Journal of the International Neuropsychological Society (2003), **9**, 815–829.

DOI: 10.1017/S1355617703960012

Attention deficit hyperactivity disorder and neurocognitive correlates after childhood stroke

JEFFREY E. MAX,[1] KATHERINE MATHEWS,[2] FACUNDO F. MANES,[3] BRIGITTE A.M. ROBERTSON,[4] PETER T. FOX,[5] JACK L. LANCASTER,[5] AMY E. LANSING,[6] AMY SCHATZ,[6] AND NICOLE COLLINGS[6]

[1]University of California, San Diego and Children's Hospital and Health Center, San Diego, California
[2]University of Iowa, Department of Pediatrics and Neurology, Iowa City, Iowa
[3]Raul Carrea Institute for Neurological Research—FLENI, Buenos Aires, Argentina
[4]GlaxoSmithKline, Research Triangle Park, North Carolina
[5]Research Imaging Center, University of Texas Health Science Center, San Antonio, Texas
[6]Children's Hospital and Health Center, Department of Psychiatry, San Diego, California

(RECEIVED March 28, 2002; REVISED August 22, 2002; ACCEPTED October 3, 2002)

Abstract

We investigated the frequency and neurocognitive correlates of attention deficit hyperactivity disorder and traits of this disorder (ADHD/Traits) after childhood stroke and orthopedic diagnosis in medical controls. Twenty-nine children with focal stroke lesions and individually matched children with clubfoot or scoliosis were studied with standardized psychiatric, intellectual, academic, adaptive, executive, and motivation function assessments. Lifetime ADHD/Traits were significantly more common in stroke participants with no prestroke ADHD than in orthopedic controls (16/28 *vs.* 7/29; Fisher's Exact $p < .02$). Lifetime ADHD/Traits in the orthopedic controls occurred exclusively in males with clubfoot (7/13; 54%). Participants with current ADHD/Traits functioned significantly worse ($p < .005$) than participants without current ADHD/Traits on all outcome measures. Within the stroke group, current ADHD/Traits was associated with significantly lower verbal IQ and arithmetic achievement ($p < .04$), more nonperseverative errors ($p < .005$), and lower motivation ($p < .004$). A principal components analysis of selected outcome variables significantly associated with current ADHD/Traits revealed "impaired neurocognition" and "inattention-apathy" factors. The latter factor was a more consistent predictor of current ADHD/Traits in regression analyses. These findings suggest that inattention and apathy are core features of ADHD/Traits after childhood stroke. This association may provide clues towards the understanding of mechanisms underlying the syndrome. (*JINS*, 2003, *9*, 815–829.)

Keywords: ADHD, Childhood stroke, Cognition, Apathy, Clubfoot, Scoliosis

INTRODUCTION

This is the first study of neurocognitive correlates of attention deficit hyperactivity disorder (ADHD) after childhood stroke. ADHD is one of the most common psychiatric syndromes which manifest after a variety of brain injuries including traumatic brain injury (TBI) (Bloom et al., 2001; Gerring et al., 1998; Max et al., 1998a; Max et al., in press), very low birth weight/premature infants (Botting et al., 1997; Lou, 1996; Whitaker et al., 1997), cerebral palsy (Breslau & Chilcoat, 2000; Ingram, 1956), epilepsy (Ounsted, 1955), childhood hemiplegia (Goodman & Graham, 1996), and encephalitis (Ebaugh, 1923). Such diverse etiologies would tend to suggest that the syndrome is a final common pathway of varied pathophysiological processes. The syndrome may be associated with a varied pattern of symptom clusters and neurocognitive correlates depending on the nature and extent of the brain injury. Pathophysiological and neurocognitive research in idiopathic ADHD is more advanced than corresponding research in ADHD that follows brain injury, yet it is far from conclusive. Therefore the investigation of poststroke ADHD and idiopathic ADHD are likely to have mutual relevance.

Children with focal stroke lesions provide a potentially useful model for the investigation of ADHD after brain injury. We recently reported a trend towards an association

Reprint requests to: Jeffrey E. Max, M.B.B.Ch, Children's Hospital and Health Center, San Diego, 3020 Children's Way, MC 5033, San Diego, CA 92123. E-mail: jmax@ucsd.edu

of ADHD and stroke lesions of the putamen in participants with lesions ≤10 cc (Max et al., 2002). In the current study, we shall report neurocognitive correlates of poststroke ADHD regardless of lesion volume. Our focus will be on intellectual, academic, adaptive, and executive functions, as well as motivation.

Intellectual Function

Children with idiopathic ADHD have a lower IQ, particularly verbal IQ, than controls. This difference is small but reaches statistical significance (Barkley, 1997). In controlled studies, this can affect comparisons of neurocognitive functions that correlate significantly with IQ. Barkley (1997) has challenged the wisdom of statistically controlling for IQ in studies of idiopathic ADHD because findings related to the independent variable of interest, ADHD, might be eliminated. Intellectual function in brain-injury-related ADHD has been studied in children with TBI. Brain-injury-related ADHD is associated with significantly lower IQ when analyses include mild to severe TBI children (Max et al., in press) and IQ scores were lower but reached statistical significance in only 1 of 2 studies when analyses were limited to more severely injured TBI participants (Gerring et al., 1998; Max et al., in press).

Academic Function

Academic deficits have been associated with idiopathic ADHD. Specifically, reading disorders are often comorbid with ADHD (Shaywitz & Shaywitz, 1994; Willcutt & Pennington, 2000). ADHD is also associated with poorer long-term
educational achievement measured in years of formal education (Wood & Felton, 1994) and poorer math skills (Nussbaum et al., 1990). In contrast, academic function associated with brain-injury-related ADHD has not been studied.

Adaptive Function

Over 70% of children with idiopathic ADHD in an epidemiological study had deficits in adaptive function (Costello et al., 1996). These deficits are often considered markers of more severe and pervasive impairments in this population (Shelton et al., 1998). However, adaptive function (Max et al., in press) or overall disability (Gerring et al., 1998) associated with brain-injury-related ADHD has been studied only in childhood TBI. Taken together, these studies indicate significantly worse functioning in brain-injury-related ADHD participants regardless of whether the samples included a full range of injury severity or only more severely injured participants.

Executive Function

Executive-function deficits have been implicated in the expression of idiopathic ADHD (e.g., Barkley, 1997). The construct of executive function is nonunitary. We report on two measures of executive function, the Wisconsin Card Sorting Test (WCST) (Grant & Berg, 1948) and the Controlled Oral Word Association Test (Borkowski et al., 1967).

The WCST is a test that demands flexibility of sorting strategies for multidimensional figures, and requires working memory and behavioral inhibition (Barkley, 1997). Children with ADHD make more perseverative errors and nonperseverative errors on the WCST than controls, but this is not a uniform finding (Barkley, 1997; Klorman et al., 1999; Pennington & Ozonoff, 1996). Performance on the WCST has not been reported in children with brain-injury-related ADHD.

The Controlled Oral Word Association Test (Borkowski et al., 1967) is a test of verbal fluency. The literature on children with ADHD is mixed with respect to documented differences in this domain of executive function (Barkley, 1997). However, tests which use letters, for example, the Controlled Oral Word Association Test, rather than semantic categories may be more challenging and more likely to discriminate children with ADHD from controls (Barkley, 1997). Verbal fluency associated with brain-injury-related ADHD has not been studied.

Motivation

There is extensive evidence for difficulties in the self-regulation of motivation, particularly persistence of effort, in children with idiopathic ADHD (Barkley, 1997). It may be that children with ADHD have a deficit in the executive-function capacity to bridge delays in reinforcement and permit the persistence of goal-directed acts (Barkley, 1997). There are no published reports of motivation or its converse, apathy, associated with brain-injury-related ADHD.

Against this background, we set out to study ADHD in children with neuroimaging evidence of focal stroke lesions, controlling for age, gender, socioeconomic status (SES), and the presence of and timing of onset of a chronic non-central nervous system (non-CNS) medical condition. (See Table 1 for categorization of ADHD with onset *after* the diagnosis of the respective medical condition: stroke and chronic non-CNS disorders.) We hypothesized, first, that significantly more children with stroke than controls would have a lifetime history of the full ADHD syndrome. Second, we hypothesized that when children with a lifetime history of the full ADHD syndrome and children with only ADHD traits (defined below) were considered as one group (*lifetime* ADHD/Traits), significantly more children with stroke than medical controls would exhibit *lifetime* ADHD/Traits. Third, we hypothesized that children with *current* ADHD/Traits (i.e., excluding resolved ADHD cases) would demonstrate significantly more impairments in intellectual, academic, adaptive, and executive functions as well as motivation than participants without *current* ADHD/Traits either when stroke and control participants were analyzed or only when participants with stroke were considered.

