

Current Literature in ADHD

Summarized by Sam Goldstein

Abikoff, H., McGough, J., Vitiello, B., McCracken, J., Davies, M., Walkup, J., et al. (2005). Sequential pharmacotherapy for children with comorbid attention deficit/hyperactivity and anxiety disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, 44, 418-427.

A recent pilot study examined sequential treatment with methylphenidate with the later addition of Fluvoxamine, an SSRI antidepressant. Children with ADHD and anxiety were first titrated to an effective dose of methylphenidate. Those who responded favorably were then treated with Fluvoxamine. A total of 81% of participants responded to the methylphenidate, suggesting that children with this combined comorbidity do in fact respond to ADHD treatments. The benefits of adding Fluvoxamine were less clear than in prior studies as the response rate to the Fluvoxamine placebo was higher than expected. Fluvoxamine treatment in this study did not cause exacerbation of anxiety or physical symptoms. These results suggest that stimulants are as effective and safe in children with ADHD and comorbid anxiety as in those with ADHD alone.

Acevedo-Polakovich, I. D., Louch, E. P., & Milich, R. (2005). TV or not TV: Questions and answers regarding television and ADHD. *ADHD Report*, 13(6), 6-11.

Although television habits are often ascribed as cause for and consequence of ADHD, most studies used to support these positions were conducted on samples of children without the disorder. These authors set out to address this question specifically in a population of children with ADHD. The authors conclude that their research suggests that children with ADHD watch more television than their nonreferred peers but that a child's home media environment may be a strong factor driving these differences. According to parent reports, children with ADHD had greater access to electronic media and

less access to print media than their nonreferred peers. Nonreferred children whose homes had the same type of media environment as children with ADHD watched as much television as these children. The authors discussed a number of possible hypotheses to explain these differences, note that thus far there has yet to be a well-controlled study examining whether television viewing causes ADHD, and also suggest the popular understanding "of the relation between television and ADHD has been unduly influenced by simplistic explanations of available data" (p. 10).

Barkley, R. A., & Fischer, M. (2005). Suicidality in children with ADHD, grown-up. *ADHD Report*, 13(6), 1-6.

The potential association of suicidality with medications used to treat ADHD necessitates investigation of this question. These authors used data from their longitudinal study of 158 hyperactive and 81 control children followed for more than 13 years. Twelve questions dealing with the topic of suicidality were asked of this sample. Six of the questions dealt with these issues during high school, and the same six were repeated again for functioning since leaving high school. The authors report that children growing up with hyperactivity/ADHD were significantly more likely to consider, attempt, and be hospitalized for suicidality during high school and were more likely to consider suicide after high school than children in the control group. When risk factors were examined individually, lifetime major depressive disorder, conduct disorder in adolescence, severity of ADHD during the teenage years, and adult follow-up and being treated with stimulant medication in high school for ADHD increased the likelihood of suicidal ideation and attempts in high school. However, when these variables were examined jointly controlling for the others, the risk of suicidal ideation in the hyperactive group, both during high school and after high school, was significantly predicted only by presence of lifetime major depressive

disorder. Nonetheless, the authors also noted that stimulant treatment remained marginally associated with suicidal ideation, even after controlling for the substantial contribution of major depressive disorder and the marginally significant association with severity of teenage ADHD. The authors suggested these findings warrant further examination in larger studies.

Bauermeister, J. J. (2005). Comparison of the DSM-IV combined and inattentive types of ADHD in a school-based sample of Latino/Hispanic children. *Journal of Child Psychology and Psychiatry, 46*, 166-179.

This study examined the validity and distinctiveness of ADHD subtypes within school-based sample of Latino/Hispanic children, ages 6 to 11, identified by classroom teachers and subsequently undergoing a comprehensive diagnostic assessment. When comparing the subtypes with each other, the inattentive subtype was associated with later onset of inattentive symptoms and higher rates of sluggish cognitive tempo. This group was also less assertive socially and had fewer externalizing symptoms than the combined type group. Both the inattentive and combined type groups exhibited lower academic achievement and more ADHD type behaviors during tasks than their non-ADHD counterparts. They also exhibited more internalizing symptoms. Parents of inattentive subtype children reported less parenting stress. These children also exhibited lower levels of adaptive functioning.

Biederman, J., Monuteaux, M. C., Mick, E., Spencer, T., Wilens, T. E., Silva, J. M., et al. (2006). Young adult outcome of ADHD: A controlled ten-year follow-up study. *Psychological Medicine, 36*, 167-179.

