The impossible dream: can psychiatry prevent psychosis?

Article in Early Intervention in Psychiatry · October 2007
DOI: 10.1111/j.1751-7893.2007.00031.x

2 authors:

Jeffrey A Lieberman
Columbia University
1,066 PUBLICATIONS 61,028 CITATIONS

Cheryl Corcoran
Columbia University
138 PUBLICATIONS 3,005 CITATIONS

Some of the authors of this publication are also working on these related projects:

Biomarkers and Predictors of Schizophrenia Pathogenesis View project

Experimental Therapeutics for Schizophrenia View project

All content following this page was uploaded by Jeffrey A Lieberman on 05 September 2014.

The user has requested enhancement of the downloaded file. All in-text references underlined in blue are added to the original document and are linked to publications on ResearchGate, letting you access and read them immediately.
The impossible dream: can psychiatry prevent psychosis?

Somewhere, something incredible is waiting to be known. – Carl Sagan

INTRODUCTION

Few things have captured the attention of the field of psychiatric research and mental health care more than the prospect of early detection of schizophrenia and intervention during its premorbid or prodromal stages to prevent its onset. Adding to the enthusiasm is the fact that this goal seems achievable and could potentially dramatically limit the consequences of the illness if not reduce the incidence of psychotic disorders. However, while the future prospect for early intervention in schizophrenia is excellent, the present is a challenge, and we have our work cut out for us. Although current efforts to reduce the duration of untreated psychosis is an unalloyed good, with reduction in suicide and preservation of function, intervention during a prepsychotic prodromal phase in schizophrenia remains controversial.

The current debate over mental health parity in the USA is illustrative. The greatest objection to equity in coverage and reimbursement of care of mental illness in the USA is the claim that ‘mental health care is often entirely disconnected from evidence’, despite an evidence base for the treatment of many disorders (Azalavitz, 4/11/07, NY Times Op-Ed). For prevention of mental illness, the evidence base is as yet still in a nascent stage. Therefore, although there is a groundswell of international interest in early intervention in psychiatry, we must remain sceptical in our beliefs and rigorous in our approaches, systematically evaluating potential strategies and only promoting those that are clearly supported by evidence. We have a golden opportunity that we cannot squander.

Three essential elements are necessary to establish early detection and intervention as the standard of care and enable its acceptance into clinical practice: (i) reliable and accurate diagnostic methods for case identification; (ii) proven methods of intervention; and (iii) the development of models of service delivery. Each of these is reviewed in turn.

DIAGNOSTIC METHODS FOR CASE IDENTIFICATION

The importance yet difficulty of identifying cases of schizophrenia in a prepsychotic stage were recognized several decades ago, by pioneers such as Emil Kraepelin and Harry Stack Sullivan. Efforts in the 1990s led to an expert consensus on prodromal symptoms, included in the DSM-III-R, which were quite non-specific, with marked prevalence found in population samples of high school students.1 Subsequently, longitudinal studies of help-seeking young people with subthreshold positive symptoms led to operationalized criteria that represented a great improvement, yielding conversion rates to psychosis of ~40–50% within 1–2 years.2,3 However, the specificity of this prodromal designation for psychosis, defined purely by behavioural features and family history, has varied over time and the conversion rate to psychosis declined.4 Also problematic, the outcome of psychosis conversion is broad and not specific to schizophrenia, including affective psychoses as well.

At present, young people at risk are now identified solely on the basis of clinical features which by themselves have low predictive value. The risks of negative effects for the many ‘false positives’ have been articulated by Warner,5 including unnecessary medication exposure and the unintended effects on young people in terms of potential reconsideration of life goals. It is clear that we must move beyond behavioural symptoms and signs in order to improve diagnostic methods for case identification.

The challenge now is to bridge the gap of knowledge between the rich descriptive phenomenology of early schizophrenia and an understanding of the underlying biology of risk and illness progression in schizophrenia. Neuropsychology has yielded some good first steps in the effort to identify biomarkers during a prodromal period, with verbal memory deficits consistently identified as a risk factor for schizophrenia in numerous high risk samples.6–8 In a previous editorial, Thomas Insel considered the power of a potential imaging biomarker for schizophrenia.9 One candidate is striatal...
dopamine release, a plausible abnormal substrate that could interact with exposures such as stress and drug abuse to yield psychosis. Genetics also holds great promise for identifying candidate biomarkers, in tandem with cognitive neuro-science and neuroimaging. Combinatorial arrangements of putative biomarkers can increase predictive power for schizophrenia among high-risk young people, and improve our diagnostic methods for case identification.