Table 1. Postmedical diagnosis ADHD/Traits in stroke and orthopedic participants

	Stroke		Orthopedic	
ADHD *current*	**12**		**3**	
Inattentive		6		2
Not otherwise specified		4		
Hyperactive/impulsive		1		
Combined type		1		1
ADHD resolved	**1**		**1**	
Not otherwise specified		1		1
ADHD partial resolution	**0**		**1**	
Not otherwise specified				1
ADHD traits	**3**		**2**	

Legend. One additional stroke participant had ADHD before the medical diagnosis. Hypothesis 1 concerned *lifetime postmedical diagnosis ADHD* ($n = 13$ in stroke cohort; $n = 5$ in orthopedic cohort) which consists of participants with a history of the full postmedical diagnosis ADHD syndrome at some point in their life (postmedical diagnosis ADHD *current*, postmedical diagnosis ADHD resolved, postmedical diagnosis ADHD partial resolution); Hypothesis 2 concerned *lifetime* postmedical diagnosis *ADHD/Traits* ($n = 16$ in stroke cohort; $n = 7$ in orthopedic cohort) which consists of participants with a history of the full postmedical diagnosis ADHD syndrome or postmedical diagnosis ADHD traits at some point in their life (postmedical diagnosis ADHD *current*, postmedical diagnosis ADHD resolved, postmedical diagnosis ADHD partial resolution, postmedical diagnosis ADHD traits); Hypothesis 3 concerns *current* postmedical diagnosis *ADHD/Traits* ($n = 15$ in stroke cohort; $n = 6$ in orthopedic cohort) which consists of participants with current postmedical diagnosis ADHD, postmedical diagnosis ADHD traits, and postmedical diagnosis ADHD in partial resolution.

METHOD

The design and concept of this study was strongly influenced by British research on psychiatric aspects of neurological disorders over the past three decades (e.g., Goodman & Graham, 1996; Rutter et al., 1970; Seidel et al., 1975). The research design, previously reported in detail (Max et al., 2002), is a cross-sectional study of children with a history of a single stroke and a medical control group. The study focus was on psychiatric outcome in children with strokes in addition to neuropsychological, academic, adaptive, executive, and family function outcomes. In accordance with previous studies (Riva & Cazzaniga, 1986; Woods, 1980), stroke participants were considered to have "early" lesions if their brain lesion occurred prenatally or up to 12 months of postnatal life. The "late" lesion group consisted of children who acquired their stroke at age 12 months or later. We matched "early" stroke participants with children with clubfoot, with the rationale that physical deformity in both groups was an early, and frequently congenital, insult. We matched "late" stroke participants with children who had scoliosis because these children were without physical deformity prior to their acquired disorders.

Inclusion criteria for stroke cases were as follows: (1) Neuroimaging documentation of a focal, nonrecurrent and nonprogressive supratentorial brain parenchymal lesion caused by a stroke before age 14 years; (2) Participants aged 5–19 years at the time of the assessment; (3) ≥1 year since stroke; and (4) English as first language. The following exclusions were applied: (1) neonatal bleeds (e.g., intraventricular hemorrhages, germinal matrix hemorrhages) potentially associated with prematurity; (2) neonatal watershed infarcts associated with hypoxia; (3) hemoglobinopathies; (4) progressive neurometabolic disorders; (5) Down's syndrome and other chromosomal abnormalities; (6) malignancy; (7) congenital hydrocephalus; (8) shunts; (9) congenital and acquired CNS infections; (10) clotting factor deficiency; (11) stroke in a pregnant minor; (12) previous organ or bone marrow transplant; (13) cerebral cysts; (14) trauma; (15) transient ischemic attack; (16) Moya Moya; (17) severe and profound mental retardation; (18) quadriplegia, triplegia, or diplegia diagnoses; (19) syndromic vascular malformations (excluding arterio-venous malformation (AVM) aneurysm ruptures); (20) systemic lupus erythematosis; and (21) multiple lesions (unless in close proximity).

Inclusion criteria for controls were as follows: Children with congenital clubfoot and children with scoliosis were individually matched to participants with stroke according to age of onset of stroke (i.e., early *vs.* late). Matching was based on gender, ethnicity, SES, and age within 1 year. Age matching had to be extended to 16 months in three cases. The following exclusion criteria were applied for controls: Orthopedic controls were excluded when they had evidence in the chart of acquired or congenital CNS injury that may be part of broader (e.g., neuromuscular) syndromes unrelated to the common idiopathic syndromes. Matching was possible for all but two children with late stroke lesions. These two late-onset stroke participants were matched with children with clubfoot.

Stroke participants evaluated included 17 with early lesions and 12 with late lesions. The strokes were ischemic in 21 cases and hemorrhagic in eight cases. Etiology included 15 idiopathic occlusive cases, two idiopathic hemorrhagic cases, four cases occurred in participants with congenital heart disease (three after cardiac surgery or catheterization and one after varicella zoster infection), five cases of arteriovenous malformation rupture, one case of ruptured angioma, one case possibly linked to comorbid ulcerative colitis, and one case followed a varicella infection. Both cases associated with varicella infections were presumed to be due to vasculitis and there was no evidence for encephalitis (Roach & Riela, 1995). The distribution of the brain lesions included seven cases of predominantly putamen lesions, nine cases of large middle cerebral artery (MCA) distribution infarcts including deep gray structures, ten cases of smaller MCA distribution fronto-temporal or temporo-parietal lesions sparing the deep gray, and three cases of parietal or parieto-occipital strokes. Forty-eight participants (including all stroke participants) were recruited from one university hospital while ten participants were recruited from a second university hospital due to the relocation of the first author (JEM).

The stroke and orthopedic groups were not significantly different on matching variables of age and SES. Respective age means (*SD*) of stroke and orthopedic participants were

12.1 (3.9) and 11.9 (3.9), $df = 56$, $t = -.135$, $p > .8$. Respective SES means (SD) of stroke and orthopedic participants were 2.45 (.95) and 2.45 (1.06), $df = 56$, $t = 0$, $p = 1.0$. There were 18 males, 27 Caucasians, and two biracial children in each of the stroke and orthopedic groups.

Measures

Psychiatric and behavioral measures

Diagnostic and Statistical Manual–Fourth Edition (DSM–IV) psychiatric diagnoses (American Psychiatric Association, 1994) were derived by utilizing a semistructured interview, the *Schedule for affective disorders and schizophrenia for school-aged children, present and lifetime version (K-SADS-PL)* (Kaufman et al., 1997). The K-SADS-PL is an integrated parent–child interview which generates diagnoses based on a clinician synthesizing data collected from parent and child separately, querying present and lifetime symptoms as well as providing data regarding the timing of symptom onset in relation to the stroke and orthopedic diagnosis. If participants have significant symptoms on questions for a particular syndrome in a K-SADS-PL screen interview, a corresponding K-SADS-PL supplementary interview module is completed to clarify the diagnosis.

The outcome measures were the diagnoses of DSM–IV ADHD and "ADHD traits." This approach recognized the dimensional nature of ADHD symptomatology (Levy et al., 1997). The diagnosis of ADHD was made when the symptom complex resulted in clinically significant impairment, even after considering overall developmental level of the child, and was not based simply on symptom counts. The ADHD subtypes (combined, predominantly inattentive, predominantly hyperactive/impulsive, *and* not otherwise specified) were applied only to participants with a clinically significant DSM–IV ADHD syndrome. The designation of ADHD traits was given to participants with a subsyndromal condition. ADHD traits were defined *a priori* as at least three of four symptoms in the screening interview for ADHD rated positive but "subthreshold" or at least one screener question rated "threshold" and at least five additional symptoms on the supplementary ADHD interview rated "subthreshold" or "threshold". The age-of-onset (7 years) criterion for ADHD was waived so that we could document the development of this behavioral syndrome in participants whose stroke or scoliosis was diagnosed later.

Fifty-seven of 58 interviews were administered by JEM, who is a board-certified child and adolescent psychiatrist, and all were videotaped. AEL, a trained Ph.D. level researcher, administered one interview. Eleven interviews were selected randomly to be rated by a second child psychiatrist, BAMR, to ascertain interrater reliability. Agreement regarding the presence of ADHD, ADHD subtype, ADHD traits, and ADHD/Traits was 100%.

The *Child Behavior Checklist* (CBCL) (Achenbach, 1991) was completed by a parent. The CBCL is a well-standardized assessment of child-behavior problems. In addition to a total behavior-problem score, the CBCL provides two "broad band" subscales (internalizing and externalizing symptoms) and eight "narrow band" scales (withdrawn, somatic complaints, anxious/depressed, social problems, thought problems, attention problems, delinquent behavior and aggressive behavior).

In addition, the *Children's Motivation Scale* (Gerring et al., 1996) was administered. This is a 16-item rating scale that measures the behavioral, cognitive, and emotional concomitants of motivation, the conceptual converse of apathy. The scale has fair-to-good test–retest reliability, internal consistency, and interrater reliability. The measure correlated significantly with an independent measure of withdrawal but not with depression. Normative samples have a mean of 50 with a standard deviation of approximately 10. Psychiatric inpatient or outpatient samples have a mean of 31 with a standard deviation of 10. Parents completed this questionnaire.

