Effects of Stimulant Medication on Neuropsychological Functioning in Young Adults With Attention-Deficit/Hyperactivity Disorder

Joseph Biederman, M.D.; Larry J. Seidman, Ph.D.; Carter R. Petty, M.A.; Ronna Fried, Ed.D.; Alysa E. Doyle, Ph.D.; Daniel R. Cohen, B.A.; Deborah C. Kenealy, B.A.; and Stephen V. Faraone, Ph.D.

Objective: The main goal of this study was to evaluate the impact of stimulant medication on executive function deficits in a group of adolescents and young adults with attention-deficit/hyperactivity disorder (ADHD; DSM-III-R criteria).

Method: Male and female subjects aged 15 to 25 years were divided into 3 groups: subjects with ADHD treated with stimulants who took their medication at the time of testing (ADHD active stimulant treatment: N = 26), subjects with ADHD who had not taken stimulant medication in the past month (ADHD no stimulant treatment: N = 94), and non-ADHD control subjects (controls: N = 133). The neuropsychological battery assessed domains of cognitive functioning known to be relevant in ADHD, including tests of executive functions and learning and memory. Data were collected from July 1998 to April 2003.

Results: The ADHD no stimulant treatment group had significantly lower aggregate scores compared with the controls for the total aggregate, working memory, interference control, processing speed, sustained attention, and verbal learning domains (all $p < .001$). The ADHD active stimulant treatment group had significantly poorer scores on the total aggregate ($p = .002$), interference control ($p < .001$), and processing speed ($p = .003$) domains compared with the controls. The ADHD active stimulant treatment subjects scored significantly higher on the domains of sustained attention ($p = .04$) and verbal learning ($p = .03$) compared with the ADHD no stimulant treatment subjects.

Conclusions: Our study showed that subjects with ADHD who took stimulant medication had higher neuropsychological measures of attention compared with subjects with ADHD who did not take stimulant medication, but differences were not found for other measures of executive function.

(J Clin Psychiatry 2008;69:1150–1156)

Received June 26, 2007; accepted Oct. 15, 2007. From the Pediatric Psychopharmacology Program of the Psychiatry Department, Massachusetts General Hospital, Boston (Drs. Biederman, Seidman, Fried, and Doyle; Messrs. Petty and Cohen; and Ms. Kenealy), and the Department of Psychiatry and Behavioral Sciences, SUNY Upstate Medical University, Syracuse, N.Y. (Dr. Faraone).

This work was financially supported, in part, by a grant numbered 5RO1 HD-36317-07 from the United States Public Health Service (National Institute of Child Health and Human Development), Rockville, Md. (Dr. Biederman). Support also came, in part, from the Neal-Kimmerly Fund for the Study of Cognition, Boston, Mass. Dr. Biederman had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Financial disclosure appears at the end of the article.

Corresponding author and reprints: Joseph Biederman, M.D., Massachusetts General Hospital, Pediatric Psychopharmacology Unit, 55 Fruit St., Warren 705, Boston, MA 02114 (e-mail: jbiederman@partners.org).

A consistent literature has documented significant associations between attention-deficit/hyperactivity disorder (ADHD) and executive function deficits (EFDs). Executive functions refer to a set of higher self-regulatory cognitive functions including the ability to inhibit, shift set, plan, organize, use working memory, problem solve, and maintain set for future goals.[1,2] Numerous studies have documented that children with ADHD are significantly more likely to manifest EFDs compared with children without ADHD.[1,3–5] Our group also documented that a high proportion of children with ADHD and associated EFDs were at significantly higher risk to have severe educational deficits compared with children with only ADHD. These deficits were characterized by over 2 times the rate of grade retention, placement in special classes, in-school tutoring, and learning disabilities compared with other children with ADHD without these deficits. These results held, even after controlling for socioeconomic status, learning disorders, and IQ scores.[6]

Despite evidence that stimulants are effective in the treatment of ADHD,[7,8] there is uncertainty as to the effects of stimulants on EFDs. While a body of literature indicates that impairment in sustained attention as measured by continuous performance tests are responsive to stimulant treatment, whether stimulants have a broader impact on other domains of executive function is not clear. While

some studies have shown improvements after treatment in areas of selective inhibition,[9] color naming,[10] and visual-spatial memory,[11] others have not. Moreover, in clinical practice, many children with ADHD continue to struggle with residual educational deficits even after treatment with stimulants, suggesting that there may be dissociation between improvement in ADHD symptoms and improvement in EFDs.

