Developmental Deficits in Adult Patients
With Arteriovenous Malformations

Ronald M. Lazar, PhD; Kathleen Connaire, RN; Randolph S. Marshall, MD; John Pile-Spellman, MD; Lotfi Hacein-Bey, MD; Robert A. Solomon, MD; Michael B. Sisti, MD; William L. Young, MD; J. P. Mohr, MD

Background: Cerebral arteriovenous malformations (AVMs) are congenital masses of arteries and veins that appear to undergo an unclear “maturation” for many years. Using structured interviews, we compared developmental history of adult patients with AVM with a comparison group of patients with cerebral tumor or aneurysm.

Objective: To determine whether a remote history of developmental abnormality in adult patients with AVM might be an early marker of cerebral status.

Design: Adult patients with AVM and a comparison group of patients with cerebral aneurysm or low-grade tumor participated in a survey.

Setting: Urban medical school-based tertiary care center.

Patients: Forty-four randomly selected patients with AVM from the Columbia–Presbyterian AVM Database. There were 32 comparison patients:15 randomly chosen patients from the institution's Cerebral Aneurysm Database and all 17 patients who underwent a biopsy from 1990 to 1995 with a diagnosis of low-grade tumor and who could be contacted.

Main Outcome Measures: A brief, structured interview adapted from the Centers for Disease Control and Prevention for its 1994 study of the prevalence of learning disabilities in American children. We defined the positive occurrence of a condition as an affirmative answer to the question, “Did ________ have (condition) during his/her school-age years?” Each patient was also asked if there had been any problems in the following skill areas: reading, writing, listening, speaking, attention, impulsivity, organization, mathematics, or drawing. The AVM size was calculated on the angiographic film by measuring its longest diameter in any dimension.

Results: Patients with AVM were significantly more likely to report a positive occurrence to any survey question (P<.05). Two thirds of all patients with AVM (66%) reported at least 1 skill difficulty during their school years, significantly more than the comparison group (P<.001). Neither the maximum AVM diameter nor the occurrence of hemorrhage as an adult differed between patients with AVM with and without early skill difficulty.

Conclusions: Patients with AVM are more likely to report a developmental learning disorder than patients with tumor or aneurysm despite the absence of other neurologic symptoms of diseases not diagnosed for another 20 years. These data support the notion that disorders of behavioral and intellectual function are sensitive markers of early cerebral status.

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PATIENTS AND METHODS

PATIENTS

The patients with AVM were 44 randomly selected individuals from the Columbia–Presbyterian AVM Database. None received surgical or other treatment for the AVM prior to or during school-age years. There were 32 comparison patients consisting of 15 randomly chosen patients from the institution’s Cerebral Aneurysm Database and all 17 patients who underwent biopsy from 1990 to 1993 that led to a diagnosis of low-grade tumor and who could be contacted. The patients with cerebral aneurysm, none of whom had an AVM, were selected as another example of a chronic cerebrovascular condition. The patients with low-grade tumor, diagnosed as having astrocytoma, oligodendroglioma, or mixed cytologic findings, represented a cohort with a developing mass lesion inferred not present early in life.

PROCEDURES

Each patient (or family member) was contacted via telephone and was administered a brief, structured interview by an individual who was blinded to clinical features at the time of presentation to our institution. The format of each question was based on the 1988 National Health Interview Survey—Child Health Supplement designed by the National Center for Health Statistics, and later used by the Centers for Disease Control and Prevention for its 1994 study of the prevalence of learning disabilities in American children. We defined the positive occurrence of a condition as an affirmative answer to the question, “Did you (or family member) have (condition) during his/her school-age years?” Patients were queried as to: educational attainment, attendance in special classes, classification as “learning disabled” (nearly all finished school prior to the enactment of Public Law 94.142 for the handicapped in 1978), delay of developmental milestones, grade retention, attendance in summer school, failing grades, need for tutoring, and class rank and average. Each patient was also asked if there had been any problems in the following skills areas: reading, writing, listening, speaking, attention, impulsivity, organization, mathematics, or drawing. The patients’ responses were tallied and data analysis was performed. The patients were told that we were collecting additional information for our database for their respective conditions. The AVM size was calculated on the angiographic film by measuring its longest diameter in any dimension. Histories of headaches and seizures were obtained from clinical records.

