

Space-Based Inhibition of Return in Children With Spina Bifida

Maureen Dennis

The Hospital for Sick Children and University of Toronto

Kim Copeland

University of Houston

David J. Francis

University of Houston

Susan E. Blaser

The Hospital for Sick Children

James M. Drake

The Hospital for Sick Children and University of Toronto

Kim Edelstein

The Hospital for Sick Children

Jon A. Frederick

University of Texas Health Science Center at Houston

Ross Hetherington

The Hospital for Sick Children and University of Toronto

Larry A. Kramer

University of Texas Health Science Center at Houston

Michael E. Brandt

University of Texas Health Science Center at Houston

Jack M. Fletcher

University of Texas Health Science Center at Houston

Inhibition of return (IOR) refers to an increase in time to react to a target in a previously attended location. Children with spina bifida meningomyelocele (SBM) and hydrocephalus have congenital dysmorphology of the midbrain, a brain region associated with the control of covert orienting in general and with IOR in particular. The authors studied exogenously cued covert orienting in 8- to 19-year-old children and adolescents (84 with SBM and 37 age-matched, typically developing controls). The exogenous cue was a luminance change in a peripheral box that was 50% valid for the upcoming target location. Compared with controls, children with SBM showed attenuated IOR in the vertical plane, a deficit that was associated with midbrain dysmorphology in the form of tectal beaking but not with posterior brain volume loss. The data add to the emerging evidence for SBM deficits in attentional orienting to salient information.

Keywords: visual attention, inhibition of return, spina bifida, midbrain, posterior cortex

Inhibition of return (IOR) refers to an increase in time to react to a target in a previously attended location (Posner & Cohen,

1984; Posner, Rafal, Choate, & Vaughan, 1985). As an adaptive function, IOR increases the chance that exploration will occur with new objects and in new locations and, thereby, provides a strategy for effective foraging in a complex visual environment (Klein, 1988, 2000). There are at least three types of IOR (Tipper, Jordan, & Weaver, 1999; Umiltà, 2001): *object-based* IOR, which follows moving objects; *object-centered* IOR, which follows parts of rotating objects; and *space-based* IOR, which is related to spatial locations. In this article, we are concerned with space-based IOR.

Maureen Dennis, Brain and Behaviour Program, The Hospital for Sick Children, Toronto, Ontario, Canada, and Departments of Surgery and Psychology, University of Toronto, Toronto, Ontario, Canada; Kim Edelstein, Brain and Behaviour Program, The Hospital for Sick Children; Kim Copeland and David J. Francis, Department of Psychology, University of Houston; Jon A. Frederick and Michael E. Brandt, Center for Computational Biomedicine, University of Texas Health Science Center at Houston; Ross Hetherington, Community Health and Knowledge Transfer, The Hospital for Sick Children, and Department of Psychology, University of Toronto; Susan E. Blaser, Department of Radiology, The Hospital for Sick Children; Larry A. Kramer, Department of Radiology, University of Texas Health Science Center at Houston; James M. Drake, Department of Surgery, The Hospital for Sick Children, and Department of Surgery, University of Toronto; Jack M. Fletcher, Department of Pediatrics, University of Texas Health Science Center at Houston.

This research was supported by National Institute of Child Health and Human Development Grant P01 HD35946, "Spina Bifida: Cognitive and Neurobiological Variability." We thank Joanne Robitaille, Jennifer Janes, Andrea Martin, Amy Boudousquie, Irene Townsend, and Susan Inwood for assistance.

Correspondence concerning this article should be addressed to Maureen Dennis, Brain and Behaviour Program, Department of Psychology, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada. E-mail: maureen.dennis@sickkids.ca

Attention may be summoned by salient information, and cues such as a luminance change at the future location of a target are termed *exogenous* because they represent externally cued orienting. Attention may also be deployed toward cognitively interesting information, and cues such as a central arrow pointing to the location of an upcoming target are termed *endogenous* because they represent internal, cognitively cued orienting. Exogenous and endogenous orienting are separable in normally developed adults (Posner, Cohen, & Rafal, 1982) such that attention is summoned automatically by exogenous cues but can also be summoned endogenously by cognitive cues.

In the canonical IOR paradigm, targets are cued exogenously by an event that appears at the future location of the target (e.g., a sensory change, such as a peripheral flash or a bright box in the target location). Cues can be facilitatory or inhibitory, depending on the time parameters between cue and target (i.e., the stimulus

onset asynchrony [SOA]). A motor response to a visual target presented at an exogenously cued location is facilitated when the target occurs shortly after the cue; reciprocally, the reaction time (RT) to an invalidly cued target increases at that SOA. As the SOA becomes longer, the response to validly cued targets is no longer facilitated and, instead, becomes slower or inhibited. RT is longer if a long-SOA cue validly indicates an upcoming target location than if cue and target location do not coincide. This inhibitory effect is termed *IOR*.

Oculomotor preparation is an important part of the mechanism of IOR (Rafal, Calabresi, Brennan, & Sciolto, 1989), as evidenced by the fact that the inhibitory effect is demonstrated both by a cue presented in the periphery while the eyes are fixated centrally and by endogenous activation of a saccade (Posner et al., 1985). IOR is not apparent with endogenously activated covert attention shifts in response to central cues that indicate where the forthcoming target will appear, which data add to evidence of the separability of exogenous and endogenous orienting in normally developed adults (Posner et al., 1982) and show that IOR is a feature of attention that is summoned automatically by salient cues rather than being summoned endogenously by cognitive cues.

The time course for the appearance of IOR depends on how efficiently attention can be removed from the cued location (Klein, 2000). The canonical IOR paradigm uses a single-cue procedure, although a double-cue procedure, in which attention is removed from a cued location after the initial peripheral cue (e.g., by brightening the central fixation point), has also been used. IOR appears earlier (at a shorter SOA) when attention is exogenously removed from the peripheral cued location by a second cue (Briand, Larrison, & Sereno, 2000; Pratt & Fischer, 2002).

IOR is evident early in development. Newborn infants show IOR following overt locational shifts (Simion, Valenza, Umiltà, & Dalla Barba, 1995; Valenza, Simion, & Umiltà, 1994). In a spatial cuing procedure without overt attentional shifts of fixation, infants older than 4 months of age show IOR (Clohessy, Posner, Rothbart, & Vecera, 1991; Richards, 2001). Six- to 18-month-old infants show an adult pattern of IOR when a double-cue procedure is used (Clohessy et al., 1991). Although the mechanism for inhibiting the return of attention to a recently attended location exists at birth, infants do not show covert shifts of attention in all spatial cuing procedures that result in both initial facilitation and later IOR (Richards, 2003).