Family psychiatric and behavioral assessments

The *Family History Research Diagnostic Criteria* (Andreasen et al., 1977) interview was conducted in most cases by a trained research assistant and in other cases by JEM. Criteria were modified to conform with Diagnostic and Statistical Manual–Third Edition–Revised (DSM–III–R) criteria. At least one parent acted as the informant. Family ratings were summarized for first-degree relatives on a four-point scale (0 to 3) (Max et al., 1998a) of increasing severity. Among specific disorders recorded in both first- and second-degree relatives was ADHD. We also recorded another variable, a merged category of ADHD or ADHD symptoms in first- and second-degree relatives. This category was purposefully broader than the first because it is difficult for family members to endorse sufficient ADHD symptoms to meet diagnostic criteria for their relatives who may in fact have ADHD.

Global family functioning was assessed by using the *McMaster Structured Interview of Family Functioning*. The interview is used to derive scores on the Clinical Rating Scale (CRS) (Miller et al., 1994). The CRS is comprised of seven domains, including global family functioning, which are rated 1–7 on a Likert Scale. Scores of 5–7 indicate healthy family function and lower scores indicate unhealthy family functioning. Two trained research assistants, who remained blind to the psychiatric findings, conducted the interviews.

Socioeconomic status (SES)

SES assessment was accomplished through the *Four Factor Index* (Hollingshead, 1975). Classification into five levels (1 to 5) (Max et al., 2002) depends on scores derived from a formula involving both mother's and father's educational levels and occupational levels. Lower scores reflect higher SES. Controls were matched within two levels of the relevant stroke participant.

Intellectual function

The *Wechsler Intelligence Scale for Children, Third Edition* (WISC–III) (Wechsler, 1991) was used. Prorated Full Scale IQ (FSIQ) was derived from a prorated Performance IQ (PIQ: Picture Arrangement, Block Design, and Coding subtests) and a prorated Verbal IQ (VIQ: Information and Similarities subtests). We applied the upper age limit norms for this test to the few participants who were above the age range for published norms.

Academic function

The *Wide Range Achievement Test, Revised* (WRAT–R, Jastak & Wilkinson, 1984) was administered to assess achievement in reading, spelling, and mathematics. The WRAT–R consists of two alternate forms with two levels (level 1 for children ages 5.0 to 11.11; level 2 for persons over 12 years of age).

Adaptive function

Adaptive functioning assessment was completed by trained research assistants using the *Vineland Adaptive Behavior Scale* interview (Sparrow et al., 1984) through a nondirective interview with the primary caretaker. The Vineland scales survey activities that the child habitually demonstrates in the environment, yielding an overall composite score and separate standard scores for Socialization, Daily Living, and Communication domains.

Executive function

A computerized version of the *Wisconsin Card Sorting Test* (WCST) (Grant & Berg, 1948) was administered to participants to assess aspects of executive function. Participants were asked to match each stimulus card (appearing at the bottom of the screen) with one of the four key cards at the top. Correct responses were signified by a "high beep" and a "dull buzz" denoted errors. Participants' responses were typed into a keyboard and there were no time limits. "Correct" sorting strategies were changed without announcement or explanation after a participant had completed ten correct sorts under a specific principle (e.g., color). A maximum of six categories across 128 cards was possible.

Verbal fluency was tested by means of the *Controlled Oral Word Association Test* (Borkowski et al., 1967). The task required participants to generate as many different words beginning with a particular letter, "F", "A", then "S" within discrete 60-s periods for each respective letter. Proper names were not permitted.

Neuroimaging

Protocol magnetic resonance imaging (MRI) scans were obtained (T1-weighted volumetric mode, SPGR/40^0, TR = 26, TE = 7, Matrix 256 × 192, NEX = 2, 1.5-mm thickness with no skip; T2-weighted multiecho, FSE/V, TR = 2350, TE = 17/102, Matrix 256 × 192, NEX = 1, 5 mm skip 1 mm). Twenty-six of 29 stroke participants underwent research scans that were the basis of their lesion location analyses. The other three participants who could not have a research MRI (due to refusal, concern about intracerebral metallic clips, and equipment failure, respectively) had lesion location determined from previous clinical computed tomography (CT) scans (2) or MRI scan (1).

A neurologist, FFM, marked the lesions on hard-copy films. Guided by these lesion markings, an experienced neuroanatomist supervised by PTF and JLL "painted" each lesion using a three-dimensional (3-D) brain-morphometrics package (Display, Montreal Neurological Institute). Lesion volume was computed in absolute units (cm^3) before and after normalization for intersubject differences in brain size (Lancaster et al., 1995). Size normalization was performed using the spatial normalization (SN) software which has the user mark the front, back, left, right, top, and bottom of the brain following anterior commissure–posterior commissure (AC–PC) alignment. SN then sized the brain along each axis to the template size, thus correcting for brain size.

Neurological exam

A standard history and examination was administered by KM or JEM. Scores on a neurological severity index were rated (Max et al., 2002). Scale items consisted of ratings of head circumference, degree of hemiparesis, function of the "good" side, and history of seizures. Higher scores reflected greater severity.

Microcephaly (< 3rd percentile) was present in 5/25 (20%) cases where head circumference was measured. There was no hemiparesis in 12/29 (41%) cases, mild hemiparesis in 4/29 (14%) cases, typical hemiparesis in 11/29 (38%) cases, and worst hemiparesis in 2/29 (7%) cases. The side of the body ipsilateral to the brain lesion was normal in 27/29 (93%) cases, had slightly decreased coordination in 1/29 (3%) cases, and was poorly coordinated in 1/29 (3%) cases. The possibility of bilateral physical signs with unilateral lesions is a well-known phenomenon (Goodman & Yude, 1997). Eleven of 29 participants (38%) had a history of seizures, but only five were receiving anticonvulsant medication (carbamezepine monotherapy in 3; carbamezepine plus mysoline in 1; phenytoin in 1) at the time of assessment, and all were in good control.

Statistical analysis

Group differences were tested with independent sample *t* tests and χ^2 (or Fisher's Exact Test) analyses when the variables of interest were continuous or categorical, respectively.

For hypotheses 1 and 2, we compared the rates of *lifetime* ADHD and *lifetime* ADHD/Traits between stroke and orthopedic participants with Fisher's Exact Test. For hypothesis 3, we correlated current intellectual, academic, adaptive, and executive functioning, and motivation in participants *currently* affected with ADHD/Traits *versus* participants not currently affected with ADHD/Traits (resolved ADHD/Traits and never any ADHD/Traits). We rea-

soned that resolved ADHD/Traits status would be accompanied by improvements in function in these various domains.

Other analyses of general interest in the description and characterization of the sample but not a part of our three hypotheses were conducted. Analyses on family history of psychiatric disorder and family history of ADHD concerned participants with any *lifetime* history of ADHD/Traits *versus* those with *no lifetime* history of ADHD/Traits. We assumed that a family history of these conditions might predispose participants to persisting *and* more transient ADHD/Traits. Similarly, we compared stroke children with a *lifetime* history of ADHD/Traits *versus* those with *no lifetime* history of ADHD/Traits with respect to onset of stroke (early *vs.* late), lesion laterality, and lesion volume. This allowed us to document both persistent and more transient correlates of these lesion characteristics.

Certain independent variables that were found to be significantly correlated ($p < .05$) with *current* ADHD/Traits from each of the domains of interest (intellectual function, academic function, adaptive function, executive function, and motivation) were chosen for a principal components analysis with a varimax rotation. This was done to extract the largest amount of meaningful variation among the independent variables of which several were conceptually related. Factors with an eigenvalue >1 were identified and named according to their dominant characteristics.

RESULTS

Incidence of ADHD

Table 1 shows the distribution of ADHD in the groups. One stroke participant was diagnosed with prestroke ADHD and was dropped from further analyses regarding the development of postmedical disorder ADHD/Traits. There were no other participants who had premorbid symptoms reaching our defined level for traits of ADHD. This yielded 28 stroke participants eligible to develop ADHD/Traits. Twelve stroke participants were diagnosed with ongoing ADHD (six inattentive, four not otherwise specified, one hyperactive/impulsive, and one combined subtype); and three had ongoing ADHD traits. One additional stroke participant had a resolved ADHD, not otherwise specified diagnosis. Participants with the "not otherwise specified" subtype had predominantly inattentive symptoms. Notably, all but two participants with ADHD/Traits or resolved ADHD/Traits had at least one hyperactivity/impulsivity symptom at threshold or subthreshold intensity on the K-SADS-PL. Only four of the 16 participants with a lifetime history of ADHD/Traits developed this problem after age 7 because their strokes occurred after that age.

