CHILD & ADOLESCENT PSYCHIATRY ALERTS

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ADHD and Diabetes

In a nationwide longitudinal study, adolescents and young adults with ADHD were more likely than their peers to have onset of type 2 diabetes. Risk was increased regardless of medical comorbidities commonly associated with diabetes—hypertension, dyslipidemia, and obesity—and long-term atypical antipsychotic use.

Methods: Data were collected from Taiwan's national health insurance program. The study cohort comprised all adolescents (aged 10–17 years) and young adults (aged 18–29 years) who received a diagnosis of ADHD in 2002–2009. Each patient was age- and gender-matched with 2 control subjects without ADHD. All patients were required to be free of any type of diabetes at inception of the cohort. Participants in whom type 2 diabetes developed were identified during follow-up lasting through 2011.

Results: The analysis included nearly 36,000 young people with ADHD and 72,000 controls. Study subjects had a mean age of nearly 13 years, and 79% were male. About 60% of those with ADHD were receiving treatment with either methylphenidate or atomoxetine.

Adolescents and young adults with ADHD had an increased incidence of type 2 diabetes compared with controls (0.83 vs 0.21 per 1000 person-years; $p<0.001$; hazard ratio [HR],* 4.01) and a shorter duration from enrollment to diabetes onset (3.17 years vs 4.08 years; $p=0.004$). Patients with ADHD also had an increased prevalence of ADHD-related comorbidities, with HRs ranging from 1.9 to 10.8 for hypertension, obesity, and dyslipidemia. Diabetes risk was greater among patients with these medical comorbidities, but after adjustment for these factors, comedication, and demographics, the risk of type 2 diabetes remained significantly elevated in patients with ADHD (HR, 2.84). Diabetes incidence was not related to use of ADHD medication. Incidence was increased in those who used atypical antipsychotics for ≥1 year (649 patients with ADHD and 55 controls), but not in those who used these medications for shorter periods.

Discussion: Previous research has identified an increased prevalence of obesity and other type 2 diabetes risk factors in young people with ADHD. In the present study, risk of type 2 diabetes was increased overall, and especially in young people who had these risk factors.

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The underlying mechanisms for the association with diabetes may be immunologic dysregulation and proinflammatory cytokine oversecretion.

Chen M-H, Pan T-L, Hsu J-W, Huang K-L, et al: Risk of type 2 diabetes in adolescents and young adults with attention-deficit/hyperactivity disorder: a nationwide longitudinal study. *Journal of Clinical Psychiatry* 2018; doi 10.4088/JCP.17m11607. From Taipei Veterans General Hospital, Taiwan; and other institutions. **Funded by the Taipei Veterans General Hospital. The authors declared no competing interests.**

Common Drug Trade Names*: atomoxetine—*Strattera*; methylphenidate—*Concerta, Ritalin

***See Reference Guide.**

Callous-Unemotional Traits and Family Function

Parents of boys with conduct disorder and a high level of callous-unemotional (HCU) traits had poorer rapport with their children than did parents of boys with conduct disorder and lower levels of these traits (LCU). Families of highly callous and unemotional children also had poorer levels of affective involvement as well as other adverse dynamics. These findings may help clinicians identify targets for family interventions.

Methods: Participant families included a boy, aged 11–16 years, who met screening criteria for a conduct disorder. Boys with autism or Asperger's syndrome, low IQ, or a neurological disorder were excluded. All boys enrolled in the trial completed the Inventory of Callous-Unemotional Traits and those who scored above the median were classified as the HCU (n=35) group. A control group of 31 typically developing (TD) boys was also included in the study. Family function was assessed using the McMaster Family Assessment Device (FAD), which has 7 subscales. Parents were also asked to write a free-form description of their child. These descriptions were then analyzed using qualitative methods to identify major themes.

Results: No differences were observed between conduct disordered youth with HCU and LCU and control families on child age or IQ, child alcohol use, birth order, number of people living in the household, parental psychopathology, child ethnicity, family structure, and parent informant. According to the assessment of family function, families of a child with HCU traits showed poorer levels of affective involvement, general functioning, and role functioning than the other groups. (See table.) However, after adjusting for child ADHD and generalized anxiety disorder, the group effects on general functioning and roles were no longer significant. For some areas of familial function, LCU youths were impaired relative to controls.

