Prefrontal and Executive Attention Network Lesions and the Development of Attention-Deficit/Hyperactivity Symptomatology

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ABSTRACT

Objective: To investigate the association between focal stroke lesions of Posner's executive attention network and a specific region of interest in the frontal lobes (orbital frontal and mesial frontal) and either attention-deficit/hyperactivity disorder (ADHD) or traits of the disorder (ADHD symptomatology). **Method:** Twenty-nine children with focal stroke lesions were studied with standardized psychiatric assessments and anatomical brain magnetic resonance imaging. The pattern of lesion overlap in subjects with ADHD symptomatology was determined. **Results:** Fifteen of 28 subjects with no prestroke ADHD were diagnosed with ADHD symptomatology at the time of assessment. The extent of lesions within the executive attention network was marginally related to ADHD symptomatology ($p = .088$; effect size = 0.66), whereas the extent of lesions in the specific frontal region of interest was significantly related to ADHD symptomatology ($p = .040$; effect size = 0.82). **Conclusions:** Lesions within Posner's executive attention network and its orbital frontal connections may be linked to important mechanisms in the expression of ADHD symptomatology after childhood stroke. These findings are consistent with functional and structural imaging findings in studies of idiopathic ADHD. *J. Am. Acad. Child Adolesc. Psychiatry,* 2005;44(5):443–450. **Key Words:** attention-deficit/hyperactivity disorder, childhood stroke, executive attention, frontal lobe.

The literature on child outcomes after both focal and diffuse brain insult suggests that these children have high rates of attention-deficit/hyperactivity disorder (ADHD) (e.g., traumatic brain injury [Max et al., 1998] and stroke [Max et al., 2002]). Neither the specific phenomenologies nor the mechanisms of ADHD secondary to these distinct types of brain injury have been studied comprehensively. This report sought to elucidate stroke lesion/ADHD correlates. In the absence of data, we believe that it is a reasonable approach to look toward findings related to idiopathic ADHD and attention network theory to guide initial research efforts to understand the neurological mechanisms underlying the expression of ADHD after childhood stroke.

Structural and functional magnetic resonance imaging (MRI) and positron emission tomography studies of idiopathic ADHD have implicated dysfunction of prefrontal corticostriatopallidal pathways as well as cerebellar hemispheres and a subregion of cerebellar vermis, which have extensive connections with the frontal lobes (see Castellanos and Tannock, 2002, for a review). The prefrontal corticostriatopallidal pathways roughly correspond with Posner's executive attention network, which is constituted by frontal mesial structures bilaterally including anterior and posterior cingulate, supplementary motor area, prefrontal region, rolandic region, and bilateral basal ganglia (Rothbart and Posner, 2001). There have been a number of studies that have implicated

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mesial frontal and/or orbital frontal areas in the pathophysiology of ADHD (Casey, 2001; Casey et al., 1997; Hesslinger et al., 2002; Rohde et al., 2003; Rubia et al., 1999). These areas are components of or closely connected with Posner's executive network, respectively. Neuropsychological and electrophysiological methods have also advanced knowledge of neural attention networks relevant to idiopathic ADHD. Tests that tap domains such as vigilance, sustained attention, and executive function have been useful in distinguishing children with ADHD from controls (Casey, 2001; Chhabidas et al., 2001; Swanson et al., 1998). Electrophysiological studies using evoked response potentials report that children with ADHD have impairments both during early perceptual processing and at later stages of processing (e.g., long latency P3 component) (van der Stelt et al., 2001). The later stage impairments correspond with deficits in executive, cognitive, and semantic selective processing, whereas the earlier stage impairments correspond with weaknesses in sensory and perceptual processes. However, a prevailing theory of mechanisms underlying idiopathic ADHD is that the disorder reflects principally a dysregulation of executive functions (Barkley, 1997). Swanson et al. (1998) have proposed a theory identifying which specific inattentive, hyperactive, and impulsive symptoms may be most closely related to Posner's anatomical attention networks (Rothbart and Posner, 2001) concerned primarily with executive functions or with sensory and perceptual functions.

