Child Psychiatry Growin' Up

Like adolescents' march toward adulthood, research on the developmental origins of mental illness steadily advances. Six articles in this month's *Journal* reflect child psychiatry's growing impact, as it profoundly shapes thinking about mental illnesses as they afflict individuals of all ages. Moreover, these articles presage a new period in the field, which encourages increasing dialogue among clinicians, clinical researchers, and neuroscientists. Together, these six articles consider the way in which childhood measures of development and behavior may presage adult patterns of behavior.

Longitudinal studies are the foundation upon which the connection between child and adult psychiatry rests, because they demonstrate the continuity between childhood behavior and adult illness. Cognitive dysfunction represents one risk factor, manifest during childhood, for adult mental illness. In the first article, a longitudinal study, Koenen et al. measured IQ between 7 and 11 years of age and then assessed psychiatric illness between 18 and 32 years of age (1). Several adult illnesses—schizophrenia spectrum disorders, major depressive disorder, and anxiety disorders—were associated with low IQ in childhood.

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The association between childhood cognitive deficits and adult illness could reflect two potential processes. First, the association could suggest that pathophysiological processes already present in the developing brain might first manifest as diminished cognitive function before ultimately being expressed as adult pathological syndromes. From this first perspective, early cognitive dysfunction and later mental illness represent alternative manifestations of the same underlying neural processes. Second, an alternative explanation is that diminished cognitive abilities reflect loss of functional brain reserve needed to buffer children's mental function when they are exposed to risks. The combination of reduced buffering capacity and exposure to stress ultimately could produce loss of brain function and manifesting mental illness in adulthood. From this second perspective, intact cognitive ability confers resilience that helps prevent adult syndromes from developing in adverse circumstances. Ultimately, evaluating these two possibilities requires direct measurement of brain structure and function in children so that neural processes can be linked to measures of risk, resilience, and changing manifestations of psychopathology over time. Five studies described in this issue applied magnetic resonance imaging (MRI) to lay the groundwork for research that will eventually test the reasonableness of such alternative hypotheses on brain-behavior associations.

As researchers entering the field during long-past periods of excitement about new technologies, we greet current enthusiasm about MRI with some skepticism. Nevertheless, articles in the current issue portend unique, transformative changes in child psychiatry. Why does MRI research engender such enthusiasm? MRI provides heretofore unseen opportunities to observe the living, functioning, thinking child's brain in action. The safety of the technique allows repeated imaging, as children enter and leave successive developmental stages. The earliest signs of alterations in normal brain function can be observed in ill children, as well as the effects of their illness and treatment on the brain structures that support the reserve of brain function that normally helps prevent illness. A combination of temporal sensitivity in functional MRI (fMRI) and anatomical precision in structural MRI (sMRI) generates data in children that can be more directly integrated with findings from basic neuroscience than previously possible. The five MRI

studies in this issue examine three separate, core aspects of pediatric mental illness, each stimulating discussions among clinicians, clinical researchers, and neuroscientists.

For the first instance, research on pediatric depression has evolved radically, from a period when the condition was viewed as nonexistent to the point where data on the condition heavily inform understanding of the adult syndrome. Promising leads for novel treatments emerge from work in animal models (2–4). This work implicates functioning within a key brain-reward node, the striatum, in ecologically valid models of depression-like behavior. The study by Forbes and colleagues, in this issue, used fMRI to generate parallel data in adolescents that support basic-clinical dialogue on development of brain-reward circuitry and its modulation by current and potentially novel treatments (5). Their data show that individual differences in striatal function reflect individual differences in adolescents' daily experiences of positive affect. Beck's fundamental insight of a systematic cognitive bias or negativity in depressed patients thus may have its roots in these individual differences in affect that are already apparent in adolescence (6). Extending research on cognition through brain imaging allows an integration of psychiatry's current theories about treatments with its future theories and their basis in neuroscience. This integration will allow us to examine the origins of cognitive bias in perturbed brain development. Such integration, in turn, encourages basic-clinical dialogue likely to transform the field. In the case of depression, this discussion can focus on developmental aspects of striatal function and its modulation by potential antidepressant therapies when children learn about the emotional salience of rewards.

