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Peripersonal spatial attention in children with spina bifida: Associations between horizontal and vertical line bisection and congenital malformations of the corpus callosum, midbrain, and posterior cortex

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Abstract

Horizontal and vertical line bisection was studied in 129 children and adolescents between 8 and 19 years of age, one group ($n = 32$) of typically developing controls and one group ($n = 97$) with spina bifida (SBM), a neurodevelopmental disorder associated with dysmorphology of the corpus callosum, posterior cortex, and midbrain. For each participant, structural brain MRIs were analyzed qualitatively to identify beaking of the midbrain tectum and corpus callosum agenesis and hypoplasia and quantitatively by segmentation and volumetric analyses of regional cortical white and gray matter. Each group showed the line length effect, whereby greater estimation errors are made with longer lines. The group with SBM differed from controls in terms of both accuracy and variability of line bisection. Children with SBM showed pseudoneglect, attending more than controls to left hemispace. The extent of rightward bisection bias was unrelated to right posterior brain volumes, although an intact corpus callosum during development moderated and normalized the exaggerated leftward line bisection bias. More children with SBM than controls attended to inferior hemispace. A normal midbrain and greater posterior cortex volume during development moderated and normalized the downward bias. Children with SBM showed more intra-subject variability than controls. Line bisection in children with SBM reflects three deficits: an exaggerated attentional bias to left hemispace, an abnormal attentional bias to inferior hemispace; and a larger zone of subjective uncertainty in bisection judgments.

Keywords: Neglect; MRI volumetrics; Midbrain; Corpus callosum; Posterior cortex

1. Introduction

The brain codes visual information with respect to different spatial frames of reference, such as the plane of

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the viewer's gaze (Shelton, Bowers, & Heilman, 1990) and viewer-centered eye, head-, torso-, shoulder-, arm- or hand-centered coordinates (Karnath, Ferber, & Himmelbach, 2001; Vallar, 1998). Peripersonal space is the part of egocentric space, within arm's reach, that is used for activities like picking up objects, drawing, or bisecting lines (Halligan, Fink, Marshall, & Vallar, 2003).

Line bisections reveal attentional biases in peripersonal space. Normal right-handed individuals bisect horizontal lines slightly to the left of center, a phenomenon termed pseudoneglect (Bowers & Heilman, 1980). This bisection bias is especially pronounced when right-handers use the left hand (Brodie & Pettigrew, 1996; Hausmann, Ergun, Yazgan, & Güntürkün, 2002; Jewell & McCourt, 2000), or bisect vertical lines above the true midpoint. The normal attentional bias is toward left and superior hemispace. Bisection error is positively correlated with line length (Halligan & Marshall, 1988) and the line length effect is such that longer lines produce greater neglect. Accuracy and variability of line bisection varies with age and presence of brain damage.

Normal adults show a range of results on line bisection tasks, from no lateralized bias, a small rightward bias, to equal numbers of leftward and rightward displacements (Bowers & Heilman, 1980; Bradshaw, Nettleton, Hathan, & Wilson, 1985; Halligan, Manning, & Marshall, 1990; Manning, Halligan, & Marshall, 1990). Some (but not all) authors have reported decreased performance accuracy in normal individuals with increasing line length (Heilman, Bowers, & Watson, 1984; Werth & Pöppel, 1988).

Age-related changes in the performance of line bisection tasks have been reported in typically developing children (e.g., Dellatolas, Coutin, & DeAgostini, 1996; van Vugt, Fransen, Creten, & Paquier, 2000). Young children show a rightward bias; with age, they become more accurate and increasingly show displacement of the subjective midpoint to the left (Hausmann, Waldie, & Corballis, 2003). The age-related shift from rightward to leftward bias in line bisection has been related to a shift from contralateral to right hemisphere control, which may reflect corpus callosum maturation (Hausmann et al., 2003).

Lack of awareness of stimuli, objects, persons, or events, termed neglect (Heilman, Watson, & Valenstein, 2002), has been most often studied in the horizontal plane (Vallar, 1998). After unilateral cortical injury, some individuals show hemispatial neglect, a profound lack of awareness of the contralesional half of space whereby they fail to identify or respond to information on the side of space contralateral to the lesion, even in the absence of contralesional peripheral sensory or motor loss. In bisecting horizontal lines, for example, they misplace their bisections toward the right, ipsilesional, side of the line. Hemispatial neglect concerns spatial attention, because the line dividing the well-attended and poorly-attended features of the object or the visual array ranges through the center of the object of regard and affects the half of the object to the left of its intrinsic midline. Not only is the rightward displacement greater in subjects with neglect than in controls, but the standard deviation of bisection displacements is also much larger (Marshall & Halligan, 1989). Neglect patients on some trials have normal reaction times in their neglected field, with their performance decrements reflecting an inability to detect and respond consistently (Anderson, Mennemeier, & Chatterjee, 2000).

Neglect involves a distributed neural system including the posterior parietal cortex, together with subcortical nuclei in the superior colliculus and pulvinar (Mesulam, 2002; Posner & Peterson, 1990; Vallar, 2001). Evidence for the role of the posterior parietal cortex, especially on the right, in line bisection (Mennemeier, Wertman, & Heilman, 1992) comes from studies of brain activation with fMRI (Fink et al., 2000; Fink, Marshall, Weiss, & Zilles, 2001), magnetic source imaging (Billingsley, Simos, Sarkari, Fletcher, & Papanicolaou, 2004), and repetitive transcranial magnetic stimulation of the posterior parietal cortex (Bjoertomt, Cowey, & Walsh, 2002).

