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Spinal lesion level in spina bifida: a source of neural and cognitive heterogeneity

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Object. The aim of this study was to evaluate whether the level of a spinal lesion is associated with variations in anomalous brain development and neurobehavioral outcomes in children suffering from the meningomyelocele form of spina bifida and hydrocephalus (SBM-H).

Methods. Two hundred sixty-eight children with SBM-H were divided into upper (T-12 and above; 82 patients) and lower (L-1 and below; 186 patients) lesion-level groups. Magnetic resonance images were qualitatively coded by radiologists and quantitatively segmented for cerebrum and cerebellum volumes. Psychometric assessments of handedness, intelligence, academic skills, and adaptive behavior were compared between lesion-level groups and also used to determine the number of children who met research-based criteria for mental retardation, attention deficit hyperactivity disorder, and learning disabilities.

The magnetic resonance images obtained in children with upper-level spinal lesions demonstrated more qualitative abnormalities in the midbrain and tectum, pons, and splenium, although not in the cerebellum, compared with images obtained in children with lower-level spinal lesions. Upper-level lesions were also associated with reductions in cerebrum and cerebellum volumes, lower scores on measures of intelligence, academic skills, and adaptive behavior, and with a higher frequency of individuals meeting the criteria for mental retardation. Hispanic children (who were also more economically disadvantaged) were more likely to have upper-level lesions and poorer neurobehavioral outcomes, but lesion-level effects were generally independent of ethnicity.

Conclusions. A higher level of spinal lesion in SBM-H is a marker for more severe anomalous brain development, which is in turn associated with poorer neurobehavioral outcomes in a wide variety of domains that determine levels of independent functioning for these children at home and school.

KEY WORDS • spina bifida • lesion level • meningomyelocele • neuropsychology • intelligence quotient • magnetic resonance imaging • pediatric neurosurgery

THE purpose of this study was to evaluate the relationship of the level of a spinal lesion to the severity of anomalous brain development and neurobehavioral outcomes in children with SBM-H. Although poorer medical and cognitive outcomes have been reported in children with upper-level spinal lesions compared with the outcomes for children with lower-level spinal lesions,[1,5,13,14] explanations for this observation have been limited and controversial. The level of spinal defect clearly explains variability in orthopedic and urological outcomes in SBM-H: the higher the lesion, the more incapacitated the child.[1,5,13,14] Other investigators have found that higher-level lesions are associated with lower IQ. The results are not consistent, however, with some studies reporting no relationship between IQ and lesion level[15,24] and others reporting that only thoracic lesions are associated with lower IQ,[14,16,20,27] or that lesions above L-2 are related to poorer outcomes.[9–11]

The differences across studies reflect variations in the size of study populations (which are usually small), socio-

Abbreviations used in this paper: ADHD = attention deficit hyperactivity disorder; ANOVA = analysis of variance; CSF = cerebrospinal fluid; df = degree of freedom; FOV = field of view; IQ = intelligence quotient; MR = magnetic resonance; SBM-H = meningomyelocele form of spina bifida with hydrocephalus; SD = standard deviation; SES = socioeconomic status; SIB-R = Scales of Independent Behavior—Revised; WJR = Woodcock-Johnson Revised.

demographic characteristics (which are rarely reported), type of spinal lesion (meningocele compared with meningomyelocele), and the exclusion of individuals with thoracic lesions.[19] The findings of one study[14] suggest that differences in IQ that vary according to lesion level are due to an association of perinatal complications with higher lesion levels; this issue is not addressed in most studies. In some studies there was no control for the status of hydrocephalus, an omission that is important to note because children with shunt-treated hydrocephalus have lower IQ scores than those seen in patients with hydrocephalus that is not sufficiently severe to warrant shunt placement.[14–16] Whether lesion level is associated with differences in the extent of brain malformation is not well established; however, this association may help explain an association between higher spinal lesions and more adverse cognitive outcomes. In older studies, Lonton[13] found that children with thoracic lesions had thinner cortical mantles than those with lumbar and sacral lesions, and Badell-Ribera, et al.,[1] found more brain defects in children with thoracic lesions.

Despite these descriptive studies, the relationship of spinal lesion level to outcome is not well understood. The brain anomalies that occur with upper and lower spinal lesions have not been directly compared using MR imaging in large, ethnically diverse populations; this is important because evidence from MR imaging studies now reveals brain anomalies not identifiable in older studies, such as congenital partial dysgenesis of the cerebellum[2] and variability in the severity of the Chiari II corpus callosum.[18] There is no study in which the relationship of lesion level to anomalous brain development in spina bifida has been examined using a principled division of spinal lesion level to determine which types of anomalous brain development are related to a specific level of spinal defect.

Principled methods for determining the level of spinal defect can be derived from research on genetic and neuroembryological factors in SBM-H. A model of neural tube malformation[25] has provided evidence of a multisite closure in which two closure initiation sites are identified in spinal development, one near the juncture of the rhombencephalon and the cervical spinal cord and another with a proposed meeting point at L1–2.[25] In support of this theory, investigators have recently found that the level of spinal lesion as determined using this model along with the factor of ethnicity accounts for genetic variability in SBM-H;[26] significantly higher frequencies of mutant genotypes related to folate metabolism were demonstrated in Hispanic mothers of children with thoracic level defects. Although these studies produced results similar to those of van Allen, et al.,[25] and divided lesion level at L1–2, a more reasonable subdivision may be at T12–L1 because vertebrae with ribs (T1–12) are likely to require different genetic programming than vertebrae without ribs (L1–sacrum).

In this study, we address the issue of the brain and behavioral differences detected in upper (thoracic) and lower (lumbar and sacral) spinal lesions in a large, well-characterized population of children with SBM-H, in relation to two primary questions. 1) What is the relationship among lesion level, brain malformation, and the clinical markers associated with SBM-H? We hypothesize that children with upper-level lesions will show more anomalies involving the cerebellum, midbrain and tectum, and corpus callosum, and more regional thinning of posterior cortical regions as determined by quantitative analyses of MR imaging studies. The reasoning underlying the latter prediction is that more severe anomalous brain development will be associated with more severe hydrocephalus. Moreover, we expect to replicate the findings that demonstrated that children with upper-level lesions will have greater problems with ambulation and bladder/bowel control as well as a higher rate of perinatal and shunt-related complications. 2) What is the relationship between lesion level and intellectual, academic, and adaptive behavior outcomes? We hypothesize that children with upper-level lesions will have lower performance levels across outcome domains and higher rates of mental retardation, learning disorders, and attention problems, conditions that reflect medical complications and brain abnormalities.

