

Abstracts

CHILD AND ADOLESCENT PSYCHIATRY

Given space limitations and varying reprint permission policies, not all of the influential publications the editors considered reprinting in this issue could be included. This section contains abstracts from additional articles the editors deemed well worth reviewing.

Meta-Analysis of Randomized, Controlled Treatment Trials for Pediatric Obsessive-Compulsive Disorder

Watson HJ, Rees CS.

Journal of Child Psychology and Psychiatry. 2008 May;49(5):489–98.

Objective: To conduct a meta-analysis on randomized, controlled treatment trials of pediatric obsessive-compulsive disorder (OCD). **Method:** Studies were included if they employed randomized, controlled methodology and treated young people (19 years or under) with OCD. A comprehensive literature search identified 13 RCTs containing 10 pharmacotherapy to control comparisons ($N = 1016$) and five cognitive-behavioral therapy (CBT) to control comparisons ($N = 161$). **Results:** Random effects modeling yielded statistically significant pooled effect size (ES) estimates for pharmacotherapy ($ES = .48$, 95% $CI = .36$ to $.61$, $p < .00001$) and CBT ($ES = 1.45$, 95% $CI = .68$ to 2.22 , $p = .002$). The results were robust to publication bias. **Conclusions:** This is the first meta-analysis of treatment RCTs for pediatric OCD. CBT and pharmacotherapy were the only treatments effective beyond control in alleviating OCD symptoms. CBT showed a greater ES than pharmacotherapy. Previous meta-analyses that included uncontrolled trials exaggerated the efficacy of both treatments.

Frontiers Between Attention Deficit Hyperactivity Disorder and Bipolar Disorder

Galanter CA, Leibenluft E.

Child Adolesc Psychiatr Clin N Am. 2008 Apr;17(2):325–46, viii–ix.

The co-occurrence of attention deficit hyperactivity disorder (ADHD) and bipolar disorder has received much recent attention in the literature. The authors review the literature examining associations between ADHD and bipolar disorder in children, and data concerning severe irritability in youth with ADHD. This article focuses on (1) population-based studies examining ADHD and bipolar disorder or ADHD and co-occurring irritability, (2) the co-occurrence and prospective relationships of ADHD and bipolar disorder in clinical samples, (3) phenomenology and assessment of bipolar disorder and ADHD, (4) treatment of comorbid ADHD and bipolar disorder, (5) family and genetic studies of ADHD and bipolar disorder, and (6) pathophysiologic comparisons between children with ADHD and irritability and bipolar disorder. We draw on the research to make clinical recommendations and highlight important directions for future research.

Understanding the Risk of Using Medications for Attention Deficit Hyperactivity Disorder with Respect to Physical Growth and Cardiovascular Function

Vitiello B.

Child Adolesc Psychiatr Clin N Am. 2008 Apr;17(2):459–74, xi.

The effects of stimulant medications and atomoxetine on physical growth and on cardiovascular function are reviewed in light of the most recent data, with attention to clinical implications and research needs. Although these medications have a favorable benefit/risk profile and do not induce clinically significant changes in growth or cardiovascular function in the majority of cases, careful patient monitoring is needed to identify individuals at risk for negative outcomes. More research is needed to elucidate the mechanism of growth suppression to estimate better the risk for rare but life-threatening events and test the effectiveness of monitoring procedures.

Management of Children with Autism Spectrum Disorders

Myers SM, Johnson CP; American Academy of Pediatrics Council on Children With Disabilities. Pediatrics 2007 Nov;120(5):1162–82. Epub 2007 Oct 29.

Pediatricians have an important role not only in early recognition and evaluation of autism spectrum disorders but also in chronic management of these disorders. The primary goals of treatment are to maximize the child's ultimate functional independence and quality of life by minimizing the core autism spectrum disorder features, facilitating development and learning, promoting socialization, reducing maladaptive behaviors, and educating and supporting families. To assist pediatricians in educating families and guiding them toward empirically supported interventions for their children, this report reviews the educational strategies and associated therapies that are the primary treatments for children with autism spectrum disorders. Optimization of health care is likely to have a positive effect on habilitative progress, functional outcome, and quality of life; therefore, important issues, such as management of associated medical problems, pharmacologic and nonpharmacologic intervention for challenging behaviors or coexisting mental health conditions, and use of complementary and alternative medical treatments, are also addressed.

A Review of Psychotherapeutic Interventions for Children and Adolescents with Eating Disorders

Rutherford L, Couturier J.

J Can Acad Child Adolesc Psychiatry. 2007 Nov;16(4):153–7.

Objective: Psychotherapeutic interventions for child and adolescent eating disorders have recently received increasing attention in the research literature. This article attempts to summarize these studies.

