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Spatial analysis after perinatal stroke: patterns of neglect and exploration in extra-personal space

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Abstract

This study was conducted to determine whether school-aged children who had experienced a perinatal stroke demonstrate evidence of persistent spatial neglect, and if such neglect was specific to the visual domain or was more generalized. Two studies were carried out. In the first, 38 children with either left hemisphere (LH) or right hemisphere (RH) damage and 50 age-matched controls were given visual cancellation tasks varying in two factors: target stimuli and stimulus array. In the second study, tactile neglect was evaluated in 41 children with LH or RH damage and 72 age-matched controls using a blindfolded manual exploration task. On the visual cancellation task, LH subjects omitted more target stimuli on the right, but also on the left, compared with controls. Children with RH lesions also produced a larger number of omissions on both the left and right sides than controls, but with poorer performance on the left. On the manual exploration task, LH children required significantly longer times to locate the target on both sides of the board than did controls. RH children had significantly prolonged search times on the left side, but not on the right, compared with controls. In both tasks, LH subjects employed unsystematic search strategies more often than both control and RH children. The search strategy of RH children also tended to be erratic when compared to controls, but only in the random arrays of the visual cancellation tasks; structure of the target stimuli improved their organization. These results demonstrate that children with early LH brain damage display bilateral difficulties in visual and tactile modalities; a pattern that is in contrast to that seen in adults with LH damage. This may result from disorganized search strategies or other subtle spatial or attentional deficits. Results of performance of RH children suggests the presence of contralateral neglect in both the visual and tactile modalities; a finding that is similar to the neglect in adult stroke patients with RH lesions. The fact that deficits in spatial attention and organizational strategies are present after very early focal damage to either the LH or the RH broadens our understanding of the differences in functional lateralization between the immature and mature brain. These results also add to evidence for limitations to plasticity in the developing brain. Our findings may have therapeutic and rehabilitative implications for the management of children with early focal brain lesions.

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Keywords

spatial neglect; perinatal stroke; extrapersonal space; tactile neglect; visual neglect

1. INTRODUCTION

Evidence regarding the persisting neurological and cognitive impairments of stroke in adults has been well established since the mid-19th century (Broca, 1861). A large number of studies have identified major lasting impairments in language, cognition, motor function, intellect, and mood in adults following stroke. In contrast, studies done in children have generally reported milder deficits and greater intellectual and functional recovery following early brain damage (Ballantyne, 1994, Ballantyne *et al.*, 2008, Trauner *et al.*, 1993). For instance, although there is initial delay in language acquisition in children with either RH or LH injury (Bates, 1997), they develop essentially normal language skills by the age of five years (Bates, 1999). Similarly, children with early brain injury reach motor milestones at nearly expected times, despite the presence of hemiparesis (Trauner *et al.*, 1993). The recovery of such cognitive and neurological functioning after very early brain damage has been attributed to the tremendous potential for reorganization in the developing brain. However, the limitations of plasticity in the developing nervous system, particularly as the brain matures, have been questioned. In this regard, recent studies have demonstrated persisting deficits in visual spatial skills (Stiles and Nass, 1991, Stiles *et al.*, 1997), interpersonal skills (Weintraub and Mesulam, 1983), prosody (Trauner *et al.*, 1996), attention (Max *et al.*, 2004), and some aspects of language (Thal *et al.*, 1991) in children with early focal brain lesions. For example, Thal *et al.* (1991) showed that children with either RH or LH damage demonstrate overall delays in lexical comprehension and production. Interestingly, left hemisphere lesions in children were associated with greater delays in expressive language and children with right hemisphere lesions were more impaired in word comprehension.

One of the commonly observed disabling conditions following stroke in adults is hemispatial neglect, or inattention to the contralateral half of an individual's extra-personal space. Although such neglect can be found following either RH or LH damage (Plummer *et al.*, 2003, Stone *et al.*, 1993), it is more common and severe and is more likely to persist when the lesion is in the RH (Bowen *et al.*, 1999, Gainotti *et al.*, 1972, Heilman and Van Den Abell, 1980). Over time, this has led to the theory that the RH of the brain distributes attention throughout extra-personal space, while the left hemisphere attends mainly to contralateral right hemispace (Heilman and Van Den Abell, 1980, Weintraub and Mesulam, 1987).