Damage to the adult corpus callosum has also been implicated in hemispatial neglect. A rightward bias with the right hand has been observed after callosal infarct (Heilman et al., 1984; Kashiwagi, Kashiwagi, Nishikawa, Tanabe, & Okuda, 1990), or section of the forebrain commissures (Corballis, 1995). Split-callosum patients neglect left personal space during right-handed gestures (Lausberg, Kita, Zaidel, & Ptito, 2003).

Altitudinal neglect, or neglect in the vertical plane, has been less commonly studied than has horizontal neglect. Shelton et al. (1990) report a patient with bilateral temporal lesions who neglected upper vertical space. Rapcsak, Cimino, and Heilman (1988) reported inattention to the vertical axis of extrapersonal space in a patient with Bálint's syndrome secondary to bilateral parietal-occipital infarction (Harvey & Milner, 1995: paralysis of voluntary eye movements, problems judging the relative positions of objects, and optic ataxia), and it was concluded that bilateral parietal damage causes spatial attention deficits in the vertical plane.

Sparse information exists on neglect in children with brain disorders. Hemispatial neglect has been observed after pre/perinatal lateralized brain lesions in preschoolers (although not in children with cerebral palsy; Katz, Cermak, & Shamir, 1998), who removed objects from the side of the board ipsilateral to the lesion before removing them from the side contralateral to the lesion, unlike controls, who showed no lateral preference (Trauner, 2003). A child with left hemisphere subdural hematoma after birth showed long-standing right-sided hemispatial neglect (Johnston & Shapiro, 1986). A preschool child with right-sided brain contusions and clinical left hemiparesis following a head injury showed left hemispatial neglect that had resolved by 6 months post-injury (Thompson, Ewing-Cobbs, Fletcher, Miner, & Levin, 1991). Ferro and Martins (1990) and Ferro, Martins, and Tavora (1984) reported six 5- to 11-year-old children with right hemisphere lesions who developed hemispatial neglect, as evidenced by omission of left-sided stimuli in cancellation tasks, rightward deviation on line bisection tasks, failure to respond to the left sides of words and sentences, and visual and motor extinction. Hemispatial neglect originating early in development has been described in one case with no evidence of structural brain injury (Manly, Robertson, & Verity, 1997). What has not been analyzed in these case studies and case series are performance variability, vertical plane asymmetries, and correlations with brain structure.

To understand the neural basis of developmental attentional asymmetries, it would be informative to study a condition with explicit compromise of one or more of the neural substrates associated with various forms of neglect identified in the mature brain. Spina bifida is a neural tube defect associated with congenital malformations of the posterior cortex, corpus callosum, and midbrain, three regions that have been implicated in neglect in the mature brain. Spina bifida meningocyelocele (SBM) is the most common and severe form of the condition. SBM is associated with profound disturbances of brain development that include abnormal formation and maturation of the posterior cortex and white matter, midbrain, corpus callosum, and cerebellum (Dennis et al., 1981, 2004; Fletcher, Dennis & Northrup, 2000; Hannay, 2000). The posterior cortex is thinner than the anterior cortex. Although the thinning is clearly bilateral, it is somewhat more pronounced in the gray matter on the right side (Fletcher et al., 2005). Children with SBM exhibit midbrain damage, most commonly in the form of beaking of the tectum, with tectal beaking being much more common in children with upper than with lower spinal lesions (Fletcher et al., 2004). Most children with SBM develop hydrocephalus, which involves enlarged cerebral ventricles and produces a range of primary and secondary effects on the brain (del Bigio, 1993; Fletcher et al., 2000). The corpus callosum is compromised by a primary agenesis of callosal structures during embryogenesis and by a secondary hypoplasia related to increased intracranial pressure and hydrocephalus.

We compared line bisection in typically developing children and children with SBM. The first goal was to compare line bisection with respect to group (SBM versus typically developing age peers), plane (horizontal versus vertical), and line length. We hypothesized that children with SBM would be less accurate and more variable than typically developing children in bisecting horizontal and vertical lines, but that both groups would show a line length effect involving greater bisection error with longer lines. The second goal was to relate line bisection to MRI-identified brain abnormalities. For vertical line bisection, we hypothesized a relation between accuracy and congenital malformations of the midbrain in the form of tectal beaking, based on the literature showing vertical neglect in adults with bilateral temporal or parietal lesions (Rapcsak et al., 1988; Shelton et al., 1990). For horizontal line bisection, we entertained two competing hypotheses. The first was that children with SBM would show left hemineglect, like both adults with right posterior lesions and typically developing younger children, and that the extent of hemineglect would be related to extent of posterior right hemisphere volume; part of the rationale for this hypothesis was that children with SBM show bilateral posterior cortical thinning that is somewhat more pronounced in the gray matter on the right side (Fletcher et al., 2005). The second hypothesis was that children with SBM would show pseudoneglect, the leftward bisection bias exhibited by typically developing older children and normal adults, and that the extent of pseudoneglect would be related to the integrity of the corpus callosum.