TABLE 1

*Summary of characteristics of 268 children with SBM-H segmented by upper- and lower-level lesion groups**

Characteristic	Total (%)	Upper Lesions (%)	Lower Lesions (%)
no. of patients	268	82	186
mean age ± SD (mos)	132.1 ± 36.1	133.1 ± 37.9	131.6 ± 35.3
sex			
female†	130 (49)	49 (60)	81 (44)
ethnicity			
caucasian	154 (58)	43 (28)	111 (72)
Hispanic	87 (32)	34 (36)	53 (61)
African American	18 (7)	3 (17)	15 (83)
Asian/other	9 (3)	2 (22)	7 (78)
SES (264 patients)			
mean ± SD	37.0 ± 14.4	34.8 ± 15.0	37.9 ± 14.1

* Lower lesions denotes those located at L-1 and below, and upper lesions, those at T-12 and above.

† $p < 0.05$.

Clinical Material and Methods

Patient Population

The study population comprised 268 children between 7 and 16 years of age with SBM-H and shunt-treated hydrocephalus who were enrolled from three primary sites. Two sites were in Houston—the Spina Bifida Clinic at Texas Children's Hospital and the Shriner's Hospital for Children. In Toronto, participants were enrolled from The Hospital for Sick Children and surrounding areas. At all sites, close relationships were established with outpatient clinics and patient registries that are maintained by pediatric neurosurgeons. Although not epidemiologically derived, the population represents a substantial number of the children with SBM-H in this age range from these geographic regions. There are considerable sociodemographic differences between patients in Houston (170 patients) and Toronto (98 patients) largely because of the large Hispanic population in Houston. Extensive analysis of cohort differences revealed few differences in the non-Hispanic Houston and Toronto cohorts in terms of sociodemographic, medical, MR imaging, and cognitive characteristics; however, the Hispanic study population is clearly different in terms of language factors and lower SES.[8]

Table 1 provides the age, sex, ethnicity, and SES of patients by lesion level. The chi-square test for all levels of ethnicity could not be computed because of the small populations of African Americans, Asians, and other ethnicities. Upper-level lesions were more common in Hispanics than in non-Hispanics ($\chi^2 = 4.37$, df 1; $p < 0.04$; 268 patients). In addition, girls (Hispanic and non-Hispanic) were more likely than boys to have upper-level lesions ($\chi^2 = 5.99$, df 1; $p < 0.02$; 268 patients). Socioeconomic status was not significantly different between the lesion-level subgroups ($F(1,260) < 1$); however, the main effect of ethnicity was significant, ($F(1,260) = 122.3$, $p < 0.0001$). The Hispanic subgroup (mean 25.3; ± 11 [SD]) was significantly lower in SES than the non-Hispanic subgroup (mean 42.7 ± 12.3 [SD]), although this difference did not interact significantly with lesion level ($F(1,260) = 3.36$, $p < 0.07$). Nonetheless, this trend will be accounted for in subsequent analyses by comparing lesion-level groups within Hispanic and non-Hispanic ethnicities, representing comparisons of lesion level that control for ethnicity and SES differences.

Data Gathering and Neuroimaging Studies

This study was approved by the institutional review boards at The University of Texas Health Science Center at Houston and The Hospital for Sick Children. After parents and children agreed to participate, written consent was obtained from parents and each child signed to indicate assent. Each participant underwent an assessment of handedness, intellectual, and academic functions that was administered by trained research assistants under the supervision of licensed neuropsychologists. Children were assessed in their primary language (English [93%] or Spanish [7%]) by a native speaker of the primary language. All instruments were adapted for use with Spanish-speaking children. With the exception of the academic tasks, the normative group was typically English speaking; there were no normative indices specific for Spanish speakers. Information was derived from parent interviews conducted in the native language by the research nurses or psychologists and from questionnaires designed to ascertain each child's developmental history, medical history, adaptive function, behavioral adjustment, and family resources. Pregnancy (infection, preterm labor, hypertension, diabetes, and other) and perinatal complications (small for gestational age, low birth weight, respiratory distress, metabolic problems, jaundice, and other) related to birth were analyzed for the presence or absence of any complications, but the actual coding was detailed, including specific complications and their treatment.

Most patients (191) underwent MR imaging of the brain specifically for this research project; some participants declined the procedure and others were unable to cooperate, refused sedation, or suffered from physical handicaps (for example, severe kyphosis) that precluded MR imaging. Images were coded by radiologists in Houston and Toronto who were blinded to patient histories and who developed conventions and a coding form. In addition, quantitative segmentation was performed on a subset of the MR images suitable for this form of analysis.

In accordance with practices established for genetic studies,[26] lesion level was determined using multiple sources—the original hospital discharge summaries, neurosurgical operative reports, and medical records at the time of birth—to attempt to identify anatomically based indicators (performed for 178 patients). Many of the birth records were old and difficult to obtain, and therefore the lesion level was determined using subsequent medical records in 90 patients; in most cases, this involved a transfer of information from the birth records. Although neuroimaging-based assessments would be ideal for this analysis, such studies are not routinely completed or are available only in the form of medical record summaries. Whereas a number of classifications have been used in older studies of spinal lesion level, we adopted the classification (thoracic compared with lumbar and sacral) based on recent research on the genetics and embryology of neural tube closure.[26] The specification of lesion level was based on the highest level apparent, even in cases where the defect was large or asymmetric.

Cognitive Tasks and Parent Rating Scales

Children completed assessments of verbal and nonverbal intelligence (Stanford-Binet Intelligence Test-IV[23]), word recognition (WJR Basic Reading[29,30]), reading comprehension (WJR Passage Comprehension[29,30]), math (WJR Calculations[29,30]), and adaptive behavior (SIB-R[4]). None of these performance measures requires significant motor output. These measures were also used to identify children who met research-based criteria for mental retardation and for learning disabilities in reading, math, or both. We identified children who met research-based criteria for ADHD based on a parent rating scale, the Swanson, Nolan, Achenbach, Pelham-IV.[22] A performance-based handedness inventory was administered to determine if lesion level was associated with differences in handedness.[13]

Magnetic Resonance Imaging. The MR images were obtained using comparable magnets (General Electric Medical Systems, Milwaukee, WI) at each site. Three imaging sequences were obtained. The initial series was for a sagittal plane spin echo T_1-weighted localizer (FOV 24 cm, TR 500 msec, TE 14 msec, 256 × 192 matrix, 3 mm with a 0.3 skip, two repetitions). The localizer was followed by two whole-brain coronal acquisitions. One series involved three-dimensional fast–spin echo T_2-weighted MR images (FOV 24 cm, TR 4000 msec, TE 102 msec, echo-train length 16, 256 × 256 matrix, one repetition with contiguous 1.7-mm coronal images). The other series involved three-dimensional spoiled-gradient echo MR images (with contiguous 1.7-mm coronal images, FOV 24 cm, TR 18 msec, TE 3 msec, flip angle 25°, 124 locations, 256 × 256 matrix, one repetition). Separate T_1- and T_2-weighted acquisitions were necessary to ensure adequate estimation of CSF compared with gray and white matter, a measure that is essential for quantitative analysis.

