

1

Youth Mental Health Toward a New Paradigm

Peter J. Uhlhaas and Stephen J. Wood

Abstract

Progress in science is frequently achieved when challenges are made to the dominant mode of thinking and novel paradigms begin to emerge, providing new frameworks to organize data and conduct empirical inquiry. To examine current thinking in the areas of youth mental health, this 28th Ernst Strüngmann Forum was convened to scrutinize early intervention and treatment for emerging mental disorders during youth. The multifaceted contributions in this volume argue that current approaches to research and intervention need to shift away from adulthood and focus on the predominant onset period for mental ill-health: youth, the period between 15–24 years of age. Wide-ranging implications emerged for diagnosis, treatment, and research. This chapter provides background to the topics addressed at this 28th Ernst Strüngmann Forum and highlights future prospects for a youth mental health paradigm.

The Challenge of Mental Health

Mental health disorders constitute a major challenge to both society and science. Syndromes such as schizophrenia, depression, anxiety, and personality disorders comprise some of the largest disease burdens worldwide, yet funding for research and treatment of these conditions is disproportionately small compared to other medical conditions (e.g., cancer, AIDS/HIV) (Woelbert et al. 2019). Moreover, the continued stigmatization of mentally ill individuals contributes to poor outcomes and barriers to help-seeking.

Currently, it is estimated that 1.1 billion people are affected worldwide by mental or substance use disorders. Moreover, in both high- and middle-income countries, significant gaps in treatment exist. For example, only one in five people from high-income countries and only one in 27 people from low- and middle-income countries receive minimally adequate treatment for depression (Global Mental Health Group 2007). For the vast majority of these people,

limited availability of existing treatments is exacerbated by a lack of efficacy for some of the most disabling features of major syndromes, such as impairments in cognitive and functional domains. Despite the promises of genetics and translational neuroscience, insights into the causal mechanisms of major syndromes remain rudimentary, and the search for biomarkers to improve diagnosis and stratification has thus far been unsuccessful. Development of novel therapies, both pharmacological and psychosocial, has also largely stalled (Hyman 2013).

One reason for the absence of significant breakthroughs in improving mental health has been the way in which research and treatment have been framed. Over the last 100 years, a cardinal feature of the existing paradigm in mental health has been its emphasis on fully established disorders in adulthood. Diagnostic and therapeutic approaches constructed around the adult have resulted in a pervasive therapeutic pessimism, in particular in regard to syndromes such as schizophrenia. Fuelled by theories that neurodegenerative processes set a person on a course for life-long disability, this pessimism frequently has become a self-fulfilling prophecy.

Rethinking Mental Health

Over the last two decades, prevailing ideas about mental illness have started to change. Insel and Fenton (2005:591), for instance, stressed that “mental disorders begin in early life and are common and protracted,” constituting “chronic diseases of the young.” Out of the entrenched attitude from the past, a more optimistic outlook has emerged: one aimed at improving mental health, in particular in young people/youth, stimulated by the early intervention approach in the psychosis movement (McGorry et al. 2008a). These early pioneers realized that to improve outcomes in people with schizophrenia, which typically emerges during the transition from adolescence to adulthood, the duration of untreated psychosis must be reduced (Marshall et al. 2005). Specialized clinics set up to detect young people during their first episode of psychosis provided an initial impetus to improve mental health, followed by the concept of clinical high-risk for psychosis (CHR-P), which served as the first blueprint for a preemptive psychiatry approach (Yung et al. 2012).

CHR-P criteria define a group of young people (usually between the age of 15 and 30, the peak onset years for psychotic disorders) who are experiencing subthreshold psychosis symptoms and/or have a genetic liability combined with a functional decline (Fusar-Poli et al. 2015). An alternative approach to CHR-P diagnosis has been the basic symptom approach, which defines risk for psychosis based on the presence of self-experienced cognitive and perceptual anomalies, which are thought to represent the earliest indicators for the development of psychosis (Schultze-Lutter et al. 2016). Meta-analysis suggests that

CHR-P criteria confer a risk of developing psychosis within a two-year period at 10–30% (Fusar-Poli et al. 2013a).

The identification of behavioral and neurobiological predictors of transition to psychosis and functional outcomes in CHR-P cohorts is an ongoing endeavor. A critical aspect of the CHR-P approach has been the identification of interventions capable of reducing the likelihood of transition to psychosis. Overall, evidence suggests that psychosocial interventions, such as cognitive behavioral therapy (CBT), reduce the risk of transition (Fusar-Poli et al. 2013a). Evidence for pharmacological interventions, however, has thus far been mixed, and research is ongoing to identify more effective ways of modifying the course of emerging psychosis in young people.