2. Methods

2.1. Participants

Participants were 129 children and adolescents between 8 and 19 years of age. The group with SBM ($N = 97$) had been identified at birth, and treated shortly thereafter with a shunt to control hydrocephalus. Twenty-seven of the children with SBM had no shunt revision, 31 had 1 revision, 25 had 2–4 revisions, 12 had 5–9 revisions, and 2 children had more than 10 shunt revisions. The control group comprised typically developing, age-matched controls ($N = 32$). All participants had IQ scores within two standard deviations (≥ 70) of the population mean of 100 on the Stanford–Binet Test of Intelligence-IV (Thorndike, Hagen, & Sattler, 1986). The mean IQ was 87.9 ± 12.2 for the group with SBM, and 107.8 ± 10.1 for the control group. The sample included 96 Caucasian, 19 Hispanic, 6 Asian, 5 African American, and 3 children classified as Other. Individuals were excluded from participation if they had neurological disorders unrelated to SBM, severe psychiatric disorder, uncontrolled seizure disorder, uncorrected sensory disorder, or inability to control the upper limbs. Participants in each group were recruited in clinics in Toronto ($N = 80$) and Houston ($N = 49$). No child recruited for the study had been identified with a visual field defect.

2.2. Brain imaging procedures

Of the 129 children who completed the line bisection task, 113 (86 with SBM, 27 controls) had a qualitative analysis of their MRI scans, and 58 (39 with SBM, 19 controls) had structural magnetic resonance (MR) brain scans that were artefact-free and that could be quantified in a manner suitable for segmentation for quantitative analysis.

2.2.1. Image acquisition

Three sets of images were acquired, including a T1-weighted coronal series for assessment of white and gray matter and a T2-weighted coronal series for assessment of CSF. To co-register and position normalize the scans, external fiducial markers were placed on the nasion, and external meatus. An initial series (spin echo T1-weighted sagittal localizer, FOV 24, TR 500, TE 14, 256×192 matrix, 3 mm skip 0.3, with two repetitions) was used for anatomical landmark identification. One whole-brain coronal series consisted of a fast spin-echo Proton density and heavily T2-weighted images. (FOV 20, TR 4000, TE1 15, TE2 112, 256 × 192 matrix, with two repetitions). This series was obtained in contiguous 1.5 mm slices across the whole brain. Another whole-brain coronal series consisted of a 3D-spoiled grass (3D SPGR) gradient echo contiguous 1.5 mm coronal series (TR 21, TE 4, Flip angle 35 degrees, 124 locations, 256 × 192 matrix, one repetition).

2.2.2. *Image preprocessing*

Prior to tissue segmentation, each slice series was stored in a single volume file and the pixel grayscale limits were expanded by increasing the gain within the 0–255 (byte data) range. Each sequence volume was then reformatted so that voxel dimensions were isotropic. The T1- and T2-weighted reformatted volumes were aligned with each other through the use of the fiducial markers. Rigid-body translation and rotation routines programmed in IDL software were used for the realignment procedure itself, which was manually and visually checked at each step. Each volume was placed within a 256 cubic voxel bounding box with the fiducial marker cross point placed at the center of the volume. The two reformatted and aligned volumes were filtered using a non-linear anisotropic diffusion filter, which increased the overall signal-to-noise ratio of each volume an average of 100% (Gerig, Kubler, Kikinis, & Jolesz, 1992). This automated non-linear filter served to sharpen areas of high intensity gradient (boundaries) and to smooth regions of low-intensity gradient within tissue borders.

2.2.3. *Automatic segmentation*

The method used a fully automated fuzzy cluster analysis that obtained whole brain and regional brain tissue and CSF volumes (Brandt, Bohan, Kramer, & Fletcher, 1994; Brandt et al., 1996). The T1-weighted scan volume, which provides superior white-gray contrast compared to the T2-weighted scan, was used to obtain white and gray matter tissue volumes. The T2-weighted scan was fuzzy clustered separately from the T1-weighted scan to extract CSF volumes, and this was used to adjust the white and gray matter volume measures obtained from the T1-weighted volume. Solution images were derived from the final computed fuzzy cluster membership values for each voxel, which could then be viewed graphically on screen and compared with the actual scan images.

For the *quantitative* analyses, separate tissue volumes (white matter, gray matter, CSF) were obtained for various cortical regions. For the present study, the regions of interest involved a region roughly representative of the posterior temporal, parietal, and occipital cortex. As the brains of children are grossly dysmorphic, we relied on methods based on a division of the corpus callosum into a precallosal region, pericallosal (including the corpus callosum) and retrocallosal region for each hemisphere (Filipek et al., 1992). In this categorization, the pericallosal region subtends the coronal brain volume extending from the most anterior to the most posterior aspect of the corpus callosum. The precallosal region extends fully frontally from the pericallosal region and the retrocallosal region extends fully posteriorly from the pericallosal region. For the present study, the regions of interest involved the retrocallosal region, roughly representative of the posterior temporal, parietal, and occipital cortex. For individuals where the posterior aspect of the corpus callosum was missing, a formula was developed based on the distance from the anterior aspect to the farthest segment of posterior brain in normal individuals and subdivided to represent the peri and retrocallosal regions. In both hemispheres, the percent retrocallosal volumes were calculated as the absolute total retrocallosal volumes divided by the absolute hemispheric retrocallosal volumes.

For the *qualitative* analyses, two pediatric neuroradiologists coded two brain regions from the MRI scans, the corpus callosum and the tectum. Few children with SBM have a normal corpus callosum, but the spectrum of abnormalities is broad. The corpus callosum coding involved presence, absence, or hypoplasia of the body, splenium, rostrum, and genu. Individual children were assigned to one of three groups: In the *No/Mild Callosum Deficit* group, all or most of the corpus callosum, including the body and splenium, was present and intact; at least one of the mid-posterior regions (the body and splenium) was present, with the second being either present or hypoplastic; and at least one of the anterior portions (the rostrum and genu) was present. In the *Callosum Hypoplastic* group, the splenium was hypoplastic and the body was either hypoplastic or present; the rostrum was absent, hypoplastic, or present; and the genu was hypoplastic or present. In the *Callosum Agenesis* group, the splenium was absent; the body was either absent or hypoplastic; and the rostrum and genu was either present, absent, or hypoplastic. These groupings are ad hoc, but designed to clearly differentiate those with corpus callosums that are mildly abnormal, those that are predominantly hypoplastic, and those characterized primarily by dysgenesis of the posterior aspect, where connectivity of the two hemispheres for spatial attention should be maximal. Fig. 1 shows mid-sagittal sections from MRI scans of children in the three groupings.