In school-age children, the time course of IOR varies with age and experimental procedure. Younger children (5–10 years old) show IOR with a double-cue procedure (MacPherson, Klein, & Moore, 2003) but not with a single-cue procedure (Brodeur & Enns, 1997); that is, younger children have delayed IOR unless a second cue at fixation removes their attention from the peripherally cued location. Older children (11–17 years old) show the adult pattern of facilitation at a short SOA and inhibition at a longer SOA for both single- and double-cue conditions (MacPherson et al., 2003).

The importance of oculomotor programming in IOR suggests that it depends on midbrain structures such as the superior colliculus (Rafal & Henik, 1994), and there are three pieces of evidence that implicate the superior colliculus in IOR. (a) Adult individuals viewing monocularly show greater IOR in the temporal than in the nasal visual field, associating IOR with the retinotectal pathway (Rafal, Henik, & Smith, 1991). (b) Individuals with brain injury

that preserves retinotectal pathways (e.g., brain-damaged patients with hemianopia, in whom the geniculostriate pathway is disturbed but the retinotectal pathway is relatively intact; Rafal et al., 1989, 1991) do show IOR. (c) Midbrain lesions produce a loss of IOR. The condition of progressive supranuclear palsy is associated with degeneration of the superior colliculus and tectal region and produces vertical gaze disorders, deficits in spatial orienting not directly caused by disorders of eye movements (Rafal & Grimm, 1981), and a lack of IOR (Rafal, Posner, Friedman, Inhoff, & Bernstein, 1988). In a patient with a lesion restricted to the right superior colliculus, IOR was evident in the visual field projecting to the intact left superior colliculus but not in the visual field projecting to the damaged right superior colliculus (Sapir, Soroker, Berger, & Henik, 1999).

Behaviorally, IOR has effects on a range of cognitive processes (e.g., Vivas & Fuentes, 2001), implying some IOR mediation by cortical structures. In patients with parietal lesions, some studies have shown null IOR effects (Posner et al., 1985), whereas others have shown an attenuated or limited IOR (Bartolomeo, Sieroff, Decaix, & Chokron, 2001; Vivas, Humphreys, & Fuentes, 2003). The finding that parietal lobe damage attenuates IOR has led to the proposal that an intact superior colliculus may be necessary but not sufficient for IOR, with biases in spatial attention needing to be implemented by the posterior parietal cortex (Danzinger, Fendrich, & Rafal, 1997; Vivas et al., 2003). Anterior cortical regions do not seem to be involved in IOR. For example, in children with the impulsive/inattentive form (Combined Type) of attention-deficit/hyperactivity disorder (ADHD), who show primarily anterior attention problems, IOR is generally similar to that observed in controls (Li, Chang, & Lin, 2003).

The developmental plasticity of the brain system for IOR is not known, because the studies of superior colliculus and parietal lesions have used adults with acquired brain damage. The fact that IOR in some form is evident in newborns, for whom visual behavior is mediated largely by the superior colliculus, suggests that the brain mechanisms for IOR are established early in life. A useful perspective on the neural basis of IOR might emerge from the study of IOR in a large, representative sample with a childhood brain disorder that explicitly compromises the midbrain and posterior cortex, neural substrates important for IOR in the mature brain. Spina bifida meningomyelocele (SBM) is one such condition.

SBM is a neural tube defect associated with malformations of the spine and brain. It involves dysraphism of the spinal cord, with a loss of sensory and motor function below the level of the spinal lesion. It is the most common severely disabling birth defect in North America, occurring in about 0.5 per 1,000 births. Spina bifida represents a heterogeneous disorder and is usually classified on the basis of the spinal dysraphism that is apparent at birth. SBM is the most common and severe form of the condition. 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; Dennis et al., 1981, 2005; Fletcher et al., 1996, 2005; Fletcher, Dennis, & Northrup, 2000; Hannay, 2000). SBM is associated with profound disturbances of brain development that include malformation of the midbrain, abnormal formation and maturation of the posterior cortex and white matter, agenesis and hypoplasia of the corpus callosum, and dysmorphology of the cerebellum involving abnor-

malities in shape and reductions in volume (Dennis et al., 2005; Dennis et al., 1981; Fletcher et al., 1996, 2000; Hannay, 2000).

The pattern of brain dysmorphology in children with SBM is one of particular relevance for the neurobiology of covert orienting in general, including IOR. This is because these children have congenital abnormalities of the midbrain and selective reductions in posterior cortical volume (Dennis et al., 1981; Fletcher et al., 1996). At a neural level, children with SBM commonly exhibit midbrain damage, mostly in the form of beaking of the tectum (Fletcher et al., 2000, 2005). They also show paralysis of upward gaze as part of their clinical symptomatology during shunt malfunctions.

At a behavioral level, children with SBM have deficits in the posterior, rather than the anterior, attention system. In an exogenous visual orienting task, children with hydrocephalus, most of whom had SBM, sustained attention to the task but were slow to disengage from an exogenous cue (Brewer, Fletcher, Hiscock, & Davidson, 2001). A recent study of covert orienting in children with SBM compared three types of cues: exogenous (luminance change in a peripheral box that was either valid or invalid for upcoming target location), endogenous arrow (a central arrow that was either valid or invalid for upcoming target location), and endogenous word (a central word that was either valid or invalid for upcoming target location). Compared with controls, children with SBM showed slowed covert orienting to both exogenous and endogenous cues and enhanced disengagement costs to exogenous (although not to endogenous) cues with a short SOA, deficits that were associated with midbrain dysmorphology and posterior brain volume loss (Dennis et al., 2005).

The nature of exogenously cued attention is explored further in the present article with specific reference to IOR. Although it is known that children with SBM show greater exogenous disengagement costs at a short SOA, it is not clear whether they show IOR at a long SOA. In a number of visual attention paradigms, such children exhibit more problems in the vertical than in the horizontal plane, but it is not clear whether IOR varies by plane. Nor is it known whether IOR varies with disorders of the midbrain in SBM, as it does in adult conditions like progressive supranuclear palsy associated with midbrain degeneration or unilateral superior colliculus lesions. The presence of midbrain and tectal abnormalities in some but not all children with SBM provides an opportunity to test hypotheses about the developmental role of the midbrain in IOR.

Little evidence exists about posterior parietal lesions and IOR. The variability of posterior cortical volumes in SBM also allows exploration of the question of the correlation between posterior cortical volumes and IOR. A study of the neurobiology of IOR in children with SBM, then, would provide not only missing information about covert orienting in this population but also information about the plasticity of brain bases of IOR.

