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Investigating Children at High Risk for Bipolar and Psychotic Disorders: Findings and Implications

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Bipolar disorders (BDs) and psychotic disorders were initially conceived as disorders of adulthood, with an occasional onset in adolescence. However, those concepts are gradually changing, and, based on recent studies of children of parents with BD and psychotic disorders, these aged constructs require intense rethinking. A series of longitudinal studies paints a new, different picture: the true beginnings of these disorders were either different or have changed.

In nearly all departments of psychiatry, adult and child-adolescent psychiatry represent 2 separate universes that did not enable continuous studies. However, in recent years, several adult and child specialists have joined forces to investigate the populations of young people at high risk for BDs and psychotic disorders and came up with identical basic findings regarding the early clinical course.

This issue of *The Canadian Journal of Psychiatry* offers 2 excellent reviews of this fruitful approach by its major proponents, Dr Anne Duffy¹ and Dr Patrick D McGorry, Dr Barnaby Nelson, Dr Sherilyn Goldstone, and Dr Alison R Yung.² They present their findings, and review the relevant literature and convergent conclusions. They report replicated evidence that, in predisposed people over time, major mood and psychotic disorders develop from nonspecific harbingers.

Based on her longitudinal studies of offspring of affected parents, Dr Duffy¹ describes the early natural history of BD as unfolding in a series of clinical stages. BDs evolve from nonspecific childhood antecedents, including anxiety and sleep problems, followed by adjustment and minor mood disturbances through early adolescence, culminating in major mood episodes in later adolescence and early adulthood. As

BDs have a forceful genetic contribution, the study of children of affected parents is an important strategy to capture this unfolding of the illness. The clinical staging model is likely to improve early detection and may enable early intervention.

Interestingly, Dr Duffy's longitudinal studies shed light on seemingly contradictory findings that emerged from earlier cross-sectional high-risk studies and studies of pediatric clinical populations. To wit, the diversity of BDs in parents appears to explain why ADHD and other cognitive difficulties are reported in some high-risk offspring studies and not in others.

Studies focusing on the early phase have also mushroomed in psychotic disorders. Dr McGorry and coauthors² introduce an ultra-high-risk (UHR) approach to identify people in the prodromal phase of psychotic disorder. UHR criteria are based on a combination of known trait and state risk factors for psychosis, including attenuated positive psychotic symptoms, brief self-limited psychotic symptoms, and a family history of psychotic disorder.

Early identification is critical, as meta-analysis, as well as systematic reviews, demonstrated that a longer duration of untreated psychosis is associated with worse outcome, poorer response to antipsychotic treatment, and greater neuroimaging changes. Moreover, intervening during the early stages appears to reduce the burden of disability and the prevalence of full-blown illness.

An imperative reason for offering these 2 papers^{1,2} here together is their striking convergence. In particular, in their longitudinal investigations, the authors have found evidence of staging during the development of the disorders. Staging, a

notion already recognized in other areas of medicine, is a more advanced way of characterizing a disorder.

These findings are both comforting and disturbing. Comforting, because we are finally learning about the early stages of major disorders from prospective observations. Disturbing, because they point to the limitations of the symptom-based approach to diagnosis, which delays any advance in developing effective early interventions. Past classifications in psychiatry were developed on the implicit assumption of lasting stability. However, we are now learning that psychopathological manifestations have changed, not only throughout history³ but also during the lives of people suffering from BDs and psychotic disorders.

Clearly, there is a problem with a system that diagnoses a person with budding schizophrenia with some type of depressive disorder and, following the guidelines, will prescribe an antidepressant that will activate the psychosis and worsen the prognosis. Similarly, it is a misfortune when a young patient from a family with BD is diagnosed with some kind of depressive illness and, according to the guidelines, will receive an antidepressant that will trigger their first manic episode, with the associated psychosocial detriment.

Moreover, as young patients move through the early stages of BD or psychosis, the traditional approach generates the illusion of multiple comorbid diagnoses and forces unnecessary polypharmacy.

The symptom-based approach serves better when the clinician is dealing with a fully developed disorder, but it is of no value when effective intervention appears to be needed most—in early onset. However, to identify patients in the early stages of BD and psychotic disorder, the clinician would have to focus on characteristics and features other than bipolar episodes or psychotic symptoms.

The present diagnostic method was developed a long time ago, under very different circumstances, and for different purposes. It is less fitting today, for use in the choice of treatment, for prognosis, for emotional problems in the community, and

for young people experiencing prodromes of major psychiatric disorders.

Clearly, a more adaptable approach is needed. Clinical staging may be one of the productive ways to carry us out of this unfortunate situation, and it may open doors for more fruitful research, including gene–environment interaction. How the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, will address these new challenges remains to be seen.

Perhaps the most important directions emerging from these longitudinal studies are the treatment implications. Emerging data support the assumption that intervening early pays off and reduces transition from less specific into specific disabling ailments. The observations also indicate that BDs, if properly recognized, can be treated in adolescence effectively, and that offspring requiring stabilizing treatment against recurrent episodes tend to respond to the same stabilizer as the parent with BD. Also, transitions from prepsychotic into psychotic disorder can be significantly reduced, even by interventions such as essential fatty acids or psychosocial interventions.

However, if the early manifestations of major disorders are not recognized for what they are, and are treated according to the traditional diagnosis, young patients may be harmed; that is, switched to a mania, triggered into a psychosis, destabilized, and induced into a later stage.

References

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