The severity of visual neglect in adults following stroke has been shown to depend on stimulus and task-related factors (Aglioti *et al.*, 1997, Leicester *et al.*, 1969, Sarri *et al.*, 2009, Weintraub and Mesulam, 1988). One of the most useful types of tests for identifying visual neglect is the cancellation test in which the subject is asked to find and visibly cross out (with a pencil) targets distributed on a sheet of paper. Weintraub and Mesulam (1988) used visual target cancellation tasks differing in stimulus (letters or geometric shapes) and spatial array (random or structured) to examine the effect of these factors on the severity of neglect. They found that patients with RH lesions demonstrated dramatic contralateral neglect when letters were presented in a random array but not in a structured array and that their subjects were better at letter detection than shape detection. Similarly, studies have found differences in performance on cancellation tests in adults according to the inclusion of non-target stimuli that must be ignored (Geldmacher, 1996, Husain and Kennard, 1997, Kaplan *et al.*, 1991), the degree of similarity between targets and non-targets (Rapcsak *et al.*,

1989), and differences in stimulus content and search field complexity (Weintraub and Mesulam, 1988).

In addition to inattention to visually presented stimuli, hemispatial neglect has also been observed in the tactile modality in brain-damaged adults (Beschlin *et al.*, 1996, Chedru, 1976, De Renzi, 1970). Tactile neglect, or neglect of stimuli in the absence of vision, has been most commonly shown using blindfolded manual exploration tasks (Liu *et al.*, 1992, Weintraub and Mesulam, 1987). The results from these studies, however, have been somewhat conflicting and difficult to generalize. For example, De Renzi and colleagues (1970) demonstrated that patients with RH brain damage and a visual field deficit show tactile neglect significantly more often than any other brain-damaged subgroup. Neglect was defined as the failure to find a marble placed contralateral to the lesion side in a maze within a 90 second time limit. This led to the hypothesis that tactile neglect is not independent from visual neglect and consequently, that unilateral spatial neglect is likely to be a disruption of a *single* attentional process. In contrast, Villardita (1987), using a similar maze test, reported that RH lesion patients with left visual neglect preferred tactile scanning of the *left* side of the maze even under no visual control. Several other studies using different experimental procedures have since reported a dissociation between visual and tactile neglect (Chokron *et al.*, 2002, Cubelli *et al.*, 1991, Marsh and Hillis, 2008). For example, Cubelli *et al.* (1991) reported in their study investigating exploration of a computer keyboard that three patients were impaired on blindfolded exploration but not on visual exploration and four patients were impaired on visual exploration but not on blindfolded exploration.

Although hemispatial neglect in adults has been the subject of a large number of studies, much less is known about this phenomenon in children following very early brain damage. In particular, there remains a paucity of information regarding laterality effects on spatial neglect in this population. Recently, Trauner (2003) demonstrated hemispatial neglect in infants and young children after *either* LH or RH damage using two object-removal preference tasks. Children with either LH or RH lesions preferentially removed objects from the side of the board ipsilateral to the lesion. This study added to evidence that early brain damage may be associated with long-term consequences in neuropsychological functioning. In addition, the fact that children with LH lesions showed contralateral neglect is in contrast to adults with LH lesions in whom neglect is rare or disappears after just weeks when it does occur (Heilman and Van Den Abell, 1980, Mesulam, 1981), suggesting differences in functional localization between the developing and adult brain. More evidence for the presence of unilateral spatial neglect in young children with brain lesions was presented in a retrospective study by Laurent-Vannier *et al.* (2003). Neglect was assessed in 12 children with acquired brain damage of various etiologies; all children exhibited various types of neglect behavior in daily activities, including drawing, writing, and reading. The same group confirmed these results in a recent study using the Teddy Bear Cancellation Test in children with acquired brain injury. Neglect of left hemispace was found in three of ten children with right-sided lesions while right hemispatial neglect was found in two of fifteen children with left-sided injuries (Laurent-Vannier *et al.*, 2006).

Given the paucity of data on neglect syndromes in children with early unilateral damage, the present study was designed to provide additional information on this phenomenon in children who had perinatal stroke. The aims of the current study were: (1) to determine whether school-aged children who experienced perinatal focal brain lesions demonstrate evidence of hemispatial neglect, either in the visual or tactile modalities, and whether there is a dissociation between visual and tactile neglect; (2) to evaluate the effect of different target stimuli and stimulus arrays on the severity of visual hemispatial neglect in these children; and (3) to explore whether early brain damage impairs search strategies in children and if this contributes to the severity of visual inattention in these patients.