In the present study, we examined IOR with respect to exogenously cued targets in the horizontal and vertical planes, and we related IOR to MRI-identified anomalies of the midbrain, a region that has been implicated in IOR in the mature brain. The behavioral hypotheses were that children with SBM would, as a group, show the typical pattern of facilitation by a valid cue at a short SOA but less IOR than controls with a valid cue at a longer SOA, particularly in the vertical plane. The brain-behavior hypothesis was that midbrain damage would be the factor that limited IOR—

specifically, that children with SBM and tectal beaking would show no or very attenuated IOR relative both to controls and to children with SBM and a more normal midbrain. The evidence for a parietal cortex role in IOR is mixed, so although we explored this question by correlating IOR with posterior cortical volumes, we entertained no specific hypotheses about this relationship.

Method

Participants

The participants were 121 children and adolescents ranging in age from 8 to 19 years, recruited from two sites: The Hospital for Sick Children in Toronto, Ontario, Canada ($n = 67$) and the University of Texas Medical School at Houston ($n = 54$). One group ($n = 84$) had been identified with and treated for SBM at birth, including placement of a shunt shortly thereafter for hydrocephalus. The other group represented typically developing, age-matched controls ($n = 37$) recruited through local advertisements, posters, and related activities. Within the group with SBM, children were seen when they were medically stable. Most children ($n = 51$) had either no or 1 shunt revision, 22 had 2–4 revisions, and 11 had 5–14 revisions. There were 16 with spinal lesions above L1 and 68 with spinal lesions below T12, the differentiation at the thoracic level reflecting genetic (Volcik, Blanton, & Northrup, 2001), neuroembryological (Park, Stewart, Khoury, & Mulinare, 1992), and neuropsychological research (Fletcher et al., 2005) supporting a subdivision at this level. Although higher spinal lesions are associated with poorer neurobehavioral outcomes (Fletcher et al., 2005), they are also associated with a greater incidence of brain anomalies. Of relevance to the study of IOR, children with upper spinal lesions are more likely than those with lower spinal lesions to show tectal beaking, with few children with upper lesions failing to show this relation (Fletcher et al., 2005). In the present sample, all but one of the children with upper lesions showed tectal beaking, whereas 43 (78%) of those with lower level lesions showed tectal beaking. Because beaking is a more theoretically relevant variable than lesion level for visual attention—and, especially, given that we cannot dissociate tectal beaking and upper level lesions—we chose to analyze the results according to tectal beaking only.

All participants had IQ scores within 2 standard deviations of the population mean of 100 (70 and above) on either the Verbal Reasoning and/or Abstract/Visual Reasoning subtests of the Stanford-Binet Test of Intelligence (4th. ed.; Thorndike, Hagen, & Sattler, 1986). Individuals were not included if they had a neurological disorder unrelated to SBM, a severe psychiatric disorder, uncontrolled seizure disorder, uncorrected sensory disorder, or an inability to control the upper limbs. In addition, controls were not included if they had identified neurobehavioral disorders, including learning and attention disorders evidenced through parent or school reports.

Table 1 summarizes data on sociodemographic variables and IQ. The group did not differ significantly in age, $t(119) = 0.93$, $p < .36$; gender, $\chi^2(1, N = 121) = 0.03$, $p < .87$; or socioeconomic status, $t(119) = 1.78$, $p < .08$. There were more children of Hispanic origin in the group with SBM, analyzed as a comparison of Hispanic and non-Hispanic participants given the low sample size in some cells, $\chi^2(1, N = 121) = 7.39$, $p < .007$. In North America, SBM is more common in Hispanic than in non-Hispanic populations. All participants were English speaking, and the socioeconomic status difference was not statistically significant.

Cued Orienting Procedure

The cued orienting task (based on Rafal et al., 1988) was administered using an IBM-compatible personal computer, coded in Micro Experimental Laboratory (Version 2.0), and scored in SAS (Version 9.0). A chin rest with a forehead bar was used to ensure a distance of 47.5 cm between the computer monitor and participant's eye level. While maintaining central

Table 1
Demographic Information for Control and Spina Bifida Meningomyelocele (SBM) Participants

Variable	Group	
	Control (<i>n</i> = 37)	SBM (<i>n</i> = 84)
Age (years; <i>M</i> ± <i>SD</i>)	14.55 ± 2.56	15.37 ± 2.86
Gender		
Male	20	40
Female	17	44
Ethnicity		
Caucasian	29	56
Hispanic	1	19
Asian	3	3
African American	2	3
Other	2	3
Socioeconomic status ^a (<i>M</i> ± <i>SD</i>)	46.00 ± 12.01	41.20 ± 14.10
Stanford-Binet composite IQ (<i>M</i> ± <i>SD</i>)	107.84 ± 9.76	88.9 ± 11.97

^a Determined by the Hollingshead (1975) four-factor scale.

fixation, participants were required to press a button when a target appeared in one of four peripheral locations on the computer screen: to the right, to the left, above, or below the central fixation point. On each trial, a cue was presented at one of two SOAs (200 or 1,000 ms prior to the target). The cue, a luminance change in one of the peripheral boxes, accurately indicated the location of the target on approximately 50% of the trials. Children completed 5 practice trials prior to each block, and then they completed two blocks of at least 80 trials each. Any trial with an RT less than 150 ms or greater than 2,000 ms was considered spoiled and was excluded from analyses; such trials were presented again after Trial 80 in each block.

Brain Imaging Procedures

Image acquisition. Three sets of images were acquired: a sagittal localizer, a T1-weighted coronal series for assessment of white and gray matter, and a T2-weighted coronal series for assessment of cerebrospinal fluid (CSF). To coregister and position-normalize the two sequences, external fiducial markers were placed on the nasion and external meatus. The sagittal localizer was a spin-echo T1-weighted series (FOV 24, TR 500, TE 14, 256 × 192 matrix, 3 mm with a 0.3-mm skip, two repetitions). One whole-brain coronal series consisted of contiguous 1.5-mm slices using a fast spin-echo proton density and heavily T2-weighted images (FOV 20, TR 4000, TE1 15, TE2 112, 256 × 192 matrix, two repetitions). The second whole-brain coronal series consisted of a 3-D-spoiled grass gradient echo contiguous 1.5-mm coronal series (TR 21, TE4, flip angle 35°, 124 locations, 256 × 192 matrix, one repetition).

Quantitative analysis. 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 nonlinear 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 nonlinear filter served to sharpen areas of high-intensity gradient (boundaries) and to smooth regions of low-intensity gradient within the tissue borders.

Automatic segmentation. The method used a fully automated fuzzy cluster analysis (Pao, 1989) that obtained whole and regional brain tissue

and CSF volumes (Brandt, Bohan, Kramer, & Fletcher, 1994, Brandt et al., 1996; Brandt, Fletcher, & Bohan, 1992). The T1-weighted scan volume, which provides superior white–gray contrast compared with 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 onscreen and compared with the actual scan images. For the quantitative analyses, separate tissue volumes (white matter, gray matter, CSF) were obtained for the posterior cortical region on the basis of a division of the corpus callosum into a precallosal region (*genu forward*), a pericallosal (including the corpus callosum) and a retrocallosal region (the regions of interest; Filipek et al., 1992). In this categorization, the retrocallosal region extended caudally from the most posterior aspect of the corpus callosum. For the present study, the regions of interest are as follows: total retrocallosal region gray matter, total retrocallosal region white matter, and total retrocallosal region CSF. The percentages of retrocallosal volumes were calculated as the absolute total retrocallosal volume for each tissue type divided by the absolute whole retrocallosal volumes.