A case controlled, 10-year prospective study of 140 youth without ADHD and 120 with ADHD between the ages of 6 and 18 was ascertained from psychiatric and pediatric sources. At the 10-year follow-up, 112 (80%) and 105 (88%) of the ADHD and controls, respectively, were reassessed (mean age = 22 years). The lifetime prevalence for disorders including mood, anxiety, antisocial, developmental, and substance were significantly greater in ADHD young adults compared to controls.

The authors conclude that by their young adult years, youth with ADHD were at high risk for a wide range of adverse psychiatric outcomes, including marketing elevated risks of antisocial, addictive, mood, and anxiety disorders. The authors suggest that their findings provide further evidence for the high morbidity associated with ADHD across the life cycle.

Carpenter, E. M., Frankel, F., Marina, M., Duan, N., & Smalley, S. L. (2004). Internet treatment delivery of parent-adolescent conflict training for families with an ADHD teen: A feasibility study. *Family Behavior Therapy, 2026*, 1-20.

These authors examined the feasibility of Internet delivery of a parent-adolescent conflict training program for families with a teenager suffering from ADHD. The authors attempted to ascertain the willingness of families to participate in a Web-based study, identify relevant issues related to confidentiality of Internet data collection, and determine participant satisfaction with this treatment protocol. Six families participated and four were compliant with participation requirements. A series of single subject linear regressions revealed that all but one participant maintained a steady log-in rate over time. Treatment compliant results, according to these authors, were rated as "promising." Participants provided high ratings of the security of the Web site and satisfaction scale scores were also above neutral.

Dickstein, D. P., Garvey, M., Pradella, A. G., Greenstein, D. K., Sharp, W. S., Castellanos, F. X., et al. (2005). Neurologic examination of abnormalities in children with Bipolar Disorder or ADHD. *Biological Psychiatry, 58*, 517-524.

ADHD and bipolar disorder in children were evaluated through an examination of neurologic abnormalities in this study. The authors performed the Revised Physical and Neurological Exam for Soft Signs in groups of children with ADHD, bipolar disorder, and controls. Then, a blind rater evaluated motor performance. Results were analyzed using multiple analyses of covariance. Participants with ADHD were impaired on repetitive task reaction time. In contrast, pediatric bipolar participants, both with and without comorbid ADHD, were impaired on sequential task reaction time. The authors

conclude that this differential pattern of soft signs by diagnosis suggested pathophysiologic differences between ADHD and bipolar disorder in children. They hypothesize that repetitive motor performance requires inhibition of nonrelevant movements. As such, ADHD participants' impairment in this domain supports the hypothesis that ADHD involves a core deficit of fronto-striatal-basal ganglia neurocircuitry. In contrast, participants with bipolar disorder caused by their impairment in sequential and motor performance appeared to reflect impaired attentional set shifting and reversal learning suggesting a different pathophysiology.

Faraone, S. V., Biederman, J., & Mick, E. (2006). The age dependent decline of ADHD: A meta-analysis of follow-up studies. *Psychological Medicine*, *36*, 159-165.

Through a meta-analysis, these authors analyzed data from published follow-up studies of ADHD. A regression model was used to separately assess the syndromic and symptomatic persistence of ADHD. When only those meeting full criteria for ADHD were defined as having "persistent ADHD," the rate of persistence was low, approximately 15% at 25 years of age. But when cases were consistent with *DSM-IV*'s current definition of ADHD in partial remission, the rate of persistence was much higher, approximately 65%. The authors conclude their results demonstrate that estimates of ADHD's persistence rely heavily on definition. Regardless of definition, however, evidence for ADHD lessens with age according to these data.

Harris, K. R., Friedlander, D. B., Sadler, B., Frizzelle, R., & Graham, S. (2005). Self-monitoring of attention versus self-monitoring of academic performance: Effects among students with ADHD in the general education classroom. *Journal of Special Education*, *39*, 145-156.

In a counterbalanced, multiple baseline across-subjects design, attention and performance monitoring were evaluated to determine potential differential effects on the on-task and spelling study behavior of six elementary students with ADHD in a general education classroom. Low self-monitoring of attention and self-monitoring of performance had positive effects on

students' on-task and spelling study behaviors. Although improvement in on-task behavior was comparable across the two interventions, self-monitoring of attention had produced substantially higher gains in spelling study behavior among four of the six students. This is the first study in which differential effects of these two interventions have been investigated among students with ADHD.