The main goal of this study was to evaluate the impact of stimulants on EFDs. Considering the morbidity and dysfunction associated with EFDs, a better understanding of the effects of stimulants on EFDs has important clinical and educational implications. If treatments with stimulants improve EFDs, they would have a much larger impact than just improvement of ADHD symptoms. If, on the other hand, stimulants were to have limited impact on EFDs, this finding would guide clinicians to more aggressively seek appropriate psychoeducational interventions for children with ADHD and associated EFDs and would drive drug discovery toward developing treatments specific to EFDs. In this analysis, we utilized data from our group's longitudinal studies of adolescents and young adults with and without ADHD to investigate the impact of stimulant medication on domains of neuropsychological functioning between treated and untreated individuals with ADHD. On the basis of the literature, we hypothesized that stimulant medication would have an effect on measures of attention but limited effects on other measures of EFDs.

METHOD

Subjects

Subjects were derived from 2 identically designed longitudinal case-control family studies of ADHD.[12,13] These studies ascertained male and female subjects aged 6 to 18 years with (N = 140 boys, N = 140 girls) and without (N = 120 boys, N = 122 girls) Diagnostic Statistical Manual of Mental Disorders, Third Edition, Revised (DSM-III-R)–diagnosed ADHD from pediatric and psychiatric clinics. This analysis reports on neuropsychological data collected at the male subjects' 10-year follow-ups[14] and female subjects' 5-year follow-ups.[15] Because of differences in age among subjects in the 2 studies, we restricted the age of the subjects in each group to the same age range in the present study. Additionally, we excluded individuals from the present analysis who had been taking medication during the past month but did not take their medication on the day of assessment (N = 31). Therefore, this analysis reports on 120 ADHD subjects (64 boys and 56 girls) and 133 control subjects (55 boys and 78 girls) between the ages of 15 and 25 years (mean = 19.2 years, SD = 2.8 years). Data were collected from July 1998 to April 2003.

A 3-stage ascertainment procedure was used to select the probands for both groups. For subjects with ADHD, the first stage was the patient's referral. The second stage confirmed the diagnosis of ADHD by using a telephone questionnaire administered to the mother. The questionnaire asked about the 14 DSM-III-R symptoms of ADHD and contained questions regarding study exclusion criteria. The third stage confirmed the diagnosis with a face-to-face structured interview with the mother. Only patients who received a positive diagnosis at all 3 stages were included. For control probands, we ascertained participants from referrals to medical clinics for routine physical examinations. In the second stage, the control mothers responded to the telephone questionnaire. Eligible controls meeting study entry criteria were recruited for the study and received the third-stage assessment (structured interview). Only subjects classified as not having ADHD at all 3 stages were included in the control group. Potential subjects were excluded if they had been adopted or if their nuclear family was not available for study. We also excluded potential subjects if they had major sensorimotor handicaps (paralysis, deafness, blindness), psychosis, autism, inadequate command of the English language, or a full-scale IQ score less than 80.

Psychiatric Assessments

All diagnostic assessments used structured interviews based upon the criteria of the DSM-III-R.[16] Psychiatric assessments of probands relied on the epidemiologic version of the Schedule for Affective Disorders and Schizophrenia for Children.[17] Diagnoses were based on independent interviews with the mothers and direct interviews of probands. Maternal reports and self-reports were combined by considering a diagnosis as positive if it was endorsed by either interview. The structured interviews assessed lifetime history of psychopathology. Subjects reported impairment for each disorder as mild, moderate, or severe.

The interviewers/psychometricians had undergraduate degrees in psychology; they were trained to high levels of interrater reliability for the assessment of psychiatric diagnosis by the first author (J.B.). We computed κ coefficients of agreement by having experienced, board-certified child and adult psychiatrists diagnose subjects from audiotaped interviews made by the assessment staff. On the basis of 173 interviews from a mixed pediatric and adult data set, the median κ for all diagnoses was .86 and for ADHD was .98. All assessment personnel were blind to proband diagnosis (ADHD or control) and ascertainment site (psychiatric or pediatric).