Qualitative Analyses

Structural MRI scans were analyzed in 94 participants (69 SBM, 25 control) with respect to qualitative analyses of the midbrain and tectum. Two pediatric radiologists coded tectal beaking as either *present* or *absent*. Figure 1 shows a normal tectum and two examples of tectal beaking from the SBM group.

Data Analyses

Cued orienting. In an earlier study of exogenous and endogenous cuing (Dennis, Edelstein, Copeland, et al., 2005), we had calculated the difference in RT between valid and invalid cues at each SOA. At the short SOA, we found a relative cost associated with cue validity, which we termed the *disengagement cost*. To study IOR, we calculated a parallel relative-cost measure at the long SOA. Using relative differences in RTs for valid and invalid cues has the additional advantage of equating individual differences in the absolute magnitude of RT among participants.

Median RTs for each child were calculated by plane (horizontal, vertical) and SOA (200 or 1,000 ms) for both validly cued targets and invalidly cued targets. To evaluate the facilitation or inhibition of RT associated with

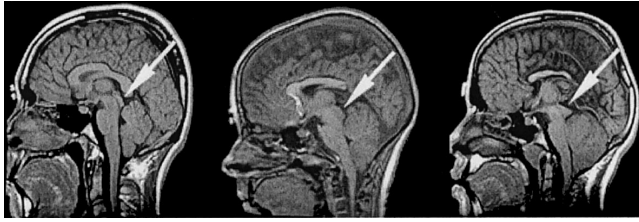


Figure 1. Tectal beaking in midsagittal structural MRI slices for a control participant with normal tectum (left), a spina bifida meningocele (SBM) participant with normal tectum (middle), and an SBM participant with beaked tectum (right). Arrows point to the midbrain-tectal area.

cue validity, we calculated the difference in median RT on valid and invalid trials for each participant by plane and SOA. Average differences in latency were compared between groups, at each plane, using a Group \times SOA repeated measures analysis of variance (ANOVA), covarying for age.

Brain structure and visual orienting. To evaluate the relationship between tectal dysmorphology and covert orienting, we analyzed RT latency differences using a Group (control, SBM—no tectal beaking, SBM—tectal beaking) \times SOA repeated measures ANOVA, covarying for age. In addition, we made partial correlations between differences in RT latency and posterior cortical volume, controlling for age.

Results

Cued Orienting

Differences in RT latency are shown in Figure 2. At the short SOA, RTs were facilitated when targets were preceded by valid cues and prolonged when targets were preceded by invalid cues, a finding that we have described as the cost of disengaging attention on invalid trials (Dennis et al., 2005). In contrast, at the long SOA, this cost of disengagement was not observed: main effect of SOA in the horizontal plane, $F(1, 118) = 14.425, p < .001$, and in the vertical plane, $F(1, 118) = 13.693, p < .001$. All participants showed a shorter RT to the invalidly cued target than to the validly cued target at the long SOA.

The effects of cue validity on latency to targets in the horizontal plane were similar for both children with SBM and controls. However, this effect was mediated by age for both groups—effect of age, $F(1, 118) = 7.256, p < .008$ —with older children showing shorter latencies. In contrast, the latency difference in responses to targets presented in the vertical plane, at both the short and the long SOA, were significantly different between groups: main effect of group in the vertical plane, $F(1, 118) = 19.615, p < .001$. Children with SBM were less responsive than controls to the

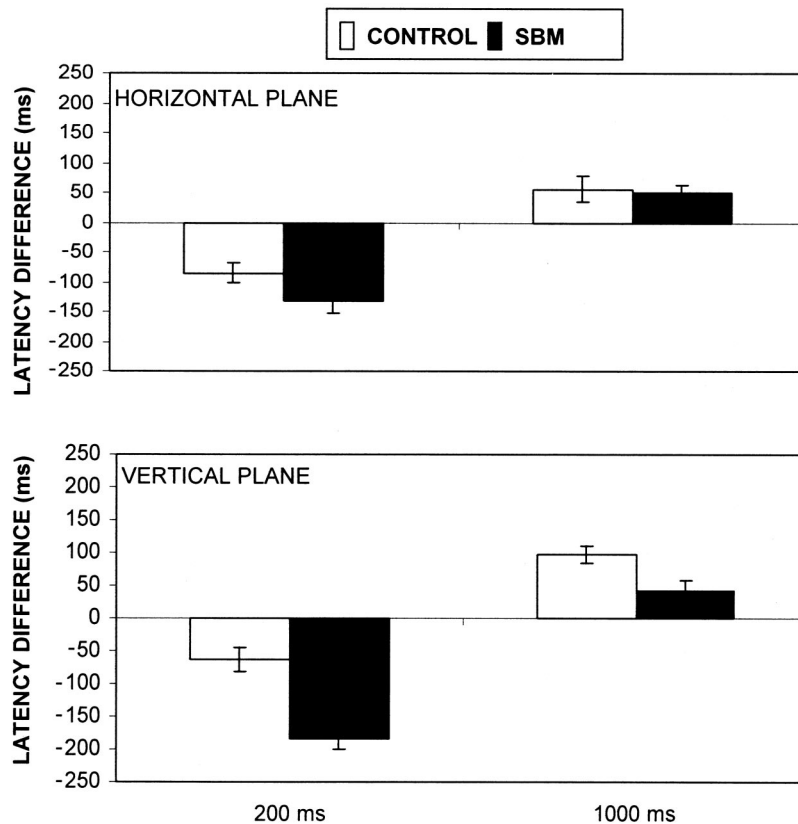


Figure 2. Latency differences in median reaction times (RTs) between validly and invalidly cued targets for spina bifida meningocele (SBM) and control group participants. The negative latency differences at the short (200-ms) stimulus onset asynchrony (SOA) are the disengagement costs associated with misdirecting attention on invalidly cued trials. At the 1,000-ms SOA, shorter RTs to invalidly cued targets result in positive latency differences, which are evidence of inhibition of return. Error bars represent standard errors of the mean.

effects of cue validity on targets in the vertical plane (see Figure 2), and this effect was not mediated by age.