Huang-Pollock, C. L., Nigg, J. T., & Carr, T. H. (2005). Deficient attention is hard to find: Applying the perceptual load model of selective attention to ADHD subtypes. *Journal of Child Psychology and Psychiatry*, *46*, 1211-1218.

These authors sought to determine whether selective attention is a primary deficit in childhood ADHD. A perceptual load paradigm was used to examine both early and late selective attention problems in children with inattentive and combined subtypes of ADHD. No evidence emerged for selective attention deficits in either of the subtypes. However, sluggish cognitive tempo was associated with abnormal early selection. The authors concluded that at least some and possibly most children with *DSM-IV*-diagnosed ADHD have normal selective attention. They suggested their results supported a move away from theories of attention dysfunction as primary in combined type ADHD. They also note that children with ADHD who demonstrate sluggish cognitive tempo warrant further study for possible early selective attention deficits.

Evans, S. W., Allen, J., Moore, S., & Strauss, E. (2005). Measuring symptoms in functioning of youth with ADHD in middle schools. *Journal of Abnormal Child Psychology*, *33*, 695-706.

This study examined the interrater agreement of teacher ratings and the relationship between ratings and observation data for ADHD symptoms in a middle school setting. Teacher ratings and observational data were collected regularly during the course of 2 academic years for middle school students diagnosed with ADHD. Findings indicated low rates of interrater agreement as well as low rates of agreement between teachers and observational data and between observational data collected in different classrooms. The interrater agreement was lowest in late fall and gradually increased during the

second half of the year. The authors discuss implications for conducting treatment outcome evaluations of school-based treatment programs and diagnostic evaluations. As it relates to ADHD, these data reinforce the need to collect behavioral samples across multiple classes and academic tasks.

Grizenko, N., Kobacina, B., Amoral, B., Schwartz, G., Ter-Stepanian, M., & Joober, R. (2006). Relationship between response to methylphenidate treatment in children with ADHD and psychopathology in their families. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*, 47-53.

Familial aggregation of psychopathology in children with ADHD who are good responders to methylphenidate was compared to those who were poor responders. A total of 118 clinically referred children 6 to 12 years of age participated in a double-blind, placebo-controlled, randomized, 2-week crossover trial of methylphenidate from 1999 to 2004. Information was collected on 342 first-degree and 1,151 second-degree relatives of children with ADHD. Forty-four participants showed mild or no improvement, and 74 showed moderate or very much improvement on methylphenidate over placebo. First-degree relatives of good responders were at significantly higher risk of ADHD than the relatives of poor responders. Second-degree relatives of good responders were at significantly higher risk of antisocial personality disorder compared to the relatives of poor responders. The authors conclude that the significantly higher presence of ADHD in the first-degree relatives and of antisocial personality in the second-degree relatives of good Ritalin responders suggest that this group may at least partially be distinct from the poor responder group on the basis of genetic determinants.

Johnston, C., Chen, M., & Ohan, J. (2006). Mothers' attribution for behavior in non-problem boys, boys with ADHD and boys with ADHD and oppositional defiant disorder. *Journal of Clinical Child and Adolescent Psychology, 35*, 60-71.

Attributions for child behavior among mothers of 38 nonproblem boys, 26 boys with ADHD, and 25 boys with ADHD and oppositional defiant disorder (ODD)

between the ages of 7 and 10 were examined. Two assessment measures were used, including the coding of causal attributions as mothers watch their children's behavior. Mothers of boys with ADHD plus ODD rated the causes of oppositional and inattentive-impulsive child behaviors as more stable and global than did mothers of nonproblem boys in identifying causes of their children's failure on laboratory tasks. Mothers of boys with ADHD plus ODD provided more child negative attributional causes than did mothers of either ADHD only or nonproblem boys. The authors discuss implications for assessing and understanding attributions in families of children with ADHD and ODD.

Moore, C. M., Biederman, J., Wozniak, J., Mick, E., Aleardi, M., Wardrop, M., et al. (2006). Differences in brain chemistry in children and adolescents with ADHD with and without comorbid bipolar disorder: A proton magnetic resonance spectroscopy study. *American Journal of Psychiatry, 163*, 316-318.

The brain chemistry in the anterior cingulate cortex of children and adolescents with ADHD alone, children with ADHD plus bipolar disorder, and children with no Axis I *DSM-IV* condition were evaluated using proton spectra analysis. Children with ADHD had a significantly higher ratio of glutamine to myo-inositol-containing compounds than children with ADHD plus bipolar disorder and unaffected children. The authors suggest that an understanding of these brain chemistry differences may provide information about the action of antimanic treatments such as lithium. They also suggest that these chemical differences may also reflect changes in serotonin and dopamine pathways.