A committee of board-certified child and adult psychiatrists resolved all diagnostic uncertainties. The committee members were blind to the subjects' ascertainment group, ascertainment site, all data collected from other family members, and all nondiagnostic data (e.g., neuropsychological tests). Diagnoses were considered positive if, based on the interview results, DSM-III-R criteria were unequivocally met to a clinically meaningful degree.

Parents and adult offspring provided written informed consent to participate, and parents also provided consent for offspring under the age of 18 years. Children and adolescents provided written consent to participate. The human research committee at Massachusetts General Hospital, Boston, approved this study.

Treatment

As this was a naturalistic study, no treatments were assigned to the subjects, nor were treatments a factor in study participation. Thus, treatment was allowed to vary by design, and all psychotropic medications were recorded as part of the diagnostic interview. We stratified subjects with ADHD by use of current psychotropic medications.

Neuropsychological Assessments

The neuropsychological battery assessed domains of cognitive functioning known to be relevant in ADHD, including tests of executive functions and learning and memory. Tests were selected to measure domains of functioning thought to be indirect indices of frontostriatal systems that have been found to be impaired in youth and adults with ADHD.[1,18–20] These functions include sustained attention, working memory, interference control, abstract problem solving/set shifting, planning/visuospatial organization, processing speed, and verbal learning.[3,21,22] Subtests were selected from several well-studied clinical instruments that purport to measure these constructs, although it should be noted that these measures may be multifactorial and may assess more than 1 domain of function. The tests included in this study were consistent with those used in our previous work.[12,13,23] As in previous studies,[12,13] tests were administered in a fixed order as follows: (1) the Rey-Osterrieth Complex Figure copy[24]; (2) the Wechsler Adult Intelligence Scale, Third Edition (WAIS-III)[25] (Wechsler Intelligence Scale for Children, Third Edition [WISC-III][26] for individuals aged < 17 years) vocabulary, digit span, and symbol search; (3) the Rey-Osterrieth Complex Figure recall; (4) the WAIS-III (WISC-III for individuals aged < 17 years) block design, arithmetic, and coding/digit symbol subtests; (5) the Auditory Continuous Performance Test (ACPT)[27]; (6) the total words learned on the California Verbal Learning Test (CVLT)[28] (CVLT-Child for individuals aged < 17 years[29]); (7) the computerized Wisconsin Card Sorting Test (WCST)[30]; and (8) the Stroop Color and Word Test.[31] The test battery usually took approximately 2 hours on 1 day to administer. Rest periods were given during the testing sessions as needed.

The Rey-Osterrieth Complex Figure was administered and scored according to the Developmental Scoring System.[32] This method was chosen because we hypothesized that subjects with ADHD would have organization (i.e., executive function) deficits in contrast to simple visuospatial deficits; the developmental scoring of Waber and Holmes assesses such strategies.[32] The organization score distinguishes executive functions from accuracy measures of visuospatial processes. Further administration and scoring details on the Rey-Osterrieth Complex Figure and application to ADHD are provided elsewhere.[21] The tests used in the study have interrater reliabilities in the 0.90s.[33]

The testers were recent college graduates who had undergraduate degrees in psychology; they were trained in neuropsychological assessment by a licensed neuropsychologist who is a coauthor (R.F.) of this article. Testers were trained to maintain the interest of subjects with positive rapport and sensitivity to fatigue. Thus, all neuropsychological function assessments were administered and scored by examiners who were unaware of all other data except for medication status of the subjects. The psychometricians administering the tests are trained to administer the testing in an exact format without any variation from the written administration. They do not administer any tests that need interpretation, they do not interpret material, and every subtest is double-checked for precise administration (tapes) and scoring. Thus, the lack of blindness to medication status would have no bearing on test results.