Posner's three-component attention network model includes executive, alerting, and sensory-orienting networks. The executive network is operational during tasks when conflict is present and when the production of a nonhabitual response is necessary (Rothbart and Posner, 2001), i.e., executive attention requires the mobilization of inhibitory attentional processes, which are elements of "cognitive control" (Casey, 2001; Casey et al., 2000; Filoteo et al., 2002; Miller and Cohen, 2001). Tasks tapping executive attention require suppression of a competing response choice or suppression of attention to a salient stimulus (Eriksen and Eriksen, 1974; Logan, 1994). Evidence from structural imaging (Casey et al., 2000), functional MRI (Casey et al., 2000), and positron emission tomography (Lee et al., 2001) studies in normal children and adults suggests that the executive attention network is subserved by the anterior cingulate, prefrontal cortex, and basal ganglia, particularly the striatum (Casey, 2001; Casey et al., 2000; Filoteo et al., 2002). These areas are part of a closely connected corticostriatopallidothalamic network.

The alerting network is involved in maintaining the alert state. This network involves control of wakefulness and arousal and phasic alertness, which is the ability to increase response readiness subsequent to external cueing (Sturm and Willmes, 2001). Structures integral to this network are the locus ceruleus, right frontal cortex (superior region of Brodmann area 6), and right parietal cortex (Posner and Petersen, 1990). In addition, the thalamus and brainstem are also activated during alerting tasks (Sturm and Willmes, 2001).

The sensory-orienting network is responsible for covert orienting to sensory, particularly visual, signals (Posner and Dehaene, 1994). This network includes the parietal lobes, temporoparietal junction, frontal eye fields, superior colliculus, and thalamus. These areas have been implicated in functional neuroimaging (Corbetta et al., 2000; Posner et al., 1988) and lesion (Posner, 1988; Sapir et al., 1999) studies.

The application of lesion studies to investigate ADHD in children with stroke is limited to one study (Max et al., 2002). We reported in an analysis of the MRI scans of 13 subjects with lesions <10 cm^3 that ADHD or traits of the disorder (ADHD/Traits) (see "Methods" for precise definition) was associated with predominantly putamen lesions at a trend level (Fisher's exact test, $p = .1$). The area of greatest lesion overlap for children with ADHD/Traits was the posterior ventral putamen. This dopamine-rich region is part of the ventral (limbic) striatum, which receives fibers from a number of sources including the medial orbital frontal cortex. Further analyses suggested that inattention and apathy are core features of ADHD/Traits (Max et al., 2003).

A second study of childhood focal stroke measured attention difficulties with a standardized behavior rating scale, the Child Behavior Checklist (CBCL) (Achenbach, 1991). *T* scores >70 on the Attention Problems scale of the CBCL were found in five of 39 children with focal stroke lesions (Trauner et al., 2001). The lesions were defined by clinical neuroradiological readings and showed that four of these five children had left hemisphere lesions and four of the five had frontal lobe involvement.

Two case reports also examined ADHD in children with focal stroke using structural imaging. In the first

case (Eslinger and Biddle, 2001), it was found that ADHD was associated with hemorrhagic damage to Brodmann areas 9, 10, 44, 45, 46, and 47 in the right prefrontal cortex, with minor involvement of premotor cortex (area 6) and the anterior insula. The frontal lesion extended through adjacent white matter to the anterior limb of the internal capsule but spared the head of the caudate. The second case reported (Castellanos et al., 2003) was of a child who had a congenital ischemic stroke involving the left caudate, left putamen, and adjacent white matter.

The findings reviewed above suggest that ADHD associated with focal stroke lesions are associated with lesions in frontal and/or basal ganglia circuits. This pattern is strikingly similar to findings related to idiopathic ADHD from structural and functional MRI and positron emission tomography studies reviewed above. In view of this similarity, we hypothesized that ADHD/Traits at the time of assessment will be associated with (1) lesions specifically in the combined mesial prefrontal and orbital frontal regions (Casey, 2001; Casey et al., 1997; Hesslinger et al., 2002; Rohde et al., 2003; Rubia et al., 1999) and (2) with lesions in Posner's executive attention network.