2. METHODS

Two studies were conducted, one utilizing a visual exploration task requiring target cancellation, and the other utilizing a manual exploration task without visual input.

2.1 Study Population

For the visual exploration task, participants consisted of 88 children between the ages of 4 years, 9 months and 16 years, 5 months. Nineteen subjects had LH lesions (13 males, 6 females; age $M = 8$ years, 9 months, $SD = 3$ years, 3 months), nineteen subjects had RH lesions (9 males, 10 females; age $M = 9$ years, 8 months, $SD = 2$ years, 8 months), and fifty subjects were typically developing controls who were age-matched to the focal lesion children (26 males, 24 females; age $M = 9$ years, 5 months, $SD = 2$ years, 7 months). All eighty-eight of the children who participated in the visual exploration task also participated in the manual exploration task. An additional 25 children participated in the manual exploration task but not the visual exploration task. For the manual exploration task, subjects consisted of 113 children between the ages of 4 years, 9 months and 16 years, 5 months. Twenty-one children had LH lesions (15 males, 6 females; age $M = 8$ years, 11 months, $SD = 3$ years, 4 months). Twenty children had RH lesions (10 males, 10 females; age $M = 9$ years, 5 months, $SD = 2$ years, 9 months). Seventy two controls were age-matched to the focal lesion children (39 males, 33 females; age $M = 9$ years, 7 months, $SD = 2$ years, 9 months).

Children in the focal brain lesion groups had a single, unilateral lesion due to ischemic or hemorrhagic infarct, which was documented by a neuroimaging procedure (either CT or MRI). Lesion occurrence was perinatal, based on medical history and hospital records. Participants were recruited through referrals from area pediatric neurologists. Exclusionary criteria included the presence of multiple lesions; history of exposure to illicit drugs in utero; history of bacterial meningitis, encephalitis, or anoxia; severe closed head trauma; or any history of a problem that might have produced more global brain damage. All focal lesion participants were able to understand and cooperate in the testing sessions. None of the participants displayed significant gaze deviation at rest.

Recruitment of control children was primarily from fliers placed in pediatricians' offices and local community centers, advertisements in parent magazines, and by word of mouth. Control participants had no significant neurological or psychiatric history, and had normal medical and developmental histories. Exclusionary criteria for control children included IQ < 85 ; history of exposure to illicit drugs in utero; severe closed head trauma; or any history of a problem that might have resulted in cognitive dysfunction.

Informed consent was obtained for all subjects prior to testing, in accordance with the procedures of the University of California, San Diego Institutional Review Board.

2.2 Neurological Examination

Children in the focal brain lesion groups underwent a standard neurological examination as part of the study. Information from these exams was used to identify those children with a visual field defect.

2.3 Neglect Tasks

2.3.1 Visual Cancellation Task

2.3.1.1 Materials: A visual cancellation task designed by Weintraub and Mesulam (1988) was used. Subjects were tested on four different conditions in which two factors were varied: target stimulus (geometric shape vs. letter) and array (random vs. structured).

Subjects were presented an 8 ½" by 11" sheet of paper in each of the four conditions. The center of the sheet was aligned with the subject's midline and the subject was not permitted to move the sheet. There were 30 targets to the left of center and 30 targets to the right of center. In the random array, the shapes or letters were randomly distributed, while in the structured array shapes or letters had an orderly arrangement. The administration of the trials was as follows: Random Shapes (RS), Random Letters (RL), Structured Shapes (SS), and Structured Letters (SL). The subject was asked to circle, with a colored pencil, all the target stimuli on each trial (the letter "A" for the letter cancellation trials and an open circle crossed with a single slanted line for the shape cancellation trials). In order to not bias search strategy, the target was presented to the subject on a separate sheet of paper. A different colored pencil was handed to the child after every ten to twelve circled items. This allowed us to assess the subject's search strategy. No time limit was given. Instead, the subject was asked to report when he/she believed they had circled all of the targets.