It is of note that the effect of SOA manifested in RT to invalidly cued targets, and not to validly cued targets (Group \times SOA repeated measures ANOVA). Neither children with SBM nor controls showed a difference in RT to validly cued targets across the two SOAs (see Figure 3). In contrast, the RTs to invalidly cued targets at the two SOAs differed significantly: main effect of SOA in the horizontal plane, $F(1, 118) = 9.93, p < .002$, and in the vertical plane, $F(1, 118) = 10.57, p < .002$.

Structure–Function Relationships: Tectal Beaking

The pattern of results described above is similar to that found when considering the role of tectal dysmorphology on RT. Differences in RT latency for children with SBM with tectal beaking, children with SBM with no tectal beaking, and typically developing controls are shown in Figure 4. We found significant effects of SOA—horizontal plane, $F(1, 90) = 18.37, p < .001$; vertical plane, $F(1, 90) = 10.14, p < .002$ —with disengagement cost associated with the short SOA and IOR associated with the long SOA.

The effects of cue validity on latencies to targets in the horizontal plane were similar for children with SBM with tectal beaking, children with SBM with no tectal beaking, and controls. In contrast, the latencies to targets presented in the vertical plane, at both the short SOA and the long SOA, were significantly different between groups: main effect of group in the vertical plane, $F(2, 90) = 5.91, p < .004$. Post hoc comparisons (controlling alpha at $p < .05$) revealed significant differences between controls and children with SBM with tectal beaking.

Structure–Function Relationships: Posterior Cortical Volume

There were no significant correlations between retrocallosal brain volumes and RT latency differences.

Discussion

Children with SBM have impairments in covert orienting that include attenuated IOR. All of the children in this study showed some basic task effects. Both children with SBM and controls exhibited a disengagement cost at the shorter SOA and IOR at the longer SOA. For both groups, the direction of the relation between valid and invalid cues changed with SOA. Children with SBM performed the task as directed and as would typically developing infants (Clohessy et al., 1991), children (MacPherson et al., 2003), and adults (Rafal & Henik, 1994). In important respects, then, the children in the study performed the exogenously cued orienting task as would typically developing children and normally developed adults.

Nevertheless, the children with SBM differed from the controls, and the results varied by plane. In the horizontal plane, children with SBM performed similarly to controls with respect to showing a disengagement cost at the shorter SOA and IOR at the longer SOA. In the vertical plane, children with SBM—in particular those with tectal beaking—had a greater disengagement cost and less IOR.

Both disengagement cost and IOR are defined by the relation between the valid and the invalid cue. For space-based IOR, the limiting factor is the invalid cue, because the groups do not differ across conditions for the valid cue. The change from a cost of disengagement at the shorter SOA to IOR at the longer SOA is related to changes in the invalid, although not to the valid, cue. Thus, it is not the case that it took either group longer to respond to the valid cue. What changed with SOA was the relation between RT to the constant valid cue and RT to the variable invalid cue. Our results are consistent with the idea that IOR biases attention toward novel locations and away from previously inspected locations, thereby making visual search more efficient (Danzinger, Kingstone, & Snyder, 1998).

Age mediated RTs to horizontally cued targets in both group comparisons, suggesting that IOR in the horizontal plane, even

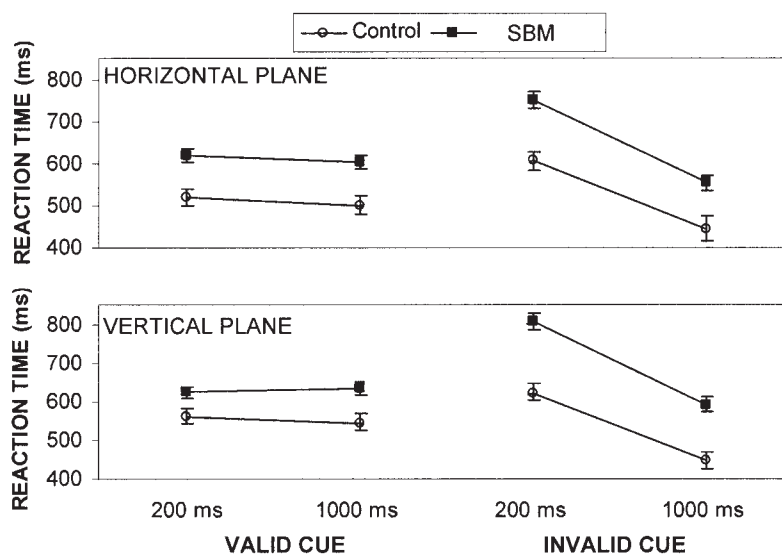


Figure 3. Median reaction times to validly and invalidly cued targets at the short (200-ms) and the long (1,000-ms) stimulus onset asynchrony for controls and in children with spina bifida meningomyelocele (SBM). Error bars represent standard errors of the mean.

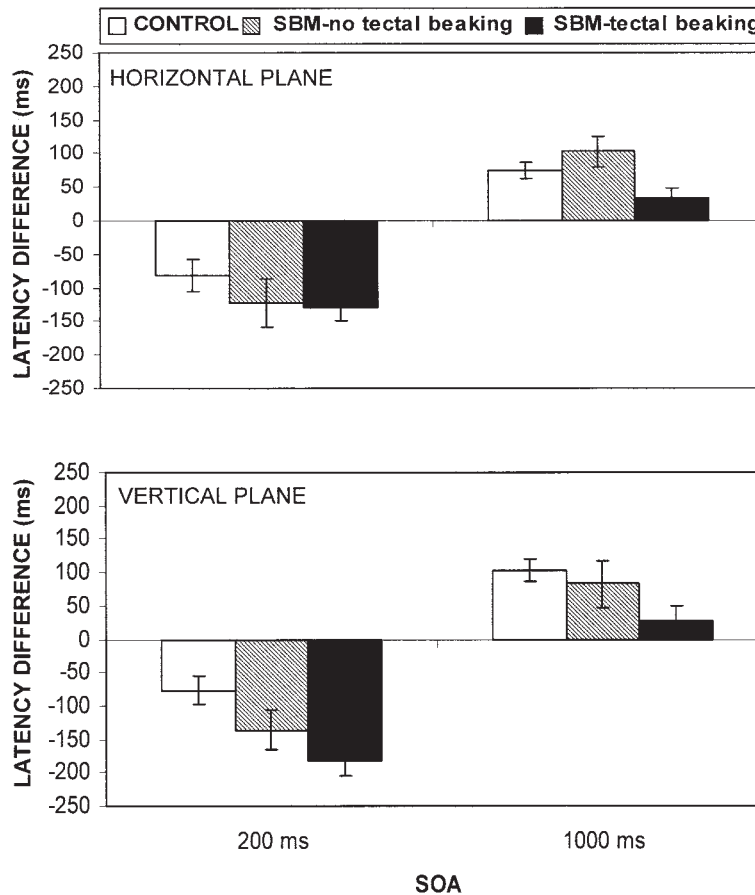


Figure 4. Comparison of latency differences between validly and invalidly cued targets for participants with spina bifida meningomyelocele (SBM) with tectal beaking, participants with SBM without tectal beaking, and control group participants. The negative latency differences at the short (200-ms) stimulus onset asynchrony (SOA) are the disengagement costs associated with misdirecting attention on invalidly cued trials. At the longer (1,000-ms) SOA, the shorter reaction times to invalidly cued targets result in positive latency differences, which are evidence of inhibition of return. Error bars represent standard errors of the mean.

though it is apparent early in life, improves in all children over the age range tested. Although the basic IOR may be apparent by 6 months of age, performance in these canonical IOR paradigms is responsive to developments marked by increasing age. Of considerable interest, age had no effect on IOR in the vertical plane.