Pelham, W. E., Manos, M., Ezzell, C., Tresco, K. E., Gnagy, E., Hoffman, N., et al. (2005). A dose-ranging study of methylphenidate transdermal system in children with ADHD. *Journal of the American Academy of Child and Adolescent Psychiatry, 44*, 522-529.

This recent study continued a series of studies being conducted as part of a Food and Drug Administration application for methylphenidate patch. This study evaluated the efficacy of a range of doses on a variety of outcome

measures for children attending a summer treatment program. Thirty-seven children ages 6 to 13 in this program were administered three doses of methylphenidate via the patch. The patch was applied either 6 through 120 min before the start of the program each day, and each condition was compared to placebo. The magnitude of dose was related to the number of points children earned on their daily report cards and in the classroom and through observational ratings of behavior in the classroom. More negative behavior was observed when the patch was applied 120 min before the program regardless of whether it was medication or placebo. These studies are consistent with other stimulant studies suggesting that increased dosages yields increased effectiveness. However, small doses of stimulants produced effects that were fairly comparable to larger ones.

Reich, W., Neuman, R., Volk, H. E., Joiner, C. A., & Todd, R. (2005). Comorbidity between ADHD and symptoms of bipolar disorder in a community sample of children and adolescents. *Twin Research and Human Genetics*, 8, 459-466.

The prevalence and frequency of comorbidity of bipolar disorder was examined with ADHD in a nonreferred population of twins. Children and adolescents ages 7 to 18 with a history of manic symptoms were identified from a population-based twin sample obtained from state birth records. The sample was enriched for ADHD, however there was also a random control sample that allowed the authors to examine population prevalence of the disorder. Juveniles with threshold or below threshold manic episodes were further assessed for comorbidity. The authors found the population prevalence of broadly defined mania in the random sample was 0.2%. The possible manic episode showed significant comorbidity with population-defined severe combined and inattentive ADHD subtypes. The authors concluded that there is a significant association of bipolar symptoms with two population-defined subtypes of ADHD. Episodes of possible bipolar disorder as defined by *DSM-IV* were uncommon in the nonreferred sample. Finally, the authors conclude that children and adolescents with ADHD appear to be only modestly at increased risk for bipolar disorder.

Reimer, B., D'ambrosio, L. A., Gilbert, J., Coughlin, J. F., Biederman, J., Surman, C., et al.

(2005). Behavior differences in drivers with ADHD: The driving behavior questionnaire. *Accident Analysis and Prevention*, 37, 996-1004.

ADHD has been linked to an increased number of driving citations, particularly for speeding and a fourfold increase in accident risk. Using three factors—errors, lapses, and violations—these authors used regression analysis to explore the impact of ADHD status, gender, and age. Results indicated that ADHD status is positively and significantly related to driving errors, lapses, and violation scores. Older participants with ADHD did not differ statistically from controls relative to errors and violations. There were no significant effects of age on error, lapse, or violation scores for control participants. Consistent with other research, gender was significantly related to violation scores but not to errors or lapses such that the males were more likely than females to report higher violation scores controlling for ADHD status and age.

Saudino, K. J., Ronald, A., & Plomin, R. (2005). The etiology of behavior problems in 7-year-old twins. Substantial genetic influence and negligible shared environmental influence for parent ratings and ratings by same and different teachers. *Journal of Abnormal Child Psychology*, 33, 113-131.

This study examined the relative contributions to teacher ratings made by genetic influences in twins rated by same and different teachers. Parents and teachers rated nearly 4,000 7-year-old identical and fraternal twin pairs on the Strengths and Differences Questionnaire. Individual differences as measured by all three raters in hyperactivity, peer problems, conduct problems, emotional symptoms, total behavior problems, and prosocial behavior were found to be substantially heritable. Shared environmental influences were often small, with the influence of nonshared environments making more substantial contributions. Parents tended to contrast their children with each other when making hyperactivity ratings, leading to greater differences between nonidentical siblings than predicted by genetic influences, while teachers displayed no such contrast effects. The authors conclude that although parents have a more intimate knowledge of their child as an individual, they also have a narrower context to make judgments about behavior, whereas teachers have greater expertise with children and observe them in a structured context. Ratings from both sources, however, did in fact yield consistent results regarding the causes of behavior problems.