Tectal beaking was coded by the neuroradiologists as either present or absent. Fig. 2 shows a normal tectum in a control child and in a child with SBM, as well as an example of tectal beaking in a child with SBM.

Individuals with SBM have lesions at various levels of the spinal cord, which provides a source of principled, within-group variability. The level of spinal lesion is related to a mutation in methylenetetrahydrofolate reductase (MTHFR), the enzyme that regulates folate-dependent remethylation of homocysteine (van der Put, van Straaten, Trijbels, & Blom, 2001). The incidence of the MTHFR mutation is higher in mothers of children with upper spinal lesions than in typically developing controls or in mothers of children with lower spinal lesions (Volcik, Blanton, & Northrup, 2001).

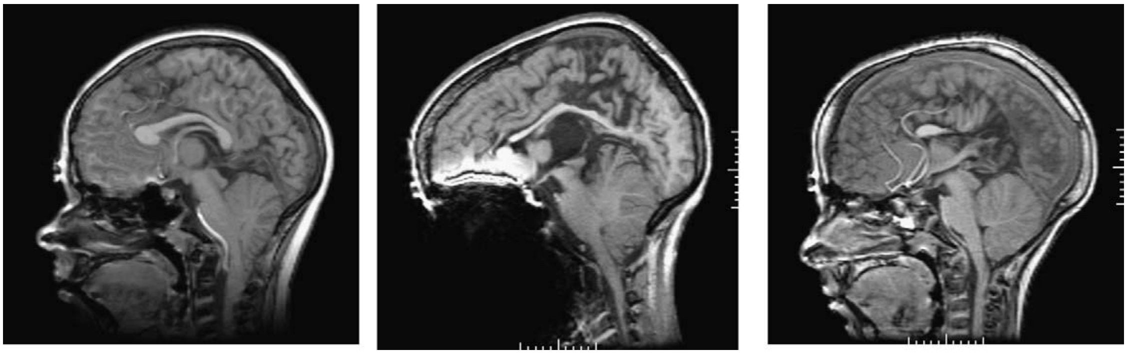

Fig. 1. Corpus callosum in mid-sagittal structural MRI slices of children with SBM. Intact corpus callosum (left), corpus callosum hypoplasia (middle), and corpus callosum agenesis (right).

The level of spinal cord lesion is of interest in the study of line bisection because it demarcates more or less severe dysmorphologies of the midbrain and corpus callosum (Fletcher et al., 2004). Participants with SBM were divided into upper spinal lesion (T12 and higher) and lower spinal lesion (L1 and lower) groups, according to current taxonomies (Fletcher et al., 2004; Park, Stewart, Khoury, & Mulinare, 1992). Children in this study with upper spinal lesions are more likely than those with lower lesions to have tectal beaking (95.2% versus 79.4%) and partial callosal agenesis (47.6% versus 27%), although the two groups are similar with respect to the frequency of a basically intact corpus callosum (19% versus 17.5%), and corpus callosum hypoplasia (33.3% versus 55.6%). All controls had a normal tectum and corpus callosum.

2.3. *Tasks*

2.3.1. *Line bisection task*

The line bisection task required the children to bisect a series of horizontal and vertical lines by estimating and then marking the midpoint of the lines in free vision. The pages with the lines were presented one at a time directly in front of the children's mid-sagittal planes, to ensure that the two main coordinate reference frames, the trunk and the head, were aligned, and also that judgment of one line was independent of judgment of any other.

Materials consisted of 16 letter-sized sheets of white paper with one black line drawn in the center of the page. Line lengths were 50, 100, 150, and 200 mm (4 trials of each length). Each participant received one of six randomly assigned line length orders. Each sheet of paper was presented twice in front of the subject's midline; one set of lines was oriented horizontally, as landscapes (28 cm × 22 cm), and the other set was oriented vertically, as portraits (22 cm × 28 cm). Order of plane was counterbalanced across subjects. The examiner identified the orientation of the papers. Participants were not allowed to turn or reposition the paper. They were given the following instructions. "I want you to take your pencil and draw a little line that cuts this line in half. Put it as close to the center of the line as you can. Do it now. [Practice item.] Good. Now I want you to do that with some more lines." The difference between the participant's bisected line length and the actual bisected line length was recorded. Measures for each participant were average deviations from the true midpoint, calculated separately for each line length.

2.3.2. *Handedness*

Like other brain-injured populations, children with spina bifida are more likely to be weakly right-handed (up 30%) or left-handed (10–20%). Handedness was assessed with an inventory consisting of eight items that the participant is asked to *perform*, often using objects, e.g., "show me how you write," and the subject is handed a pencil. Each item is

Fig. 2. Tectal beaking in mid-sagittal structural MRI slices. Control participant with normal tectum (left), SBM participant with normal tectum (middle), and SBM participant with beaked tectum (right). Arrows point to midbrain/tectal area.

scored on a zero-one basis, with one indicating use of the right hand. Individuals with a score of 0–1 are considered strongly left-handed, while individuals with a score of 7–8 are considered strongly right-handed. Scores in between are considered to indicate “weak” handedness depending on the direction. Children used their preferred hand, whether right or left, to perform the line bisections.

