within six months of the onset of psychosis (82% compared to 60%).[3] Unfortunately, the evidence for such a relationship between DUP and negative symptoms or social functioning at followup is less consistent. Irrespective of its relationship to long-term treatment outcome, longer DUP in itself represents significant unnecessary suffering and distress for patients and their families. In another study of pathways to care at the PEPP, it was observed that the mean delay between onset of the current episode of psychosis and initiation of adequate treatment was 61.1 weeks with a median of 21.1 weeks.[4] This delay is comparable to the average reported in other studies.[2] Family physicians were a first point of contact for almost 40% of patients once psychosis had occurred, and were involved in 55% of patient cases. This finding is consistent with findings from Australia.[5] It would, therefore, appear that approaches to reduce DUP involving primary health-care providers, such as family physicians, should become a priority in first episode psychoses programs.

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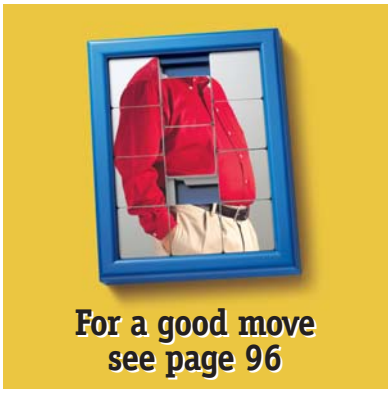
How does early intervention work?

The strategies used at the PEPP, and at other centres in Australia, Norway, and Denmark, consist of materials providing brief descriptions of psychosis, likely early signs and symptoms, and potential advantages of prompt intervention. This information is presented in the form of posters, pamphlets, bookmarks, calendars, and film clips. In addition, presentations to family physicians and community agencies are also undertaken. Ongoing liaisons are established with guidance counselling services at high schools, community colleges, and universities. Research evaluation of these strategies for early identification of psychoses is in progress, and findings are not yet published.



Intervention during prepsychotic phase

Prodromal symptoms of schizophrenia consist of non-psychotic and behavioural changes prior to the onset of psychosis (Table 2). It may be argued that accurate identification and effective treatment of the prodrome of psychosis offers hope for reducing the DUP and improving outcome. Unfortunately, the prodromal symptoms not only lack specificity as predictors of psychosis, but may also last up to several years. Even in selected at-risk cases, the conversion to psychosis is typically less than 50%.[6] Thus, it is not surprising that questions have been raised about the ethics of treating individuals who may not develop a psychotic disorder. Nevertheless, there have been two published studies and one ongoing study of intervention during the prodrome. An earlier study in the U.K. identified prodromal symptoms based on the Diagnostic and Statistical Manual of mental disorders, revised third edition (DSM-III-R) criteria and utilized psychosocial interventions and low-dose medications. On the basis of comparison with a historical control group, it was concluded that intervention resulted in a tenfold reduction in the incidence of schizophrenia.[7] In a prospective, randomized, open intervention trial in Australia, the patients received either a low-dose antipsychotic and cognitive therapy, or were allocated to receive a control condition of supportive case management. In the first six months, 9.7% of the treatment group showed a transition to psychosis, compared to 35.7% in the control group. Individuals not making the transition to psychosis also showed significant improvement in symptoms and functioning.[8]

There is no consensus as of yet whether, and under what circumstances, low-dose antipsychotic medication should be given to individuals who are not psychotic. Clearly, it is a decision that at-risk individuals need to make after consultation with their physicians. An alternate is the provision of followup observation/assessment and/or psychological intervention to such individuals, and the provision of prompt treatment depending on the severity of symptoms or the behavioural consequences thereof.

What is important to remember?

The presentation of bizarre psychotic symptoms is readily identified. However, many other contextual aspects of a psychotic illness may hinder early recognition. For example, it is often difficult to distinguish between early signs of psychotic illness and adolescence adjustment issues; comorbid substance use; subtle disturbances in mood, cognition, social interaction and perception; and eccentricities of thinking and behaviour. Prompt accessibility to expert assessment and treatment service which is tailored to the needs of the first-episode psychosis patient is, therefore, essential. Many early-intervention or first-episode programs for the treatment of psychotic disorders have been established throughout

Table 3
Benefits of early intervention

- A reduction of length of the acute illness. A treatment delay does appear to be a significant, independent predictor of remission.
- Long-term benefits in a variety of outcomes
- Enthusiasm and optimism may, in themselves, be some of the most powerful tools for improving outcome.

the world, and Canada is taking a leading role, with programs in several provinces.