2.3.1.2 Measures: The data collected for each test condition consisted of target omissions and error commissions on the left and right halves of the page. This was calculated by folding the test sheet in half along the vertical axis, and counting the number of target omissions and commissions on each half of the page. The time from the "go" signal to when the subject indicated he/she was done was also noted for each subject during each trial. Three characteristics of the search strategy were recorded. The origin of search was defined as the location of the first circled target on each trial. The possible indices were "left," "right," and "center." The progression of search was defined as the *initial* progression of the search. The possible indices were "left-to-right," "right-to-left," and "undefined/center" if the child did not progress towards the left or the right. Organization during the search was rated as "systematic" if the child proceeded in a successive vertical or horizontal pattern and as "unsystematic" if the child proceeded in any other approach.

2.3.2 Manual Exploration Task

2.3.2.1 Materials: A large cork-board (70 × 91.4 cm) was placed on a flat surface in front of the subject, with the center of the board at the midline of the subject's body. After two practice trials under visual guidance, the subject was blindfolded for the remainder of the task. A plastic pinhead was placed in one of nine predetermined locations on the board and the subject was instructed to feel around the board as quickly as possible with their preferred hand to find the pinhead. The locations were distributed symmetrically on the left, middle, or right side of the board. The child's preferred hand was placed at the bottom center of the board before each trial. Trials were videotaped for later detailed assessment of the search strategy.

2.3.2.2 Measures: The time from the "go" signal to when the subject found the pinhead was recorded for each trial. The average time to locate the pinhead on each side of the board was calculated. Three measures of search strategy were noted: origin, progression, and degree of organization of search (Figure 1). The origin of search was defined as where the child placed his/her hand on the board and touched the board to feel for the pinhead. The indices for origin were "left," "right," and "center." To be considered originating on the left or right, the child's hand must have started at least one-hand-width away from the center of the board. Progression was defined as *initial* progression. If the child progressed to the right, a score of "left to right" was given. If the child progressed to the left, a score of "right to left" was given. If the child originated in the center, the direction in which the child progressed greater than a metric of one-hand-width was scored. An "N/S – not scorable" was given if the child's progression was not scorable. A child's search was considered systematic if the child proceeded in successive vertical or horizontal sweeps or in a spiral movement. The spiral search strategy was only considered systematic if the child used an outward to inward or

inward to outward strategy and covered at least half the board in width and height. Any other search strategies were considered unsystematic. If the child found the pinhead on initial progression or if there was too little information, an “N/S – not scorable” was given. Some participants used a patting strategy – this was noted and a score of “systematic – patting” or “unsystematic – patting” was given. In addition to scoring the degree of organization, the approach chosen – horizontal, vertical, or spiral – was noted.

2.4 Statistical Analysis

In both studies, independent *t*-tests were used to explore group differences in performance (LH vs. control, RH vs. control, and LH vs. RH). For the visual exploration study, analyses were based on the number of omissions on the left and right halves of the page, as well as the time needed for completion in each of the four trials. To assess performance differences between groups in the manual exploration task, analyses were done on the mean number of seconds taken to locate the pinhead on the left and right sides of the board using the preferred hand. Dependent *t*-tests were used to examine within group (LH lesion, RH lesion, and control groups) differences in performance on the left and right on the visual cancellation task and the manual exploration task. Each lesion group was compared to controls with respect to the frequency of employed search strategies in the two studies using χ^2 tests. If the absolute value of a residual was greater than 2.00, it was concluded to have a major influence on a significant chi-squared test statistic. Finally, given that some of the lesion children had visual field deficits, independent *t*-tests were used to examine the effect of visual field deficit on performance within each lesion group in each of the studies. Alpha was set at .05 in all statistical analyses.

3. RESULTS

3.1 Visual Exploration

3.1.1 Age—There was no significant difference in ages for the control, LH, and RH groups.

3.1.2 Target Omissions—The mean number of target omissions per hemispace for each group on each trial of the cancellation test is summarized in Table 1. Control children produced very few errors (Figure 2). However, they missed more targets on the right half of the page than on the left, summed across all trials, $t(46) = -2.019$, $p = .049$. [We offer two explanations for this: (1) the contribution of learned left-to-right reading habits or (2) since the majority of our subjects were right handed, there might be partial occlusion of the right side by the right hand. There were too few left-handed controls ($n = 5$) to provide sufficient information for statistical analysis.] Control children did significantly worse on the two letters tasks than on the two shapes tasks (Letters Total Omissions: $M = 4.6$, $SD = 4.51$; Shapes Total Omissions: $M = 2.25$, $SD = 2.02$; $t(46) = -3.63$, $p = .001$). These children did not perform significantly differently on the structured and random arrays.

