Psychiatric Treatment of Children and Adolescents

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

Preventing Onset of Anxiety Disorders in Offspring of Anxious Parents: A Randomized Controlled Trial of a Family-Based Intervention

Ginsburg GS, Drake KL, Tein JY, et al.

Am J Psychiatry (Epub ahead of print, Sep 25, 2015)

OBJECTIVE: The authors examined the efficacy of a family-based intervention to prevent the onset of anxiety disorders in offspring of anxious parents. **METHOD:** Participants were 136 families with a parent meeting DSM-IV criteria for an anxiety disorder and one child 6–13 years of age without an anxiety disorder. Families were randomly assigned to the family-based intervention (N=70) or to an information-monitoring control condition (N=66). All families were expected to complete assessments, administered by blind interviewers, at baseline, at the end of the intervention (or 8 weeks after randomization) and at 6- and 12-month follow-ups. Onset of any anxiety disorder and anxiety symptom severity (assessed using the Anxiety Disorders Interview Schedule for Children) at 12 months were the primary and secondary outcome measures, respectively. **RESULTS:** The incidence of child anxiety disorders was 31% in the control group and 5% in the intervention group (odds ratio=8.54, 95% CI=2.27, 32.06). At the 1-year follow-up, youths in the control group also had higher anxiety symptoms ratings than those in the intervention group. Effect sizes were medium to large (0.81 at 6 months and 0.57 at 12 months for anxiety symptoms), and the number needed to treat was 3.9 at 12 months. Significant moderators included baseline levels of child anxiety; significant mediators were parental distress and modeling of anxiety. Child maladaptive cognitions and parental anxiety did not mediate outcomes. **CONCLUSIONS:** A brief psychosocial prevention program holds promise for reducing the 1-year incidence of anxiety disorders among offspring of anxious parents.

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Extended-Release Guanfacine for Hyperactivity in Children With Autism Spectrum Disorder

Scahill L, McCracken JT, King BH, et al.

Am J Psychiatry (Epub ahead of print, Aug 28, 2015)

OBJECTIVE: Hyperactivity, impulsiveness, and distractibility are common problems in children with autism spectrum disorder (ASD). Extended-release guanfacine is approved for children with attention deficit hyperactivity disorder but not well studied in ASD. **METHOD:** In a multisite, randomized clinical trial, extended-release guanfacine was compared with placebo in children with ASD accompanied by hyperactivity, impulsiveness, and distractibility. **RESULTS:** Sixty-two subjects (boys, N=53; girls, N=9; mean age=8.5 years [SD=2.25]) were randomly assigned to guanfacine (N=30) or placebo (N=32) for 8 weeks. The guanfacine group showed a 43.6% decline in scores on the Aberrant Behavior Checklist-hyperactivity subscale (least squares mean from 34.2 to 19.3) compared with a 13.2% decrease in the placebo group (least squares mean from 34.2 to 29.7; effect size=1.67). The rate of positive response (much improved or very much improved on the Clinical Global Impression-Improvement scale) was 50% (15 of 30) for guanfacine compared with 9.4% (3 of 32) for placebo. A brief cognitive battery tapping working memory and motor planning showed no group differences before or after 8 weeks of treatment. The modal dose of guanfacine at week 8 was 3 mg/day (range: 1–4 mg/day), and the modal dose was 3 mg/day (range: 2–4 mg/day) for placebo. Four guanfacine-treated subjects (13.3%) and four placebo subjects (12.5%) exited the study before week 8. The most common adverse events included drowsiness, fatigue, and decreased appetite. There were no significant changes on ECG in either group. For subjects in the guanfacine group, blood pressure declined in the first 4 weeks, with return nearly to baseline by endpoint (week 8). Pulse rate showed a similar pattern but remained lower than baseline at endpoint. **CONCLUSIONS:** Extended-release guanfacine appears to be safe and effective for reducing hyperactivity, impulsiveness, and distractibility in children with ASD.

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Sex and Gender Differences in Autism Spectrum Disorder: Summarizing Evidence Gaps and Identifying Emerging Areas of Priority

Halladay AK, Bishop S, Constantino JN, et al.