Initially, the early intervention movement was firmly rooted in improving the outcome of psychotic disorders, especially in schizophrenia. Its scope has now been broadened to target emerging mental disorders of youth more generally, due to two important observations.

First, young people with CHR-P criteria rarely present solely with signs of psychosis. In the large majority of cases, they display a range of other symptoms that defy the idealized DSM-5 categories. Indeed, the CHR-P concept has been referred to as a “pluripotent risk stage” (McGorry et al. 2018a) for a range of mental health outcomes, of which psychosis is only one. This is supported by follow-up data which highlight that CHR-P individuals who do not transition to psychosis will, in the majority of cases, show nonpsychotic disorders that are associated with a significant impact on functional outcomes (Lin et al. 2015).

Second, emerging epidemiological evidence has pinpointed a crucial aspect of mental health: all major syndromes—schizophrenia, depression, personality disorders, and substance abuse, which constitute approximately 75% of mental disorders—begin before the age of 24 years (Kessler et al. 2005; Kim-Cohen et al. 2003), with a significant proportion of 15- to 24-year-olds affected by mental illness at any one time (McCrone et al. 2008). Prevalence has increased over recent decades (Collishaw et al. 2004; Rutter and Smith 1995) and is likely to continue to do so (McCrone et al. 2008). Data from the National Comorbidity Study Adolescent Supplement indicate that 40% of 13- to 17-year-olds in the United States had a mental disorder in any one year (Kessler et al. 2012). These findings are supported by large prospective cohort studies, such as the Great Smoky Mountains Study, which show that by age 21, 61% of participants had experienced a diagnosable mental disorder; this increased to 83% when sub-threshold disorders (with functional impairment) were included (Copeland et al. 2011). Even when these disorders resolve, they can have lasting impacts on economic and social outcomes in later life (Gibb et al. 2010). Accordingly, these data emphasize that the time frame between 12 and 24 years of age constitutes *the developmental period* with the most pronounced manifestation of mental health disorders.

These findings have fundamental implications for the ways in which mental disorders are researched, diagnosed, and treated. To further the development of a youth mental health paradigm and establish trajectories for future research and intervention to pursue, we proposed this Ernst Strüngmann Forum to address collectively the questions and challenges in the field.

Core Themes

Three main themes, described below, provided a conceptual backdrop to this Forum and were used to focus our efforts. Any discussion of youth mental health, however, can easily be hampered when there is a lack of clear definitions. Terms such as *adolescence* or *youth*, for instance, are understood differently in different contexts (for an in-depth discussion, see Torous et al., this volume). Thus, qualifying these contexts proved important during our discussions. Now, as we prepare to pass along the results, we confront again the issue of terminology. Since there is no way to reconcile the multiple aspects involved, we have recommended that the WHO guidelines be used when reference is made to adolescents (10–19 years of age) and youth/young people (15–24 years of age). This was a pragmatic decision—one that we hope will not detract from the highly dynamic nature of this developmental stage of transition from adolescence to adulthood.

Rethinking Diagnostic Systems in Mental Health

Current diagnostic systems (DSM-5, ICD-10) have undergone extensive critique in recent years due to the lack of construct validity of major categories, the lack of biological markers, and high comorbidity for the large majority of disorders. One area that has received less attention, however, is the developmental aspect of psychopathology and the resulting challenges to current nosology. The clinical picture of emerging mental illnesses in young people is often complicated by mixed symptom patterns and frequent comorbid substance use (Sawyer et al. 2000). This may reflect the fact that the earliest manifestation of these conditions (in adolescence or youth) comes in the form of undifferentiated “subsyndromal” symptoms; that is, before a clear-cut diagnosable illness emerges.

This contrasts the long-standing assumption that mental disorders constitute categorical entities. It also highlights the limitation of current diagnostic systems, which are likely to reflect (artificial) end points of developmental trajectories. Indeed, research to identify genes that confer risk to individual syndromes have found instead that the genes are frequently shared across different DSM-5 categories (Owen 2014), consistent with long-standing evidence of comorbidity for most syndromes (Plana-Ripoll et al. 2019). While approaches that highlight the importance of comorbidity and transdiagnostic factors in adult mental health conditions are increasingly being recognized (Fusar-Poli et

al. 2019), unclear diagnostic boundaries in emerging mental disorders are the rule, not the exception. This underlines an urgent need for novel approaches to define “disorders” and “caseness” in youth, as in clinical staging models that have been proposed to guide intervention (McGorry et al. 2006).

Rethinking Treatment

A fundamental implication of the emergence of the majority of mental disorders during youth is the importance of early intervention. Both at subsyndromal and threshold levels, mental disorders are costly, from personal and societal viewpoints. Disorders can lead to substantial disability, long-term morbidity, welfare dependency, and premature mortality (Butterworth and Berry 2004; Killackey et al. 2006) at a period when major developmental processes occur to determine the path that a young person follows, in terms of vocational and social milestones.