3. Results

The line bisection group data are shown in Fig. 3 (deviation from the horizontal midpoint as a function of line length and group) and Fig. 4 (deviation from the vertical midpoint as a function of line length and group). Comparisons of absolute deviations from the midpoint between groups were made using group (SBM, CON) × line (50, 100, 150, 200 mm) × plane (horizontal, vertical) repeated measures analysis of variance. Analyses of significant effects were conducted using Bonferroni-corrected comparisons. The repeated measures ANOVA revealed a significant line × group interaction, $F(3, 125) = 2.77$, $p = 0.04$, and a significant plane × group interaction $F(1, 127) = 8.37$, $p = 0.004$. In addressing the two interactions, we examined the effect of line length separately for horizontal and vertical lines, recognizing that the effect of line length may be comparable for both line directions because the 3-way interaction was not statistically significant.

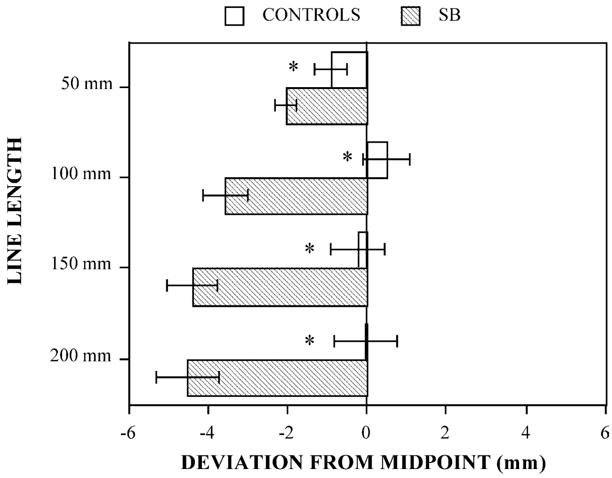

Fig. 3. Line bisection estimation errors in millimeters (mean ± S.E.M.) for horizontal lines. Negative numbers represent average midpoint estimates to the left of the actual value. (*) Denotes significant difference between children with SBM and controls.

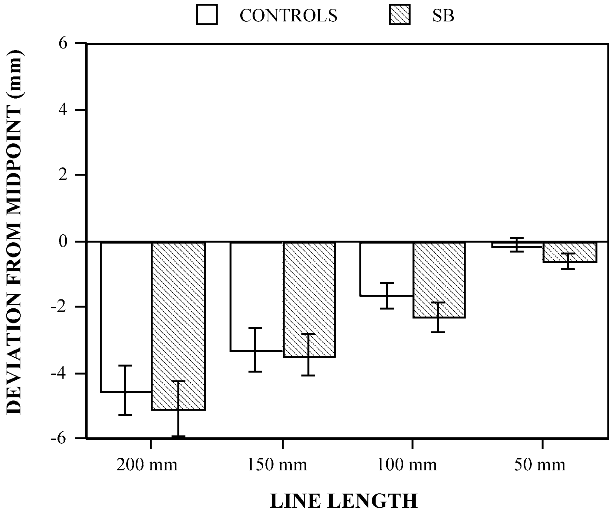

Fig. 4. Line bisection estimation errors in millimeters (mean ± S.E.M.) for vertical lines. Negative numbers represent average midpoint estimates below the actual value.

3.1. Horizontal line bisection

Children with SBM were less accurate than controls in horizontal line bisection (group × line repeated measures ANOVA, main effect of group: $F(1, 127) = 14.99$, $p = 0.001$). Controls made only very small estimation errors in bisecting horizontal lines of any length. Children with SBM made significantly larger estimation errors than controls in the horizontal plane. Unlike controls, who had a high level of accuracy, children with SBM exhibited increasing deviations from the true midline on the line bisection task as line length increased (group × line interaction: $F(3, 125) = 3.70$, $p = .014$); that is to say, they showed a line length effect. Children with SBM showed a left-sided bias (pseudoneglect) for horizontal line bisection. The direction of their errors of the midpoint of the horizontal lines was to the left of the true midpoint.

Individual children were subgrouped according to whether their horizontal line bisections showed a rightward or a leftward bias. The characteristics of these subgroups are shown in Table 1.

Compared to controls, children with SBM showed greater leftward bias (group × lateral bias between-groups ANOVA, $F(2, 91) = 7.16$, $p = 0.001$). The lateral bias subgroups do not differ significantly in terms of chronological age, or the frequency of upper versus lower spinal lesions ($p > 0.05$). For children with SBM and upper lesions, handedness is comparably distributed across lateral bias subgroups. In the subgroup of SBM children with lower lesions, however, more

Table 1
Horizontal line bisection by leftwards vs. rightwards bias in children with SBM and typically developing controls

Group	Leftward bias	Rightward bias
Control		
N (% within group)	19 (59.4%)	13 (40.6%)
Age (mean ± S.E.M.)	142.5 ± 6.9	152.8 ± 7.3
N (%) left-handed	1 (5.3%)	1 (7.7%)
N (%) right-handed	18 (94.7%)	12 (92.3%)
SBM		
N (% within group)	(75.3%)	24 (24.7%)
Age (mean ± S.E.M.)	143.7 ± 3.7	159.8 ± 7.7
N (%) left-handed	19 (26%)	2 (8.3%)
N (%) right-handed	54 (74%)	22 (91.7%)