Mol Autism (Epub ahead of print, Jun 13, 2015)

One of the most consistent findings in autism spectrum disorder (ASD) research is a higher rate of ASD diagnosis in males than females. Despite this, remarkably little research has focused on the reasons for this disparity. Better understanding of this sex difference could lead to major advancements in the prevention or treatment of ASD in both males and females. In

October of 2014, Autism Speaks and the Autism Science Foundation co-organized a meeting that brought together almost 60 clinicians, researchers, parents, and self-identified autistic individuals. Discussion at the meeting is summarized here with recommendations on directions of future research endeavors.

Sleep in Children With Psychiatric Disorders

Ramtekkar U, Ivanenko A

Semin Pediatr Neurol 2015; 22:148–155

Sleep disturbances are common in pediatric psychiatric disorders and constitute key elements in diagnostic symptomatology of various primary psychiatric disorders including bipolar disorder, depression, and anxiety disorder. Although sleep is not included in key defining criteria of some impairing illnesses such as obsessive-compulsive disorder and schizophrenia, these disorders present with a very high prevalence of sleep disturbances. The interaction between sleep and psychopathology is very complex with significant interrelationship in development, severity, and prognosis of psychiatric disorders and comorbid sleep disturbances. The research ranging from small intervention case series to large epidemiologic studies demonstrated the role of specific sleep complaints in specific psychiatric diagnoses. However, the research using objective instruments such as polysomnography and actigraphy remains limited in youth with psychiatric disorders. The intervention studies using pharmaceutical treatment specifically focusing on sleep disturbances in psychiatric disorders are also sparse in the pediatric literature. Early identification of sleep disturbances and behavioral management using cognitive behavior therapy-based tools appear to be the most effective approach for treatment. The use of psychotropic medications such as selective serotonin reuptake inhibitors for the treatment of primary psychiatric disorder often alleviate the psychological barriers for sleep but may lead to emergence of other sleep issues such as restless leg syndrome. The safety and efficacy data of hypnotics for primary sleep disorders are limited in pediatrics and should be avoided or used with extreme caution in children with comorbid sleep and psychiatric problems.

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Longitudinal Trajectories and Associated Baseline Predictors in Youths With Bipolar Spectrum Disorders

Birmaher B, Gill MK, Axelson DA, Goldstein BI, et al.

Am J Psychiatry 2014; 171:990–999

OBJECTIVE: The authors sought to identify and evaluate longitudinal mood trajectories and associated baseline predictors in youths with bipolar disorder. **METHOD:** A total of 367 outpatient youths (mean age, 12.6 years) with bipolar disorder with at least 4 years of follow-up were included. After intake, participants were interviewed on average 10 times (SD=3.2) over a mean of 93 months (SD=8.3). Youths and parents were interviewed for psychopathology, functioning, treatment, and familial psychopathology and functioning. **RESULTS:** Latent class growth analysis showed four different longitudinal mood trajectories: "predominantly euthymic" (24.0%), "moderately euthymic" (34.6%), "ill with improving course" (19.1%), and "predominantly ill" (22.3%). Within each class, youths were euthymic on average 84.4%, 47.3%, 42.8%, and 11.5% of the follow-up time, respectively. Multivariate analyses showed that better course was associated with higher age at onset of mood symptoms, less lifetime family history of bipolar disorder and substance abuse, and less history at baseline of severe depression, manic symptoms, suicidality, subsyndromal mood episodes, and sexual abuse. Most of these factors were more noticeable in the "predominantly euthymic" class. The effects of age at onset were attenuated in youths with lower socioeconomic status, and the effects of depression severity were absent in those with the highest socioeconomic status. **CONCLUSIONS:** A substantial proportion of youths with bipolar disorder, especially those with adolescent onset and the above-noted factors, appear to be euthymic over extended periods. Nonetheless, continued syndromal and subsyndromal mood symptoms in all four classes underscore the need to optimize treatment.

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Adult Diagnostic and Functional Outcomes of DSM-5 Disruptive Mood Dysregulation Disorder

Copeland WE, Shanahan L, Egger H, Angold A, et al.