Subjects with LH lesions made more errors than controls on the left *and* right half of the page (Figure 2). Similar to controls, in every trial, LH lesion children showed a trend toward missing more targets on the right half of the page than on the left. The average number of targets omitted on the right half of the page, summed across all trials, was significantly greater than the average number of targets omitted on the left half the page, $t(18) = -2.242$, $p = .038$. LH children did significantly worse on the two letters tasks than on the two shapes tasks, (Letters Total Omissions: $M = 18.89$, $SD = 18.34$; Shapes Total Omissions: $M = 12.53$, $SD = 14.63$; $t(18) = -2.815$, $p = .011$). Interestingly, LH children did not perform differently between the two halves of the page on the shapes tasks, but on the two letters tasks, LH children made significantly more errors on the right than on the left half of the

page (Letters Omissions on Left: $M = 7.89$, $SD = 9.04$; Letters Omissions on Right: $M = 12.52$, $SD = 14.63$; $t(18) = -2.17$, $p = .044$.)

Children with RH lesions also produced significantly more errors than controls on the left and right halves of the page (Figure 2). In every trial, with the exception of Random Letters (in which subjects performed the same on the left and right halves of the page,) RH lesion children showed a trend toward missing more targets on the left half of the page than on the right (Figure 3), a pattern which is the reverse of that seen in controls, although these analyses did not meet significance. All of these subjects, except for one child, were right-handed (the left-handed child did not perform differently from the rest of the group on any test). RH lesion children did not perform differently when the stimulus material was varied (letters vs. shapes) or when the array was varied (random vs. structured).

Between the lesion groups, LH lesion children produced significantly more errors on the right half of the page compared to RH lesion children, but not on the left half the page (Figure 2).

No significant difference was found in the number of omissions on the left and right half of the page on each trial or summed across all trials when children with visual field deficits were compared with those who had no evidence of visual field deficits for either the LH or RH group (LH group, left side of page $t(8) = 0.514$, $p = .621$, right side of page $t(8) = 0.535$, $p = .607$; RH group, left side of page $t(7) = 0.139$, $p = .893$, right side of page $t(7) = 0.597$, $p = .569$).

Subjects in each group made almost no commission errors on any of the trials.

3.1.3 Mean Time to Completion—The mean time to completion on each trial and time summed across all four trials of the cancellation test is summarized in Table 1. Both of the lesion groups required significantly more time to complete each visual cancellation task than did the controls (Figure 4). No significant difference was found in the amount of time needed to complete the tasks between children with and without visual field deficits.

3.1.4 Search Strategies—Data on the search strategies employed by controls, LH, and RH subjects summed across the four trials of the cancellation task is presented in Table 2. On average, control subjects began their search on the left on almost 80% of trials. The progression for controls was from left-to-right on the page 80.63% of the time, from right-to-left 14.8% of the time, and in an undefined pattern only 4.6% of the time. The choice to progress in a left-to-right manner was most pronounced when they were presented with a structured array of letters. With a small number of exceptions, controls progressed in systematic horizontal or vertical sweeps on the page on all four trials.

LH lesion children originated their search less often on the left side of the page compared to controls. Instead, they chose to start in the center more than twice as often as the controls. This was most pronounced in the Structured Letters trial in which controls began their search in the center 6.1% of the time, while LH children started in the center 21.1% of the time. The initial progression pattern used by LH subjects also differed than controls in that they progressed in an undefined pattern significantly more often than did controls. Children with LH lesions were more unsystematic in their search strategy compared to controls as well and they were not aided in their search strategy by organization of the shapes or letters. In fact, children with LH lesions were the most unorganized in their search strategies, even when compared to RH children. LH children employed unsystematic search strategies 43.4% of the time.

Children in the RH lesion group differed significantly from controls on origin and organization. These children originated their search on the right more than twice as frequently as controls. Despite this, their progression did not differ significantly from that of controls. RH subjects used unsystematic search strategies twice as often as control children. Interestingly, when analyses were completed for individual trials, RH lesion children used unsystematic strategies more often than controls only in the *random* arrays; structured arrays of the shapes and letters improved their organization.