Statistical Analysis

The z scores were created for each neuropsychological score using the means and standard deviations of the control subjects. Therefore, the z score for the control group had a mean of zero for all neuropsychological variables. All z scores were scored in the same direction of effect; that is, a lower score translates to poorer performance. We then created domain scores based on the domain of neuropsychological functioning that each test is purported to measure. Thus, working memory consisted of the Wechsler scores on oral arithmetic and digit span as well as the ACPT memory and interference scores. The interference control domain comprised the Stroop color-word and interference scores. Set shifting consisted of the WCST categories completed and perseverative and nonperseverative errors. Visuospatial organization included the Rey-Osterrieth Complex Figure copy and recall organization scores. Processing speed was comprised of Stroop word and color-naming items, as well as the Wechsler digit symbol and symbol search subtests. The domains of sustained attention and verbal learning each had only 1 test score included. The sustained attention domain used ACPT vigilance score, while verbal learning used total words learned (trials 1–5) of the CVLT. Domain scores were created by taking the mean of the z score variables in the same neuropsychological domain. An overall aggregate score was calculated as the mean of all neuropsychological scores. Each domain score was compared between groups using analysis of covariance that controlled for age and gender. If a domain score significantly differed between groups, pair-

Table 1. Demographics of Adolescents and Young Adults With ADHD With and Without Stimulant Treatment and Controls

Demographic	Controls (N = 133)	ADHD Active Stimulant Treatment (N = 26)	ADHD No Stimulant Treatment (N = 94)	Test Statistic	p Value
Age, range, y	15–25	15–24	15–25	NA	NA
Age, mean ± SD, y	18.9 ± 2.9	18.3 ± 2.3	20.1 ± 2.7	F = 6.80 df = 2,250	.001
Education, mean ± SD, y	12.8 ± 2.2	12.0 ± 1.9	12.6 ± 2.0	F = 1.40 df = 2,249	.25
Gender (male), N (%)	55 (41)	11 (42)	53 (56)	χ^2 = 5.25 df = 2	.07
Ethnicity (white), N (%)	123 (92)	26 (100)	91 (97)	χ^2 = 3.69 df = 2	.16
Socioeconomic status, mean ± SD	1.7 ± 0.8	1.6 ± 0.8	1.8 ± 1.0	χ^2 = 1.69 df = 2	.43

Abbreviations: ADHD = attention-deficit/hyperactivity disorder, NA = not applicable.

wise comparisons were made between the 3 groups. All tests were 2-tailed with an α set at 0.05.

RESULTS

Subjects with ADHD were grouped based on their treatment status as follows: (1) ADHD probands treated with stimulants who took their medication at the time of testing (ADHD active stimulant treatment: N = 26) and (2) ADHD probands who had not taken stimulant medication in the past month (ADHD no stimulant treatment: N = 94). Comparisons were made between these ADHD groups and non-ADHD controls (controls: N = 133). Table 1 includes demographic information for the 3 groups. The ADHD active stimulant treatment and ADHD no stimulant treatment groups did not differ in the lifetime severity of their ADHD (58% vs. 64% with severe impairment, respectively, $\chi^2 = 0.3$, df = 1, p = .57).

Neuropsychological scores (not z scored) for each of the 3 groups are presented in Table 2. Scores were grouped by their respective neuropsychological domains. Figure 1 shows the mean aggregate scores of the 3 groups. The ADHD no stimulant treatment group had significantly lower aggregate scores compared with the controls for the total aggregate (F = 46.04; df = 1,223; p < .001; Cohen's d = 0.92), working memory (F = 34.86; df = 1,223; p < .001; Cohen's d = 0.80), interference control (F = 22.50; df = 1,221; p < .001; Cohen's d = 0.65), processing speed (F = 28.65; df = 1,223; p < .001; Cohen's d = 0.73), sustained attention (F = 14.88; df = 1,216; p < .001; Cohen's d = 0.54), and verbal learning (F = 22.23; df = 1,223; p < .001; Cohen's d = 0.64). The ADHD active stimulant treatment group had significantly poorer scores on the total aggregate (F = 9.56; df = 1,155; p = .002; Cohen's d = 0.67), interference control (F = 18.07; df = 1,154; p < .001; Cohen's d = 0.92), and processing speed (F = 8.99; df = 1,155; p = .003; Cohen's d = 0.65) compared with the controls. The ADHD active stimulant treatment subjects scored higher on sustained attention (F = 4.47; df = 1,111; p = .04; Cohen's d = 0.48) and verbal learning (F = 5.13; df = 1,115; p = .03; Cohen's d = 0.51) compared with the ADHD no stimulant treatment subjects.