METHODS FOR INTERVENTION

In addition to accurate case identification, we must determine the optimal interventions for the prepsychotic stages of schizophrenia. Currently, we have insufficient evidence for the effectiveness of interventions and only a theoretical understanding of the pharmacology of prepsychotic stages of schizophrenia. The results of clinical trials in a putative prodromal period in schizophrenia thus far have been promising, in that they suggest that psychosis may be at least forestalled in young people at risk. But our knowledge of the pathophysiology of the prodromal stage of schizophrenia and by extension the optimal therapeutics is as yet limited. Although they may be effective it is not clear that antipsychotics are the most appropriate treatment for this stage of illness and may be too costly in terms of serious side-effects, including metabolic effects and weight gain, especially in adolescents. What does it say about our knowledge of disease pathophysiology and therapeutic innovation if we use a single class of medications (albeit at different doses) for every stage of the illness?

In the absence of a clear understanding of the pathophysiology of emerging schizophrenia, clinical investigators have utilized more general preventive strategies, such as neuroprotection with lithium or omega fatty acids, or psychological treatments that target cognitive symptoms and problematic behaviours. Although the findings are preliminary, these strategies have met with some success. The optimal interventions will likely be derived through a better understanding of the pathogenesis of the emerging illness itself. This is a complex task, as brain maturation during adolescence is a dynamic process with shifts in grey and white matter, synaptic remodelling, changes in connectivity and shifts in receptor expression for neurotransmitters implicated in schizophrenia, including dopamine and glutamate.

MODELS OF SERVICE DELIVERY

Mental health-care services are typically located in hospital and clinic settings. However, to effectively orchestrate a strategy for early detection and intervention, populations at risk and affected persons who are or will become symptomatic will need to be engaged in community settings. Herein lies the problem articulated earlier – that we generally have systems of care which are not conducive to finding the target population and providing what would be truly efficacious for them.

The importance of mobile outreach teams and specialized care is demonstrated by randomized clinical trials in Europe for first-episode psychosis patients, which show that with integrated treatment strategies, first-episode psychosis patients can be diagnosed earlier, have fewer relapses and have significant reduction in both positive and negative symptoms. There is some evidence to suggest that this strategy may be effective for prepsychotic schizophrenia as well.

Education is also important. Quasi-experimental studies comparing geographical regions demonstrate that multimedia informational campaigns targeting young people can improve mental health literacy and increase help seeking. Further, when informational campaigns focusing on psychosis are accompanied by easy access to assessment, regional differences are found for duration of untreated psychosis, suicidal behaviour and negative symptom severity in first-episode psychosis patients.

Overall, these studies demonstrate that it is possible to address mental illness and its risk at a population level, which is necessary if prepsychotic intervention in schizophrenia is to become the standard of care.

CONCLUSION

We have demonstrated the political will and proven capacity to address mental illness as a public health issue, but are still limited in our identification of risk states and effective prevention strategies. The powerful tools of neuroscience – neuropsychology, neuroimaging, neurophysiology and genetics – hold great promise for the development of diagnostic methods and novel interventions for the prevention of serious mental illnesses in adulthood. A more complete understanding of the pathological mechanisms that underlie schizophrenia and other disorders will facilitate diagnosis and inform the design of innovative, safe and effective interventions. Then we will truly be able to realize the promise of this
revolutionary new approach to prevent serious mental illness.

Jeffrey Lieberman and Cheryl Corcoran
Department of Psychiatry, Columbia University,
New York, USA

REFERENCES


10. McGorry PD, Yung AR, Phillips LJ et al. Randomized controlled trial of interventions designed to reduce the risk of progression to first-episode psychosis in a clinical sample with sub-threshold symptoms. *Arch Gen Psychiatry* 2002; 59: 921–8.