METHOD

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 research questions addressed in this article do not concern the control group. We identified children with stroke at one university hospital by means of a record review, supervised by a pediatric neurologist, guided by the *ICD-9* codes for stroke and congenital cerebral palsy. Assent from the child and written consent from parents/guardians were obtained in accordance with the institutional review board–approved protocol.

Inclusion criteria for stroke cases were (1) neuroimaging documentation of a focal, nonrecurrent, and nonprogressive supratentorial brain parenchymal lesion caused by a stroke before age 14; (2) subjects aged 5 to 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) transplant status; (13) cerebral cysts; (14) trauma; (15) transient ischemic attack; (16) moyamoya; (17) severe and profound mental retardation; (18) quadriplegia, triplegia, or diplegia diagnoses; (19) syndromic vascular malformations (excluding arteriovenous aneurysm ruptures); (20) systemic lupus erythematosus; and (21) multiple lesions (unless in close proximity).

Stroke subjects evaluated included 12 with lesions acquired from age 1 year and 17 with lesions acquired before age 1 year (12 with a prenatal lesion and five with a postnatal lesion acquired between 1 and 270 days of life). The strokes were ischemic in 21 cases and hemorrhagic in eight cases. Etiology was idiopathic occlusive in 15 cases and idiopathic hemorrhagic in two cases; four cases occurred in subjects with congenital heart disease (three after cardiac surgery or catheterization and one after varicella zoster infection). There were five cases of arteriovenous malformation rupture and one case of ruptured angioma; one case was possibly linked to comorbid ulcerative colitis, and 1 case followed a varicella infection. The distribution of the brain lesions included seven cases of predominantly putamen lesions, nine large middle cerebral artery distribution infarcts including deep gray structures, 10 smaller middle cerebral artery distribution frontotemporal or temporoparietal lesions sparing the deep gray, and three cases of parietal or parietooccipital strokes. One of the 29 subjects had ADHD before her idiopathic occlusive stroke and was dropped for the analyses presented in this article. There were 18 males and 27 white and two biracial children. Mean age (SD) was 12.1 (3.9) years.

Psychiatric, Behavioral, and Intellectual Function Measures

The Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997) was conducted by a board-certified child and adolescent psychiatrist. The K-SADS-PL is a semistructured, integrated parent-child interview that generates diagnoses, including ADHD, based on synthesizing data collected separately from the parent and child. Because we recognized the dimensional nature of ADHD symptomatology (Levy et al., 1997), we studied not only the diagnosis of ADHD but also considered ADHD/Traits, defined as subsyndromal symptoms within the ADHD diagnostic category. Subthreshold and threshold criteria are clearly defined in the K-SADS-PL for each symptom and relate to frequency and/or severity of the symptom. The diagnosis of ADHD was made when the symptom complex resulted in clinically significant impairment, after considering the overall developmental level of the child, and was not based simply on symptom counts (Faraone et al., 1995). The ADHD subtypes (predominantly inattentive, predominantly hyperactive/impulsive, combined, and not otherwise specified) were applied only to participants with a clinically significant ADHD syndrome. 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 at onset (7 years) criterion for ADHD was waived so that we could document the development of this behavioral syndrome in subjects who had a stroke later. The psychiatric assessments were made blind to the neuroimaging findings. Reliability checks using videotapes of 11 randomly selected interviews yielded excellent interrater agreement (100%) for diagnosis of ADHD/Traits.

The CBCL (Achenbach, 1991) was completed by a parent. The CBCL is a well-standardized assessment of child behavior problems. We characterized the groups with and without ADHD/Traits in terms of the attention problems scale.

The WISC, Third Edition (WISC-III) (Wechsler, 1991) was used. Prorated Full Scale IQ was derived from a prorated Performance IQ (Picture Arrangement, Block Design, and Coding subtests) and a prorated Verbal IQ (Information and Similarities subtests).