Table 2. Neuropsychological Scores (mean ± SD) of Adolescents and Young Adults With ADHD With and Without Stimulant Treatment and Controls

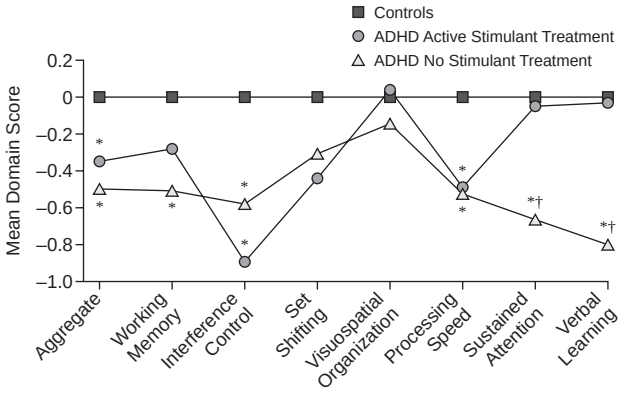
Domain	Controls (N = 133)	ADHD Active Stimulant Treatment (N = 26)	ADHD No Stimulant Treatment (N = 94)
Working memory			
Arithmetic[a]	12.2 ± 3.0	10.8 ± 3.7	10.2 ± 3.1
Digit span[a]	11.4 ± 2.9	10.6 ± 3.3	10.4 ± 2.9
CPT memory	20.6 ± 3.2	19.9 ± 3.0	18.9 ± 3.3
CPT interference	26.7 ± 6.5	25.8 ± 6.6	23.1 ± 6.8
Interference control			
Stroop color-word[b]	53.8 ± 10.0	43.8 ± 10.0	46.8 ± 10.2
Stroop interference[b]	56.1 ± 8.5	49.4 ± 7.4	52.2 ± 7.7
Abstract problem solving/ set shifting			
Categories	5.9 ± 0.5	5.5 ± 1.4	5.7 ± 1.0
Perseverative errors[b]	60.1 ± 10.7	57.6 ± 12.7	57.9 ± 12.7
Nonperseverative errors[b]	54.8 ± 7.7	52.5 ± 8.1	52.6 ± 8.8
Planning visuospatial organization			
Copy organization	10.5 ± 3.0	10.3 ± 3.1	9.7 ± 3.4
Delay organization	9.4 ± 3.5	9.9 ± 3.5	9.4 ± 3.8
Processing speed			
Digit symbol[a]	11.2 ± 2.9	9.5 ± 3.1	8.8 ± 3.1
Symbol search[a]	11.2 ± 2.8	10.0 ± 2.8	10.2 ± 2.7
Stroop word[b]	46.6 ± 7.5	43.7 ± 8.3	43.3 ± 8.6
Stroop color[b]	46.6 ± 7.9	42.2 ± 7.8	42.4 ± 7.8
Sustained attention			
ACPT vigilance	29.3 ± 1.0	29.2 ± 1.0	28.6 ± 2.1
Verbal learning			
CVLT	58.4 ± 7.4	58.1 ± 9.3	52.4 ± 10.9

[a]Scaled score.
[b]T score.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, ACPT = Auditory Continuous Performance Test, CVLT = California Verbal Learning Test.

DISCUSSION

This study analyzed neuropsychological data from a large sample of well-characterized youth with and without

Figure 1. Domains of Standardized Neuropsychological Scores in Adolescents and Young Adults With ADHD With and Without Stimulant Treatment and Controls[a]



[a]All comparisons $p < .05$ and adjusted for age and gender.
*Versus controls.
†Versus ADHD active stimulant treatment group.
Abbreviation: ADHD = attention-deficit/hyperactivity disorder.

ADHD ascertained from psychiatric and pediatric referral sources. Results showed that subjects with ADHD who were not taking stimulants on the day of testing displayed robust neuropsychological deficits relative to non-ADHD controls, while subjects with ADHD who took stimulant treatment did not display some of these deficits. Results indicate heterogeneity in the effects of stimulants on neuropsychological functioning, with the largest effects being on measures of sustained attention (ACPT) and verbal learning (CVLT), while the weakest effects were on measures of specific domains of executive function including organization/planning (Rey-Osterrieth Complex Figure), working memory (Wechsler digit span and oral arithmetic), and set shifting (WCST). These findings suggest that stimulants may have a limited effect on EFDs in individuals with ADHD.