Nine of 16 stroke children with a lifetime history of ADHD/Traits had other DSM–IV psychiatric disorders present at the time of assessment: oppositional defiant disorder, 4; personality change disorder, 3; separation anxiety disorder, 2; agoraphobia without panic, 2; social phobia, 2; depressive disorder not otherwise specified, 2; simple phobia, 2; overanxious disorder, 1; chronic motor tic disorder, 1; chronic vocal tic disorder, 1; and stereotypic movement disorder, 1.

Three orthopedic controls had ADHD (two inattentive and one combined type). Two orthopedic participants had ADHD traits, and one had a completely resolved ADHD (not otherwise specified subtype). One other orthopedic participant had a partially resolved ADHD (not otherwise specified subtype) with only two inattentive symptoms current at the time of the assessment. The latter participant was assigned to the ADHD/Traits grouping. Table 2 shows demographic, lesion, and ADHD characteristics of each participant.

These data confirmed our first hypothesis: 13/28 (46%) of stroke participants had a *lifetime* history of the full ADHD syndrome compared with 5/29 (17%) of orthopedic controls (Fisher's Exact Test, $p < .03$). Our second hypothesis was likewise confirmed: 16/28 (57%) eligible stroke participants compared with 7/29 (24%) orthopedic participants had lifetime ADHD/Traits (ADHD, ADHD traits, partially remitted ADHD, or resolved ADHD) (Fisher's Exact Test, $p < .02$). The surprisingly high rate of ADHD/Traits among the orthopedic participants was accounted for exclusively by males with clubfoot (7/13; 54%).

Table 3 shows CBCL scores of participants with and without ADHD/Traits. The ADHD/Traits group was significantly more impaired regarding attention problems and showed a statistical trend regarding increased total behavior scores in analyses of the entire cohort and of stroke participants only. The ADHD/Traits children showed a statistical trend for increased aggressive behavior in analyses of the entire cohort and for delinquent behavior in analyses of stroke participants only.

Outcome in stroke and control participants

To provide context for the analyses concerning ADHD/Traits, Table 4 shows comparisons of intellectual, academic, adaptive, and executive function, as well as motivation between stroke and orthopedic participants. Children with stroke scored significantly worse than orthopedic controls in all domains except motivation.

Characteristics of children with ADHD/Traits

The child with partially resolved ADHD was considered in the ADHD/Traits group for all analyses. However, there were no meaningful changes in the analyses when this child was excluded from the ADHD/Traits group.

Entire cohort

Children with ADHD/Traits were significantly more impaired than children without ADHD/Traits regarding intellectual, academic, and adaptive functioning, WCST measures, motivation, and family psychiatric history (Tables 5–7). The ADHD/Traits group was not signifi-

Table 2. Demographic, lesion, and ADHD characteristics of participants

Participant ID	Age (years)	Sex	Age at onset	Etiology	Lesion laterality	Lesion location	ADHD status	CBCL attention
1	8	F	4 yrs	Idiopathic Occ.	R	Putamen	Inattentive	70
1c	9	F	7 yrs	Scoliosis			None	50
2	11	M	Pre	Idiopathic Occ.	R	P/P-Occip.	Inattentive	81
2c	11	M	Pre	Clubfoot			None	50
3	12	F	1 day	Idiopathic Hem.	L	Fr-T/Temp-P	Inattentive	62
3c	13	F	Pre	Clubfoot			None	50
4	15	M	10 yrs	Occ. Ulcerative Coliitis	L	Ant-lat Temporal	Inattentive	63
4c	15	M	12 yrs	Scoliosis			None	50
5	15	F	13 yrs	Hem. AVM	L	Fr-T/Temp-P	Inattentive	50
5c	15	F	12 yrs	Scoliosis			None	57
6	19	M	11 yrs	Hem. AVM	L	MCA	Inattentive	61
6c	18	M	10 yrs	Scoliosis			None	50
7	6	M	3 yrs	Idiopathic Occ.	R	Putamen	NOS	54
7c	6	M	Pre	Clubfoot			None	50
8	8	M	Pre	Idiopathic Occ.	L	MCA	NOS	50
8c	9	M	Pre	Clubfoot			Inattentive	65
9	9	M	8 yrs	Cardiac Postvaricella Zoster	R	Putamen	NOS	54
9c	10	M	7 yrs	Scoliosis			None	69
10	11	M	Pre	Idiopathic Occ.	R	MCA	NOS	50
10c	11	M	Pre	Clubfoot			Inattentive	67
11	5	F	1 day	Idiopathic Hem.	L	Ant-lat Temporal	H/I	68
11c	5	F	Pre	Clubfoot			None	50
12	14	F	Pre	Idiopathic Occ.	L	Putamen	Combined	67
12c	15	F	Pre	Clubfoot			None	50
13	13	F	Pre	Idiopathic Occ.	L	Putamen	NOS Resolved	57
13c	14	F	Pre	Clubfoot			None	66
14	6	M	Pre	Idiopathic Occ.	L	P/P-Occip.	Traits	50
14c	6	M	Pre	Clubfoot			Traits	57
15	16	M	9 mos	Cardiac Postcathederization	R	MCA	Traits	78
15c	17	M	Pre	Clubfoot			None	50
16	17	M	5 yrs	Occ. Varicella Zoster	R	Putamen	Traits	61
16c	17	M	13 yrs	Scoliosis			None	50
17	15	F	10 yrs	Idiopathic Occ.	R	Fr-T/Temp-P	Prestroke ADHD	75
17c	15	F	12 yrs	Scoliosis			None	50
18	7	M	Pre	Idiopathic Occ.	R	Fr-T/Temp-P	None	50
18c	7	M	Pre	Clubfoot			None	51
19	8	M	5 yrs	Hem. AVM	L	MCA	None	*
19c	7	M	Pre	Clubfoot			None	50
20	8	M	Pre	Idiopathic Occ.	R	Fr-T/Temp-P	None	50
20c	7	M	Pre	Clubfoot			Combined	70
21	10	M	1 day	Cardiac Postsurgery	R	P/P-Occip.	None	50
21c	11	M	Pre	Clubfoot			None	60
22	12	M	Pre	Idiopathic Occ.	R	MCA	None	51
22c	11	M	Pre	Clubfoot			Traits	50
23	12	F	9 yrs	Hem. AVM	R	Fr-T/Temp-P	None	51
23c	12	F	7–8 yrs	Scoliosis			None	50
24	13	F	Pre	Idiopathic Occ.	L	MCA	None	50
24c	13	F	Pre	Clubfoot			None	50
25	13	F	5 yrs	Hem. AVM	R	Fr-T/Temp-P	None	50
25c	13	F	11 yrs	Scoliosis			None	50
26	14	M	Pre	Idiopathic Occ.	L	Putamen	None	50
26c	14	M	Pre	Clubfoot			NOS resolved	50
27	14	M	2.5 mos	Cardiac Post Surgery	R	Fr-T/Temp-P	None	50
27c	14	M	Pre	Clubfoot			NOS part resol	51
28	16	M	10 yrs	Angioma	R	MCA	None	50
28c	16	M	14	Scoliosis			None	50
29	19	F	Pre	Idiopathic Occ.	L	MCA	None	64
29c	19	F	Pre	Clubfoot			None	50

Legend. Participants are listed according to ADHD status of stroke participants in the hierarchical order of Table 1 and then according to age at evaluation. Each stroke participant is followed by the individually matched orthopedic control designated with a "c" at the end of the subject ID. * No CBCL score is available for this participant. Ant-lat = anterior lateral; AVM = arterio-venous malformation; CBCL = Child behavior checklist; F = female; Fr-T/Temp-P = Fronto-temporal/temporo-parietal lesions sparing the deep gray structures; H/I = hyperactive/impulsive; Hem. = hemorrhage; L = left; M = male; MCA = large middle cerebral artery distribution infarcts including deep gray structures; mos = months; N/A = not applicable; NOS = not otherwise specified; Occ = occlusive; P/P-Occip. = Parietal/Parieto-Occipital; part resol = partial resolution; Pre = prenatal; R = right; yrs = years.