There is a growing recognition that a profound redesign of services and intervention is required. In 2010, early intervention for mental illness was established as a top priority in the U.K. Medical Research Council Mental Health Strategy (MRC Strategic Review Group 2010), which delineated the need to “identify individuals at risk in order to target intervention.”

Despite the importance and high prevalence of mental disorders in young people, individuals with emerging mental disorders face major difficulties in accessing appropriate treatment (Singh 2009). This is partly due to the “gap” in care between child and adult mental health services as well as to a reluctance to seek help, stigma, and negative attitudes toward professionals (McGorry 2007; Rickwood et al. 2007). In the U.S. National Comorbidity Study, only a little more than one-third of adolescents with a mental disorder received mental health care, but this tended to be directed toward childhood-onset conditions, such as attention deficit hyperactivity disorder. Moreover, less than one in five adolescents with disorders of youth onset (anxiety, substance use disorders) received care (Merikangas et al. 2011).

Current treatment paradigms, at both the service and individual level, focus on diagnosis. Typically, official diagnostic systems, such as the DSM-4 and ICD-10, were derived from chronic samples, where the impression of stability and validity is enhanced (Cohen and Cohen 1984). Early clinical features are not differentiated from those that become apparent as a disorder persists. Such diagnoses are not useful in guiding early intervention or treatment of less severe cases, and do not further our understanding of the processes involved in the emergence of disorders.

It is essential that a different approach be developed. Diagnosis needs to be refined so that treatments can be selected in a safer, more effective manner, and prognosis must be accurately assessed. Such an alternative approach would allow for the array of biological disturbances at differing phases of the illness

to be better defined and reappraised within an appropriate clinical-pathological framework.

Rethinking Research

The emergence of major mental disorders during youth highlights the need to identify the unique factors that contribute to their manifestation during this developmental period. Until recently, an essential dogma was the assumption that fundamental properties of cortical networks are sculpted mainly *in utero* and the early postnatal years. Accordingly, later developmental stages were assumed to have little or no effect on the functional characteristics and anatomical layout of large-scale networks. Recently, however, a range of disciplines from basic neuroscience to neuroimaging has provided evidence that the period between 15 and 24 years of age is associated with profound changes in behavior and cognition as well as the underlying neural processes, including modifications in neurotransmitter systems, reorganization of functional networks, and ongoing changes in anatomical parameters (Lee et al. 2014a).

While these processes have increasingly been described in detail, critical links to emerging psychopathology still remain to be established. Indeed, the close correlation between the onset of certain disorders, such as anxiety, and ongoing brain maturational processes, for instance in fear extinction (Pattwell et al. 2011), suggests that aspects of psychopathology may be directly linked to changes in neural circuits during youth. If true, such a framework could have wide-ranging implications for understanding the etiology of major mental disorders as well as treatment. Furthermore, monitoring normative developmental trajectories might provide opportunities to identify individuals at greater risk for mental disorders. Central to this effort will be research that links individual variability in these trajectories to clinical outcomes, and the extent to which multiple domains of cognitive performance and neurobiological assessment can be combined into a cogent risk score (Marquand et al. 2019).

Emerging evidence on the profound changes that take place in neural processing and behavior during youth carries important implications for interventions. Currently, the majority of psychosocial and pharmacological treatments that are applied to emerging mental disorders during youth were originally developed for adult populations. Accordingly, one important consequence of the youth mental health paradigm may be that interventions must consider developmental modifications to correct aberrant maturational processes so that therapeutic efficacy can be maximized. For example, interventions aimed at targeting social functioning need to recognize the specific developmental time course of social cognition across adolescence and adjust their contents accordingly (Bartholomeusz et al. 2011). Similarly, pharmacological therapies need to account for the ongoing maturational changes in basic circuit properties.

Our Approach

To “rethink” these core topics, experts from clinical research, neuroscience, health policy as well as developmental and social psychology worked collectively at this Forum to address the nature of psychopathology, its underlying causal factors, and mechanisms. Throughout, the overarching goal was to generate understanding that would move us further away from the current paradigm (i.e., diagnostic and therapeutic approaches designed to address fully established mental disorders in adults), toward one centered on the emergent nature of mental ill-health and the necessity for early intervention in youth. The results of this multifaceted dialogue are captured in this volume, organized around the following primary topics:

1. *Epidemiology, classification, and diagnostic issues.* The transition from childhood to adulthood is associated with the highest incidence of mental disorders across the life span (Costello et al. 2011), yet current classification frameworks were developed to fit the psychopathological presentation of adult populations. Thus, they perform poorly during early stages of mental illness. Several alternatives to the prevailing diagnostic approach have been suggested: the Research Domain Criteria developed by the National Institute of Mental Health (Cuthbert and Insel 2010, 2013), the Hierarchical Taxonomy of Psychopathology (HiTOP) (Kotov et al. 2018), network theory (Borsboom 2017), and the Psychopathology (“p”) Factor (Caspi et al. 2014; Caspi and Moffitt 2018). Although all of these approaches embrace a transdiagnostic approach, they focus on different aspects of psychopathology, and none incorporates a longitudinal perspective or considers developmental context:
 - How can emerging psychopathologies best be characterized?
 - Are there early features that indicate trajectories toward mental disorders?
 - What are the temporal sequences and stages of the differential evolution of premorbid phases?
 - What is the relationship between normal functional trajectories and trajectories for psychopathology?
 - What are the best indicators of need for intervention during the unfolding course of mental disorders?
2. *Context for emerging mental disorders: biological, psychological, and sociocultural processes.* The transition from childhood to adulthood is a developmental period that is highly influenced by social and cultural context, but our understanding of the way these contexts interact with individual differences (e.g., genetic variation) to generate or moderate psychopathology is limited. Combined with known transcultural variation in mental health, there is a critical need to increase understanding of the general applicability of models in youth mental health. This is

likely to be important for the development of appropriate interventions and services as well as the identification of risk and resilience factors.

- Which key precursors are susceptible to contextual modification?
 - Which contextual factors confer resilience and risk for emerging psychopathology?
 - How can we characterize/quantify social and cultural context in the context of psychopathology?
 - How do these precursors and risk and resilience factors evolve over time and interact?
3. *Biological mechanisms underlying risk for psychopathology.* A large body of evidence has accumulated over the years, from a range of disciplines, on the profound modifications in the anatomy and functionality of large-scale networks as well as basic circuit modifications during the transition from adolescence to adulthood (Lee et al. 2014a). Because of the temporal coincidence of these changes with the expression of major mental disorders during this period, we need to understand whether the developmental events at the neural and behavioral level constitute vulnerability for emerging psychopathologies. If so, this could point toward opportunities for understanding the etiology as well as possible interventions.
- What are the core modifications to circuit properties during the transition from childhood to adulthood?
 - How might animal models guide our understanding of the development of psychopathology and interventions?
 - How do earlier risk factors interact with the expression of mental disorders in youth?
 - What are the implications for the development of biomarkers during this period?
 - How can these findings inform the development of interventions?
4. *Developing and implementing prevention and early intervention.* Given the clear evidence supporting the emergence of major mental disorders in young people, the continued division of mental health services along the same developmental lines (child vs. adult), as practiced in other areas of medicine, seems perverse. Actually developing and implementing services for young people has, however, presented a range of challenges across different cultures, communities, and health systems. Developing such services relies on decisions about boundaries between those who are well and those who have a disorder. Labeling and over-treatment are key concerns. Such boundaries also tend to be influenced by available resources, which vary by country and health system.
- What political, economic, and systemic issues need to be addressed to deliver effective prevention and early intervention?

- How can translational basic science be used to improve assessment, treatment, and clinical decision making?
- What are the prospects of delivering interventions to young people through e-mental health and how might these be studied?
- What might be the optimal way to adapt and establish youth mental health services in current health systems?
- How might interventions consider the social, cultural, economic, and political contexts in which the transition from childhood to adulthood takes place?

Future Steps

Paradigmatic changes in science do not occur linearly: they follow a landscape of dynamic systems, characterized by local minima and bifurcations that can suddenly give rise to new system properties. So, too, may be the path that is followed toward a youth mental health paradigm.

We hope that the multifaceted exchanges from this Forum will contribute to shift attention away from the dominant paradigm in mental health toward a new approach: one focused on understanding emerging mental ill-health and early interventions in youth. Undoubtedly, this is an ambitious goal. Yet in the absence of significant advances and unfulfilled promises in the field, we are propelled forward by the urgent need to respond to the ever-increasing burden that mental health places on individuals and societies.

It is our sincere hope that the ideas and proposals outlined in this volume, as well as the open questions that remain, will provide a roadmap for research to follow over the next decade. Practices, perspectives, and methods need to be reconceptualized and reframed. This is a herculean task, reliant on vision, commitment, and collaboration.

From “Youth Mental Health: A Paradigm for Prevention and Early Intervention,”
edited by Peter J. Uhlhaas and Stephen J. Wood. Strüngmann Forum Reports, vol. 28,
Julia R. Lupp, series editor. Cambridge, MA: MIT Press. ISBN 978-0-262-04397-7