Method: The current literature was reviewed using the PubMed and Embase databases under the search terms eating disorders, child, adolescent, and psychotherapy. Here we will present a practical overview of the current evidence for psychotherapeutic interventions in this clinical population. **Results:** There have been some very promising findings with regards to specific types of therapy for anorexia nervosa (AN), bulimia nervosa (BN) and binge eating disorder (BED). **Conclusions:** The best evidence available suggests that family-therapy models are most effective for treating adolescents with AN, and that CBT models are most effective for adolescent BN, although family-based treatment may also be effective for adolescents with BN. Too few studies have been done on BED in adolescents to draw any conclusions; however CBT, IPT and DBT are all theoretically promising.

The Treatment for Adolescents With Depression Study (TADS): Long-Term Effectiveness and Safety Outcomes

March JS, Silva S, Petrycki S, Curry J, Wells K, Fairbank J, Burns B, Domino M, McNulty S, Vitiello B, Severe J.

Archives of General Psychiatry 2007 Oct;64(10):1132–43.

Context: The Treatment for Adolescents With Depression Study evaluates the effectiveness of fluoxetine hydrochloride therapy, cognitive behavior therapy (CBT), and their combination in adolescents with major depressive disorder. **Objective:** To report effectiveness outcomes across 36 weeks of randomized treatment. **Design and Setting:** Randomized, controlled trial conducted in 13 academic and community sites in the United States. Cognitive behavior and combination therapies were not masked, whereas administration of placebo and fluoxetine was double-blind through 12 weeks, after which treatments were unblinded. Patients assigned to placebo were treated openly after week 12, and the placebo group is not included in these analyses by design. **Participants:** Three hundred twenty-seven patients aged 12 to 17 years with a primary DSM-IV diagnosis of major depressive disorder. **Interventions:** All treatments were administered per protocol. **Main Outcome Measures:** The primary dependent measures rated blind to treatment status by an independent evaluator were the Children's Depression Rating Scale-Revised total score and the response rate, defined as a Clinical Global Impressions-Improvement score of much or very much improved. **Results:** Intention-to-treat analyses on the Children's Depression Rating Scale-Revised identified a significant time \times treatment interaction ($P < .001$). Rates of response were 73% for combination therapy, 62% for fluoxetine therapy, and 48% for CBT at week 12; 85% for combination therapy, 69% for fluoxetine therapy, and 65% for CBT at week 18; and 86% for combination therapy, 81%

for fluoxetine therapy, and 81% for CBT at week 36. Suicidal ideation decreased with treatment, but less so with fluoxetine therapy than with combination therapy or CBT. Suicidal events were more common in patients receiving fluoxetine therapy (14.7%) than combination therapy (8.4%) or CBT (6.3%).

Conclusions: In adolescents with moderate to severe depression, treatment with fluoxetine alone or in combination with CBT accelerates the response. Adding CBT to medication enhances the safety of medication. Taking benefits and harms into account, combined treatment appears superior to either monotherapy as a treatment for major depression in adolescents.

3-Year Follow-up of the NIMH MTA Study

Jensen PS, Arnold LE, Swanson JM, Vitiello B, Abikoff HB, Greenhill LL, Hechtman L, Hinshaw SP, Pelham WE, Wells KC, Conners CK, Elliott GR, Epstein JN, Hoza B, March JS, Molina BS, Newcorn JH, Severe JB, Wigal T, Gibbons RD, Hur K.

J Am Acad Child Adolesc Psychiatry. 2007 Aug;46(8):989–1002

Objective: In the intent-to-treat analysis of the Multimodal Treatment Study of Children With ADHD (MTA), the effects of medication management (MedMgt), behavior therapy (Beh), their combination (Comb), and usual community care (CC) differed at 14 and 24 months due to superiority of treatments that used the MTA medication algorithm (Comb+MedMgt) over those that did not (Beh+CC). This report examines 36-month outcomes, 2 years after treatment by the study ended. **Method:** For primary outcome measures (attention-deficit/hyperactivity disorder [ADHD] and oppositional defiant disorder [ODD] symptoms, social skills, reading scores, impairment, and diagnostic status), mixed-effects regression models and orthogonal contrasts examined 36-month outcomes. **Results:** At 3 years, 485 of the original 579 subjects (83.8%) participated in the follow-up, now at ages 10 to 13 years, (mean 11.9 years). In contrast to the significant advantage of MedMgt+Comb over Beh+CC for ADHD symptoms at 14 and 24 months, treatment groups did not differ significantly on any measure at 36 months. The percentage of children taking medication >50% of the time changed between 14 and 36 months across the initial treatment groups: Beh significantly increased (14% to 45%), MedMed+Comb significantly decreased (91% to 71%), and CC remained constant (60%–62%). Regardless of their treatment use changes, all of the groups showed symptom improvement over baseline. Notably, initial symptom severity, sex (male), comorbidity, public assistance, and parental psychopathology (ADHD) did not moderate children's 36-month treatment responses, but these factors predicted worse outcomes over 36 months, regardless of original treatment assignment. **Conclusions:** By 36 months, the earlier advantage of having had 14 months of the medication algorithm was no longer apparent, possibly due to age-related decline in ADHD symptoms, changes in medication management intensity, starting or stopping medications altogether, or other factors not yet evaluated.