Table 3. Child behavior checklist scores and ADHD

Entire cohort (T-scores)	ADHD active/traits/ partial resolution [Mean (*SD*) *n* = 21]	No ADHD/resolved [Mean (*SD*) *n* = 35]	*dF*	*t*	*p*
Total	53.1 (11.5)	46.9 (11.4)	54	−2.00	.051
Externalizing behavior	51.1 (11.1)	46.2 (10.1)	54	−1.67	ns
Internalizing behavior	51.2 (10.2)	49.3 (10.9)	54	−.66	ns
Withdrawn	53.8 (6.8)	53.5 (5.2)	54	−.17	ns
Somatic complaints	57.8 (7.1)	54.5 (7.1)	54	−1.66	ns
Anxious/depressed	54.2 (5.7)	53.8 (5.7)	54	−.23	ns
Social problems	57.8 (9.9)	54.1 (7.3)	33.0	−1.49	ns
Thought problems	53.8 (6.0)	52.5 (4.7)	54	−.90	ns
Attention problems	60.9 (9.5)	52.2 (5.0)	26.7	−3.90	**.001**
Delinquent behavior	54.6 (6.8)	53.4 (6.1)	54	−.71	ns
Aggressive behavior	55.1 (6.6)	52.4 (5.5)	54	−1.70	.095
Stroke participants only (T-scores)	**ADHD active/traits/ partial resolution (*N* = 15)**	**No ADHD/resolved (*N* = 12)**	***dF***	***t***	***p***
Total	54.8 (12.7)	45.5 (13.0)	25	−1.87	.073
Externalizing behavior	52.3 (11.9)	45.3 (9.6)	25	−1.64	ns
Internalizing behavior	53.9 (10.8)	47.3 (10.8)	25	−1.57	ns
Withdrawn	55.3 (7.6)	52.8 (5.0)	25	−1.02	ns
Somatic complaints	58.3 (7.8)	54.8 (6.9)	25	−1.02	ns
Anxious/depressed	55.7 (6.1)	53.5 (6.5)	25	−.92	ns
Social problems	59.4 (11.1)	54.1 (5.6)	21.6	−1.62	ns
Thought problems	55.3 (6.6)	52.9 (4.6)	25	−1.08	ns
Attention problems	61.3 (10.2)	51.9 (4.3)	19.7	−3.23	**.004**
Delinquent behavior	56.2 (7.5)	51.7 (4.0)	22.1	−2.02	.055
Aggressive behavior	55.6 (7.4)	52.0 (3.7)	21.5	−1.65	ns

Note. ns = not significant.

cantly different regarding verbal fluency, global family function, family history of ADHD, family history of ADHD/ADHD symptoms, age, and gender (16/36 males *vs.* 5/21 females).

Stroke participants only

Analyses limited to stroke participants that compared stroke participants with ADHD/Traits to stroke participants without ADHD/Traits revealed the following (Tables 5–7): Children with ADHD/Traits were significantly more impaired regarding VIQ, arithmetic scores, and certain executive function measures (WCST total errors and nonperseverative errors). The groups were not significantly different regarding age, gender (10/18 males *vs.* 5/10 females), neurological severity summary score, seizure activity history (6/15 participants with ADHD/Traits had a seizure history compared with 4/13 participants without ADHD/Traits), FSIQ, PIQ, reading, spelling, adaptive function, family function, family history of ADHD, and family history of ADHD/ADHD symptoms. Neither were the groups significantly different in terms of perseverative aspects of executive function (responses and errors) on the WCST or verbal fluency.

Principal component analysis

Independent variables found to be significantly correlated ($p < .05$) with ADHD/Traits from each of the domains of interest (intellectual function, academic function, adaptive function, executive function, and motivation) were chosen for a principal components analysis for the following reasons: *VIQ* was selected because it provides a more accurate reflection of overall intellectual function in stroke participants than PIQ (and therefore FSIQ) due to motor impairments such as hemiplegia (Goodman & Yude, 1996). *Reading* standard score was selected from the significant academic function tests because of the well-known comorbidity of reading disability and ADHD (Shaywitz & Shaywitz, 1994; Willcutt & Pennington, 2000). The *Vineland adaptive behavior composite* was chosen because it captures overall adaptive function. Both *perseverative errors* (standard score) and *nonperseverative errors* (standard score) were selected from the WCST because these measures reflect distinct domains of information processing. Finally, the *total score on the Children's Motivation Scale* was chosen.

These six variables were then entered into a principal components analysis with a varimax rotation. The two-factor final solution is shown in Table 8. We termed the first

Table 4. Intellectual, academic, adaptive, and executive function, and motivation in stroke and control participants

	Stroke ($n = 29$) Mean (*SD*)	Orthopedic ($n = 29$) Mean (*SD*)	*dF*	*t*	*p*
IQ variables[a]					
PIQ	84.5 (20.4)	100.4 (15.2)	56	−3.38	**.001**
VIQ	90.9 (16.5)	105.8 (13.9)	56	−3.74	**.0005**
FSIQ	86.6 (18.0)	103.5 (13.1)	56	−4.08	**.0005**
Academic function[b]					
Reading	80.8 (17.7)	101.0 (14.0)	56	−4.82	**.0005**
Spelling	84.5 (17.3)	101.5 (16.2)	56	−3.86	**.0005**
Arithmetic	81.6 (19.0)	98.4 (19.3)	56	−3.33	**.002**
Adaptive function[c]					
Communication	80.5 (15.8)	97.1 (13.6)	56	−4.30	**.0005**
Daily living skills	80.1 (15.3)	99.5 (18.5)	56	−4.35	**.0005**
Socialization	84.5 (16.3)	94.7 (13.7)	56	−2.58	**.013**
Adaptive behavior composite	77.3 (14.7)	96.3 (17.9)	56	−4.41	**.0005**
Executive function (*Wisconsin Card Sorting Test*)					
Total # errors (SS)	94.8 (18.9) $n = 28$	108.4 (14.8) $n = 27$	53	2.97	**.004**
Perseverative responses (SS)	96.3 (20.4) $n = 28$	110.9 (16.5) $n = 27$	53	2.90	**.005**
Perseverative errors (SS)	96.0 (20.4) $n = 28$	110.6 (16.4) $n = 27$	53	2.90	**.005**
Nonperseverative errors (SS)	97.1 (18.2) $n = 28$	105.7 (13.3) $n = 27$	53	2.00	**.05**
Conceptual level responses (SS)	94.0 (18.2) $n = 28$	108.7 (15.5) $n = 27$	53	3.22	**.002**
COWA (percentile)	24.9 (28.4)	39.0 (34.9)	56	1.70	.095
Motivation[d]	42.5 (9.9) $n = 23$	46.9 (8.9) $n = 23$	44	−1.58	ns

Legend. Means (*SD*) of standard scores (SS).
[a]Wechsler Intelligence Scales for Children–Third Edition.
[b]Wide Range Achievement Test–Revised.
[c]Vineland Adaptive Behavior Scales.
[d]Children's Motivation Scale.
COWA = Controlled Oral Word Association; PIQ = Performance IQ; VIQ = Verbal IQ; FSIQ = Full Scale IQ; ns = not significant.

factor the "impaired neurocognition" because it was correlated highly with general intellectual function, specific reading ability, overall adaptive function, and perseveration which is typically considered to reflect a measure of neurological integrity. We termed the second factor the "inattention–apathy" because it was correlated highly with nonperseverative errors (which reflects inattention) and low motivation/apathy. The derived "impaired neurocognition" and the "inattention–apathy" factors, respectively, captured 56.5% and 18.3% (total 74.7% with rounding) of the variance within the set of independent variables entered. The results were similar when the analyses were repeated utilizing only the stroke participants: the derived "impaired neurocognition" and the "inattention–apathy" factors, respectively, captured 51.6% and 25.5% (total 77.2% with rounding) of the variance within the set of independent variables entered.

Logistic regression analyses were conducted for the presence of ADHD/Traits using both the "impaired neurocognition" and the "inattention–apathy" factors. The first regression which included stroke and orthopedic participants was significant (−2 log likelihood $\chi^2 = 37.79$, $df = 2$, $p < .00005$), and correctly predicted 77.8% of the ADHD/Traits cases. Furthermore, each factor independent of the other significantly contributed to the presence of ADHD/Traits: "inattention–apathy" factor (Wald $\chi^2 = 10.23$, $df = 1$, $p < .002$) and "impaired neurocognition" factor (Wald $\chi^2 = 4.12$, $df = 1$, $p < .05$). The second regression based on only stroke participants was also significant (−2 log likelihood $\chi^2 = 19.52$, $df = 2$, $p < .003$), and correctly predicted 82.6% of the ADHD/Traits cases. However, only the "inattention–apathy" factor (Wald $\chi^2 = 5.71$, $df = 1$, $p < .02$) significantly contributed to the presence of ADHD/Traits when simultaneously entered in the regression with the "impaired neurocognition" factor (Wald $\chi^2 = .76$, $df = 1$, $p > .38$).

Lesion correlates of lifetime ADHD/Traits

Lifetime ADHD/Traits was not significantly related to whether the lesion onset was *early* or *late* (9/17 children with early lesions *vs.* 7/11 children with late lesions had this behavior disturbance). Lifetime ADHD/Traits was not significantly related to lesion laterality (7/15 children with right-sided lesions *vs.* 9/13 children with left-sided lesions had this behavior disturbance). Finally, lesion volume, which was highly skewed, was not significantly related to lifetime ADHD/Traits (Mann–Whitney *U* Test = 70.0): the mean rank of lesion volume for the participants with and without lifetime ADHD/Traits was 12.7 ($n = 15$) and 13.5 ($n = 10$), respectively.