Second, similar basic and clinical research on frontostriatal circuitry informs conceptualizations of attention deficit hyperactivity disorder (ADHD). Studies in rodents and nonhuman primates suggest that modulation of frontostriatal function by psychostimulants is a possible basis for the effects of these drugs in ADHD (7, 8). Consistent with this possibility, Qiu and colleagues used sMRI to show that the shape of the caudate and anterior and ventral putamen nuclei of the striatum is compressed and their volume is diminished in boys with ADHD (9). Such structural alterations may reflect either illness-related effects or the toxic effects of treatment. Shaw and colleagues examined these two possibilities by comparing the change in cortical thickness between 12 and 16 years of age in children with ADHD who were treated or not treated with stimulants, compared to typically developing children (10). The children who were not treated lost more cortical thickness than either the treated or typically developing children. This suggests that psychostimulant treatment does not cause alterations in brain structure. While studies in rodents raise concerns about potential adverse effects of stimulants (8), the data of Shaw et al. alleviate some of these concerns. Considered alone, neither this earlier basic work in rodents nor the current imaging work in children generates definitive insights on the risks and benefits of ADHD treatment. Considered together, however, a mutually informative basic-clinical dialogue provides a new opportunity to arrive at such insight.

Finally, the field has struggled to generate algorithms that might identify children at particularly high risk for poor outcomes from disruptive behavioral abnormalities. Emerging basic work suggests that differences in the engagement of brain circuitry by motivationally salient stimuli may distinguish among healthy children and children with behavior disorders, such as ADHD and conduct disorder. Moreover, this brain circuitry may be most perturbed in those children facing a particularly high risk for poor outcome. Some of this work focuses on the salience of rewards, encoded in frontostriatal circuitry, as described in the previous paragraph. Other work focuses on the salience of punishments, encoded in the amygdala and associated frontal circuitry.

Two studies reported in this issue used fMRI to extend this work to children. Rubia and colleagues focused on brain-reward circuitry to demonstrate that children with ADHD can be differentiated from children with conduct disorder on the basis of the sensitivity of their brains to rewards (11). Children with conduct disorder have diagnos-

tically specific diminished activation of the reward circuitry of the orbitofrontal cortex. Similarly, Jones and colleagues focused on brain systems encompassing the amygdala that are typically engaged by punishments and threatening circumstances (12). This extends considerable work in laboratory animals demonstrating that early-life individual differences in response to punishments mediate long-term behavioral trajectories (13). Jones and colleagues showed that callous-unemotional traits in children are associated with amygdala hyposensitivity to fearful faces. These findings support the hypothesis that children's relative lack of neural response to adverse or fearful stimuli predicts deviant adult behavioral profiles. Eventually, this information may be used to predict long-term outcomes and to tailor treatments individually targeted toward underlying neural dysfunction associated with different forms of behavior disorders. The consonance of the imaging findings in children with those from laboratory animals may provide models for discovery of new neurobiological treatments. The reward and punishment biases demonstrated by brain imaging may likewise inform new psychotherapeutic treatments, just as the observation of negative cognitive biases informed Beck's development of cognitive therapy for depression.

Taken together, these six articles chart the ever-increasing promise of research on pediatric mental illnesses. In a steady progression of findings, longitudinal research lays bare the developmental roots of virtually all chronic psychopathologies. When integrated with modern imaging techniques, this work shows that alterations in brain function and structure associated with adult mental illnesses manifest early in development. Such evidence of early pathological change suggests that treatment for pediatric mental disorders should not be delayed simply because youth is normally considered to be a carefree time of life or because there is reluctance to intervene while children are still developing. Instead, these articles provide evidence that the developmental process itself is already awry. Now more than ever, dialogue among clinicians, clinical researchers, and basic researchers supports the developmental conceptualization of mental disorders. Child psychiatry has matured into a field that shapes not only the ways in which we conceptualize the roots of most mental illnesses but also the ways in which they are treated.

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