Neuroimaging

To assess lesion location and the proportion of the attention networks of interest that were damaged, MRI scans were obtained for 26 of the children with stroke (T_1-weighted volumetric mode, SPGR/40 degrees, TR/TE = 26/7 milliseconds, NEX = 2, X/Y/Z = 1 × 1.5 × 1 mm thickness with no skip; T_2-weighted dual-echo, FSE/V, TR = 2350, TE = 17/102, NEX = 1, X/Y/Z = 1 × 1 x 5 mm thickness with 1-mm skip). Three other children could not have research MRI scans, and their lesion analysis was derived from clinical scans (two computed tomography; one MRI). A neurologist who was blind to the neuropsychiatric data marked the lesions on hard copy films and represented the lesions on two-dimensional templates (Damasio and Damasio, 1989). The regions identified included 14 frontal lobe regions (F01–F14; five mesial aspect areas, five lateral aspect areas, four orbital aspect areas), 12 temporal lobe regions (nine lateral/superior aspect areas, three mesial aspect areas), six parietal lobe areas (P01–P06; two inferior parietal lobule, four superior parietal lobule), seven occipital lobe regions, two insula regions, four basal ganglia regions (BG1–BG4; two caudate, two lenticular nucleus), four thalamic areas (TH1–TH4), three internal capsule areas, the hypothalamus, and three corpus callosum components. The proportion of each damaged area was coded as follows: 0 = no damage; 1 = <25% damaged; 2 = 25%–75% damaged; 3 = >75% damaged.

MRI analyses also generated three-dimensional (volume) measures. Guided by the lesion markings made by the neurologist, an experienced neuroanatomist ''painted'' each lesion using a three-dimensional brain morphometrics package (Paus et al., 1996). Lesion volume was computed in native and Talairach coordinate systems for intersubject differences in brain size. The computerized Talairach atlas (Lancaster et al., 2000) was used to obtain anatomical labels for painted lesions. The Talairach Region Extraction software was used to calculate volumes of anatomical structures that were covered by painted lesions.

We derived scores for the combined mesial prefrontal and orbital frontal region of interest by summing lesion scores in the mesial prefrontal region (F04) and orbital frontal area (F11–F14).

Areas for each of the attention networks were defined as follows: executive attention network = frontal midline structures (F01–F05) bilaterally including anterior and posterior cingulate, supplementary motor area, prefrontal region, rolandic region, and bilateral basal ganglia (BG1–BG4); alerting network = right inferior parietal lobule (P01–P02), right superior regions of Brodmann area 6 (F03 and F08), and right thalamus (TH1–TH4); sensory-orienting network = bilateral parietal lobes (P01–P06), bilateral thalamus (TH1–TH4), and bilateral frontal eye fields (F08). Damage totals (0–3) in each of the defined areas of each anatomical attention network were summed to derive lesion scores for the respective networks. For example, the maximum possible score for the executive network (9 regions × 3) was 27, alerting network (8 regions × 3) was 24, and sensory-orienting network (11 regions × 3) was 33. Three-dimensional volumes were computed based on Talairach Daemon structures as follows: executive attention network = bilateral anterior cingulum, posterior cingulum, superior frontal gyrus, paracentral lobule, caudate, lentiform, and claustrum; alerting network = right inferior parietal lobule, right precentral and superior frontal gyri, and right thalamus; sensory-orienting network = bilateral parietal lobes, bilateral sublobar areas, bilateral thalamus, and bilateral precentral gyri. The bivariate correlations between the two- and three-dimensional lesion measures were quite high for the executive, alerting, and sensory-orienting attention networks (r = 0.91, 0.76, and 0.79, respectively).

Statistical Analyses

Lesion scores in the specific combined mesial prefrontal and orbital frontal location as well in the executive attention network were compared between groups with ADHD/Traits and no ADHD/Traits by independent sample t tests. To provide context, but unrelated to our hypotheses, the groups were similarly compared on age at assessment, symptom counts, CBCL Attention Problem Scale score, lesion scores in the alerting and sensory-orienting networks, Full Scale IQ, and by Fisher's exact test for gender, timing of stroke onset, and lesion laterality differences.