Table 5. Characteristics of ADHD

Entire cohort	ADHD active/traits/ partial resolution [Mean (*SD*) *n* = 21]	No ADHD/ resolved [Mean (*SD*) *n* = 36]	*dF*	*t*	*p*
Age	11.0 (4.1)	12.5 (3.7)	55	1.50	ns
Socioeconomic status	2.67 (1.02)	2.28 (.94)	55	−1.46	ns
Family function	4.74 (.81) *n* = 19	5.11 (1.11) *n* = 35	52	1.31	ns
IQ variables[a]					
PIQ	83.1 (18.3)	98.6 (18.0)	55	3.10	**.003**
VIQ	88.2 (16.2)	104.6 (14.5)	55	3.95	**.0005**
FSIQ	84.5 (16.6)	101.8 (15.2)	55	4.00	**.0005**
Academic function[b]					
Reading	81.4 (19.3)	96.2 (16.7)	55	3.05	**.004**
Spelling	83.2 (16.9)	98.3 (17.7)	55	3.15	**.003**
Arithmetic	80.1 (22.1)	95.9 (18.2)	55	2.93	**.005**
Adaptive function[c]					
Communication	78.0 (15.0)	95.0 (14.9)	55	4.13	**.0005**
Daily living skills	80.7 (16.5)	95.6 (19.3)	55	2.96	**.004**
Socialization	82.2 (16.4)	94.5 (13.6)	55	3.04	**.004**
Adaptive behavior composite	75.7 (14.8)	93.6 (18.1)	55	3.84	**.0005**
Motivation[d]	39.4 (10.4) *n* = 18	48.1 (7.4) *n* = 28	44	3.35	**.002**
Stroke subjects only	**ADHD active/traits/ partial resolution (*N* = 15)**	**No ADHD/resolved (*N* = 13)**			
Age	11.5 (4.4)	12.2 (3.4)	26	.51	ns
Socioeconomic status	2.73 (1.10)	2.00 (.82)	26	−1.98	ns
Family function	4.69 (.75) *n* = 13	5.08 (1.19)	24	.99	ns
IQ variables[a]					
PIQ	80.4 (19.0)	90.5 (21.5)	26	1.31	ns
VIQ	84.8 (17.0)	98.2 (13.8)	26	2.26	**.033**
FSIQ	81.2 (17.3)	93.8 (17.5)	26	1.91	ns
Academic function[b]					
Reading	77.1 (19.3)	83.9 (15.7)	26	1.01	ns
Spelling	80.4 (16.7)	87.7 (17.5)	26	1.13	ns
Arithmetic	74.6 (21.2)	89.2 (13.7)	24.2	2.20	**.038**
Adaptive function[c]					
Communication	75.4 (16.0)	85.4 (14.6)	26	1.72	ns
Daily living skills	79.5 (18.6)	81.2 (11.8)	26	.30	ns
Socialization	80.5 (18.3)	90.2 (12.7)	26	1.61	ns
Adaptive behavior composite	73.9 (16.1)	81.5 (13.0)	26	1.36	ns
Motivation[d]	37.1 (9.2) *n* = 12	48.5 (7.1) *n* = 11	21	3.31	**.003**
Neurological severity	2.13 (2.03)	1.92 (1.38)	26	−.32	ns

Legend. Means (*SD*) of standard scores.
[a]Wechsler Intelligence Scales for Children–Third Edition.
[b]Wide Range Achievement Test–Revised.
[c]Vineland Adaptive Behavior Scales.
[d]Children's Motivation Scale.
PIQ = Performance IQ; VIQ = Verbal IQ; FSIQ = Full Scale IQ; ns = not significant.

DISCUSSION

The main finding from this study was that ADHD development after stroke in children occurred at a rate (46%; 13/28) which was significantly higher than ADHD occurring after an orthopedic diagnosis in controls (17%; 5/29). We found also that when children with ADHD, ADHD traits, ADHD in partial resolution, and resolved ADHD were combined (lifetime ADHD/Traits), the rate in the stroke group (57%; 16/28) was significantly higher than the rate in the orthopedic control group (24%; 7/29). These increased rates could not be explained by differences in age, gender, SES, race, family function, family history of ADHD, or the presence of a chronic medical condition requiring medical attention.

Table 6. Tests of executive function and ADHD

Entire cohort	ADHD active/traits/ partial resolution ($n = 19$)	No ADHD/ resolved ADHD ($n = 35$)	*dF*	*t*	*p*
Wisconsin Card Sorting Test					
Total # errors (SS)	87.7 (16.7)	108.5 (14.7)	52	4.75	**.0005**
Perseverative responses (SS)	91.4 (20.7)	109.7 (16.5)	52	3.57	**.001**
Perseverative errors (SS)	90.8 (20.5)	109.6 (16.4)	52	3.68	**.001**
Nonperseverative errors (SS)	89.3 (14.3)	107.5 (13.9)	52	4.55	**.0005**
Conceptual level responses (SS)	88.6 (17.1)	107.8 (15.6)	52	4.20	**.0005**
Controlled Oral Word Association Test (percentile)	26.4 (31.8) $n = 21$	35.7 (32.9) $n = 36$	55	1.04	ns
Stroke only	**ADHD active/traits/ partial resolution ($n = 14$)**	**No ADHD/ resolved ADHD ($n = 13$)**	***dF***	***t***	***p***
Total # errors (SS)	86.4 (16.2)	102.1 (18.4)	25	2.35	**.027**
Perseverative responses (SS)	91.1 (20.9)	100.6 (19.6)	25	1.22	ns
Perseverative errors (SS)	90.4 (20.7)	100.9 (19.7)	25	1.35	ns
Nonperseverative errors (SS)	87.4 (14.6)	106.1 (17.0)	25	3.06	**.005**
Conceptual level responses (SS)	87.3 (16.1)	99.9 (18.6)	25	1.90	ns
Controlled Oral Word Association Test (percentile)	25.0 (27.6) $n = 15$	25.7 (31.3)	26	.07	ns

Note. SS = standard score. ns = not significant.

The differences were therefore probably related to the brain lesion or its complications.

The differences in incidence of lifetime ADHD/Traits between the two groups may have actually been greater were it not for an unexpectedly high rate of lifetime ADHD/Traits in males with clubfoot (7/13; 57%) which accounted entirely for the occurrence of lifetime ADHD/Traits in orthopedic controls. A specific association between ADHD and clubfoot has not been noted before; however, there is some evidence that minor physical anomalies are overrepresented in children with attention deficit disorder and their first-degree relatives (Deutsch et al., 1990). If the association between ADHD and males with clubfoot is replicated in a larger orthopedic clinic sample of children consecutively diagnosed with clubfoot, this may have implications in the search for genetic markers for both conditions.

Differences on neurocognitive measures between children (stroke plus orthopedic controls) with *current* ADHD/Traits and those with no *current* ADHD/Traits reflected the dominant influence of the stroke condition on function. This was true for intellectual, academic, adaptive, and executive function. However, this was not the case for motivation which was not significantly different between stroke and orthopedic groups but was significantly lower in children (stroke plus orthopedic controls) with ADHD. Therefore, this is a clue that the neural substrate of low motivation or apathy may play a central role in the pathophysiology of ADHD/Traits.

Table 7. ADHD and family psychiatric history

Entire cohort	ADHD active/traits/ partial resolution/resolved ($n = 20$)	No ADHD ($n = 34$)	*dF*	*t*	*p*
Family psychiatric history score	1.70 (1.08)	1.09 (1.03)	52	−2.08	.043
Family history of ADHD	7/20	5/34	1		ns
Family history of ADHD or ADHD symptoms	8/20	10/34	1		ns
Stroke cohort	**ADHD active/traits/ partial resolution/resolved ($n = 13$)**	**No ADHD ($n = 12$)**	***dF***	***t***	***p***
Family psychiatric history score	1.77 (1.01)	1.00 (1.21)	23	−1.73	ns
Family history of ADHD	4/13	1/12	1		ns
Family history of ADHD or ADHD symptoms	4/13	4/12	1		ns

Note. ns = not significant.

Table 8. Rotated factor matrix of independent variables of interest

	All participants		Stroke participants only	
	Impaired neurocognition factor	Inattention–apathy factor	Impaired neurocognition factor	Inattention–apathy factor
Verbal IQ (SS)[a]	.84	.27	.88	.16
Reading (SS)[b]	.94	−.05	.92	−.21
Adaptive behavior composite (SS)[c]	.76	.37	.74	.45
Perseverative errors (SS)[d]	.68	.42	.79	.18
Nonperseverative errors (SS)[d]	.24	.82	.22	.83
Motivation total[e]	.13	.85	.02	.90

Note. SS = standard score.
[a]Wechsler Intelligence Scales for Children–Third Edition.
[b]Wide Range Achievement Test–Revised.
[c]Vineland Adaptive Behavior Scales.
[d]Wisconsin Card Sort Test.
[e]Children's Motivation Scale.