Early intervention means more than intervening early. Such intervention needs to also focus on the nature and content of treatment.[9] This is especially relevant in first-episode psychosis, as most patients are adolescents and young adults with specific psychosocial needs and sensitivity to pharmacologic treatments. These individuals generally live with their families, are adjusting to their developmental phase, and are more likely than not using/abusing drugs or alcohol. Possible disruptions to these individuals' academic goals and fear of not returning to normal can also be traumatizing experiences. All these factors are important considerations for a comprehensive treatment plan.

What about medications?

Atypical antipsychotic medications are generally accepted as first-line treatment. However, since most individuals are previously unexposed to medications, they are likely to respond to a comparatively low dose. This low-dose strategy is also supported by D2 receptor occupancy studies.[10] The lower dose is also better-tolerated, hence the hope for fewer or no side-effects. Evidence is accumulating, however, which shows that some atypical medications may be associated with weight gain and undesirable metabolic side-effects. The goal is to use the minimum dose effective in achieving remission of symptoms and return to a premorbid level of functioning.

Take-home message

- There is no consensus whether, and under what circumstances, low-dose antipsychotic medication should be given to individuals who are not psychotic.
- Taking such medication is a decision that at-risk individuals need to make after consulting their physicians.
- Atypical antipsychotic medications are generally accepted as first-line treatment. However, most individuals are previously unexposed to medications, and are therefore likely to respond to a comparatively low dose.
- Early intervention means more than intervening early. Such intervention needs to also focus on the nature and content of treatment.
- In addition to the needs of the family, support, education, and coping strategies are extremely important.

There is no consensus as to how long the antipsychotic medication should be continued. At the PEPP, it is recommended that patients continue to take the minimum effective dose of atypical antipsychotics for at least one year following remission of symptoms. Clinical experience shows that patients generally continue to be prescribed indefinitely, as long as they choose, or until they insist on tapering/discontinuing their antipsychotic medications. Few patients (less than 10%) agree only to participate in psychologic interventions and/or case management/medical appointments, and do not accept antipsychotic medications.

What is psychosocial intervention?

The basic principles of psychosocial interventions are partially derived from the more general research literature on schizophrenia, but modified to the specific needs of first-episode patients. These interventions include:

- engagement in treatment and development of a therapeutic alliance,
- education about the illness,
- assistance with cognitive and other skills required for a return to school,
- employment initiative programs,
- interventions for anxiety or other comorbid conditions,
- addressing substance use/abuse, and
- providing opportunities for peer support.

In addition, the needs of the family in terms of their involvement in care, support, education, and coping strategies are extremely important. Most early intervention programs utilize a variety of psychosocial interventions aimed at improving outcome, and prevent recurrence/relapse of psychosis after initial improvement. It is our intention and hope that such interventions are beneficial to individuals with first episode psychosis (Table 3). The efficacy of such interventions in first-episode patients needs to be evaluated in controlled studies. CME

References
1. Wyatt RJ: Neuroleptics and the natural course of schizophrenia. Schizophrenia Bulletin 1991;17(2):325-351.
2. Norman RM, Malla AK: Duration of untreated psychosis: A critical examination of the concept and its importance. Psychological Medicine 2001; 31(3):381-400.
3. Malla AK, Norman RMG, Manchanda R, et al: Status of patients with first episode psychosis after one year of phase-specific community-oriented treatment. Psychiatric Services 2002; 53(4):458-63.
4. Norman RMG, Malla AK, Verdi MB, et al: Understanding delay in treatment for first episode psychosis. Psychological Medicine 2004; 34 (in press).
5. Lincoln CV, McGorry P: Who cares? Pathways to psychiatric care for young people experiencing a first episode of psychosis. Psychiatric Services 1995; 46(11):1166-71.
6. McGorry PD, Yung A, Phillips L: Ethics and early intervention in psychosis: Keeping up the pace and staying in step. Schizophrenia Research 2001; 51(1):17-29.
7. Falloon IR: Early intervention for first episode of schizophrenia: A preliminary exploration. Psychiatry 1992; 55(1):4-15.
8. Schaffner KF, McGorry PD: Preventing severe mental illness: New prospects and ethical challenges. Schizophrenia Research 2001; 51(1):3-15.
9. Malla AK, Norman RMG: Treating psychosis: Is there more to early intervention then interviewing early? Canadian Journal of Psychiatry 2001; 46: 645-8.
10. Kapur S, Zipursky R, Jones C, et al: Relationship between dopamine D2 occupancy, clinical response and side effects: A double blind PET study of first episode schizophrenia. American Journal of Psychiatry 2000; 157(4):514-20.

Net Readings

1. Prevention & Early Intervention Program for Psychoses: *www.pepp.ca*
2. Early Psychosis Prevention and Intervention Centre: *www.eppic.org.au*

www.stacommunications.com

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