RESULTS

Occurrence of ADHD/Traits

ADHD/Traits was present in 15 of 28 (54%) children with stroke at the time of the assessment. The total was made up of 12 children who had the full syndrome of ADHD (including six with the inattentive type, four with the not otherwise specified type, one with the hyperactive/impulsive type, and one with the combined type) and three children who had only traits of ADHD. ADHD not otherwise specified type was characterized by mostly inattentive symptoms. Counts of inattentive and hyperactive/impulsive symptoms rated by the interviewer were significantly higher in the group of children with ADHD/Traits versus those without ADHD/Traits at the time of the assessment (Table 1). The classification of the three children with only traits of ADHD depended on the presence of at least three subthreshold symptoms on the screening interview in two children and depended on at least one threshold symptom on the screening interview plus at least five threshold/subthreshold symptoms on the supplementary ADHD interview in one child. Eight of the 15 children with ADHD/Traits had other psychiatric disorders present at the time of the assessment: oppositional defiant disorder (four children); personality change disorder (three children); social phobia (two children); depressive disorder not otherwise specified (two children); separation anxiety disorder (one child); agoraphobia without panic (one child); simple phobia (one child); chronic motor tic disorder (one child); chronic vocal tic disorder (one child); and stereotypic movement disorder (one child).

The distribution of lesion mean scores (SD; range) in the combined mesial prefrontal and orbital frontal area was 1.46 (3.07; 0–12). The distribution of lesion mean scores (SD; range) in the attention networks was as follows: executive network 2.96 (3.56; 0–14); alerting network 1.89 (3.25; 0–12); sensory-orienting network 5.60 (6.86;

TABLE 1
Demographic and Clinical Data for Stroke Subjects With and Without ADHD/Traits at the Time of the Assessment

	No ADHD/Traits (n = 13)	ADHD/Traits (n = 15)	t	df	p
Age at assessment, yr (SD)	12.2 (3.4)	11.5 (4.4)	0.51	26	NS
Inattentive threshold symptoms, mean (SD)	0.2 (.8)	5.5 (2.7)	7.1	16.95	.000
Hyperactive/impulsive threshold symptoms, mean (SD)	0.0 (.0)	1.4 (2.5)	2.14	14.00	.05
Inattentive subthreshold symptoms, mean (SD)	0.2 (.6)	1.3 (1.3)	2.86	19.93	.01
Hyperactive/impulsive subthreshold symptoms, mean (SD)	0.1 (.3)	1.5 (1.4)	3.74	15.25	.002
CBCL Attention Problem scale, mean (SD)	51.9 (4.3) n = 12	61.3 (10.2)	–3.23	19.7	.004
Full Scale IQ, mean (SD)[a]	93.8 (17.5)	81.2 (17.3)	1.91	26	NS
Stroke onset					Fisher's exact
Early	9	8		1	NS
Late	4	7			
Lesion laterality					
Right	8	7		1	NS
Left	5	8			
Gender					
Male	8	10		1	NS
Female	5	5			

Note: ADHD/Traits = traits of attention-deficit/hyperactivity disorder; CBCL = Child Behavior Check list; Early = stroke acquired prenatally or before age 1 year; Late = stroke acquired from age 1 year; NS = not significant.
[a]WISC-III prorated Full Scale IQ.

0–26). The 28 stroke participants could be individually classified according to the distribution of lesioned attention networks as follows: executive attention network alone (n = 8), combined executive attention and sensory-orienting network (n = 6), executive attention and sensory-orienting and alerting network (n = 4), sensory-orienting and alerting network (n =6), sensory-orienting network alone (n = 2), no attention network (n = 2). These data confirm that stroke lesions in children are quite varied and are frequently localized within the proposed attention networks.