There were 76 patients in the study: 40 were women and 36 were men. Ages at time of our clinical interview and levels of education attained are shown in Table 1, with 2-tailed t tests revealing no significant differences between the AVM and comparison group. Among patients with AVM, 28 had left cerebral lesions and 16 had lesions in the right hemisphere. For the patients with tumor, 10 had lesions in the left hemisphere and 7 in the right hemisphere. Comparable locations could not be established in the patients with aneurysm. Of the 44 patients with AVM, 11 presented with hemorrhage as adults but none before 20 years of age. All but 1 of the patients with cerebral aneurysm presented with hemorrhage. Only 1 patient with AVM was found to have onset of seizures before 15 years of age, and only 4 patients with AVM were found to have onset of recurrent headaches, usually diagnosed as having “migraine,” before 15 years of age.

The distribution of respondents were the following: 64% of the patients with AVM provided responses regarding their learning histories while 44% of the tumor or aneurysm group provided their own histories, a difference that was not statistically significant. Thirty-three patients with AVM (75%) reported a positive occurrence to any survey question whereas only 13 patients (41%) in the comparison group reported a positive instance of a developmental, school, or behavior problem ($\chi^2 = 4.28; P < .05$). Table 2 shows the frequency of patients in each group who responded that a particular problem had occurred during their public school years. All the specific skills deficiencies (eg, reading or writing) were collapsed into a single category so that the percentages would reflect the number of patients reporting one or more skill difficulties since some difficulties, such as attentional problems and impulsivity, are not mutually exclusive. Class rank and average are omitted because more than 25% of patients or family members could not produce this information. Two thirds of all patients with AVM (66%) reported that they had experienced difficulty with at least 1 skill area during their school years, in contrast to the comparison group in which there were

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<th>Table 1. Patient Demographics</th>
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<td>Mean ± SD</td>
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<tr>
<td>Age, y</td>
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<td>Attained education, y</td>
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*AVM indicates arteriovenous malformation.
†† Test, $P = .17$ (not significant).
‡‡ Test, $P = .04$ (not significant).

whether a remote history of developmental learning abnormality might be a marker of early cerebral dysfunction. We contrasted learning and behavioral history in patients with AVM to a comparison group composed of patients with low-grade cerebral tumor verified by a biopsy or cerebral aneurysm.

gone widened distribution of some language functions. It seems reasonable to hypothesize that the brain responded to some provocative stimulus earlier in life when there appears to be greater capacity for redistribution of function.

Since patients with AVM are typically asymptomatic in their younger years, we wanted to determine
significantly fewer patients reporting such problems ($\chi^2 = 12.41; P < .001$). There were trends favoring the AVM group with regard to receiving tutoring, attendance in special classes and in summer school, diagnosis of learning disabled, and delays in developmental milestones, but none of these categories were reported with significantly greater frequency. Of 11 patients with AVM who presented as adults with hemorrhage, 8 had a history of skill problems, but of the 28 who did not present with hemorrhage, 18 had a history of developmental problems, a difference that was not statistically significant ($P > .5$).

The Figure shows that of 29 patients with AVM who indicated skill difficulty, reading was the most common disorder. Of these 12 patients who reported reading difficulty, there was an equal proportion occurring in patients with left and right hemisphere lesions. Impulsivity, disorganization, drawing problems, mathematical problems, and writing disorders were also reported with lesions in either hemisphere. Male and female patients with AVM were equally likely to indicate deficits. The maximum AVM diameter of the AVM in those with a skill difficulty (mean, 3.5 cm) and those without this history (mean, 3.2 cm) was not statistically different ($P > .5$). Reading difficulty was reported only by 2 patients with tumor or aneurysm. Only 1 specific skill defect (attention deficit) was reported by as many as 3 patients in the comparison group.

Patients with AVM were more likely to report a developmental disorder in learning or behavior than age- and education-matched patients with cerebral tumor or aneurysm despite the absence of other disease symptoms not diagnosed, on average, for another 20 years.

According to the 1994 Centers for Disease Control and Prevention survey, approximately 17% of American children have either a learning disability, behavior problem, or difficulty with speech. The verbal report by our AVM group was 4 times this rate. In contrast, the report by patients in the comparison group was not statistically different from the general population. That most patients in the AVM group completed high school indicates that these developmental problems were not grossly disabling abnormalities. Nevertheless, these data provide additional support for the notion that disorders of higher intellectual and behavioral function can serve as more sensitive markers of early cerebral dysfunction than physical signs and symptoms.

The distribution of patients ($n = 44$) with arteriovenous malformation (AVM) reporting a positive history for each of the 9 specific skill disorders queried in the survey.