The dissociation between horizontal and vertical planes is of some interest and is consistent with both experimental and clinical data on these children suggesting that the vertical plane is especially vulnerable. Children with SBM have more difficulty bisecting lines in the vertical plane than in the horizontal plane, and they show altitudinal neglect (Dennis, Edelstein, Frederick, et al., in press). Clinically, they show a Parinaud syndrome during shunt blocks whereby they have a limitation of upward gaze. Although the children with SBM were not symptomatic during testing, it does appear that the vertical plane is notably vulnerable to attention deficits in this population (see also Dennis, Edelstein, Frederick, et al., in press), which raises the question of whether visual attention in the vertical plane is driven by a failure to make vertical eye movements. The answer appears to be negative. In the basic Posner (1980) paradigm, covert attention is studied with the eyes

fixated on a central point. In the present study, even when the eyes were fixated on a central location, children with SBM had trouble disengaging from the exogenous cue and inhibiting return to the attended location. These problems are ones of attention, not simply eye movement problems (which, to be sure, may affect other visual perception tasks). The visual attention deficits of children with SBM, then, appear to include deficient oculomotor programming. What is not yet known is whether these deficiencies can be ameliorated by means of a second cue to draw attention back from the peripherally cued location.

Recent computational models of the superior colliculus propose that its function is to generate saccades and bring visual and motor information together in a common reference frame (Optican, 1995). Specifically, retinotectal pathways are important for reflex orienting to exogenous signals and for linking covert attention to the oculomotor systems of overt orienting (Rafal et al., 1988). The present data extend information about the role of the superior colliculus in exogenous orienting. Our children with SBM and tectal beaking were slower at covert orienting to exogenous cues as well as at other types of visual attention involving overt movement

of the effectors (Dennis, Edelstein, Frederick, et al., in press), which suggests that the superior colliculus is important for both overt and covert orienting in children.

The functions of exogenous orienting are delimited, and an overwhelming body of evidence implicates the midbrain in these functions. Our data support a prominent role for the midbrain and suggest that cortical mechanisms play a limited role in exogenous orienting, unlike other forms of attention (Dennis et al., 2005; Dennis, Edelstein, Frederick, et al., in press). Thus, we found no relations among posterior brain-volume measures and IOR. The posterior cortex does not seem to be significant for IOR in children with SBM, from which it may be inferred that cortical mechanisms do not take over the functions of the midbrain. Our data do not provide support for the proposal that an intact superior colliculus is necessary but not sufficient for IOR, with biases in spatial attention needing to be implemented by the posterior parietal cortex (Danzinger, Fendrich, & Rafal, 1997; Vivas et al., 2003). To be sure, we studied space-based IOR, and it is possible that a cortical role is important in other forms, such as object-based IOR, which may involve a type of inhibitory tagging of objects.

In better delineating the attention deficit of children with SBM, the present data also sharpen the differences between attention disorders in different developmental disorders. In comparison with children with SBM, children with the impulsive/inattentive form of ADHD (Combined Type) can disengage but not sustain attention, whereas children with SBM can sustain attention but cannot disengage (Brewer et al., 2001). In a recent study, we extended this finding to show that children with SBM have difficulty disengaging from exogenous cues but not from endogenous cues (Dennis, Edelstein, Copeland, et al., 2005). Here, we further elaborated this comparison by showing that children with SBM have attenuated IOR in the vertical plane, whereas children with ADHD appear to perform similarly to controls on IOR tasks (Li et al., 2003). Moreover, children with ADHD show normative but sluggish patterns on the Posner paradigm, with the exception of some asymmetric patterns (Brewer et al., 2001; Epstein, Connors, Erhardt, March, & Swanson, 1997; Swanson et al., 1991). Children with SBM cannot orient attention to salient information; children with ADHD cannot sustain attention to interesting information.

Structure–function congruence for IOR was observed in SBM, a neurodevelopmental disorder associated with midbrain damage. Furthermore, we observed a relation between brain compromise and outcome: In those children with the most severe developmental damage to the midbrain and tectum, evidenced by tectal beaking, the effects on IOR were most evident.

The present data bear on the developmental plasticity of the brain system for IOR. Because IOR in some form is evident in newborns, for whom visual behavior is mediated largely by the superior colliculus, it is likely that the brain mechanisms for IOR are established early in life. Infants with SBM as young as 7 months of age show difficulties in age-appropriate visual attention paradigms that require orienting and disengaging of attention (Landry, Lomax-Bream, & Barnes, 2003). The present data support this view at both a behavioral and a neuroanatomical level, showing that problems with the midbrain in neuroembryogenesis are associated with IOR deficits similar to those resulting from midbrain lesions acquired in adult life. The developmental plasticity of the midbrain and tectum appears to be limited both in hamsters (Finlay, Marder, & Cordon, 1980) and in human chil-

dren. Covert-orienting deficits exist similarly in congenital midbrain dysmorphology and adult midbrain degeneration, then, and they likely contribute to the visuomotor deficits that have been described in each of these conditions (e.g., Dennis, Fletcher, Rogers, Hetherington, & Francis, 2002; Rafal et al., 1988).

Genetic-embryological heterogeneity (spinal lesion level), brain dysmorphology (tectal beaking), and IOR are associated in children with SBM by virtue of the link between tectal beaking and spinal lesion level (Fletcher et al., 2005). Children with upper spinal lesions reliably have tectal beaking, and individuals with tectal beaking are those with the most severe IOR deficits. This provides further evidence (see Dennis, Edelstein, Frederick, et al., in press) about the tripartite link between gene, brain, and behavior in this condition.

The functional effects of limitations in IOR are considerable. Although automatic orienting to new information has defensive and social adaptive advantages, the tight linkage of orienting with IOR facilitates strategic, voluntary environmental search without continual distraction by repeated extraneous stimulation (Rafal & Henik, 1994). The link between orienting and IOR appears to be less tight in children with SBM, at least for the vertical plane. The implications of this for strategic visual search are less clear. It may be relevant that in tasks of rapid visual naming of common objects, such children are slow not because of naming deficits per se but because they need fillers and scaffolds to support their serial visual naming (Dennis, Hendrick, Hoffman, & Humphreys, 1987).