Table 1 provides demographic data and illustrates that age, gender, age at stroke onset, and lesion laterality were not significantly different for the subjects grouped according to the presence or absence of ADHD/Traits. Full Scale IQ in the group with ADHD/Traits was lower than the group without ADHD/Traits, but this difference was not statistically significant. T scores on the CBCL Attention Problem Scale rated by the parent differentiated the groups as would be expected and provide support for the diagnostic classification. The mean T score on the CBCL Attention Problem Scale for three children with only traits of ADHD was 63 (range 50–78). The distribution of lesion volume was markedly skewed and was not significantly different (Mann-Whitney U = 76.0; p = .96) between the groups (rank order = 12.9; 37.9 ± 51.7 cm^3 versus rank order = 13.1; 44.0 ± 79.3 cm^3 for the no-ADHD/Traits and ADHD/Traits groups, respectively).

Our first hypothesis that lesions in the mesial and orbital prefrontal region would be significantly associated with ADHD/Traits was confirmed (p = .040; effect size 0.82) (Table 2). Our hypothesis that, based on evidence for executive deficits in children with ADHD, lesion size in the executive attention network would be most closely associated with ADHD/Traits, was not confirmed (Table 2). We found a marginally significant association between ADHD/Traits and lesion size in the executive network (p = .088). However, the effect size was 0.66 (moderate), which suggests the nonsignificant finding may be related to the small sample size and limited power. We did not find any association of ADHD/Traits with lesion size in the alerting or sensory-orienting network. The pattern was similar when the three children with only traits of ADHD were

TABLE 2
Relationship of Mesial Prefrontal/Orbital Frontal Lesions and Posner's Attention Networks With ADHD/Traits

	No ADHD/Traits (n = 13)	ADHD/Traits (n = 15)	t	df	p
Mesial prefrontal and orbital frontal lesion score[a,c]	0.23 (0.60)	2.53 (3.91)	–2.25	14.76	.040
Network lesion score					
Executive network[a,d]	1.77 (2.05)	4.00 (4.29)	–1.79	20.65	.088
Alerting network	2.54 (3.50)	1.33 (3.02)	.98	26	.337
Sensory-orienting network	6.85 (7.41)	4.53 (6.40)	.89	26	.384
	No ADHD/Traits (n = 13)	ADHD full syndrome[b] (n = 12)			
Mesial prefrontal and orbital frontal lesion score[a,e]	0.23 (0.60)	2.83 (4.24)	–2.11	11.41	.058
Network lesion score					
Executive network[a,f]	1.77 (2.05)	4.33 (4.60)	–1.78	14.94	.096
Alerting network	2.54 (3.50)	.92 (2.39)	1.34	23	.193
Sensory-orienting network	6.85 (7.41)	4.17 (6.48)	.96	23	.348

[a]Levene's test for equality of variances was not assumed; [b]Children with only traits of ADHD were excluded; [c]Effect size = 0.82; [d]Effect size = 0.66; [e]Effect size = 0.86; [f]Effect size = 0.72.

excluded from the analyses, i.e., slightly larger effect sizes but only marginally significant associations of ADHD with the anatomical areas of interest (Table 2).

DISCUSSION

The major finding of this study is that ADHD/Traits was significantly associated with focal stroke lesions involving mesial prefrontal and orbital frontal areas. In addition, we found a moderate effect size and a statistical trend for the association between ADHD/Traits and lesions within Posner's executive attention network. These findings are related because the mesial prefrontal area is part of the defined executive attention network, which itself has close connections with orbital frontal areas. Our findings are consistent with a burgeoning literature that has implicated prefrontal corticostriatopallidothalamic pathways in the pathophysiology of idiopathic ADHD.

The current findings expand our earlier findings by building the case that ADHD/Traits is associated with specific lesion distribution, although unrelated to laterality, rather than nonspecific lesion volume in children with stroke (Max et al., 2002). Earlier findings showed that children with stroke have an increased rate of ADHD/Traits compared with closely matched orthopedic controls (Max et al., 2003). When the sample was limited to children with small lesions (<10 cc), ADHD/Traits was associated with predominantly putamen lesions at a trend level (Max et al., 2002). This striatal structure is a component of the executive attention network. This study therefore strengthens the case that the executive attention network and its connections are involved in the expression of ADHD/Traits.