Quantitative Segmentation. Because of the presence of artifacts, not all of the images that could be reviewed for qualitative analysis were suitable for quantitative analysis. The procedures for quantitative segmentation of the MR images were developed specifically for children with hydrocephalus and utilized semiautomated tissue segmentation based on a fuzzy C-means clustering algorithm to differentiate gray matter, white matter, and CSF.[3,7] All slices

TABLE 2

Proportion of the SBM-H study population with clinical markers segmented by upper- and lower-lesion groups

Clinical Marker	Total	Upper Lesions	Lower Lesions
no. of patients	268	82	186
birthweight in g (253 patients) mean ± SD	3258 ± 627	3254 ± 550	3260 ± 660
gestational age in wks (241 patients) mean ± SD	38.9 ± 2.5	38.8 ± 2.8	38.9 ± 2.4
history of pregnancy complications (263 patients)	0.19	0.18	0.20
history of perinatal complications (235 patients)	0.24	0.24	0.24
shunt revisions			
0	0.24	0.23	0.24
1	0.32	0.37	0.30
2–4	0.33	0.29	0.35
5–9	0.08	0.07	0.09
>10	0.03	0.04	0.03
shunt infections (264 patients)	0.26	0.29	0.24
ambulatory status*			
normal	0.01	0.0	0.01
independent	0.19	0.01	0.26
w/ support	0.30	0.09	0.40
unable to walk	0.50	0.90	0.33
neurogenic bladder (264 patients)	0.96	0.95	0.96
oculomotor abnormalities (256 patients)	0.38	0.45	0.35
seizure disorder			
no. of patients	258	78	180
none	0.76	0.74	0.77
yes, not undergoing treatment	0.15	0.14	0.16
yes, under treatment	0.10	0.12	0.07

* $p < 0.0001$ for comparison between upper- and lower-lesion groups.

for which the cerebrum or cerebellum could be identified were segmented. For the cerebrum, the segmentation solution included the absolute tissue volumes for the whole brain, each hemisphere, and three front-to-back cerebral regions within each hemisphere—precallosal, pericallosal, and retrocallosal.[6] In this categorization, the pericallosal region subtended the coronal brain volume extending from the most anterior to the most posterior aspect of the corpus callosum. The precallosal region extended fully frontally from the pericallosal region and the retrocallosal region extended fully posteriorly from the pericallosal region.

The cerebellum is usually grossly malformed in children with SBM-H, and such abnormalities make it difficult to perform reliable manual subdivisions. From the coronal series, we identified primary fissures to the left and right of the middle cerebellar slice on MR images from normally developing children. In general, the vermis represented approximately 11% of the total cerebellum. We used this estimate to define a medial cerebellar volume by identifying the areas 5.5% on either side of the midline, with the remainder being defined as the left or right lateral regions; therefore the medial cerebellar volume was a proxy for the vermis volume, although the procedures allow reliable estimates of these regions. Cerebellar volumes by tissue type are generated for the whole cerebellum and for single medial and two lateral regions.

Statistical Analysis

To address the first question concerning the relationship among lesion level, anomalous brain development, and clinical markers, frequency of abnormalities for clinical markers and MR imaging–qualitative data were computed and compared by using lesion level using the chi-square test. The quantitative brain imaging data for cerebrum and cerebellum were analyzed for effects of lesion level, region, hemispheres, and tissue type by using a multivariate approach to repeated-measures ANOVA.

The second set of data analyses addressed the relationship of lesion level to intellectual, academic, and adaptive behavior outcomes. Missing data were largely due to the inability of lower-functioning children to complete more demanding tasks and to parents who declined an interview or failed to return forms. Much of the missing data represented eight children with severe mental retardation (four with upper-level, four with lower-level lesions) who could not perform any of the tasks, but whose parents did provide the adaptive behavior assessment. Two children had severe oral language difficulties and did not complete tasks requiring verbal responses. Standard multivariate approaches to repeated measures would drop cases with incomplete data. To maximize the available data, we used a mixed-models approach to unbalanced repeated-measures ANOVA by using SAS PROC MIXED version 8.01 (SAS, Inc., Cary, NC). This approach allowed inclusion of children who could perform any of the tasks within a set of variables so that domain-level comparisons among groups with SBM-H would not be biased by exclusion of the lowest-functioning cases.

Results

Clinical Markers

Table 2 summarizes common clinical markers associated with SBM-H for the group as a whole and by lesion level. Ambulation status was the only clinical marker that differentiated upper and lower lesions. As expected, children with upper-level lesions were more likely to be nonambulatory ($\chi^2 = 73.7$, df 1; $p < 0.0001$; 268 patients). The lesion-level groups did not differ in birth weight, gestational age, pregnancy complications, perinatal complications, shunt revisions, shunt infections, neurogenic bladder, oculomotor abnormalities, or seizure status ($p > 0.10$).

Hand Preference

Upper spinal lesions were associated with incompletely lateralized hand preferences. Children with upper-level lesions were more likely than those with lower-level lesions to be non–right handed ($\chi^2 = 7.77$, df 2; $p < 0.03$; 257 patients). The difference was largely due to a higher rate of mixed handedness in children with upper-level lesions (23%) than lower-level lesions (11%), leading to lower numbers of strongly right-handed children in the upper-level lesion group (53%) compared with the lower-level group (67%). The two groups were comparable in the rates of strongly left-handed children (upper 22% and lower 24%).

TABLE 3

Qualitative abnormalities found via MR imaging by lesion level

Variable	Upper Lesions (%)	Lower Lesions (%)
no. of patients	56	135
midbrain	34 (61)	72 (55)
tectum*	54 (96)	107 (80)
axial beaking	48 (86)	99 (74)
sagittal beaking	36 (64)	57 (43)
posterior fossa (small)*	55 (98)	121 (90)
pons*	55 (98)	107 (79)
medulla	54 (96)	120 (90)
falx (fenestrated)*	53 (96)	113 (84)
cerebellum	56 (100)	133 (96)
small	24 (44)	51 (39)
dysplastic	53 (95)	114 (85)
upward herniation	41 (73)	81 (60)
vermis	52 (93)	109 (81)
hemispheres*	53 (95)	98 (73)
tonsils	27 (48)	73 (54)
Chiari malformation		
Type II	54 (96)	122 (90)
Type I	0 (0)	4 (3)
corpus callosum		
rostrum		
normal	13 (23)	34 (25)
dysgenic	26 (46)	54 (40)
hypoplastic	17 (30)	47 (35)
genu		
normal	18 (32)	54 (40)
dysgenic	3 (5)	3 (2)
hypoplastic	35 (63)	78 (58)
body		
normal	4 (7)	13 (10)
dysgenic	2 (4)	1 (01)
hypoplastic	50 (89)	12 (90)
splenium*		
normal	3 (5)	18 (13)
dysgenic	25 (45)	82 (61)
hypoplastic	28 (50)	35 (26)

* $p < 0.05$.