Psychopharmacology of Pediatric Bipolar Disorder: A Review

Smarty S, Findling RL.

Psychopharmacology (Berl). 2007 Mar;191(1):39–54. Epub 2006 Nov 9.

Rationale: Pediatric bipolar disorder (PBD) is a chronic and debilitating psychiatric illness. It is associated with many short-term and long-term complications including poor academic and social performance, legal problems and increased risk of suicide. Moreover, it is often complicated by other serious psychiatric disorders including attention deficit hyperactivity disorder, oppositional defiant disorder, conduct disorder and substance use disorders. For these reasons, there is a need for effective treatment for PBD. **Objectives:** To review available data from published reports of the treatment of PBD, highlighting those treatment practices for which there is scientific evidence. To suggest directions for future research. **Materials and Methods:** A comprehensive Medline search was performed to identify published reports from 1995 to 2006. Reports with the greatest methodological stringency received greater focus. **Results:** There is limited evidence from double-blind, placebo-controlled trials regarding the treatment of PBD. Available data suggests that lithium, some anticonvulsants and second-generation antipsychotics may be equally beneficial in the acute monotherapy for youth with mixed or manic states. However, because of limited response to acute monotherapy, there is increased justification for combination therapy. There is very limited data on the treatment of the depressed phase of bipolar illness in the youth. Also, very few studies have addressed the treatment of comorbidities and maintenance/relapse prevention in

PBD. **Conclusion:** Although significant progress was made in the treatment of youth with bipolar disorder, there is a need for more methodologically stringent research to more precisely define evidence-based treatment strategies for PBD.

Treatment for Adolescents with Depression Study (TADS): Safety Results

Emslie G, Kratochvil C, Vitiello B, Silva S, Mayes T, McNulty S, Weller E, Waslick B, Casat C, Walkup J, Pathak S, Rohde P, Posner K, March J; Columbia Suicidality Classification Group; TADS Team.

J Am Acad Child Adolesc Psychiatry. 2006 Dec;45(12):1440–55.

Objective: To compare the rates of physical, psychiatric, and suicide-related events in adolescents with MDD treated with fluoxetine alone (FLX), cognitive-behavioral therapy (CBT), combination treatment (COMB), or placebo (PBO). **Method:** Safety assessments included adverse events (AEs) collected by spontaneous report, as well as systematic measures for specific physical and psychiatric symptoms. Suicidal ideation and suicidal behavior were systematically assessed by self- and clinician reports. Suicidal events were also reanalyzed by the Columbia Group and expert raters using the Columbia-Classification Algorithm for Suicidal Assessment used in the U.S. Food and Drug Administration reclassification effort. **Results:** Depressed adolescents reported high rates of physical symptoms at baseline, which improved as depression improved. Sedation, insomnia, vomiting, and upper abdominal pain occurred in at least 2% of those treated with FLX and/or COMB and at twice the rate of placebo. The rate of psychiatric AEs was 11% in FLX, 5.6% in COMB, 4.5% in PBO, and 0.9% in CBT. Suicidal ideation improved overall, with greatest improvement in COMB. Twenty-four suicide-related events occurred during the 12-week period: 5 patients (4.7%) in COMB, 10 (9.2%) in FLX, 5 (4.5%) in CBT, and 3 (2.7%) in placebo. Statistically, only FLX had more suicide-related events than PBO ($p = .0402$, odds ratio (OR) = 3.7, 95% CI 1.00–63.7). Only five actual attempts occurred (2 COMB, 2 FLX, 1 CBT, 0 PBO). There were no suicide completions. **Conclusions:** Different methods for eliciting AEs produce different results. In general, as depression improves, physical complaints and suicidal ideation decrease in proportion to treatment benefit. In this study, psychiatric AEs and suicide-related events are more common in FLX-treated patients. COMB treatment may offer a more favorable safety profile than medication alone in adolescent depression.

The Texas Children's Medication Algorithm Project: Revision of the Algorithm for Pharmacotherapy of Attention-Deficit/Hyperactivity Disorder

Pliszka SR, Crismon ML, Hughes CW, Corners CK, Emslie GJ, Jensen PS, McCracken JT, Swanson JM, Lopez M; Texas Consensus Conference Panel on Pharmacotherapy of Childhood Attention Deficit Hyperactivity Disorder.