These findings are all the more remarkable because the lesion in affected subjects often extended to involve areas outside the executive attention regions of interest. Thus, even though our subjects had focal lesions, the study was unlike rare case reports (Eslinger and Biddle, 2001) in which behavioral correlates of very specific isolated lesions are described. Our methodology is unique not only in childhood stroke research but also with respect to adult focal lesion research. Researchers typically investigate a group of patients with circumscribed lesions in a specific area that is believed to contribute to a behavioral syndrome or cognitive construct and then determine whether this group is different than a control group (often another group of patients with circumscribed lesions in areas thought not to contribute to the behavioral syndrome or cognitive construct under study) (Eslinger and Grattan, 1993; Filoteo et al., 2002). Our study, on the other hand, has taken a different approach, by examining patients with damage to varying brain regions, characterizing the extent of this damage, and then determining whether the damage contributes to specific deficits or syndromes. This

approach takes advantage of variability in lesion size and lesion location to further knowledge of brain-behavioral relationships underlying ADHD/Traits.

The expression of inattentive and hyperactivity/impulsivity symptoms in children with stroke was indistinguishable phenomenologically but potentially different neurocognitively from idiopathic ADHD. The clinical profile of the children with ADHD was dominated by inattentive symptoms rather than hyperactivity/impulsivity. Therefore, it is interesting to note that the inattentive symptoms were associated with executive attention network and not alerting or sensory-orienting network lesions. There has been much debate whether the combined type of ADHD, which is defined clinically by impairing hyperactive/impulsive as well as inattentive symptomatology, bears the same pathophysiology and neuropsychological profile as the predominantly inattentive type of ADHD. There are those who consider executive function deficits, including disinhibition manifested as hyperactivity/impulsivity, as the core deficit in children with ADHD (Barkley, 1997). However, there is evidence that the inattentive dimension is more closely related to cognitive dysfunction than is the hyperactive/impulsive symptom dimension (Chhabidas et al., 2001; Nigg et al., 2002). Our findings would support this line of evidence and expand it to suggest that even inattentive ADHD induced by a form of brain injury has its neuroanatomical underpinnings within the frontal lobes and executive attention network.

Limitations

Wide ranges in age at onset, age at test, and time since stroke, which could be strengths in a large cohort of children with stroke, were limitations in our small sample. The small sample sizes limited the power of statistical comparisons and a high number of comparisons (Max et al., 2002, 2003) risks spurious findings. Participants included several children with congenital heart disease carefully selected to exclude children with hypoxic events. Nevertheless, the findings could be confounded by possible chronic hypoxia. Prestroke ADHD status was carefully assessed in the clinical interview. Yet there remains the possibility that a proportion of subjects with congenital conditions or even conditions with onset in the first few years of life may have developed ADHD/Traits regardless of their stroke. This problem was mitigated by using a control group in the larger study that also failed to find an association between family history of ADHD and children with ADHD/Traits (Max et al., 2003). The psychiatrist did not have the benefit of a teacher's report to guide diagnostic decisions.

Clinical Implications

The findings from this study are potentially useful in elucidating the pathophysiology of ADHD after stroke. Although these findings do not yet provide direct implications for understanding mechanisms or treatment of children with idiopathic ADHD, a direction of future studies seems clear. Follow-up studies should employ larger samples of children with childhood stroke with sufficient power to test the association of ADHD/Traits and the extent of lesions in the executive attention network and to confirm the association of ADHD/Traits with the extent of lesions in the mesial and orbital frontal areas. Patients with focal cerebellar lesions should be included in future studies because of the now recognized association between cerebellar structure and ADHD (Castellanos and Tannock, 2002). Furthermore, studies should be conducted to investigate a possible neuropsychological profile of ADHD/Traits after stroke, and if there appears to be an identifiable profile, contrast this profile directly with that of patients with idiopathic ADHD. Such studies will provide new information regarding stroke in children, reveal neural mechanisms underlying various types of attention deficits, clarify the basis of the attention problems that so frequently accompany early neurological insults in children, and possibly even find leads in the investigation of biological substrates of idiopathic ADHD.

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