The differences in neurocognitive measures between stroke participants with or without *current* ADHD/Traits were more limited but informative. These differences included significantly lower VIQ, lower arithmetic scores, more nonperseverative errors on the WCST, and lower motivation. Particularly striking was the fact that VIQ of stroke children with no *current* ADHD/Traits was in the average range compared with below average scores for *current* ADHD/Traits children. As noted before, VIQ is considered a more accurate measure of overall intelligence than PIQ or FSIQ in the stroke population (Goodman & Yude, 1996).

In contrast to VIQ, academic scores were depressed in the non-ADHD/Traits stroke participants and the ADHD/Traits stroke participants. Only scores for arithmetic were significantly different between the ADHD/Traits and non-ADHD/Traits groups. The specificity of this finding is unclear because reading and spelling scores were also lower but not significantly so. It is possible that in stroke participants, children with ADHD/Traits have a pattern of injury and/or a pattern of neuronal repair that disproportionately affects working memory, visual memory, and visual-spatial skills, whose recruitment is central to the completion of arithmetic tasks.

The increase in nonperseverative errors but not perseverative errors on the WCST in stroke participants with *current* ADHD/Traits compared with stroke participants with no *current* ADHD/Traits suggested that this group had difficulty with the marshalling of nonspecific attention to task. In fact, stroke participants with no *current* ADHD/Traits had scores in the average range on this and other measures recorded from the WCST. This is consistent with the predominant difference found in a study of idiopathic ADHD in which children with ADHD, combined type differed from controls only in nonperseverative errors on the WCST (Klorman et al., 1999). Furthermore, with respect to verbal fluency, the other executive function test assessed, the absence of significant differences between stroke *versus* control participants and between those with and without ADHD/Traits suggests that additional measures would have to be employed to document possible specific executive function deficits in children with poststroke ADHD/Traits.

The factor analysis of independent variables which were significantly associated with ADHD/Traits yielded "impaired neurocognition" and "inattention–apathy" factors. This supported earlier research that idiopathic ADHD is associated with *cognitive* differences including small but significant IQ decreases, and academic function and adaptive function deficits. The *"neuro"* component of the "impaired neurocognition" factor reflects the finding of increased perseverative errors typically associated with brain damage. Logistic regression demonstrated that the "inattention–apathy" factor was a more consistent predictor than the "impaired neurocognition" factor in accounting for *current* ADHD/Traits. This suggests that inattention and apathy are core impairments with respect to ADHD/Traits and that the syndrome is not merely a reflection of more general cognitive impairment.

Clinically, it is important to differentiate (1) inattention related to ADHD or depressive disorder, and (2) apathy limited to "personality change due to stroke, apathetic subtype" (American Psychiatric Association, 1994; Max et al., 1998b) or apathy which may be part of a depressive disorder. Inattention and apathy loaded on the same factor and they also tend to respond to similar treatment, for example, stimulants (Marin et al., 1995). This suggests that they may have related neural mechanisms. Not surprisingly, the CBCL profile exhibited by the children with ADHD/Traits showed significant increases on the attention problems scale which includes hyperactivity/impulsivity symptoms. These children tended to have increased total problems as well as aggressive and delinquent behaviors. At the level of the individual, we found that just over half the children with ADHD/Traits had comorbid externalizing and/or internalizing psychiatric disorders. The psychiatric interview and

CBCL findings support the position that we have not simply identified a group of children with compromised attentional resources related to brain damage and measurable by neuropsychological tests, but rather DSM–IV ADHD with comorbid psychiatric problems probably related to brain damage.

Striking by the absence of an apparent association was the relationship between ADHD and family history of ADHD. This is a departure from the pattern seen in idiopathic ADHD. There was however a significant association of intensity of family psychiatric history and ADHD, which suggests the existence of a relatively less specific and less direct relationship between family psychopathology and ADHD. Most cases of ADHD were children with stroke. It is likely that in the apparent absence of a relationship with familial ADHD, lesion location (Max et al., 2002) and possibly dysfunctional neuronal circuits or connections resulting from imperfect reparative processes (Goodman, 1989) may be implicated in the manifestation of poststroke ADHD.

We must acknowledge a number of limitations in this study. First, the sample is small and findings on larger samples of carefully screened children with stroke and their appropriate controls are needed. Nevertheless, this represents one of the largest reports of childhood stroke. Second, about one-third of the orthopedic control children were recruited from a different site than the children with stroke. Unknown biases may be operative as a result of this. However, all controls were carefully selected to match the participants in age, gender, SES, and the presence of a chronic medical condition. Furthermore, the stroke and control groups did not differ on family function or family psychiatric history. Third, the psychiatric interviewer was not blinded to the group affiliation of the participants. However, excellent interrater reliability was recorded with another child psychiatrist who watched randomly selected videotaped psychiatric interviews and who was blind to group affiliation of the participants. In addition, a parent-completed behavioral questionnaire found significant differences in attention problems in the group diagnosed with ADHD/Traits by clinical interview. Fourth, premorbid ADHD status was carefully assessed in the clinical interview. Yet there remains the possibility that some proportion of participants with congenital conditions or even conditions with onset in the first few years of life may have developed ADHD/Traits regardless of their medical condition. This problem was mitigated by using a control group and also by the finding of a lack of association between family history of ADHD and children with ADHD/Traits. Fifth, the stroke sample is not an epidemiological sample but rather represents the results of a case-finding strategy of children diagnosed with stroke at a university teaching hospital. The stroke children were *not* referred for their psychiatric disorders including ADHD/Traits but rather for neurological diagnosis, treatment for cardiac problems, or orthopedic procedures for residual neurologically based musculoskeletal problems. The controls were subject to similar referral biases. Sixth, the psychiatrist did not have the benefit of a teacher's report in reaching diagnostic decisions.

FUTURE DIRECTIONS

ADHD after childhood stroke should be further clarified. This will require a larger sample of stroke participants and controls. It will be important to confirm the preponderance of ADHD, inattentive and the "not otherwise specified" subtypes and its association with apathy. Other neurocognitive correlates should be investigated including dimensions of executive function such as inhibitory control. Direct measures of attention would clarify the attentional problem more specifically (Posner & Peterson, 1990). A larger study should investigate structural lesion–ADHD correlates and functional imaging studies in ADHD participants may reveal characteristic patterns of abnormal activation on neurocognitive tasks including tests of attention. A comparison group of children with idiopathic ADHD would help clarify what might be specific in terms of the neurocognitive profile of poststroke ADHD. Finally, a treatment study would provide critically important clinical data about whether children with poststroke ADHD benefit in a similar manner to children with idiopathic ADHD.

ACKNOWLEDGMENTS

We thank Chris Cook for image processing, Stephan Arndt for statistical consultation, and Damien Ihrig and Jennifer Smith for data collection and/or management. This study was supported by NARSAD (Dr. Max); T32 MH18399 (Dr. Robertson); and UTHSCSA portion of 5 PO2 MH52176-07 (NIMH, NIDA, NCI) (Dr. Fox).

REFERENCES

Achenbach, T.M. (1991). *Manual for the Child Behavior Checklist/4-18 and 1991 Profile*. Burlington, Vermont: University of Vermont Department of Psychiatry.

American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). Washington, DC: American Psychiatric Association Press.

Andreasen, N.C., Endicott, J., Spitzer, R.L., & Winokur, G. (1977). The family history method using research diagnostic criteria: Reliability and validity. *Archives of General Psychiatry*, *34*, 1229–1235.

Barkley, R.A. (1997). *ADHD and the nature of self-control*. New York: The Guilford Press.

Bloom, D.R., Levin, H.S., Ewing-Cobbs, L., Saunders, A.E., Song, J., Fletcher, J.M., & Kowatch, R.A. (2001). Lifetime and novel psychiatric disorders after pediatric traumatic brain injury. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*, 572–579.

Borkowski, J.G., Benton, A.L., & Spreen, O. (1967). Word fluency and brain damage. *Neuropsychologia*, *5*, 135–140.

Botting, N., Powls, A., & Cooke, R.W.I. (1997). Attention deficit hyperactivity disorders and other psychiatric outcomes in very low birthweight children at 12 years. *Journal of Child Psychology and Psychiatry*, *8*, 931–941.

Breslau, N. & Chilcoat, H.D. (2000). Psychiatric sequelae of low birth weight at 11 years of age. *Biological Psychiatry*, *47*, 1005–1011.

Costello, E.J., Angold, A., Burns, B.J., Erkanli, A., Stangl, D.K., & Tweed, D.L. (1996). The Great Smoky Mountains Study of Youth: Functional impairment and serious emotional disturbance. *Archives of General Psychiatry*, *53*, 1137–1143.