Between-Group Differences in Affective Involvement FAD Scores

Study group	Comparison group	Effect size†	Significance
HCU	TD	-1.17	p<0.01
HCU	LCU	-0.62	p=0.03
LCU	TD	-0.69	p=NS

†Negative effect size* indicates poorer status in the study group

Parents' qualitative descriptions of their child differed depending on the child's level of callous-unemotional traits. Parents of HCU children often described their child as unpredictable and changeable, or loving and bubbly but volatile if stressed. Parents of LCU children described lower levels of changeability, which seemed less problematic. Boys with HCU traits were described as able to turn on the charm to gain something, but those with LCU traits were described as spontaneously kind. Parents typically saw the behavior of boys in the HCU trait group as problematic, while those whose boys had LCU traits normalized the behavior, calling it cheeky or quirky, endearing, or typical of a teenage boy. Although parents of HCU boys cared for their child, there was more sense of a close, affectionate relationship in the families of boys with lower levels.

Discussion: Affective involvement, as operationalized on the FAD, refers to such aspects of function as self-centeredness and using others for personal gain. The study results indicate

children with this characteristic can have a substantial negative impact on collaborative family functioning. General family functioning is probably improved in LCU families by parents' ability to normalize their child's behavior and empathize with the challenges he faces. Role functioning—the extent to which an individual fulfills his functions and responsibilities in the family—was impaired in both clinical groups but especially the families with an HCU child.

Roberts R, McCrory E, Joffe H, DeLima N, et al: Living with conduct problem youth: family functioning and parental perceptions of their child. *European Child & Adolescent Psychiatry* 2018;27 (May):595–604. From University College London; and Cardiff University, U.K. **Funded by the UK Medical Research Council; and an award from the Royal Society. The authors declared no competing interests.**

***See Reference Guide.**

Pharmacotherapy for School Refusal

Despite the urgent nature and significant consequences of school refusal behavior, there have been very few studies of pharmacological treatments to guide clinical decision-making, according to a literature review. The limited data suggest that pharmacotherapy can be a useful adjunct to psychological therapy in children with comorbid anxiety or depression. Contributing factors unrelated to anxiety and depression, such as bullying, learning disorders, and psychosocial adversity, should also be addressed.

The review included randomized clinical trials and quasi-experimental studies that included ≥10 participants and evaluated pharmacotherapy for school refusal in children and adolescents. The search identified only 6 reports describing 7 studies, most published between the 1970s and 1990s, that included a total of 306 children. In all of the studies, medications were compared with placebo, other drugs, or no pharmacotherapy in children or adolescents who were also receiving psychosocial interventions. All of the studies were underpowered to show a statistically significant benefit of medication, but a few suggested they may have been helpful.

Two studies examined the effect of fluoxetine combined with cognitive behavioral therapy (CBT). In 1 study, fluoxetine was compared with no treatment in 82 children refusing to go to school because of mood disorder. After 12 weeks, fluoxetine was associated with a higher rate of return to school (82% vs 72%), with an effect size* of 0.24 that was not statistically significant. Anxiety, depression, and global illness severity improved equally in both treatment groups. In the second study, 62 patients meeting criteria for anxiety disorders received 12 sessions of CBT in conjunction with fluoxetine, placebo, or no medication. All treatment groups experienced improvement in anxiety and depression. Rates of return to school ranged from 44% to 56% (effect size, 0.34 for improvement in attendance with fluoxetine vs placebo), but the between-group difference was not significant.

Four randomized trials and 1 open-label study examined the effects of tricyclic antidepressants on school refusal. In 1 study, imipramine was superior to placebo in improving school attendance to ≥75% of school hours in children receiving CBT (70% vs 28%; effect size, 1.27; $p<0.001$). However, this study had a relatively small sample size (63 children) and did not correct for multiple statistical comparisons. In 3 additional studies, no positive effects of imipramine on school refusal were found. Clomipramine was also ineffective in a placebo-controlled trial in 46 children receiving tailored individual therapy. Likewise, alprazolam did not produce response in a group of 24 children.

Taken together, these studies indicate that children with school refusal and comorbid depression or anxiety generally had improvement in their school refusal with psychological therapy, with or without pharmacotherapy. Although data on pharmacological treatment are sparse and newer antidepressants (e.g., SSRIs and SNRIs) do not appear to have been evaluated, the authors suggest combined pharmacotherapy and psychosocial treatment may be warranted because of

the serious nature of school refusal along with the fact that children with anxiety disorders make up a large subset of school refusal patients.