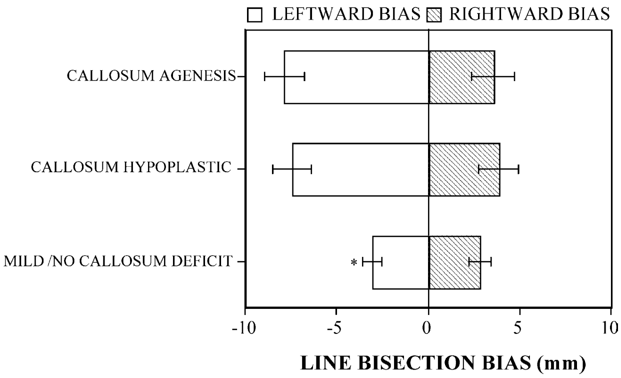

Fig. 5. Degree and direction of horizontal line bisection bias by corpus callosum subgroup.

left-handers than right-handers show a leftward line bisection bias, $\chi^2(1) = 4.20$, $p = 0.04$.

Spearman correlations were run to explore relations between the degree of lateral line bisection bias and measures of brain volume from the MRI structural scans. No significant relations were found in either control ($n = 9$) or SBM ($n = 7$) group between rightward line bisection bias and right retrocallosal brain volumes. For controls with a leftward line bisection bias ($n = 10$), there were significant correlations between degree of leftward bias and both left ($r = 0.62$, $p = 0.06$) and right ($r = 0.68$, $p = 0.03$) retrocallosal cerebrospinal volume measures, such that larger volumes were associated with a smaller leftward bias. No significant correlations between leftward line bisection and retrocallosal volumes were evident for the group with SBM ($n = 32$).

The degree and direction of horizontal line bisection bias by corpus callosum subgroup is shown in Fig. 5. A between-groups ANOVA for leftwards lateral bias was significant, $F(2, 79) = 8.04$, $p = 0.001$. The *No/Mild Callosum Deficit* group showed less leftward line bisection bias than either the *Callosum Hypoplastic* or the *Callosum Agenesis* group. No group differences were found in the ANOVA for rightwards lateral bias.

3.2. Vertical line bisection

For vertical lines, children with SBM and typically developing children were similarly accurate. They showed a similar size of estimation error for the vertical line lengths. Both groups showed the line length effect (i.e., they exhibited increasing deviations from the true midline on the line bisection task as line length increased). The two groups also showed a similar direction of estimation error, and estimated the midpoint of the line to be below the true midpoint.

As with the horizontal task, individual children were categorized according to whether their vertical line bisections showed an upward or a downward bias. The characteristics of these subgroups are shown in Table 2.

There are no group differences in downward bias, although the groups differ in upward bias (group × vertical bias between-groups ANOVA, $F(2, 96) = 4.29$, $p = 0.017$). Nearly all of the control children show an upward bias, or preference for superior hemispace. Around one-third of the SBM children show a downward bias, or preference for inferior hemispace. The vertical bias subgroups do not differ in terms of chronological age or the relative frequency of upper versus lower spinal lesions.

Table 2
Vertical line bisection by upper vs. lower bias in children with SBM and typically developing controls

Group	Downward bias	Upward bias
Control		
N (% within group)	3 (9.4%)	29 (90.6%)
Age (mean ± S.E.M.)	148.7 ± 25.8	146.5 ± 5.1
N (%) left-handed	0 (0%)	2 (6.9%)
N (%) right-handed	3 (100%)	27 (93.1%)
SBM		
N (% within group)	29 (29.9%)	68 (70.1%)
Age (mean ± S.E.M.)	143.6 ± 6.8	149.5 ± 4.0
N (%) left-handed	3 (10.3%)	18 (26.5%)
N (%) right-handed	26 (89.7%)	50 (73.5%)

Spearman correlations were run to explore relations between the degree of vertical line bisection bias and measures of brain volume from the MRI structural scans. In the SBM group with a downward vertical line bisection bias ($n = 12$), a significant negative relation was found between degree of downward bias and total retrocallosal gray matter volume ($r = -0.62$, $p = 0.03$), such that those children with less posterior cortex volume show more downward bias, that is, they attend more to inferior hemispace. Brain volume measures could not be correlated with downward bias for the control group because of the small sample size ($N = 2$). In controls with upward vertical line bisection bias ($n = 17$) extent of bias was correlated with whole brain cerebrospinal fluid ($r = -0.51$, $p = 0.04$). The SBM group with an upward bias ($n = 27$) showed no significant correlations with brain volumes.

The degree and direction of vertical line bisection bias by tectal dysmorphology grouping is shown in Fig. 6. A between-groups ANOVA for upward bias approached significance, $F(2, 80) = 2.89$, $p = 0.062$, with inspection showing that only the SBM group with tectal beaking differed from controls in showing more upward bias. No group differences were found in the ANOVA for upward bias.

3.3. Variability in line bisection

Variability in line bisection responses was also compared. Standard deviations for individual participants' mean responses were averaged by group and comparisons between the average variability scores were made using group × plane repeated measures ANOVA. For both horizontal and vertical line bisection, children with SBM showed more variability in their line bisection estimates compared to controls. They showed significantly larger intra-subject standard deviations (Table 3; $F(1, 127) = 7.60$, $p = 0.007$).