Am J Psychiatry 2014; 171:668–674

OBJECTIVE: Disruptive mood dysregulation disorder (DMDD) is a new disorder for DSM-5 that is uncommon and frequently co-occurs with other psychiatric disorders. Here, the authors test whether meeting diagnostic criteria for this disorder in childhood predicts adult diagnostic and functional outcomes. **METHOD:** In a prospective, population-based study, individuals were assessed with structured interviews up to six times in childhood and adolescence (ages 10 to 16 years; 5,336 observations of 1,420 youths) for symptoms of DMDD and three times in young adulthood (ages 19, 21, and 24–26 years; 3,215 observations of 1,273 young adults) for psychiatric and functional outcomes (health, risky/illegal behavior, financial/educational functioning, and social functioning). **RESULTS:** Young adults with a history of childhood DMDD had elevated rates of anxiety and depression and were more likely to meet criteria for more than one adult disorder relative to comparison subjects with no history of childhood psychiatric disorders (noncases) or individuals meeting criteria for psychiatric disorders other than DMDD in childhood or adolescence (psychiatric comparison subjects). Participants with a history of DMDD were more likely to have adverse health outcomes, be impoverished, have reported police contact, and have low educational attainment as adults compared with either psychiatric or noncase comparison subjects.

CONCLUSIONS: The long-term prognosis of children with DMDD is one of pervasive impaired functioning that in many cases is worse than that of other childhood psychiatric disorders.

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Psychological Therapies for the Treatment of Post-Traumatic Stress Disorder in Children and Adolescents (Review)

Gillies D, Taylor F, Gray C, O'Brien L, et al.
Evid Based Child Health 2013; 8:1004–1116

BACKGROUND: Post-traumatic stress disorder (PTSD) is highly prevalent in children and adolescents who have experienced trauma and has high personal and health costs. Although a wide range of psychological therapies have been used in the treatment of PTSD there are no systematic reviews of these therapies in children and adolescents. **OBJECTIVES:** To examine the effectiveness of psychological therapies in treating children and adolescents who have been diagnosed with PTSD. **SEARCH METHODS:** We searched the Cochrane Depression, Anxiety and Neurosis Review Group's Specialized Register (CCDANCTR) to December 2011. The CCDANCTR includes relevant randomized controlled trials from the following bibliographic databases: CENTRAL (the Cochrane Central Register of Controlled Trials) (all years), EMBASE (1974 -), MEDLINE (1950 -) and PsycINFO (1967 -). We also checked reference lists of relevant studies and reviews. We applied no date or language restrictions. **SELECTION CRITERIA:** All randomized controlled trials of psychological therapies compared with a control, pharmacological therapy or other treatments in children or adolescents exposed to a traumatic event or diagnosed with PTSD. **DATA COLLECTION AND ANALYSIS:** Two members of the review group independently extracted data. If differences were identified, they were resolved by consensus, or referral to the review team. We calculated the odds ratio (OR) for binary outcomes, the standardized mean difference (SMD) for continuous outcomes, and 95% confidence intervals (CI) for both, using a fixed-effect model. If heterogeneity was found we used a random-effects model. **MAIN RESULTS:** Fourteen studies including 758 participants were included in this review. The types of trauma participants had been exposed to included sexual abuse, civil violence, natural disaster, domestic violence and motor vehicle accidents. Most participants were clients of a trauma-related support service. The psychological therapies used in these studies were cognitive behavioral therapy (CBT), exposure-based, psychodynamic, narrative, supportive counseling, and eye movement desensitization and reprocessing (EMDR). Most compared a psychological therapy to a control group. No study compared psychological therapies to pharmacological therapies alone or as an adjunct to a psychological therapy. Across all psychological therapies, improvement was significantly better (three studies, N=80, OR 4.21, 95% CI 1.12 to 15.85) and symptoms of PTSD (seven studies, N=271, SMD -0.90, 95% CI -1.24 to -0.42), anxiety (three studies, N=91, SMD -0.57, 95% CI -1.00 to -0.13) and depression (five studies, N=156, SMD -0.74, 95% CI -1.11 to -0.36) were significantly lower within a month of completing psychological therapy compared with a control group. The psychological therapy for which there was the best evidence of effectiveness was CBT. Improvement was significantly better for up to a year following treatment (up to one month: two studies, N=49, OR 8.64, 95% CI 2.01 to 37.14; up to one year: one study, N=25, OR 8.00, 95% CI 1.21 to 52.69). PTSD symptom scores were also significantly lower for up to one year (up to one month: three studies, N=98, SMD -1.34, 95% CI -1.79 to -0.89; up to one year: one study, N=36, SMD -0.73, 95% CI -1.44 to -0.01), and depression scores were lower for up to a month (three studies, N=98, SMD -0.80, 95% CI -1.47 to -0.13) in the CBT group compared with a control. No adverse effects were identified. No study was rated as a high risk for selection or detection bias but a minority were rated as a high risk for attrition, reporting and other bias. Most included studies were rated as an unclear risk for selection, detection and attrition bias. **AUTHORS' CONCLUSIONS:** There is evidence for the effectiveness of psychological therapies, particularly CBT, for treating PTSD in children and adolescents for up to a month following treatment. At this stage, there is no clear evidence for the effectiveness of one psychological therapy compared with others. There is also not enough evidence to conclude that children and adolescents with particular types of trauma are more or less likely to respond to psychological therapies than others. The findings of this review are limited by the potential for methodological biases, and the small number and generally small size of identified studies. In addition, there was evidence of substantial heterogeneity in some analyses which could not be explained by subgroup or sensitivity analyses. More evidence is required for the effectiveness of all psychological therapies more than one month after treatment. Much more evidence is needed to demonstrate the relative effectiveness of different psychological therapies or the effectiveness of psychological therapies compared with other treatments. More details are required in future trials in regards to the types of trauma that preceded the diagnosis of PTSD and whether the traumas are single event or ongoing. Future studies should also aim to identify the most valid and reliable measures of PTSD symptoms and ensure that all scores, total and subscores, are consistently reported.