Tobon A, Reed M, Taylor J, Bloch M: A systematic review of pharmacologic treatments for school refusal behavior. *Journal of Child and Adolescent Psychopharmacology* 2018; doi 10.1089/cap.2017.0160. From Yale Child Study Center, New Haven, CT; and other institutions. **This review was conducted without external funding. One study author disclosed a potentially relevant financial relationship with a commercial source.**

Common Drug Trade Names*: clomipramine—*Anafranil*; fluoxetine—*Prozac*; imipramine—*Tofranil

***See Reference Guide.**

Nonpharmacological Treatments for ADHD

Despite widespread use, a systematic review of recent studies found little evidence to provide new guidance on use of nonpharmacological interventions for ADHD.

Methods: The review encompassed English-language, controlled or observational studies that were published from 2009 to late 2016 or were included in clinical trial registries. Studies were required to include ≥50 subjects. Participants were children or adolescents, aged ≤17 years, receiving a non-pharmacological treatment for ADHD, either alone or in combination with medication. The treatments included psychosocial, behavioral, or school interventions; cognitive training; biofeedback or neurofeedback; parent behavior training; dietary supplements; elimination diets; vision training; and chiropractic. Comparison treatments could include other nonpharmacological interventions, FDA-approved medications, placebo, usual care, or wait-listing. Study outcomes were changes on standardized symptom scores or progress toward patient-identified goals. Strength of evidence was assessed based on 5 criteria: study limitations, consistency, directness, precision, and reporting bias.

Results: A total of 54 studies were identified. Evidence suggested that in addition to improvements in ADHD symptoms, cognitive behavioral therapy may alleviate depression and anxiety, as well as oppositional-defiant and conduct-disorder symptoms in young people with ADHD. Studies comparing neurofeedback with other nonpharmacological interventions had generally positive results, but no significant differences were found between neurofeedback and methylphenidate (*Ritalin*) or combined treatment. Cognitive training was more effective than a waitlist control, but not more effective than other nonpharmacological treatments. Evidence did not support fatty acids, vitamin D, or zinc supplementation or other dietary/herbal interventions. Findings for child and/or parent training and ginkgo biloba supplementation were mixed. In a single study, an elimination diet had positive results.

Discussion: The authors note several important limitations of the included studies: most had short follow-up periods, there were variations in outcome, and reporting of comparative statistical analyses was inconsistent. While the comparisons were not generally supportive of nonpharmacological treatment, the studies were too small to determine if there is a subgroup of children or adolescents who might benefit from a particular approach.

Goode A, Coeytaux R, Maslow G, Davis N, et al: Nonpharmacologic treatments for attention-deficit/hyperactivity disorder: a systematic review. *Pediatrics* 2018; doi 10.1542/peds.2018-0094. From Duke University, Durham, NC; and other institutions. **Funded by the Agency for Healthcare Research and Quality; and the National Institute of Child Health and Human Development. One of 14 study authors disclosed relevant financial relationships; the remaining authors declared no competing interests.**

Parent-Only Intervention for Anxiety Disorders

A brief, parent-only group cognitive behavioral training resulted in symptomatic improvement in children with anxiety disorders. Although preliminary, these results support the potential of parent-only anxiety programs without the direct involvement of the child.

Methods: The study enrolled 42 families referred from a university-affiliated outpatient clinic. Children were aged 6–12 years and met DSM-IV-TR criteria for a primary diagnosis of

generalized anxiety disorder, separation anxiety disorder, social phobia, or specific phobia. All children were receiving an SSRI at a stable dose for ≥8 weeks before study entry. Families were randomly assigned to the intervention or to a wait-list control. The active treatment was the parent component of the FRIENDS for Life intervention, which is aimed at empowering parents to recognize and deal with their own anxiety and to use these skills to help their children. The program was offered in 2 groups, each with 10 parents, in 6 weekly sessions.

Results: Of the 20 families randomly assigned to the intervention, 15 participated in enough sessions to be included in the outcome analysis. Children in both groups had a mean age of about 8 years, social anxiety and generalized anxiety disorder were the most common primary diagnoses, and ADHD was the most common comorbidity.

Parents in the intervention group reported significant improvement in family functioning on the Global Relational Assessment of Functioning (p=0.04) and a reduction in their child's emotional symptoms on the Strengths and Difficulties Questionnaire (p=0.007), as well as a significant decrease in their own depression on the Depression-Anxiety-Stress Scale (p=0.006). Clinicians reported that children in the CBT group showed significant improvement in Child Global Assessment Scale scores, compared with controls (p=0.001). Outcomes did not differ between the groups on child self-report measures.