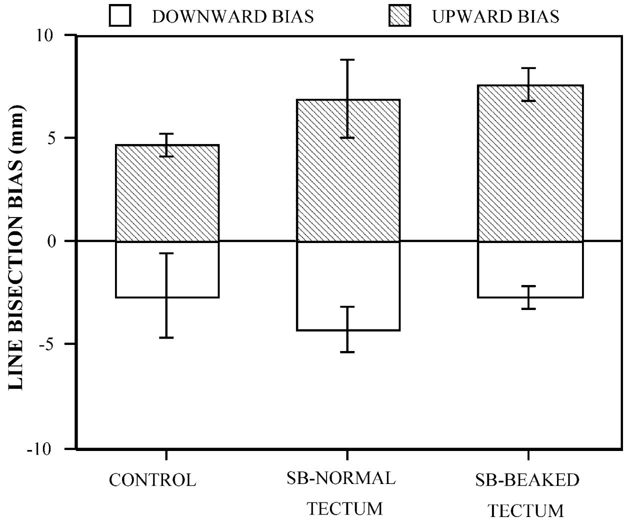

Fig. 6. Degree and direction of vertical line bisection bias by tectal beaking subgroup.

Table 3
Average standard deviation of estimation errors (±S.E.M.) in the line bisection task in children with SBM and controls, by plane

Group	Horizontal plane	Vertical plane
Control	4.33 ± 0.68	3.66 ± 0.24
SBM	5.24 ± 0.35	5.44 ± 0.32

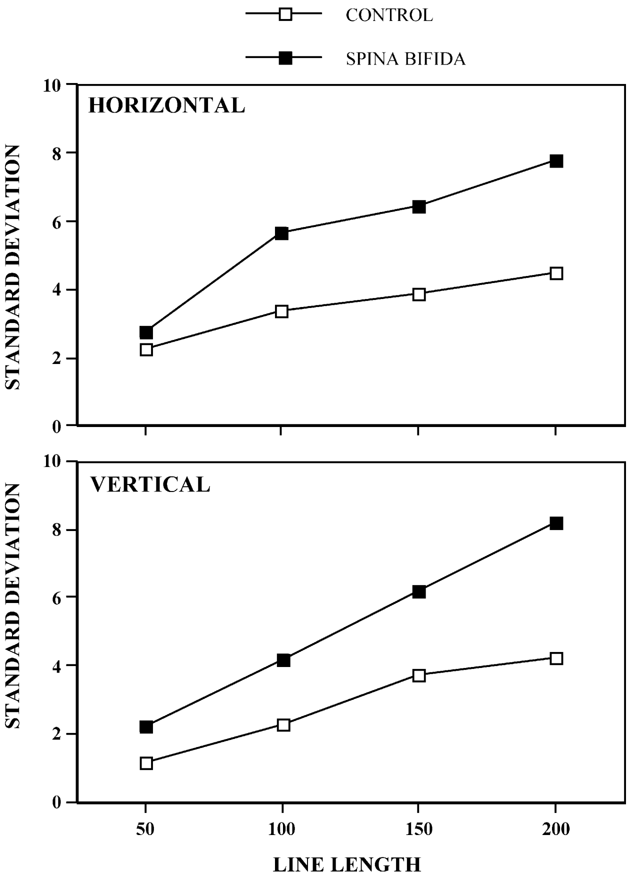

Fig. 7. Intra-individual standard deviations plotted as a function of group and line length for both horizontal and vertical planes.

Intra-individual deviation was plotted as a function of line length for both horizontal and vertical planes (Fig. 7). Variability increased more steeply as a function of line length in children with SBM than in controls for both horizontal (slope SBM 0.032, control 0.015) and vertical (slope SBM 0.040, control 0.021) lines. In the horizontal plane, there was a sharp increase in variability between 50 and 100 mm for the children with SBM.

There was no correlation between extent of horizontal and vertical biases within individuals.

4. Discussion

Children with SBM approached the line bisection task like controls and normal and brain-injured adults, for example, exhibiting increasing deviations from the true midline on the line bisection task as line length increased. Nevertheless, line bisection in children with SBM differed from age peers in terms of an exaggerated attentional bias to left hemispace, an abnormal attentional bias to inferior hemispace, and an enhanced Weber fraction, a larger zone of subjective uncertainty in making bisection judgments.

Two competing hypotheses were entertained about horizontal line bisection. No support was found for the first, that children with SBM would show a right horizontal bisection bias, like adults with right posterior lesions and younger children. As a group, children with SBM did not show an exaggerated rightward bias; even those children with a rightward bias were no more strongly right-biased than controls; and, in the subgroup of children with a right line bisection bias, the degree of rightward bias was not related to right retrocallosal brain volume, a proxy for right parietal lesions. The data provide no support for the idea that right hemisphere damage in children with SBM destroys the left half of a map of object space. Support was found for the second hypothesis, that children with SBM show the leftward bisection bias of typically developing older children and normal adults. Most children with SBM bisected horizontal lines to the left of center, as do normal right-handed adults and typically developing older children. The SBM subgroup with a left-sided bisection bias included more left-handers than did the group with a rightward line bisection bias, in keeping with the findings that pseudoneglect is more pronounced in adult left-handers (Brodie & Pettigrew, 1996; Hausmann et al., 2003; Jewell & McCourt, 2000) and typically developing non-right-handed children (van Vugt et al., 2000). As a group, children with SBM show a form of line bisection bias that is an exaggeration of that shown by non-right-handed typically developing children.