Deutsch, C.K., Matthysse, S., Swanson, J.M., & Farkas, L.G. (1990). Genetic latent structure analysis of dysmorphology in attention deficit disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *29*, 189–194.

Ebaugh, F.G. (1923). Neuropsychiatric sequelae of acute epidemic encephalitis in children. *American Journal of Diseases of Children*, *25*, 89–97.

Gerring, J.P., Freund, L., Gerson, A.C., Joshi, P.T., Capozzoli, J., Frosch, E., Brady, K., Marin, R.S., & Denckla, M.B. (1996). Psychometric characteristics of the Children's Motivation Scale. *Psychiatry Research*, *63*, 205–217.

Gerring, J.P., Brady, K.D., Chen, A., Vasa, R., Grados, M., Bandeen-Roche, K.J., Bryan, R.N., & Denckla, M.B. (1998). Premorbid prevalence of ADHD and development of secondary ADHD after closed head injury. *Journal of the American Academy of Child and Adolescent Psychiatry*, *37*, 647–654.

Goodman, R. & Graham, P. (1996). Psychiatric problems in children with hemiplegia: Cross sectional epidemiological survey. *British Medical Journal*, *312*, 1065–1069.

Goodman, R. & Yude, C. (1996). IQ and its predictors in childhood hemiplegia. *Developmental Medicine and Child Neurology*, *38*, 881–890.

Goodman, R. & Yude, C. (1997). Do unilateral lesions of the developing brain have side-specific psychiatric consequences in childhood? *Laterality*, *2*, 103–115.

Goodman, R.N. (1989). Neuronal misconnections and psychiatric disorder: Is there a link? *British Journal of Psychiatry*, *154*, 292–299.

Grant, D.A. & Berg, E.A. (1948). A behavioral analysis of degree of reinforcement and ease of shifting to new responses in a Weigl-type card sorting problem. *Journal of General Psychology*, *38*, 404–411.

Hollingshead, A.B. (1975). *Four factor index of social status*. New Haven, Connecticut: Yale University.

Ingram, T.T.S. (1956). A characteristic form of overactive behaviour in brain damaged children. *Journal of Mental Science*, *102*, 550–558.

Jastak, S. & Wilkerson, G.S. (1984). *Wide Range Achievement Test: Administration manual*. Wilmington, Delaware: Jastak Associates.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Williamson, D., & Ryan, N. (1997). Schedule for affective disorders and schizophrenia for school-age children—present and lifetime version (K-SADS-PL): Initial reliability and validity data. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 980–988.

Klorman, R., Hazel-Fernandez, L.A., Shaywitz, S.E., Fletcher, J.M., Marchione, K.E., Holahan, J.M., Stuebing, K.K., & Shaywitz, B.A. (1999). Executive functioning deficits in attention-deficit/hyperactivity disorder are independent of oppositional defiant or reading disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, *38*, 1148–1155.

Lancaster, J.L., Glass, T.G., Lankipalli, B.R., Downs, H., Mayberg, H., & Fox, P.T. (1995). A modality-independent approach to spatial normalization. *Human Brain Mapping*, *3*, 209–223.

Levy, F., Hay, D.A., McStephen, M., Wood, C., & Waldman, I. (1997). Attention-deficit hyperactivity disorder: A category or a continuum? Genetic analysis of a large-scale twin study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*, 737–744.

Lou, H.C. (1996). Etiology and pathogenesis of attention-deficit hyperactivity disorder (ADHD): Significance of prematurity and perinatal hypoxic-haemodynamic encephalopathy. *Acta Paediatrica*, *85*, 1266–1271.

Marin, R.S., Fogel, B.S., Hawkins, J., Duffy, J., & Krupp, B. (1995). Apathy: A treatable syndrome. *Journal of Neuropsychiatry and Clinical Neuroscience*, *7*, 23–30.

Max, J.E., Arndt, S., Castillo, C.S., Bokura, H., Robin, D.A., Lindgren, S.A., Smith, W.L., Jr., Sato, Y., & Mattheis, P.J. (1998a). Attention-deficit hyperactivity symptomatology after traumatic brain injury: A prospective study. *Journal of the American Academy of Child and Adolescent Psychiatry*, *37*, 841–847.

Max, J.E., Castillo, C.S., Lindgren, S.D., & Arndt, S. (1998b). The neuropsychiatric rating schedule: Reliability and validity. *Journal of the American Academy of Child and Adolescent Psychiatry*, *37*, 297–304.

Max, J.E., Fox, P.T., Lancaster, J.L., Kochunov, P., Mathews, K., Manes, F.F., Robertson, B.A.M., Arndt, S., Robin, D.A., & Lansing, A.E. (2002). Putamen lesions and the development of attention-deficit/hyperactivity symptomatology. *Journal of the American Academy of Child and Adolescent Psychiatry*, *41*, 563–571.

Max, J.E., Mathews, K., Lansing, A., Robertson, B.A.M., Fox, P., Lancaster, J., Manes, F.F., & Smith, J. (2002). Psychiatric disorders after childhood stroke. *Journal of American Academy of Child and Adolescent Psychiatry*, *41*, 555–562.

Max, J.E., Lansing, A.E., Koele, S.L., Castillo, C.S., Bokura, H., Schachar, R., Collings, N., & Williams, K.E. Attention deficit hyperactivity disorder in children and adolescents following traumatic brain injury. *Developmental Neuropsychology* (in press).

Miller, I.W., Kabacoff, R.I., Epstein, N.B., & Bishop, D.S. (1994). The development of a clinical rating scale for the McMaster model of family functioning. *Family Process*, *33*, 53–69.

Nussbaum, N.L., Grant, M.L., Roman, M.J., Poole, J.H., & Bigler, E.D. (1990). Attention deficit disorder and the mediating effect of age on academic and behavioral variables. *Journal of Developmental and Behavioral Pediatrics*, *11*, 22–26.

Ounsted, C. (1955). The hyperkinetic syndrome in epileptic children. *Lancet*, *2*, 303–311.

Pennington, B.F. & Ozonoff, S. (1996). Executive function and developmental psychopathology. *Journal of Child Psychology and Psychiatry*, *37*, 51–87.

Posner, M.I. & Petersen, S.E. (1990). The attention system of the human brain. *Annual Reviews of Neuroscience*, *13*, 25–42.

Riva, D. & Cazzaniga, L. (1986). Late effects of unilateral brain lesions sustained before and after age one. *Neuropsychologia*, *24*, 423–428.

Roach, E.S. & Riela, A.R. (1995). Inflammatory vascular disorders. In E.S. Roach and A.R. Riela (Eds.), *Pediatric Cerebrovascular Disorders* (2nd ed., pp. 121–139). Armonk, New York: Futura Publishing Company, Inc.

Rutter, M., Graham, P., & Yule, W. (1970). A neuropsychiatric study in childhood. *Clinics in Developmental Medicine*, Nos. 35/36. London, UK: Heinemann/Spastics International Medical Publications.

Seidel, U.P., Chadwick, O.F., & Rutter, M. (1975). Psychological

disorders in crippled children. A comparative study of children with and without brain damage. *Developmental Medicine and Child Neurology*, *17*, 563–573.

Shaywitz, B.A. & Shaywitz, S.E. (1994). Learning disabilities and attention disorders. In K. Swaiman (Ed.), *Principles of pediatric neurology* (pp. 1119–1151). St. Louis, Missouri: Mosby.

Shelton, T.L., Barkley, R.A., Crosswait, C., Moorehouse, M., Fletcher, K., Barrett, S., Jenkins, L., & Metevia, L. (1998). Psychiatric and psychological morbidity as a function of adaptive disability in preschool children with aggressive and hyperactive-impulsive-inattentive behavior. *Journal of Abnormal Child Psychology*, *26*, 475–494.

Sparrow, S.S., Balla, D., & Cicchetti, D. (1984). *The Vineland Adaptive Behavior Scales*. Circle Pines, Minnesota: American Guidance Services.

Wechsler, D. (1991). *Wechsler Intelligence Scale for Children–Third Edition*. New York: Psychological Corporation.

Whitaker, A.H., Van Rossem, R., Feldman, J.F., Schonfeld, I.S., Pinto-Martin, J.A., Torre, C., Shaffer, D., & Paneth, N. (1997). Psychiatric outcomes in low-birth-weight children at age 6 years: Relation to neonatal cranial ultrasound abnormalities. *Archives of General Psychiatry*, *54*, 847–856.

Willcutt, E.G. & Pennington, B.F. (2000). Comorbidity of reading disability and attention-deficit/hyperactivity disorder: Differences by gender and subtype. *Journal of Learning Disabilities*, *33*, 179–191.

Wood, F.B. & Felton, R.H. (1994). Separate linguistic and attentional factors in the development of reading. *Topics in Language Disorders*, *14*, 42–57.

Woods, B.T. (1980). The restricted effects of right-hemisphere lesions after age one: Wechsler test data. *Neuropsychologia*, *18*, 65–70.