Discussion: The few prior studies of parent-only interventions in childhood anxiety disorder were mostly conducted in preschool children. Results of the present study, including the disagreement between child and parent or clinician ratings of improvement, are consistent with the earlier studies. This may be explained by a lack of sensitivity of measurement tools, reluctance of children to report their anxiety accurately, or a lag in improvement in anxiety management and habituation to fears.

Salari E, Shahrivar Z, Mahmoudi-Gharaei J, Shirazi E, et al: Parent-only group cognitive behavioral intervention for children with anxiety disorders: a control group study. *Journal of the Canadian Academy of Child and Adolescent Psychiatry* 2018;27 (April):130–136. From Azad University of Medical Sciences, Mashad, Iran; and other institutions. **Source of funding not stated. The authors declared no competing interests.**

Intensive Community Treatment After Discharge

Following hospitalization for a psychiatric emergency, an intensive, community-based treatment to integrate adolescents into outside life was associated with reduced hospital use in the following 6 months. Effects on psychopathology and other study outcomes were mixed.

Methods: The study enrolled 106 individuals, aged 12–17 years, who had received inpatient psychiatric care for ≥72 hours. After stabilization, enrolled patients were randomly assigned to supported discharge service (SDS) or to usual care. SDS was delivered by teams consisting of a child and adolescent psychiatrist, several specialized nursing clinicians, and various administrative and support staff. Clinicians began working with patients within 72 hours after admission and were involved in discharge planning, developing customized care plans, psychological interventions, and assisting the patient with re-integration into school. Special features of the program included a small case load, the team approach, weekly formal and informal team meetings, and work with informal support systems. The duration and intensity of treatment was flexible and based on clinical need. Usual care was delivered by the hospital and by standard community mental health agencies.

The primary study outcomes, assessed at 6 months by blinded raters, were the number of bed-days of inpatient psychiatric treatment; change in the Children's Global Assessment Scale (CGAS), a measure of functioning; and the self-report Strengths and Difficulties Questionnaire (SDQ). In addition to these outcomes, the investigators conducted a cost-benefit analysis using the outcomes of CGAS scores and quality-adjusted life-years (QALYs).

Results: During the 6 months of follow-up, SDS was associated with fewer hospital bed-days than usual care (median, 34 vs 50 days; p=0.04). CGAS and SDQ scores did not differ between the 2 treatment groups at 6 months. However, SDS was associated with a marked difference in the rate of multiple incidents of deliberate self-harm: 24% with SDS and 42% for usual care (odds ratio,* 0.18; p=0.008). Adolescents in the SDS group were also more likely than the usual-care group to have returned to community schools at the end of 6 months (81% vs 51%; odds ratio, 4.14; p=0.001). Results of the economic analysis suggest that SDS is less expensive and more effective than usual care in improving the CGAS score. In terms of QALYs, usual care was not more cost-effective than SDS.

Study Rating*—17 (100%): This study met all criteria for a randomized controlled trial.

Ougrin D, Corrigall R, Poole J, Zundel T, et al: Comparison of effectiveness and cost-effectiveness of an intensive community supported discharge service versus treatment as usual for adolescents with psychiatric emergencies: a randomised controlled trial. *Lancet Psychiatry* 2018;5 (June):477–485. From King's College, London, U.K.; and other institutions. **Funded by the National Institute for Health Research; and other sources. The authors declared no competing interests.**

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Effect Size: The effect size represents the amount of change in outcome that can be attributed to treatment, where 0.2 indicates a small effect, 0.5 a medium effect, and 0.8 a large effect. It is relatively independent of clinical significance, and large effect sizes do not ensure treatment efficacy.

Hazard Ratio: A measure of the risk of an event relative to exposure, or the probability of an event occurring in an exposed group versus a non-exposed group. A hazard ratio of 0.5 indicates that 1 group has half the risk of the other group.

Odds Ratio: A comparison of the probability of an event in 2 groups. An odds ratio of 1 implies that the event is equally likely in both groups. An odds ratio greater than 1 indicates that the event is more likely to occur in that group than in the comparison group.

Study Rating: A measure of how well a study conforms to quality standards. The study rating uses a checklist system based on the comprehensive Strength of Evidence Report from the Evidence-based Practice Center Program of the Agency for Healthcare Research and Quality (AHRQ). The rating checklists are posted at www.alertpubs.com.

"Change is the law of life and those who look only to the past or present are certain to miss the future."—John F. Kennedy

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