The study of IOR in children with SBM, who have significant brain dysmorphologies in the midbrain, is informative. First, it increases understanding of the range of covert orienting deficits in this condition. Second, it allows delineation of similarities and differences with other disorders of attention, such as ADHD. Third, it provides converging developmental evidence for the importance of the midbrain as a critical component of the system for covert orienting of attention.

References

- Bartolomeo, P., Sieroff, E., Decaix, C., & Chokron, S. (2001). Modulating the attentional bias in unilateral neglect: The effects of strategic set. *Experimental Brain Research, 137*, 432–444.
- Brandt, M. E., Bohan, T. P., Kramer, L. A., & Fletcher, J. M. (1994). Estimation of CSF, white and gray matter volumes in hydrocephalic children using fuzzy clustering of MR images. *Computerized Medical Imaging and Graphics, 18*, 25–34.
- Brandt, M. E., Bohan, T. P., Thorstad, K., Beaver, S. R., Davidson, K. C., Francis, D. J., et al. (1996). Reliability of brain structure morphometry in hydrocephalic children using MR images. *Magnetic Resonance Imaging, 14*, 649–655.
- Brandt, M. E., Fletcher, J. M., & Bohan, T. P. (1992). Estimation of CSF, white, and gray matter volumes from MRIs of hydrocephalic and HIV-positive subjects. *Proceedings of SimTec/WNN*, 643–650.
- Brewer, V. R., Fletcher, J. M., Hiscock, M., & Davidson, K. C. (2001). Attention processes in children with shunted hydrocephalus versus attention deficit–hyperactivity disorder. *Neuropsychology, 15*, 185–198.
- Briand, K. A., Larrison, A. L., & Sereno, A. B. (2000). Inhibition of return in saccade and manual response systems. *Perception & Psychophysics, 62*, 1512–1524.
- Brodeur, D. A., & Enns, J. T. (1997). Covert visual orienting across the lifespan. *Canadian Journal of Experimental Psychology, 51*, 20–35.
- Clohesy, A. B., Posner, M. I., Rothbart, M. K., & Vecera, S. P. (1991). The development of inhibition of return in early infancy. *Journal of Cognitive Neuroscience, 3*, 345–350.

- Danzinger, S., Fendrich, R., & Rafal, R. D. (1997). Inhibitory tagging of locations in the blind field of hemianopic patients. *Consciousness and Cognition*, 6, 291–307.
- Danzinger, S., Kingstone, A., & Snyder, J. J. (1998). Inhibition of return to successively stimulated locations in a sequential visual search paradigm. *Journal of Experimental Psychology: Human Perception and Performance*, 24, 1467–1475.
- del Bigio, M. (1993). Neuropathological changes caused by hydrocephalus. *Acta Neuropathologica*, 18, 573–585.
- Dennis, M., Edelman, K., Copeland, K., Francis, D., Hetherington, R., Frederick, J., et al. (2005). Covert orienting to exogenous and endogenous cues in children with spina bifida. *Neuropsychologia*, 42, 976–987.
- Dennis, M., Edelman, K., Frederick, J., Copeland, K., Francis, D., Blaser, S. E., et al. (in press). 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. *Neuropsychologia*.
- Dennis, M., Fitz, C. R., Netley, C. T., Harwood-Nash, D. C. F., Sugar, J., Hendrick, E. G., et al. (1981). The intelligence of hydrocephalic children. *Archives of Neurology*, 38, 607–615.
- Dennis, M., Fletcher, J. M., Rogers, T., Hetherington, R., & Francis, D. (2002). Object-based and action-based visual perception in children with spina bifida and hydrocephalus. *Journal of the International Neuropsychological Society*, 8, 95–106.
- Dennis, M., Hendrick, E. B., Hoffman, H. J., & Humphreys, R. P. (1987). The language of hydrocephalic children and adolescents. *Journal of Clinical and Experimental Neuropsychology*, 9, 593–621.
- Epstein, J. N., Conners, C. K., Erhardt, D., March, J. S., & Swanson, J. M. (1997). Asymmetrical hemispheric control of visual-spatial attention in adults with attention deficit hyperactivity disorder. *Neuropsychology*, 11, 467–473.
- Filipek, P., Richelmen, C., Kennedy, D., Rademacher, J., Pitcher, D., Zidel, S., & Caviness, V. S. (1992). Morphometric analysis of the brain in developmental language disorders and autism. *Annals of Neurology*, 32, 475.
- Finlay, B. L., Marder, K., & Cordon, D. (1980). Acquisition of visuomotor behaviour after neonatal tectal lesions in the hamster: The role of visual experience. *Journal of Comparative and Physiological Psychology*, 94, 506–518.
- Fletcher, J. M., Bohan, T. P., Brandt, M. E., Kramer, L. A., Brookshire, B. L., Thorstad, K., et al. (1996). Morphometric evaluation of the hydrocephalic brain: Relationships with cognitive development. *Child's Nervous System*, 12, 192–199.
- Fletcher, J. M., Copeland, K., Frederick, J., Blaser, S. E., Kramer, L. A., Hannay, H. J., et al. (2005). Spinal lesion level in spina bifida meningocele: A source of neural and cognitive heterogeneity. *Journal of Neurosurgery: Pediatrics*, 102(Suppl. 3), 268–279.
- Fletcher, J. M., Dennis, M., & Northrup, H. (2000). Hydrocephalus. In K. O. Yeates, M. D. Ris, & H. G. Taylor (Eds.), *Pediatric neuropsychology: Research, theory, and practice* (pp. 25–46). New York: Guilford Press.
- Gerig, G., Kubler, O., Kikinis, R., & Jolesz, F. A. (1992). Nonlinear anisotropic filtering of MRI data. *IEEE Transactions on Medical Imaging*, 11, 221–231.
- Hannay, H. J. (2000). Functioning of the corpus callosum in children with early hydrocephalus. *Journal of the International Neuropsychological Society*, 6, 351–361.
- Hollingshead, A. B. (1975). *Four-Factor Index of Social Status*. Unpublished manuscript, Yale University.
- Klein, R. M. (1988, August 4). Inhibitory tagging system facilitates visual search. *Nature*, 334, 430–431.
- Klein, R. M. (2000). Inhibition of return. *Trends in Cognitive Sciences*, 4, 138–147.
- Landry, S., Lomax-Bream, L., & Barnes, M. (2003). The importance of early motor and visual functioning for later cognitive skills in preschoolers with and without spina bifida. *Journal of the International Neuropsychological Society*, 9, 175.
- Li, C.-S. R., Chang, H.-L., & Lin, S.-C. (2003). Inhibition of return in children with attention deficit hyperactivity disorder. *Experimental Brain Research*, 149, 125–130.
- MacPherson, A. C., Klein, R. M., & Moore, C. (2003). Inhibition of return in children and adolescents. *Journal of Experimental Child Psychology*, 85, 337–351.
- Optican, L. M. (1995). A field theory of saccade generation: Temporal-to-spatial transform in the superior colliculus. *Vision Research*, 35, 3313–3320.
- Pao, Y. H. (1989). *Adaptive pattern recognition and neural networks*. Reading, MA: Addison-Wesley.
- Park, C. H., Stewart, W., Khoury, M. J., & Mulinare, J. (1992). Is there etiologic heterogeneity between upper and lower neural tube defects? *American Journal of Epidemiology*, 136, 1491–1493.
- Posner, M. I. (1980). Orienting of attention. *Quarterly Journal of Experimental Psychology*, 32, 3–25.
- Posner, M. I., & Cohen, Y. (1984). Components of visual orienting. In H. Bouma & D. G. Bouwhuis (Eds.), *Attention and performance X: Control of language processes* (pp. 531–556). Hillsdale, NJ: Erlbaum.
- Posner, M. I., Cohen, Y., & Rafal, R. D. (1982). Neural systems control of spatial orienting. *Philosophical Transactions of the Royal Society of London, Series B*, 298, 187–198.
- Posner, M. I., Rafal, R. D., Choate, L., & Vaughan, J. (1985). Inhibition of return: Neural basis and function. *Cognitive Neuropsychology*, 2, 211–228.
- Pratt, J., & Fischer, M. H. (2002). Examining the role of the fixation cue in inhibition of return. *Canadian Journal of Experimental Psychology*, 56, 294–301.
- Rafal, R. D., Calabresi, P. A., Brennan, C. W., & Sciolto, T. K. (1989). Saccade preparation inhibits reorienting to recently attended locations. *Journal of Experimental Psychology: Human Perception and Performance*, 15, 673–685.
- Rafal, R. D., & Grimm, R. J. (1981). Progressive supranuclear palsy: Functional analysis of the response to methysergide and antiparkinsonian agents. *Neurology*, 31, 1507–1518.
- Rafal, R. D., & Henik, A. (1994). The neurology of inhibition. In D. Dagenbach & T. H. Carr (Eds.), *Inhibitory processes in attention, memory, and language* (pp. 1–51). San Diego, CA: Academic Press.
- Rafal, R. D., Henik, A., & Smith, J. (1991). Extrageniculate contribution to reflex visual orienting in normal humans: A temporal hemifield advantage. *Journal of Cognitive Neuroscience*, 3, 351–358.
- Rafal, R. D., Posner, M. I., Friedman, J. H., Inhoff, A. W., & Bernstein, E. (1988). Orienting of visual attention in progressive supranuclear palsy. *Brain*, 111, 267–280.
- Richards, J. E. (2001). Cortical indices of saccade planning following covert orienting in 20-week-old infants. *Infancy*, 2, 135–157.
- Richards, J. E. (2003). The development of visual attention and the brain. In M. de Haan & M. H. Johnson (Eds.), *The cognitive neuroscience of development* (pp. 73–98). Hove, England: Psychology Press.
- Sapir, A., Soroker, N., Berger, A., & Henik, A. (1999). Inhibition of return in spatial attention: Direct evidence for collicular generation. *Nature Neuroscience*, 2, 1053–1054.
- Simion, F., Valenza, E., Umiltà, C., & Dalla Barba, B. D. (1995). Inhibition of return in newborns is temporo-nasal asymmetrical. *Infant Behavior and Development*, 18, 189–194.
- Swanson, J. M., Posner, M., Potkin, S., Bonforte, S., Youpa, D., Fiore, C., et al. (1991). Activating tasks for the study of visual-spatial attention in ADHD children: A cognitive anatomic approach. *Journal of Child Neurology*, 6, S117–S125.