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A Meta-Analysis of Risk Factors for Post-Traumatic Stress Disorder in Children and Adolescents

Trickey D, Siddaway AP, Meiser-Stedman R, et al.
Clin Psychol Rev 2012; 32:122–138

Post-traumatic stress disorder (PTSD) is a complex and chronic disorder that causes substantial distress and interferes with social and educational functioning. Consequently,

identifying the risk factors that make a child more likely to experience traumatic distress is of academic, clinical and social importance. This meta-analysis estimated the population effect sizes of 25 potential risk factors for PTSD in children and adolescents aged 6–18 years across 64 studies (N=32,238). Medium to large effect sizes were shown for many factors relating to subjective experience of the event and post-trauma variables (low social support, peri-trauma fear, perceived life threat, social withdrawal, comorbid psychological problem, poor family functioning, distraction, PTSD at time 1, and thought suppression); whereas pre-trauma variables and more objective measures of the assumed severity of the event generated small to medium effect sizes. This indicates that subjective peri-trauma factors and post-event factors are likely to have a major role in determining whether a child develops PTSD following exposure to a traumatic event. Such factors could potentially be assessed following a potentially traumatic event in order to screen for those most vulnerable to developing PTSD and target treatment efforts accordingly. The findings support the cognitive model of PTSD as a way of understanding its development and guiding interventions to reduce symptoms.

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Depression in Adolescence

Thapar A, Collishaw S, Pine DS, et al.
Lancet 2012; 379:1056–1067

Unipolar depressive disorder in adolescence is common worldwide but often unrecognized. The incidence, notably in girls, rises sharply after puberty and, by the end of adolescence, the 1 year prevalence rate exceeds 4%. The burden is highest in low-income and middle-income countries. Depression is associated with substantial present and future morbidity, and heightens suicide risk. The strongest risk factors for depression in adolescents are a family history of depression and exposure to psychosocial stress. Inherited risks, developmental factors, sex hormones, and psychosocial adversity interact to increase risk through hormonal factors and associated perturbed neural pathways. Although many similarities between depression in adolescence and depression in adulthood exist, in adolescents the use of antidepressants is of concern and opinions about clinical management are divided. Effective treatments are available, but choices are dependent on depression severity and available resources. Prevention strategies targeted at high-risk groups are promising.

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