3.2 Manual Exploration

3.2.1 Age—There was no significant difference in ages for the control, LH, and RH groups.

3.2.2 Time to Completion—Mean values for the time taken to locate the target pinhead on the left and right sides of the board are summarized in Table 3. Subjects with LH lesions required a longer time to find the pinhead on the left *and* right sides of the board, compared to controls. Similar to the results in the visual neglect test, both the control children and LH lesion children showed a trend of taking a longer time to find the pinhead when it was placed on the right side of the board than on the left, although within group differences did not meet significance. Children with RH lesions required significantly longer times on the left side, but not on the right, compared to controls. Similar to the findings of the visual cancellation test, RH lesion children showed the opposite pattern to controls in that they spent less time to find the pinhead on the right side than on the left, although within group differences did not meet significance.

There was no significant difference in the mean time to locate the target on either side of the board for either the LH or RH group when children with visual field deficits were compared with children without visual field deficits (LH group, left side of board, $t(10) = 1.08$, $p = .304$, right side of board, $t(10) = 1.34$, $p = .211$; RH group, left side of board, $t(8) = 1.54$, $p = .161$, right side of board, $t(8) = 1.02$, $p = .339$).

3.2.3 Search Strategies—Data on the search strategies utilized by each group summed across the nine trials of the manual exploration task are presented in Table 4. Controls started their search in the center of the board 92.03% of the time. This is most likely because before each trial, the participant was asked to place their preferred hand on the bottom center of the board. The control group then progressed to the right 37.65% of the time and to the left 62.35% of the time. Although a quantitative analysis was not done, children in the control group often alternated between progressing toward the left and right sides of the board on each trial. Our explanation for this is that the children were reflecting on where the pinhead was placed in the previous trial and then searching for the tack on the opposite side of the board on the next trial. In contrast to the visual exploration task, the majority of control children proceeded in an unsystematic fashion on the board; only 28.43% of the time did the children employ systematic strategies.

LH lesion children also originated their search in the center of the board over 90% of the time. Their initial progression did not differ significantly from that of the control group. However, similar to the results in the visual cancellation task, LH lesion children employed systematic strategies less than half as often as the control children.

Children in the RH lesion group originated their search in the center 92.98% of the time, on the left 6.47% of the time, and on the right only 0.55% of the time. Interestingly, these children progressed towards the right significantly more frequently than the controls and LH lesion children; they progressed to the right 51.75% of the time and to the left 48.25% of the

time. The pattern of their organization strategies did not differ significantly from that of controls.

4. DISCUSSION

This study contributes valuable new information to the sparse literature on the persisting deficits in spatial attention in children with early unilateral brain damage. To our knowledge, except for isolated case reports, this study is the first to explore hemispatial neglect in the tactile domain in children with perinatal stroke. In addition, although differences in the severity of visual hemispatial neglect depending on the nature of stimuli have been the subject of many studies in adults, the present study provides the initial insights of these effects in children with early brain injury.

The present study demonstrated evidence of *both* visual and tactile spatial neglect in children with unilateral brain damage from perinatal stroke. Children with LH damage demonstrated bilateral difficulties on both tasks in that they produced more target omissions on the visual cancellation task on both the left and right halves of the page and required more time to locate a target on the manual exploration task on both the left and right sides of the board, compared to controls. LH children also demonstrated poorer performance on the right side of space, compared to the left, in both tasks. Children with RH damage had a larger number of omissions on both the left and right halves of the page compared to controls in the visual cancellation task, but demonstrated poorer performance on the left. In the manual exploration task, RH lesion children required longer times on the left side of the board, but not on the right, compared to controls. In both tasks, RH lesion children showed the opposite pattern to children in the control and LH groups in that they had greater deficits on the left side than on the right. These results provide evidence for contralateral neglect after very early RH damage in children in both the tactile and visual domains.

