Pediatric Psychopharmacology

DOI 10.1055/s-0042-112819
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Georg Thieme Verlag KG
Rüdigerstraße 14
70469 Stuttgart
ISSN 0176-3679

Thieme

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In this issue, Koelk and Plener provide an insightful update on the current status of pharmacotherapy for children and adolescents with psychiatric disorders. From their review, it is evident that recently much progress has been made in understanding the possible therapeutic benefit and risks of psychiatric medications during development. Controlled clinical trials have been conducted to test the acute efficacy of the most commonly used medications used to treat attention deficit/hyperactivity disorder (ADHD), mood and anxiety disorders in children and adolescents. These data have allowed a number of meta-analyses to be performed, thus achieving the highest level of methodological evidence in medicine. For example, we now know that compared to a placebo control stimulant medications have on average a large effect size in ADHD, whereas antidepressants have a small effect size in depression and a medium effect size in anxiety disorders. Studies are also available that have directly compared pharmacotherapy to psychosocial therapy, and monotherapy to combined therapy [1]. These data are useful to inform clinicians, families, and policy makers, and have informed the current clinical practice guidelines for the care of youths with emotional and behavioral disturbances.

Research has revealed both the value and the limitations of the current psychopharmacological approaches to mental illness during development. Current treatments are not curative. While effective in decreasing specific symptoms such as inattention, hyperactivity, mood instability, aggression, and anxiety, it remains unclear if medications can modify the trajectory of illness and improve functional prognosis. The great promise of psychiatric interventions in child psychiatry rests on the evidence that basically all psychopathology is developmental and the first manifestations of mental illness typically occur in the first two decades of life. Therefore, early identification and treatment should offer the best opportunity for preventing the long-term sequelae of mental illness and improving the overall level of functioning. It is, however, extremely difficult to demonstrate long-term effectiveness of treatment interventions. In fact, on the one hand, long-term randomized controlled trials have questionable feasibility given that, with time, patients leave the assigned treatment arms for different reasons. For example, in a trial of antipsychotics in early onset psychosis, despite the absence of a placebo condition, only 12% of youths were still receiving the original study treatment at the end of the 44-week study [2]. Uncontrolled studies, on the other hand, suffer from treatment selection biases as more severely impaired patients may stay longer on medications whereas milder patients tend to discontinue them, thus creating a non-causal association between pharmacotherapy and worse outcome [3]. However, there is indirect evidence that early treatment of severe mental illness, such as psychosis, is linked to better distal prognosis [4].

Safety concerns are obviously paramount when treating children, and the review underscores the need to pay great attention to possible adverse effects of psychiatric medications. The paradoxical finding that antidepressant medications increase the incidence of episodes of suicidal ideation and suicidal attempts in young people has caused much controversy and debate [5]. The mechanism through which suicidality may be induced by antidepressants is unclear, especially because suicidal ideation as measured with depressive symptom rating scales decreases on average during treatment [6]. It seems that a small proportion of young patients, however, react negatively to the pharmacological intervention. Slow titration of medication and careful monitoring during treatment are therefore necessary. Also of great concern are the adverse metabolic effects of second-generation antipsychotics, which have been increasingly used to treat non-psychotic conditions such as aggression and irritability. Because reversing obesity and impaired insulin sensitivity is often difficult, approaches to prevent the onset of these metabolic toxicities should be systematically developed and implemented.

Quite appropriately, the review underscores the need to use medications in the context of a comprehensive treatment approach that includes psychosocial interventions and, as appropriate, specific psychotherapies. The value of combined treatment is evident in the case of anxiety disorder and obsessive-compulsive disorder as well as, to a lesser degree, in depression, particularly for consolidating improvement and preventing relapse [7].

Looking forward into the more distant future of pediatric psychopharmacology as a field of research and clinical care, one could envision the development of pharmacotherapies specifically targeted to correcting the mechanisms of illness. This will require a more complete understanding of the underlying biological psychopathology of mental illness, a situation that is now possible only for certain disorders such as fragile X syndrome or Rhett's syndrome [8]. Indeed, to turn the remarkable advances of neuroscience into effective and safe interventions to prevent and treat mental disorders in children is one of the most challenging tasks of pediatric psychopharmacology research.

Note

The opinions and assertions presented here are the private views of the author, and are not to be construed as official statements of the National Institute of Mental Health, the National Institutes of Health, or the U.S. Department of Health and Human Services.

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received 24.06.2016
revised 24.06.2016
accepted 04.07.2016

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DOI http://dx.doi.org/10.1055/s-0042-112819
Published online: 2016
Pharmacopsychiatry

ISSN 0176-3679

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