TABLE 4

Quantitative analysis of MR imaging studies for cerebral cortex by upper- and lower-lesion level groups

Location	Mean Volume ± SD (mm^3)	
	Upper Lesion (25 patients)	Lower Lesion (61 patients)
whole brain	1,210,657 ± 140,528	1,293,298 ± 133,899
gray*	754,507 ± 84,183	806,512 ± 83,363
white*	332,919 ± 82,768	371,065 ± 49,861
CSF	123,214 ± 69,938	115,701 ± 58,085
lt precallosal		
gray	78,168 ± 17,050	80,842 ± 21,519
white	27,210 ± 8,607	28,798 ± 7504
CSF	5979 ± 6859	6538 ± 4512
rt precallosal		
gray	78,601 ± 19,327	80,066 ± 20,609
white	29,841 ± 9877	31,912 ± 7898
CSF	6124 ± 6448	6770 ± 4848
lt pericallosal		
gray*	187,796 ± 25,916	201,249 ± 21,803
white*	93,618 ± 23,564	103,174 ± 14,346
CSF	41,352 ± 30,871	37,823 ± 23,453
rt pericallosal		
gray*	191,557 ± 23,763	204,960 ± 20,522
white*	94,814 ± 24,861	107,311 ± 15,058
CSF	34,894 ± 20,220	32,184 ± 15,135
lt postcallosal		
gray*	108,456 ± 19,720	121,722 ± 17,420
white*	47,585 ± 13,558	53,816 ± 10,471
CSF	20,224 ± 13,739	19,277 ± 13,329
rt postcallosal		
gray*	110,442 ± 17,114	118,256 ± 18,288
white*	39,338 ± 12,827	45,472 ± 10,877
CSF	14,640 ± 8950	31,309 ± 8197

* $p < 0.05$.

Frequency of MR Imaging Abnormalities

Children with upper spinal lesions had higher frequencies of MR imaging–detected abnormalities involving major structures known to be implicated in SBM-H (Table 3). The frequency was significantly greater for upper- than for lower-level lesions for the tectum ($\chi^2 = 8.39$, df 1; $p < 0.004$; 190 patients), posterior fossa ($\chi^2 = 3.63$, df 1; $p < 0.05$; 190 patients), pons ($\chi^2 = 5.89$, df 1; $p < 0.02$; 191 patients), falx ($\chi^2 = 5.29$, df 1; $p < 0.02$; 190 patients), cerebellar hemispheres ($\chi^2 = 8.65$, df 1; $p < 0.004$; 190 patients), and the splenium of the corpus callosum ($\chi^2 = 7.50$, df 1; $p < 0.03$; 190 patients). Cerebellar anomalies were highly frequent in both groups but generally did not occur at a different rate.

Quantitative MR Imaging Data

Cerebrum. Quantitative segmentation of the cerebrum revealed significant lesion-level differences in both whole and regional cerebral volumes. Because the population size (86 patients) was smaller for the quantitative MR imaging–data analyses, the ethnicity variable was dropped from the analysis. The 25 children with SBM-H and upper-level lesions and 61 with lower-level lesions did not differ in age (mean age at neuroimaging examination 11.5 years), SES, ethnicity, or sex.

The overall pattern of findings (Table 4) indicated that children with upper-level lesions had smaller brain volumes than those with lower-level lesions ($F(1,84) = 6.56$, $p < 0.02$). The groups did not differ in terms of CSF ($F(1,85) < 1$). Children with upper-level lesions, however, had less gray matter ($F(1,84) = 6.86$, $p < 0.01$), and less white matter ($F(1,84) = 6.91$, $p < 0.01$).

To evaluate regional patterns, a multivariate ANOVA was conducted on interactions involving Lesion Level (Upper, Lower), Region (Precallosal, Pericallosal, Retrocallosal), Hemisphere (Right, Left), and Tissue (Gray, White, CSF). Patterns of regional thinning were similar between groups, with no significant interactions involving group and region. Both groups had lower volumes of gray and white matter, and more CSF in the retrocallosal and pericallosal regions but not in the precallosal region (Tissue–Region $F(4,8) = 190.1$, $p < 0.0001$). This pattern was more pronounced in the right hemisphere for gray matter ($F(4,81) = 24.9$, $p < 0.0001$). The highest level significant interaction involving group was the Lesion Level-Hemisphere-Tissue interaction ($F(2,83) = 4.28$, $p < 0.02$). Examining Lesion Level–Hemisphere interactions for each type of tissue revealed no differences involving CSF; however, the Lesion Level–Hemisphere interaction was significant for gray matter ($F(1,84) = 5.66$, $p < 0.02$). Compared with children with lower-level lesions, children with upper-

TABLE 5

Quantitative analysis of MR imaging studies for the cerebellum by upper- and lower-lesion groups

Location	Mean Volume ± SD (mm^3)	
	Upper Lesion (28 patients)	Lower Lesion (63 patients)
medial		
gray	12,216 ± 3927	14,491 ± 2791
white	2930 ± 1305	2930 ± 1305
CSF	1143 ± 698	1292 ± 578
lat		
gray*	55,708 ± 15,850	59,773 ± 12,508
white*	20,392 ± 5753	24,808 ± 5557
CSF*	2489 ± 893	3366 ± 1209
whole	94,880 ± 26,164	116,950 ± 18,759
gray*	67,902 ± 19,594	84,257 ± 14,839
white*	23,343 ± 6797	28,033 ± 6287
CSF*	3634 ± 1373	4658 ± 1661

* $p < 0.05$.

level lesions had less gray matter in both hemispheres, especially in the right. For white matter, the Lesion Level–Hemisphere interaction was not significant ($F(1,85) = 2.78$, $p < 0.10$); however, the Lesion Level–Tissue effect was significant ($F(2,83) = 1644.4$, $p < 0.0001$), indicating the absence of significant differences in CSF and significantly lower volumes of gray and white matter found in the whole-brain analysis ($p < 0.01$).