The strengths of this report include a large well-characterized sample of teenagers and young adults with and without ADHD of both sexes. An additional strength is the reliance on a battery of clinical neuropsychological measures that have been shown to distinguish between individuals with and without ADHD.[20] Additionally, prior studies have documented that the executive function impairments measured with this neuropsychological battery have been shown to predict educational deficits. The subjects with ADHD who were actively being treated with stimulants had better scores in the domains of sustained attention and verbal learning compared with the ADHD subjects who had not taken stimulants within the last month. The effect size using Cohen's d for sustained attention was 0.48 and for verbal learning was 0.51, both of which are less than the effect of stimulants on ADHD symptoms (about 0.9).[8]

Our findings for sustained attention are consistent with a body of literature documenting similar results using other continuous performance tests.[34,35] Our sustained attention domain comprised the vigilance subtest of the ACPT,[27] and the results are consistent with the literature. Given that these subtests were designed to target attention, which is 1 of the core components of ADHD, the better function on these measures is not surprising. Our other significant finding (verbal learning) was consistent with a study by Buschke and Fuld[36] that showed significant improvement in verbal recall of words presented over 5 trials. Our verbal memory finding was based on total trials (1–5) of the CVLT (CVLT-Child and -Second Edition versions). This score reflects appropriate encoding of the words into short-term memory as well as the ability to retrieve them. Yet, in addition to aspects of memory and learning, this measure also requires sustained attention while the word list is verbalized to the subject.

In contrast, stimulant treatments did not affect interference control and processing speed. Since these are measures of EFDs, these results are consistent with the dissociation between the effects of stimulants on attentional deficits and their effects on EFDs. These findings are also consistent with the literature that found other tests of EFDs, such as the Tower of London,[37] did not show significant medication effects.

If confirmed, these results may have important implications for clinicians and educators. Considering the well-documented history of EFDs on educational functions, our findings emphasize the need to define ADHD and EFDs as entities needing separate and equally important intervention. Our results may begin to explain the apparent dissociation between stimulant-associated improvement in core symptoms of ADHD and academic performance. Our results support the need to target neuropsychological deficits in clinical practice for appropriate remediation approaches.

Our results should be considered in light of some methodological limitations. Since the majority of our subjects were white, our results may not generalize to other ethnic groups. Because the sample was referred, we do not know if our results will generalize to children with ADHD in the general population. Since subjects were naturalistically treated, our results need confirmation from prospective randomized clinical trials. Although attempts were made to exclude many of the primary diagnoses that can have an impact on cognitive functioning, subjects could have been exposed to substances or mild head trauma between the baseline testing and follow-up. If a major problem was identified during the structured interview, it would have been brought to the attention of the primary investigator of the study, and the data would have been deleted.

Our sample was ascertained with DSM-III-R criteria and not that of the DSM-IV. Biederman and colleagues[38]

showed that 93% of children with a DSM-III-R diagnosis also received a DSM-IV diagnosis. However, our results may represent averages of potentially cognitively heterogeneous subgroups, so future work should determine if the effects of stimulants on cognitive function vary by DSM-IV ADHD subtypes.

Despite these considerations, our study showed that subjects with ADHD who took stimulant medication had higher neuropsychological measures of attention than subjects with ADHD who did not take stimulant medication, but differences were not found for other measures of executive function. As such, future studies should look to develop appropriate interventions to aid individuals with ADHD in this area of dysfunction.