Snyder, J., Prichard, J., Schrepferman, L., Patrick, M. R., & Stoolmiller, N. (2004). Child impulsiveness-inattention, early peer experiences and the development of early onset conduct problems. *Journal of Abnormal Child Psychology, 32*, 579-594.

This longitudinal study examined the relationship of the development of conduct problems from both trait and experiential perspectives. Two hundred and sixty-seven males and females were assessed at kindergarten entry and again at three time points, ending at the conclusion of second grade. Assessment of inattentive/impulsive traits were based on parent and teacher report as well as classroom observations and measures of working memory. Peer measures included playground observations and sociometric ratings. Using linear growth models, conduct problems at entry and progression during a 2-year period were significantly predicted by trait/symptom assessments made by parents and teachers. For boys, peer rejection and negative interactions mediated initial levels and growth of conduct problems for parent ratings. For teacher ratings, the mediation relationship was significant only for growth. Outcome for girls was more complex, with social factors alone mediating symptoms/ trait impact for conduct problems. Overall, peer problems continued to have strong additive effects on the severity of conduct problems. The authors suggest that trait-like problems could be used to identify children who may require intervention, whereas social interactions could be a target for such interventions.

Stevenson, J., Asherson, P., Hay, D., Levy, F., Swanson, J., Thapar, A., et al. (2005). Characterizing the ADHD phenotype for genetic studies. *Developmental Science, 8*, 115-121.

This article provides an excellent overview of advances in research on the association between ADHD symptoms and genetics. The review focuses on methods to accurately define ADHD symptoms predicted by genetic variation. The article reviews categorical and dimensional approaches, the need for multiple reporters of children's behavior, and most important, a system to sort out genetic causes of common comorbidities with ADHD.

selecting atomoxetine therapy for children with ADHD. *Pharmacotherapy, 25*, 1541-1549.

In this survey of more than 40,000 patients, atomoxetine therapy was found to systematically be preferred for patients with psychiatric comorbidities. In the time frame between April and December 2003, individuals were 1.5 times more likely to begin medication therapy with atomoxetine than stimulants. It is interesting that frequent use of behavioral health care services led to predisposal to start treatment with atomoxetine relative to a stimulant but not for individuals with obesity. Alcohol dependence but not drug dependence or drug abuse was predictive of the selection of atomoxetine over a short-acting stimulant.

Whalen, C., Henker, B., Ishikawa, S. S., Jamner, L. D., Floro, J. N., Johnston, J. A., et al. (2006). An electronic diary study of contextual triggers and ADHD: Get ready, get set, get mad. *Journal of the American Academy of Child and Adolescent Psychiatry, 45*, 166-174.

Across 7 days, mothers and 25 children with ADHD taking stimulant medication, and mothers and 25 children without ADHD between the ages of 7 and 12 years were provided electronic diary reports approximately every 30 min between nonschool hours. The child and maternal perceptions of behaviors, moods, and interaction quality during preparatory and transitional activities were compared with those during other activities. Maternal reports revealed that child symptomatic behaviors and negative moods, maternal negative moods, and parent-child disagreement were elevated in the ADHD but not in the comparison group while getting ready versus other activities. Children's self-ratings also revealed situational effects indicating that school-age children with ADHD can provide meaningful self-reports using carefully structured electronic diaries. Even when children with ADHD are receiving stimulant pharmacotherapy, these data suggest that preparatory tasks of daily living are especially challenging and disproportionately linked to child behavior problems, parent negative affect, and contentious interactions. These data provide support for the need for combined medical and psychosocial treatments in ADHD.

Van Brunt, D. L., Johnston, J. A., Ye, W., Pohl, G. M., Sun, P. J., Sterling, K. L., et al. (2005). Predictors of

Wilens, T., Kratochvil, C., Newcorn, J., & Gao, H. (2006). Do children and adolescents with ADHD

respond differently to atomoxetine? *Journal of the American Academy of Child and Adolescent Psychiatry*, 45, 149-157.

These authors report data contrasting the efficacy and tolerability of atomoxetine between children and adolescents with ADHD. Efficacy measures included response rate, times to response, and mean changes from baseline to

end point on a number of rating scales. There were no statistically significant differences in the overall effects on ADHD symptoms, response rates, or time to response between age groups. Children but not adolescents had a higher rate of somnolence and headache relative to placebo. No other clinically meaningful treatment differences were seen in adverse event rates, vital signs, weight, height, laboratory values, or ECG between children and adolescents.