Cerebellum. Cerebellar volumes, overall and regional, were reduced in children with upper spinal lesions (Table 5). For the cerebellum, there were 91 children (mean age 11.5 years) who underwent neuroimaging studies, the results of which were adequate for segmentation. The upper- (28 patients) and lower-level (63 patients) lesion groups did not differ in age, sex, ethnicity, or SES. As Table 5 indicates, children with upper-level lesions had smaller cerebellar volumes than children with lower-level lesions ($F(1,89) = 20.85$, $p < 0.0001$). The group with upper-level lesions had greater CSF volumes ($F(1,89) = 8.14$, $p < 0.002$), less gray matter ($F(1,89) = 19.21$, $p < 0.0001$), and less white matter ($F(1,89) = 10.31$, $p < 0.002$). A Lesion Level-Region (Lateral, Medial)-Tissue multivariate ANOVA interaction was significant ($F(2,88) = 10.08$, $p < 0.0001$). Evaluating the Lesion Level–Region interactions for each tissue type revealed that for CSF, lesion-level groups differed significantly in lateral ($F(1,89) = 11.82$, $p < 0.0001$), but not medial regions ($F(1,89) = 1.13$, $p < 0.30$). For gray matter, group differences were significant for lateral ($F(1,89) = 20.71$, $p < 0.0001$), and medial regions ($F(1,89) = 9.92$, $p < 0.003$). For white matter, significant differences were apparent for lateral ($F(1,89) = 11.98$, $p < 0.0008$), but not medial ($F(1,89) = 1.23$, $p < 0.28$) regions.

Neurobehavioral Assessments

Neurobehavioral outcomes were generally poorer for children with upper spinal lesions. Table 6 summarizes patterns of neurobehavioral outcomes across domains by ethnicity and lesion level, showing whether upper spinal lesions were more strongly associated with outcome. It also summarizes MR imaging and medical findings.

Tables 7 through 9 provide data on IQs, academic skills, and functional outcome measures (means and SDs) for the group with SBM-H as a whole and by ethnicity and lesion level, calculated to provide a mean of 100 ± 15. The tables have been organized to show comparisons of lesion-level groups within ethnicity because lesion-level groups within ethnicity do not differ significantly in SES. In Table 6, an interaction of lesion level and ethnicity implies that different patterns will be apparent depending on ethnicity. A main effect of lesion level indicates that lesion-level groups differ regardless of ethnicity. Examining the data in Tables 7 through 9, it is apparent that on each variable showing a significant difference, children with SBM-H who have upper-level lesions or who are Hispanic performed more poorly than children who have lower-level lesions or who are not Hispanic. Interaction of ethnicity and lesion level were generally not apparent. Specific tests for interactions and main effects follow for each variable set.

TABLE 6

Summary of the patterns across domains, indicating where upper- and lower-lesion outcomes were different when comparisons were made with the entire upper-lesion subgroup

Lesion Level Deficit	Upper Lesions	Upper Lesions, Hispanic	Upper Lesions, non-Hispanic	No = Lesion Level Difference
clinical markers				
shunt revisions				+
eye disorders				+
seizures				+
ambulation	+			
non–rt handedness	+			
brain				
posterior fossa	+			
midbrain & pons	+			
cerebellum				+
corpus callosum (splenium)	+			
corpus callosum (other structures)				+
cerebral volume	+			
gray matter	+			
white matter	+			
CSF				+
cerebellar volume	+			
gray matter	+			
white matter	+			
CSF	+			
neurobehavioral outcome				
intelligence	+			
reading	+			
mathematics	+			
general adaptation	+			
motor	+			
personal living	+			
social communication		+		
community living		+		
mental retardation		+		
ADHD*				
learning disability		+		

* This row is blank because it was the only outcome where children with lower level lesions in the non-Hispanic subgroup had the poorest outcomes.

Intelligence. An Ethnicity–Lesion Level ANOVA for the Stanford-Binet composite score (based on all four subtests) revealed only main effects of Ethnicity ($F(1,257) = 15.02$,

TABLE 7

Summary of results for the Stanford-Binet Intelligence Test-4 by upper- and lower-lesion groups and comparisons of lesion-level groups within ethnicities to control for the effects of ethnicity

Stanford-Binet Intelligence Scale	Total	Hispanic		Non-Hispanic	
		Upper Lesions	Lower Lesions	Upper Lesions	Lower Lesions
composite					
no. of patients	258	31	52	47	130
mean ± SD	80.2 ± 16.9	66.3 ± 14.4	79.4 ± 15.0	79.0 ± 13.6	84.4 ± 17.6
Verbal					
no. of patients	258	31	52	47	128
mean ± SD	85.5 ± 19.5	66.5 ± 22.3	78.9 ± 18.4	86.3 ± 13.5	92.6 ± 17.1
Visual					
no. of patients	260	31	52	47	130
mean ± SD	85.4 ± 17.4	75.1 ± 13.0	88.9 ± 14.8	84.2 ± 17.2	87.0 ± 18.6

$p < 0.0001$), and Lesion Level ($F(1,257) = 16.57$, $p < 0.0001$). Children with SBM-H and upper-level lesions (73.9 ± 15.2) or who were Hispanic (74.5 ± 16) obtained lower scores on the composite IQ than those with lower level lesions (83 ± 17) or who were not Hispanic (82.9 ± 16.7). Figure 1 demonstrates a trend for larger differences between lesion-level groups in Hispanics than non-Hispanics, but the interaction did not meet the critical level of alpha adopted for this study ($p < 0.05$).

Does the relative superiority of verbal over nonverbal IQ occur similarly in SBM-H groups with upper and lower spinal lesions? Table 7 indicates that only the non-Hispanic lower-level lesion subgroup had higher Verbal than Visual scores, but this difference is not large enough to contribute to an interaction of Lesion Level and Ethnicity. Most studies demonstrating a relative Verbal IQ superiority exclude children with IQ scores in the range of mental retardation. An Ethnicity–Lesion Level–Subtest (Verbal, Visual) mixed-model ANOVA was completed for the Verbal Reasoning and Visual/Abstract Reasoning standard scores of the Stanford-Binet. The Ethnicity Score interaction ($F(1,254) = 28.92$, $p < 0.0001$) and the Ethnicity–Lesion Level interaction ($F(1,254) = 4.26$, $p < 0.04$), were significant. As Table 7 indicates, the Ethnicity–Score interaction reflects the opposite direction of Verbal and Visual scores in the Hispanic and non-Hispanic subgroups: regardless of lesion level, non-Hispanics obtained higher verbal than nonverbal scores ($t(254) = 2.59$, $p < 0.01$), whereas Hispanics showed higher nonverbal than verbal scores ($t(254) = 4.78$, $p < 0.0001$). The Ethnicity–Lesion Level interaction indicates that when the means were calculated across the Verbal and Visual scores (due to the absence of an interaction), Hispanics with upper-level lesions obtained lower scores than Hispanics with lower-level lesions ($t(254) = 3.89$, $p < 0.0001$); non-Hispanics did not show a significant effect of lesion level ($t(254) = 1.78$, $p < 0.08$), although a trend for lower scores in the upper-level group is apparent. Thus, the interaction reflects the larger differences between lesion level groups in the Hispanic cohort than the non-Hispanic subgroup, but lesion-level differences are apparent in both cohorts favoring the lower-level group.