The age-related shift from rightward to leftward bias for young children in horizontal bisection parallels the shift from contralateral to right hemisphere control associated with corpus callosum maturation (Hausmann et al., 2003). Individuals with an intact corpus callosum showed less leftward line bisection bias than either the group with callosal hypoplasia or the group with congenital callosal agenesis. Either agenesis or hypoplasia resulted in similar leftward bias, suggesting that corpus callosum anomalies influence lateral attentional asymmetry through incomplete myelination (hypoplasia) as much as through agenesis. A normally myelinated corpus callosum is important for the development of line bisection: An intact corpus callosum appears to normalize the degree of line bisection bias, and an abnormal corpus callosum produces not so much an abnormal rightward bias as an exaggerated leftward bias. Models of line bisection asymmetry that involve hemispheric imbalance provide a better fit for the SBM horizontal line bisection data than do models involving hemispheric lesions, although explicit predictions from gradients of dysfunction in such models have not been tested (e.g., that the ability of a stimulus to hold attention decreases from right-to-left across the visual field).

The results are not associated with visual field deficits. Visual field deficits are rare in children with SBM. Lennerstrand and Gallo (1990) tested 18 children with spina bifida and Chiari malformations on tangent screen or Goldmann perimetry and found that none had a visual field defect. There is no evidence for visual field deficits in children in the present line bisection study: in a study of cued covert orienting (Dennis et al., 2005) requiring them to fixate a central point and press a button when they detected unpredictably occurring targets in each of four visual fields (upper left, upper right, lower left, lower right), they detected targets in all four quadrants as rapidly as controls.

Children with SBM have a higher than normal incidence of abnormal horizontal eye movements (e.g., Flett & Saunders, 1993), most of which are correctable (Biglan, 1995). The most common problem, strabismus, is identified and surgically corrected early, usually in infancy. While it is possible that horizontal eye movement anomalies produce more variability in line bisection, it is not clear how these would have resulted in lateralized rather than non-lateralized horizontal bisection biases.

Overall group accuracy for vertical line bisection was similar in SBM and control groups. In bisecting vertical lines, children with SBM and typically developing children both estimated the midpoint of the line to be below the true midpoint, made significantly larger estimation errors with longer lines, and showed a similar size of estimation error for the vertical line lengths. Superior performance for visually pointing in the lower visual field has been argued to reflect a functional bias for controlling skilled movements in this region of space (Danckert & Goodale, 2001). However, nearly all controls showed an attention bias towards superior hemispace, whereas one-third of the SBM children showed an atypical preference for inferior hemispace to the extent that they had less total retrocallosal volume.

Bilateral parietal compromise is associated with mixed patterns of visual perceptual deficits. Hemispatial neglect may, but need not, co-occur with vertical attentional asymmetries and optic ataxia (Corbetta, Kincade, & Shulman, 2002; Damasio & Benton, 1979; Harvey & Milner, 1995) and in children with SBM (Dennis, Fletcher, Rogers, Hetherington, & Francis, 2002).

The midbrain, part of the posterior attention system (Posner & Peterson, 1990), appears to be important for vertical attentional asymmetries in SBM. Controls showed less upward gaze bias than the group with SBM, especially those with tectal beaking. A limitation in upward gaze (Parinaud syndrome, involving III nerve palsy) is a sign of shunt block, and, although children with SBM were not symptomatic during testing, the relation between subclinical vertical gaze problems and vertical line bisection remains to be studied.

Horizontal and vertical attentional asymmetries are dissociable in both typically developing and brain-injured children and adults. Normal developmental changes in horizontal and vertical line bisections do not proceed in parallel (van Vugt et al., 2000). In children with SBM, horizontal and vertical bisection biases are uncorrelated and are related to different patterns of brain dysmorphology. Horizontal and vertical line bisections dissociate in normal and adults (Shelton et al., 1990), although many brain-injured patients show spatial neglect in both planes (Mark & Heilman, 1988). Some neglect phenomena (e.g., the center of mass effect, whereby people saccade to the center of a group of items; Coren & Hoenig, 1972) are more pronounced in the vertical than in the horizontal plane (Shuren, Jacobs, & Heilman, 1997).

The developmental neurobiology of vertical line bisection is similar to that in the mature brain; the developmental neurobiology of horizontal line bisection is not. Integrity of the bilateral posterior cortex and the midbrain is important for vertical line bisection in both the immature and the mature brain, whereas integrity of the right posterior hemisphere is more important for horizontal line bisection in the mature brain than in the immature brain, which requires developmental integrity of the corpus callosum. Neither the midbrain nor the cerebellum appears significantly functionally plastic (Dennis et al., 2004; Dennis, Hetherington, Spiegler, & Barnes, 1999).

Normal and pathological performance on line bisection tasks has been explained as a combination of two impairments (Marshall & Halligan, 1989). The first is a lateralized right-to-left approach to an ‘indifference zone’, or approximate area of perceived middle of the line; the second is a non-lateralized (zone of greater subjective uncertainty. Increased line bisection variability in children with SBM may mean a greater zone of subjective uncertainty, or, alternatively, trial-to-trial variation in strategy, whereby individuals approach the indifference zone sometimes from the left, and sometimes from the right (Manning et al., 1990). The latter would be consistent with the idea of an inconsistent lateral dominance for spatial attention in SBM, and perhaps also consistent with a higher than normal incidence of left-handedness.

Finally, the data provide the information about the nature of a tripartite gene-brain-behavior link in children with SBM. Genetic-embryological heterogeneity (indexed by spinal lesion level) produces a pattern of brain dysmorphology (including corpus callosum dysmorphology and tectal beaking, Fletcher et al., 2004) that is associated with neurocognitive disorders of visual attention.

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