Financial disclosure: **Dr. Biederman** is currently receiving research support from Bristol-Myers Squibb, Eli Lilly, Janssen, McNeil, Otsuka, Shire, National Institute of Mental Health (NIMH), and National Institute of Child Health and Human Development [NICHD]; is a consultant to or advisory board member for Janssen, McNeil, Novartis, and Shire; and is a speaker for Janssen, McNeil, Novartis, Shire, and UCB Pharma. In previous years, **Dr. Biederman** received research support, consultation fees, or speaker's fees from Abbott, AstraZeneca, Celltech, Cephalon, Eli Lilly, Esai, Forest, GlaxoSmithKline, Gliatech, National Alliance for Research on Schizophrenia and Depression, New River, National Institute on Drug Abuse, Novartis, Noven, Neurosearch, Pfizer, Pharmacia, The Prechter Foundation, The Stanley Foundation, and Wyeth. **Dr. Fried** has received research support from, served as a consultant to, or served on the speakers or advisory boards for NIMH, McNeil, Eli Lilly, and Pfizer. **Dr. Doyle** has served as a consultant to Novartis, NIMH, McNeil, Eli Lilly, and Pfizer and has served on the speakers or advisory boards for or received grant/research support from NIMH, McNeil, Eli Lilly, and Pfizer. **Dr. Faraone** has received research support from, served as a consultant to, or served on the speakers or advisory boards for Eli Lilly, McNeil, Shire, Noven, Cephalon, NIMH, NICHD, and National Institute of Neurological Disorders and Stroke. **Dr. Seidman**, **Messrs. Petty and Cohen**, and **Ms. Kenealy** report no other financial affiliations relevant to the subject of this article.