Academic Skills. Academic competencies were weaker in children with either upper-level lesions or in those who were Hispanic. The Ethnicity score ($F(2,500) = 13.27$, $p < 0.0001$) and Lesion Level score ($F(2,500) = 3.99$, $p < 0.02$) interactions were significant. Examining each subtest separately revealed significant effects of Lesion Level ($t(500) = 2.54$, $p < 0.02$) and Ethnicity ($t(500) = 4.38$, $p < 0.0001$) for Basic Reading, indicating significantly lower word-reading skills in Hispanic and upper-level subgroups, but no interaction. A similar pattern was apparent for Passage Comprehension (Lesion Level: $t(500) = 3.75$, $p < 0.0002$; Ethnicity: $t(1,500) = 5.84$, $p < 0.0001$) and Calculations (Lesion Level: $t(500) = 4.22$, $p < 0.0001$; Ethnicity: $t(1,500) = 2.70$, $p < 0.008$). The data in Table 8 indicate a tendency for the difference in math scores to be larger between Hispanic children with upper- and lower-level le-

TABLE 8

Summary of results for academic skills, including means and SDs for WJR basic reading, passage comprehension, and calculations by upper- and lower-lesion groups

WJR Test Component	Total	Hispanic		Non-Hispanic	
		Upper Lesions	Lower Lesions	Upper Lesions	Lower Lesions
Basic Reading					
no. of patients	255	29	52	47	126
mean ± SD	90.1 ± 24.5	71.4 ± 28.5	84.9 ± 27.8	91.3 ± 22.6	96.1 ± 19.9
Passage Comprehension					
no. of patients	253	29	52	47	125
mean ± SD	87.6 ± 24.8	62.0 ± 26.5	81.2 ± 29.3	88.6 ± 19.6	95.9 ± 18.7
Calculations					
no. of patients	256	29	53	47	127
mean ± SD	76.4 ± 26.6	56.5 ± 30.8	79.9 ± 28.0	74.6 ± 23.9	80.3 ± 24.0

TABLE 9

*Summary of functional outcome measures for the SIB-R by upper- and lower-lesion group**

SIB-R Component	Total	Hispanic		Non-Hispanic	
		Upper Lesions	Lower Lesions	Upper Lesions	Lower Lesions
no. of patients	258	33	52	47	126
broad independence	57.8 ± 22.8	37.8 ± 22.4	58.3 ± 20.3	52.4 ± 18.4	64.9 ± 21.9
motor	31.5 ± 33.3	6.2 ± 13.0	36.1 ± 30.9	11.5 ± 22.1	43.7 ± 34.6
social	84.8 ± 23.6	65.8 ± 31.1	84.4 ± 21.5	87.8 ± 19.4	88.8 ± 21.3
personal living	51.1 ± 27.0	35.7 ± 29.6	49.8 ± 25.9	45.0 ± 23.9	57.9 ± 25.9
community living	64.0 ± 24.6	43.8 ± 29.9	62.9 ± 20.1	65.4 ± 23.4	69.3 ± 22.5

*Mean values are represented as the means ± SD.

sions than their non-Hispanic counterparts, although the essential finding is lower scores across academic domains for those with upper-level lesions or from the Hispanic subgroup.

Adaptive Behavior. An analysis of the composite score from the SIB-R revealed a parallel with other neurobehavioral evaluations in this study and indicated lower levels of adaptive behaviors (which make significant demands for motor and urological independence) in children with upper-level lesions and who are Hispanic (Fig. 1). The Ethnicity–Lesion Level ANOVA for the SIB-R composite yielded significant main effects of Ethnicity ($F(1,254) = 14.50$, $p < 0.002$) and Lesion Level ($F(1,254) = 35.35$, $p < 0.0001$), but no interaction ($F(1,254) = 1.32$, $p < 0.26$).

An evaluation of the four SIB-R domains (Community Living, Social Communication, Motor, Personal Living) yielded a significant Lesion Level-Ethnicity-Domain interaction ($F(3,762) = 4.48$, $p < 0.004$). Examining each subtest separately revealed significant Lesion Level–Ethnicity interactions for Social Communication ($F(1,257) = 7.75$, $p < 0.006$) and Community Living ($F(1,257) = 5.44$, $p < 0.03$), although not for the Motor and Personal Living Domains ($F(1,257) < 1$). The Social Communication domain yielded a significant lesion-level effect for Hispanics ($t(762) = 3.32$, $p < 0.0009$), but not for non-Hispanics ($t(764) < 1$). A similar interaction and pattern of differences was apparent on the Community Living Skills domain, with lesion-level effects in Hispanic ($t(762) = 3.41$, $p < 0.0007$) but not non-Hispanic ($t(762) < 1$) subgroups. These domains are sensitive to language-based skills. In the Motor domain lesion-level effects were apparent for the Hispanic cohort ($t(762) = 5.33$, $p < 0.0001$) and the non-Hispanic cohort ($t(726) = 7.49$, $p < 0.0001$). Children with upper lesions scored lower than children with lower-level lesions in their respective subgroups. A similar effect of lesion level was apparent for Personal Living in both the Hispanic ($t(762) = 2.52$, $p < 0.02$) and non-Hispanic ($t(762) = 3.01$, $p < 0.003$) subgroups. The interaction reflects greater effects of upper-level lesions on Motor and Personal Living Domains, both of which assess functional outcomes contingent in part on motor and urological independence.

Major Disorders of Development

Table 10 provides the percentages of children with upper- and lower-level lesions who met research-based criteria for mental retardation, ADHD, and learning disabilities involving word recognition and math. The ADHD and learning disabilities data reflect only those children not meeting criteria for mental retardation. Overall, 22% of children with SBM-H failed to meet criteria for one or more of these categories. There was no significant difference in the number of children with upper-level (17%) and lower-level lesions (24%) with no disability ($\chi^2 = 1.38$, df 1; $p < 0.25$; 262 patients), most likely because children with upper-level lesions are more likely to meet criteria for mental retardation.

Mental Retardation. Spinal lesion level was associated with mental retardation in the Hispanic, although not in the non-Hispanic, subgroup. There is controversy over definitions of mental retardation, such as the weighting of IQ and adaptive behavior quotients and where to put the cut point on both (IQ scores of 70 compared with 75). Using empirical criteria, we defined "mental retardation" as Stanford-Binet-4 composite and SIB-R scores two SDs below the mean of 100 (< 70), excluding the Motor score from the adaptive behavior composite.