J Am Acad Child Adolesc Psychiatry. 2006 Jun;45(6):642–57.

Objective: In 1998, the Texas Department of Mental Health and Mental Retardation developed algorithms for medication treatment of attention-deficit/hyperactivity disorder (ADHD). Advances in the psychopharmacology of ADHD and results of a feasibility study of algorithm use in community mental health centers caused the algorithm to be modified and updated. **Method:** We convened a consensus conference of academic clinicians and researchers, practicing clinicians, administrators, consumers, and families to revise the algorithms for the pharmacotherapy of ADHD itself as well as ADHD with specific comorbid disorders. New research was reviewed by national experts, and rationales were provided for proposed changes and additions to the algorithms. The changes to the algorithms were discussed and approved both by the national experts and experienced clinicians from the Texas public mental health system. **Results:** The panel developed consensually agreed-upon algorithms for ADHD with and without comorbid disorders. The major changes included elimination of pemoline as a treatment option, adding atomoxetine to the algorithm, and refining guidelines for treating ADHD with comorbid depression, aggressive behaviors, and tic disorders. **Conclusions:** Medication algorithms for ADHD can be modified to keep abreast of developments in the field. Although these evidence- and consensus-based treatment recommendations may be a useful approach to guide the treatment of ADHD in children, additional research is needed to determine how these algorithms can be used to maximally benefit child outcomes.

The Age-Dependent Decline of Attention Deficit Hyperactivity Disorder: A Meta-Analysis of Follow-up Studies

Faraone SV, Biederman J, Mick E.
Psychol Med. 2006 Feb;36(2):159–65.

Background: This study examined the persistence of attention deficit hyperactivity disorder (ADHD) into adulthood. **Method:** We analyzed data from published follow-up studies of ADHD. To be included in the analysis, these additional studies had to meet the following criteria: the study included a control group and it was clear from the methods if the diagnosis of ADHD included subjects who did not meet full criteria but showed residual and impairing signs of the disorder. We used a meta-analysis regression model to separately assess the syndromatic and symptomatic persistence of ADHD. **Results:** When we define only those meeting full criteria for ADHD as having 'persistent ADHD', the rate of persistence is low, approximately 15% at age 25 years. But when we include cases consistent with DSM-IV's definition of ADHD in partial remission, the rate of persistence is much higher, approximately 65%. **Conclusions:** Our results show that estimates of ADHD's persistence rely heavily on how one defines persistence. Yet, regardless of definition, our analyses show that evidence for ADHD lessens with age. More work is needed to determine if this reflects true remission of ADHD symptoms or is due to the developmental insensitivity of diagnostic criteria for the disorder.

Risperidone for the Core Symptom Domains of Autism: Results from the Study by the Autism Network of the Research Units on Pediatric Psychopharmacology

McDougle CJ, Scahill L, Aman MG, McCracken JT, Tierney E, Davies M, Arnold LE, Posey DJ, Martin A, Ghuman JK, Shah B, Chuang SZ, Swiezy NB, Gonzalez NM, Hollway J, Koenig K, McGough JJ, Ritz L, Vitiello B.
American Journal of Psychiatry 2005 Jun;162(6):1142–8.

Objective: Risperidone has been found efficacious for decreasing severe tantrums, aggression, and self-injurious behavior in children and adolescents with autistic disorder (autism). The authors report on whether risperidone improves the core symptoms of autism, social and communication impairment and repetitive and stereotyped behavior. **Method:** The database from an 8-week double-blind, placebo-controlled trial (N = 101) and 16-week open-label continuation study (N = 63) of risperidone for children and adolescents with autism was used to test for drug effects on secondary outcome measures: scores on the Ritvo-Freeman Real Life Rating Scale, the Children's Yale-Brown Obsessive Compulsive Scale, and the maladaptive behavior domain of the Vineland Adaptive Behavior Scales. **Results:** Compared to placebo, risperidone led to a significantly greater reduction in the overall score on the Ritvo-Freeman Real Life Rating Scale, as well as the scores on the subscales for sensory motor behaviors (subscale I), affectual reactions (subscale III), and sensory responses (subscale IV). No statistically significant difference was observed, however, on the subscale for social relatedness (subscale II) or language (subscale V). Risperidone also resulted in significantly greater reductions in scores on the Children's Yale-Brown Obsessive Compulsive Scale and Vineland maladaptive behavior domain. This pattern of treatment response was maintained for 6 months. **Conclusions:** Risperidone led to significant improvements in the restricted, repetitive, and stereotyped patterns of behavior, interests, and activities of autistic children but did not significantly change their deficit in social interaction and communication. Further research is necessary to develop effective treatments for the core social and communicative impairments of autism.