REFERENCES

1. Pennington BF, Ozonoff S. Executive functions and developmental psychopathology. J Child Psychol Psychiatry 1996;37:51–87
2. Sergeant JA, Geurts H, Oosterlaan J. How specific is a deficit of executive functioning for attention-deficit/hyperactivity disorder? Behav Brain Res 2002;130:3–28
3. Seidman LJ, Biederman J, Faraone SV, et al. Toward defining a neuropsychology of attention-deficit/hyperactivity disorder: performance of children and adolescents from a large clinically referred sample. J Consult Clin Psychol 1997;65:150–160
4. Barkley RA, ed. ADHD and the Nature of Self-Control. New York, NY: Guilford; 1997
5. Houghton S, Douglas G, West J, et al. Differential patterns of executive function in children with attention-deficit/hyperactivity disorder according to gender and subtype. J Child Neurol 1999;14:801–805
6. Biederman J, Monuteaux M, Seidman L, et al. Impact of executive function deficits and ADHD on academic outcomes in children. J Consult Clin Psychol 2004;72:757–766
7. Faraone SV, Biederman J, Kiely K. Cognitive functioning, learning disability, and school failure in attention-deficit/hyperactivity disorder: a family study perspective. In: Beitchman J, ed. Language, Learning and Behavior Disorders. Essex, England: Cambridge University Press; 1996:247–271
8. Faraone SV. Understanding the effect size of ADHD medications: implications for clinical care. Medscape Psychiatry Ment Health 2003;8
9. Bedard AC, Ickowicz A, Logan GD, et al. Selective inhibition in children with attention-deficit/hyperactivity disorder off and on stimulant medication. J Abnorm Child Psychol 2003;31:315–327
10. Bedard AC, Ickowicz A, Tannock R. Methylphenidate improves Stroop naming speed, but not response interference, in children with attention-deficit/hyperactivity disorder. J Child Adolesc Psychopharmacol 2002; 12:301–309
11. Bedard AC, Martinussen R, Ickowicz A, et al. Methylphenidate improves visual-spatial memory in children with attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 2004;43: 260–268
12. Biederman J, Faraone SV, Mick E, et al. Clinical correlates of ADHD in females: findings from a large group of girls ascertained from pediatric and psychiatric referral sources. J Am Acad Child Adolesc Psychiatry 1999;38:966–975
13. Biederman J, Faraone S, Milberger S, et al. A prospective 4-year follow-up study of attention-deficit/hyperactivity and related disorders. Arch Gen Psychiatry 1996;53:437–446
14. Biederman J, Monuteaux M, Mick E, et al. Young adult outcome of attention-deficit/hyperactivity disorder: a controlled 10-year prospective follow-up study. Psychol Med 2006;36:167–179
15. Biederman J, Monuteaux M, Mick E, et al. Psychopathology in females with attention-deficit/hyperactivity disorder: a controlled, five-year prospective study. Biol Psychiatry 2006;60:1098–1105
16. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised. Washington, DC: American Psychiatric Association; 1987
17. Orvaschel H. Psychiatric interviews suitable for use in research with children and adolescents. Psychopharmacol Bull 1985;21:737–745
18. Tannock R, Banaschewski T, Gold D. Color naming deficits and attention-deficit/hyperactivity disorder: a retinal dopaminergic hypothesis. Behav Brain Funct 2006;2:4
19. Seidman LJ, Doyle AE, Fried R, et al. Neuropsychological function in adults with attention-deficit/hyperactivity disorder. Psychiatr Clin North Am 2004;27:261–282
20. Willcutt EG, Doyle AE, Nigg JT, et al. Validity of the executive function theory of ADHD: a meta-analytic review. Biol Psychiatry 2005; 57:1336–1346
21. Seidman LJ, Benedict KB, Biederman J, et al. Performance of children with ADHD on the Rey-Osterrieth Complex Figure: a pilot neuropsychological study. J Child Psychol Psychiatry 1995;36:1459–1473
22. Seidman LJ, Biederman J, Weber W, et al. Neuropsychological function in adults with attention-deficit/hyperactivity disorder. Biol Psychiatry 1998;44:260–268
23. Doyle AE, Wilens T, Kwon A, et al. Neuropsychological functioning in youth with bipolar disorder. Biol Psychiatry 2005;58:540–548
24. Rey A. L'examen psychologique dans les cas d'encephalopathie traumatique. Les Archives de Psychologie 1941;28:286–340
25. Wechsler D, ed. Wechsler Adult Intelligence Scale III [manual]. San Antonio, Tex: The Psychological Corporation; 1997
26. Wechsler D, ed. Manual for the Wechsler Intelligence Scale for Children. 3rd Edition. San Antonio, Tex: The Psychological Corporation, Harcourt Brace Jovanovich, Inc; 1991
27. Seidman LJ, Breiter HC, Goodman JM, et al. A functional magnetic resonance imaging study of auditory vigilance with low and high information processing demands. Neuropsychology 1998;12:505–518
28. Delis DC, Kramer JH, Kaplan E, et al, eds. California Verbal Learning Test-Adult Version. New York, NY: The Psychological Corporation; 1987
29. Delis D, Kramer J, Kaplan E, et al, eds. The California Verbal Learning Test-Children's Version. San Antonio, Tex: Psychological Corporation; 1994
30. Heaton RK, Chelune GJ, Talley JL, et al, eds. Wisconsin Card Sorting Test Manual: Revised and Expanded. Odessa, Fla: Psychological Assessment Resources, Inc; 1993
31. Golden CJ, ed. Stroop Color and Word Test: A Manual for Clinical and Experimental Use. Chicago, Ill: Stoelting Co; 1978
32. Waber D, Holmes JM. Assessing children's copy productions of the Rey-Osterrieth Complex Figure. J Clin Exp Neuropsychol 1985;7: 264–280
33. Lezak M, ed. Neuropsychological Assessment. New York, NY: Oxford University Press; 1995
34. Bouffard R, Hechtman L, Minde K, et al. The efficacy of 2 different

dosages of methylphenidate in treating adults with attention-deficit/hyperactivity disorder. Can J Psychiatry 2003;48:546–554
35. Musten LM, Firestone P, Pisterman S, et al. Effects of methylphenidate on preschool children with ADHD: cognitive and behavioral functions. J Am Acad Child Adolesc Psychiatry 1997;36:1407–1415
36. Buschke H, Fuld PA. Evaluating storage, retention, and retrieval in disordered memory and learning. Neurology 1974;24:1019–1025
37. Kempton S, Vance A, Maruff P, et al. Executive function and attention-deficit/hyperactivity disorder: stimulant medication and better executive function performance in children. Psychol Med 1999;29:527–538
38. Biederman J, Faraone SV, Weber W, et al. Correspondence between DSM-III-R and DSM-IV attention-deficit/hyperactivity disorder (ADHD). J Am Acad Child Adolesc Psychiatry 1997;36:1682–1687

Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Childhood and Adolescent Mental Health section. Please contact Karen D. Wagner, M.D., Ph.D., at kwagner@psychiatrist.com.

© COPYRIGHT 2008 PHYSICIANS POSTGRADUATE PRESS, INC.