Overall, 62 (23%) of those patients with SBM-H met criteria for mental retardation, a rate that was higher in those with upper-level lesions (28 patients or 34% of the upper-level group) than lower-level lesions (34 patients or 18% of the lower-level group; $\chi^2 = 8.06$, df 1; $p < 0.005$; 268 patients). This association was most apparent in the Hispanic subgroup with upper-level lesions, where 20 of the 34 children (59%) with upper-level lesions met criteria for mental retardation, compared with 12 of the 53 non-Hispanic children (23%) with lower-level lesions ($\chi^2 = 11.66$, df 1; $p < 0.0006$; 87 patients). This association of lesion level and mental retardation was not apparent in the non-Hispanic cohort, in which approximately 17% of those patients with either upper- or lower-level lesions met the criteria.

Attention Deficit Hyperactivity Disorder. In contrast to the results for mental retardation, spinal lesion level was predictive of attention disorders in the non-Hispanic group, although not in the Hispanic group. Children were divided into putative ADHD subtypes by using statistical cutoff scores based on norms for the average response per item for the parent-based Swanson, Nolan, Achenbach, Pelham-IV Inattention and Hyperactivity/Impulsivity Scales.[22] Table 10 shows that 34% of those with SBM-H and no evidence of mental retardation met criteria for ADHD, with most (26% of the entire nonmentally retarded cohort) representing the Predominantly Inattentive Type. This means that while problems with attention are common in children with SBM-H, they are relatively specific in form; however, ADHD subtypes (combining the Combined and Hyperac-

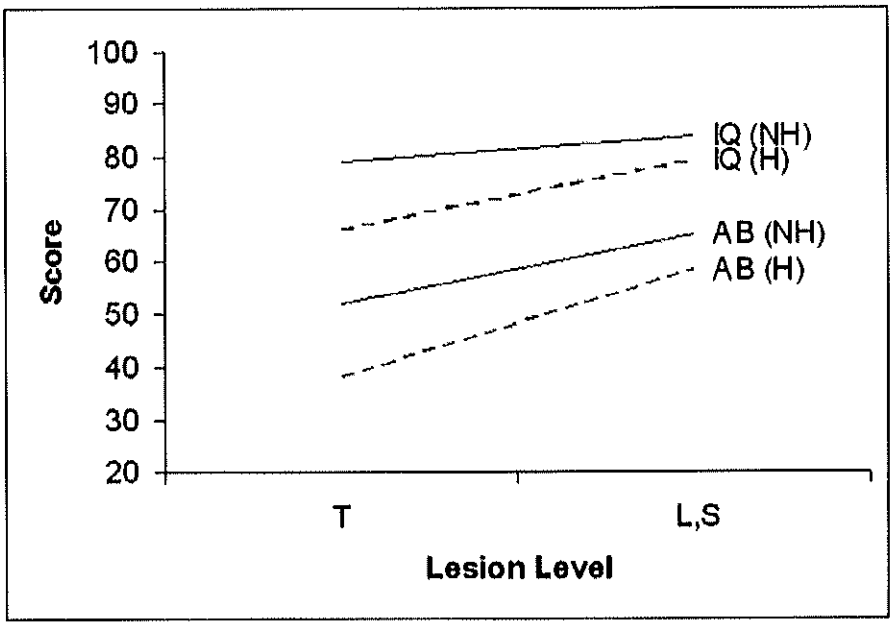

FIG. 1. Graph demonstrating IQ and adaptive behavior (AB) outcomes by lesion level (thoracic [T] compared with lumbar [L] and sacral [S]) and ethnicity (Hispanic [H] or non-Hispanic [NH]). Children with upper-level lesions show poorer outcomes in both domains within each ethnicity, which controls for differences in SES.

tive–Impulsive Types into one group due to small subgroup sizes) were not significantly associated with lesion level ($\chi^2 = 5.29$, df 2; $p < 0.08$; 206 patients). Collapsing across subtypes shows that 34% (51 patients) of those with lower-level lesions and 35% (19 patients) of those with upper-level lesions met criteria for one of the ADHD subgroups. The difference is that children with upper-level lesions are rarely rated as hyperactive–impulsive, which is not surprising considering that most are nonambulatory. Unlike mental retardation, there was no significant association of ADHD status and lesion level in the Hispanic subgroup ($\chi^2 = 3.48$, df 2; $p < 0.18$; 55 patients); the association was significant in the non-Hispanic subgroup ($\chi^2 = 8.48$, df 2; $p < 0.02$; 151 patients).

Learning Disabilities. Based on our definition, learning disabilities were not strongly related to spinal lesion level. We used low achievement cut points (25th percentile and below), which are reliable markers for learning disabilities in children who do not meet criteria for mental retardation,[21] to identify learning disabilities in reading (word recognition–WJR Word ID) and math (WJR Calculations). Table 10 shows that about 58% of the group that did not meet criteria for mental retardation and had adequate assessment data (204 patients) met criteria for learning disabilities.

In reviewing the data for those who met criteria for reading and math forms of learning disabilities (ignoring overlap), problems involving reading (word recognition) occurred in only 2% of the group. Math problems were more frequent, representing 29% of the group with SBM-H. When overlap was examined, 26% had evidence of academic difficulties in both reading and math. Altogether, more than 50% of children with SBM-H and no evidence of mental retardation displayed math difficulties. There was no significant association of learning disabilities status (adding the small number of reading disabilities to the math and reading impaired group) and lesion level ($\chi^2 = 4.27$, df 2; $p < 0.12$; 204 patients), with approximately 54% of those patients with lower-level lesions and 68% of those with upper-level lesions having evidence of learning disabilities. Within ethnicities, there was an association of learning disabilities status and lesion level in the Hispanic subgroup ($\chi^2 = 7.24$, df 2; $p < 0.03$; 54 patients) but not the non-Hispanic subgroup ($\chi^2 = 1.36$, df 2; $p < 0.51$; 150 patients). Although the sample size is small, Hispanic children with upper-level lesions were more likely to display reading and math disabilities than other forms of learning disabilities (Table 10).

Discussion

We considered two primary questions concerning the effects of lesion level on the development of the brain in patients with SBM-H and on neurobehavioral outcomes. Our findings indicate that children with upper- and lower-level spinal lesions differ in terms of both anomalous brain development and behavioral outcomes; upper-level lesions were associated with significantly more compromise than were lower lesions. Virtually all the comparisons (Table 6) indicate that, regardless of ethnicity, children with upper-level lesions have poorer outcomes.

Anomalous Brain Development and Lesion Level

Spinal lesion level constitutes a visible source of phenotypic diversity in SBM-H, explained in part by genetic factors.[26] Our findings indicate that the genetic variability expressed as spinal lesion level is also related to broader,

nonvisible phenotypic diversity in the form of severity of regional anomalous brain development. Children with upper-level lesions had more anomalous brain development in the midbrain, tectum, and corpus callosum than those with lower-level lesions. Moreover, quantitative analysis of the cerebrum and cerebellum revealed that both were smaller in children with upper-level lesions. For the cerebrum, the differences reflected less gray and white matter in those with upper-level defects with no regional specificity other than a tendency to be more reduced in the right than left hemispheres.