<table>
<thead>
<tr>
<th>Skill Disorder</th>
<th>AVM Group (n = 44)</th>
<th>Tumor or Aneurysm Group (n = 32)</th>
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<tbody>
<tr>
<td>Difficulty with specific skills</td>
<td>66</td>
<td>25†</td>
</tr>
<tr>
<td>Received tutoring</td>
<td>28</td>
<td>6</td>
</tr>
<tr>
<td>Special classes</td>
<td>16</td>
<td>6</td>
</tr>
<tr>
<td>Attended summer school</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Diagnosis of learning disabled</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>Delay in milestones</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Failed a class</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Retained in a school grade</td>
<td>9</td>
<td>12</td>
</tr>
</tbody>
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*AVM indicates arteriovenous malformation.
†$x^2 = 13.83; P < .001$. 

There was no statistical difference in the report of delayed developmental milestones (speech, language, or motor function) between the AVM and the tumor or aneurysm group, suggesting that despite the likely presence of some primitive form of an AVM at birth there may not have been any functional consequences before the age of 3 or 4 years. This finding supports the notion that the reorganization of brain function reported in our previous work may not have occurred until patients were well into the language development period. The hypothesis that the presence of a cerebral lesion at birth, per se, is not sufficient to produce relocalization of function has received support from studies of cortical stimulation in patients with epilepsy. In the series of children undergoing dominant temporal lobectomy by Devinsky et al., patients with onset of epilepsy at a mean age of 5.8 years were more likely to demonstrate anteriorly distributed temporal (lobe) language representation than children at 12 years of age. Conversely, mapping language by electrical stimulation of chronically implanted subdural electrodes in 34 patients, Duchowny et al. found that cerebral injury acquired after birth was more likely to produce displacement of language than lesions present at birth.

It should be noted that the vast majority of children with learning difficulties do not have an associated brain lesion measurable on computed tomography or magnetic resonance imaging, and it is not suggested herein that children diagnosed as being learning disabled should routinely undergo imaging. Rather, our data suggest that on retrospective analysis, patients with cerebral AVM have
a high incidence of developmental learning problems. Because of the relative absence of seizure and headache histories before 15 years of age in our AVM sample, this study does not provide new information to child neurologists regarding when to perform neuroimaging (usually magnetic resonance imaging) and the current “best practice” is to do so in all cases when migraine is asymmetrical and there are learning disabilities. A limitation of this study is the lack of family history data with regard to learning disabilities and attention-deficit/hyperactive disorder, but, to our knowledge, there are so few studies demonstrating genetic linkage for AVMs that relationships to other neurologic or behavioral conditions have not yet been established. Moreover, the likelihood of coincident learning problems to such a high degree in the families of our patients with AVM appears extremely small. If a larger sample had been obtained, there probably would have been a statistical difference between the tumor or aneurysm group and the general population, but such a finding would not likely alter the discrepancy between our AVM and comparison group. Nevertheless, the presence of reading disorders in patients with AVMs in either hemisphere may be a marker of the developing lesion or a reflection of an as yet incomplete redistribution of function that occurs during development.

The hemodynamic effects of shunt flow through an AVM on surrounding brain are incompletely understood and controversial. Not only is this interest driven by a desire to clarify mechanisms of cerebrovascular regulation in health and disease but also because altered cerebral hemodynamics have been implicated in the pathogenesis of pretreatment neurologic deficits and posttreatment complications. An intuitively derived but unproven paradigm continues to serve as an explanation for instances of pretreatment deficits, often attributed to cerebral “steal.”

14,15 and certain catastrophic posttreatment complications of brain swelling and intracranial hemorrhage, termed circulatory breakthrough10,11 and normal perfusion pressure breakthrough.18 This paradigm is based to a large extent on the observation that in some patients high-feeding artery flow reduces perfusion pressure in neighboring vascular territories.19-21 Reduction in perfusion pressure may place these vascular territories at or below the lower limit of autoregulation by a combination of arterial hypotension and venous hypertension, which may account for the occurrence of focal neurologic deficits. The evidence for such a pathomechanism is largely indirect and speculative.14,15 It has been postulated that chronic arteriolar vasodilation may result in vasomotor paralysis, both at sites near and distant from the AVM. Experimental evidence, however, for the pathophysiological link between pretreatment hypotension and posttreatment hyperemia and subsequent swelling and hemorrhage is lacking.22

The results of our study suggest that causes of neurologic dysfunction in patients harboring AVMs is likely to be far more subtle and complicated than any simplistic attempt to attribute them to hemodynamic failure. In fact, study of these developmental problems in patients with AVM may be a useful model for understanding neural organization and dysfunction for a variety of more common cerebral disease states.

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Reprints: Ronald M. Lazar, PhD, Cerebral Localization Laboratory, Neurological Institute, Columbia—Presbyterian Medical Center, 710 W 168th St, New York, NY 10032.

REFERENCES