- Thorndike, R. L., Hagen, E. P., & Sattler, J. M. (1986). *The Stanford-Binet Intelligence Scale* (4th ed.). Itasca, IL: Riverside.
- Tipper, S. P., Jordan, H., & Weaver, B. (1999). Scene-based and object-centered inhibition of return: Evidence for dual orienting mechanisms. *Perception & Psychophysics*, *61*, 50–60.
- Umiltà, C. (2001). Mechanisms of attention. In B. Rapp (Ed.), *The handbook of cognitive neuropsychology: What deficits reveal about the mind* (pp. 135–158). Philadelphia: Psychology Press.
- Valenza, E., Simion, F., & Umiltà, C. (1994). Inhibition of return in newborns. *Infant Behavior and Development*, *17*, 293–302.
- Vivas, A. B., & Fuentes, L. J. (2001). Stroop interference is affected in inhibition of return. *Psychonomic Bulletin & Review*, *8*, 315–323.
- Vivas, A. B., Humphreys, G. W., & Fuentes, L. J. (2003). Inhibitory processing following damage to the parietal lobe. *Neuropsychologia*, *41*, 1531–1540.
- Volcik, K. A., Blanton, S. H., & Northrup, H. (2001). Examinations of methylenetetrahydrofolate reductase C677T and A1298C mutations—and in utero viability. *American Journal of Human Genetics*, *69*, 1150–1153.

Received November 21, 2003

Revision received March 5, 2004

Accepted May 24, 2004 ■

Members of Underrepresented Groups: Reviewers for Journal Manuscripts Wanted

If you are interested in reviewing manuscripts for APA journals, the APA Publications and Communications Board would like to invite your participation. Manuscript reviewers are vital to the publications process. As a reviewer, you would gain valuable experience in publishing. The P&C Board is particularly interested in encouraging members of underrepresented groups to participate more in this process.

If you are interested in reviewing manuscripts, please write to Demarie Jackson at the address below. Please note the following important points:

- To be selected as a reviewer, you must have published articles in peer-reviewed journals. The experience of publishing provides a reviewer with the basis for preparing a thorough, objective review.
- To be selected, it is critical to be a regular reader of the five to six empirical journals that are most central to the area or journal for which you would like to review. Current knowledge of recently published research provides a reviewer with the knowledge base to evaluate a new submission within the context of existing research.
- To select the appropriate reviewers for each manuscript, the editor needs detailed information. Please include with your letter your vita. In your letter, please identify which APA journal(s) you are interested in, and describe your area of expertise. Be as specific as possible. For example, “social psychology” is not sufficient—you would need to specify “social cognition” or “attitude change” as well.
- Reviewing a manuscript takes time (1–4 hours per manuscript reviewed). If you are selected to review a manuscript, be prepared to invest the necessary time to evaluate the manuscript thoroughly.

Write to Demarie Jackson, Journals Office, American Psychological Association, 750 First Street, NE, Washington, DC 20002-4242.