The groups were relatively similar in qualitative cerebellar anomalies, but they differed in the size of the posterior fossa and the presence of anomalies of the midbrain and tectum. There were, however, quantitative differences in the lateral cerebellum, which is an indication that neocerebellar functions may be more compromised in those with upper lesions. Children with upper-level lesions were also more likely to suffer from dysgenesis of the splenium. The greater association of splenial dysgenesis with upper-level lesions may indicate more severe disruption of neuroembryogenesis because the splenium develops later than the body and genu.[2]

The differences between lesion-level groups do not appear to represent the effects of hydrocephalus; not only were the lesion-level groups similar in the number of shunt revisions and infections, they did not differ in patterns of regional thinning or CSF volumes from MR imaging–based quantitative analyses. Furthermore, lesion-level groups did not differ in the perinatal variables that are potentially related to outcome. There are other factors that could contribute to poorer outcomes that were not assessed in this study, such as initial ventriculomegaly, ventriculitis, or the timing of shunt infections in newborns; however, the overall incidence of infections is low in our contemporary cohort. A prospective study would be needed to evaluate these possibilities.

Neurobehavioral Outcomes, Anomalous Brain Development, and Lesion Level

Upper spinal lesions were also associated with greater impairment in intellectual, academic, and adaptive behavior, and in a higher rate of mixed handedness. Previous studies have attempted to attribute, at least in part, the associations of upper-level defects and poorer scores on measures of intelligence to the location of the spinal lesion, reflecting the well-known link of motor outcome and lesion level.[28] Our results indicate that the lesion-level effect occurs more broadly and includes academic function, adaptive behavior, and those intellectual functions in which there is no significant requirement for motor output.

Other aspects of the performance patterns across the lesion-level subgroups are noteworthy. Lesion level has a greater impact on motor than cognitive function, although both domains are affected (Fig. 1). Pervasive impairments in intellectual functions occur primarily when the upper-level defect occurs in association with Hispanic ethnicity, a factor that is also associated with a higher number of economically disadvantaged families. In contrast, non-Hispanic children with lower-level lesions have higher verbal than nonverbal IQ, better word recognition than math performance, and stronger adaptive behavior in areas involving social communication. This pattern is consistent with common clinical descriptions associated with SBM-H, but is more apparent in non-Hispanic children with lower-level lesions who predominate in most studies of outcomes in SBM-H. Previous studies of SBM-H have not included large numbers of Hispanic children.

Role of Ethnicity, Cultural Factors, and SES

The Hispanic patients, predominantly Mexican–American children in this study, were not only more likely to harbor upper-level lesions, they were also more economically disadvantaged. Because most Hispanics in this study were economically disadvantaged, it may seem difficult to disentangle the effects of ethnicity and SES; however, the critical comparison is between lesion-level groups within Hispanic and non-Hispanic cohorts, where lesion-level groups are comparable in SES. In Table 6, most measures show the effects of lesion level and of ethnicity, but no interactions; therefore, this pattern cannot simply reflect the interactive effects of SES and the greater incidence of anomalous brain development associated with lesion level because the differences are observed within the comparably disadvantaged Hispanic cohort. There may be a relationship between the environmental factors related to SES and eth-

TABLE 10

Summary of research-based definitions of mental retardation, ADHD, and learning disabilities by upper- and lower-lesion groups

Disability	Total (%)	Hispanic (%)		Non-Hispanic (%)	
		Upper Lesions	Lower Lesions	Upper Lesions	Lower Lesions
no. of patients	268	34	53	48	133
no disability (262 patients)	59 (22)	3 (5)	14 (25)	13 (25)	29 (23)
mental retardation	62 (23)	20 (59)	12 (23)	8 (17)	22 (17)
ADHD (IQ>70; 206 patients)					
no ADHD	136 (66)	13 (93)	30 (73)	22 (55)	71 (64)
inattentive	53 (26)	0 (0)	7 (17)	18 (45)	28 (25)
impulsive	4 (2)	1 (7)	1 (2)	0 (0)	2 (2)
combined	13 (6)	0 (0)	3 (7)	0 (0)	10 (9)
no learning disability (204 patients)	86 (42)	1 (3)	19 (46)	16 (40)	50 (46)
only reading	5 (3)	0 (0)	1 (2)	0 (0)	4 (4)
only math	60 (29)	5 (39)	6 (15)	16 (40)	33 (30)
reading & math	53 (26)	7 (54)	15 (37)	8 (20)	23 (21)

nicity that make it more likely that economically disadvantaged and/or Hispanic cohorts experienced more frequent upper-level defects. Dietary factors may be especially critical as a factor related to the heritability of SBM-H and lesion level.[26] The effects of poverty on language and cognitive development are well known and are reflected in the only two measures that indicate interactions of ethnicity and lesion level (Social Communication and Community Living); nevertheless, poverty and SES do not account for the overall pattern of effects of lesion level in this study.

Cultural and religious factors do not adequately explain the relationship between lesion level and ethnicity observed in this study, including the higher rate of upper-level defects in the Hispanic group, who are predominantly Catholic. Epidemiological research has found that the highest pregnancy termination rates occur in women who are 18 to 29 years old, unmarried, African American or Hispanic, or economically disadvantaged[12] and that Hispanic women are most likely to have undergone an abortion compared with ethnic subgroups of US-born non-Hispanic women.[17] Regardless of ethnicity and religious preferences, parents typically do not terminate fetuses with nonlethal defects.[27]

Implications for Practice

The common perception of SBM-H is that it is an orthopedic disorder that results in difficulties with ambulation and bladder function. In fact, the neural component of SBM-H produces consistent difficulties in adaptive domains that extend beyond intelligence. Children with SBM-H have a high rate of learning disabilites, particularly in math. In addition, attention problems are common and usually need to be treated, given the significant impact of such problems on functioning at home and school. Physicians following children with SBM-H need to be aware of these types of problems and be prepared to identify and treat them as they arise. In discussing the long-term outcomes of SBM-H with parents, particular attention should be devoted to learning and attention difficulties, and to the probable explanation for these difficulties, which involves anomalous brain development associated with SBM-H. This study provides guidelines for physicians concerning the factors (lesion level, ethnicity, SES) that increase the risk for more adverse outcomes.

Conclusions

A higher level of spinal lesion in SBM-H is a marker for more severe anomalous brain development, which is associated with poorer neurobehavioral outcomes. Lesion level provides a link for genetic, neural, and cognitive variability. Such variability indicates that neurobehavioral outcomes involving learning and attention need to be carefully monitored and treated when necessary. Genetic variability influences neuroembryological development, which leads to variations that disrupt the normal interconnected development of both spine and brain; the higher the lesion, the more malformed the brain, and the more malformed the brain, the poorer the neurobehavioral outcome.

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