The pattern of bilateral inattention seen in children in the LH group differs from what is known about adults with LH lesions. Contralateral inattention has been shown in adults with left cerebral lesions, although it is much less severe and often transient, compared to the neglect following right sided lesions (Bowen *et al.*, 1999, Gainotti *et al.*, 1972, Heilman and Van Den Abell, 1980), whereas bilateral neglect or inattention to extra-personal space is more likely to be found in adults with RH lesions (Weintraub and Mesulam, 1987). Thus, our LH subjects are more reminiscent of adults with RH lesions, suggesting a difference in brain organization for spatial attention in the developing brain as opposed to the mature brain. Similar differences in the localization of cerebral functions between the immature and adult brain have also been observed in other cognitive domains, most prominently in aspects of language. Unlike the profile in adults with strokes, early brain damage to *either* hemisphere results in initial language delay. Bates and colleagues (1997) found that children with RH lesions are at a greater risk for delays in language comprehension, whereas early LH injury results in impairment of expressive vocabulary and grammar; this is in direct contradiction with the typical findings in adults with stroke. These data in the domain of language together with the pattern of spatial attention deficits found in the current study suggest that the same behaviors may be mediated by different neural substrates in the developing and mature brain.

One potential explanation for the patterns of performance seen in our study is that children with LH lesions display significantly impaired search strategies. LH lesion children exhibited inefficient, unsystematic strategies more often than both the control and RH lesion children in both visual and tactile domains. The fact that their erratic search strategy was not aided by organization of the target stimuli is also evidence for impaired organizational skills. In contrast, unsystematic search strategies have been demonstrated in adults with lesions of

the right hemisphere (Ishiai *et al.*, 1990, Samuelsson *et al.*, 2002, Weintraub and Mesulam, 1988). For example, Weintraub and Mesulam (1988) demonstrated that patients with right sided lesions began their search on cancellation tests on the right side of the page and then searched erratically, whereas LH patients adopted a systematic horizontal or vertical approach, similar to controls. Although disorganized visual search has been shown in adults with hemispatial neglect, the two are not necessarily associated (Chatterjee *et al.*, 1992, Donnelly *et al.*, 1999, Mark *et al.*, 2004). Indeed in 2004, Mark *et al.* demonstrated that in a group of 18 adult stroke patients, there were no correlations between performance on cancellation tests and various search organization measures, suggesting that organization of visual search strategy and spatial inattention to extra-personal space are not related. The authors hypothesized that impaired search strategies may be under the control of an unspecified executive functioning mechanism. Our results in children with LH lesions provide evidence for this theory. It is possible that children with LH lesions have disrupted executive functioning, resulting in disordered search strategies, and therefore, poorer performance bilaterally on both tasks. Deficits in executive functioning were recently reported in children with focal frontal lobe lesions, although no effects of side of lesion were seen (Jacobs *et al.*, 2007).

An alternative explanation for the observed differences in spatial attention early in development relates to the differences in hierarchical processing that are mediated by the two hemispheres. The right hemisphere is believed to play a dominant role in perceptually integrating external stimuli to form a coherent whole, whereas the left hemisphere appears to attend to details or local elements of a stimulus (Fink *et al.*, 1996; Navon, 1977). These patterns have been demonstrated both in adults with unilateral brain damage (Delis, Kiefner & Fridlund, 1988) and in children after early unilateral stroke (Stiles *et al.*, 1997). If children with left hemisphere damage are unable to adequately attend to parts of the whole, they may have great difficulty with search tasks and also with organizing those searches. In contrast, children with right hemisphere damage might have difficulty in synthesizing the details into a coherent whole. These perceptual differences have also been implicated as a theoretical explanation for the fact that children with early right hemisphere damage may actually have more difficulty acquiring language than children with early left hemisphere injury (Bates *et al.*, 1997), suggesting that hierarchical processing may extend to multiple modalities. To our knowledge, this has not been tested for haptic stimuli, but would be of great interest for future studies.

Children with RH lesions demonstrated contralateral neglect behaviors in both visual and tactile tasks, similar to those in adults. The neglect observed in these children was subtle but noteworthy in that the pattern of performance seen in children with RH lesions was the reverse of that seen in control and LH children in both the visual and tactile modalities. The fact that children in the RH lesion group preferred to either start their search on the right or progress towards the right more often than the two other groups also lends evidence to the presence of contralateral neglect in these children. Similar observations of the persistence of deficits following early damage to the RH have been found in other domains, most notably the domain of visuospatial cognition (e.g., Netelenbos and Rooij, 2004, Schatz *et al.*, 2000, Vicari *et al.*, 1998). For example, Netelenbos and Rooij (2004) found that very early damage to the RH, but not the LH, results in deficits in locating visual targets presented within and beyond the field of view. The persistence of contralateral neglect found in RH children in the present study, coupled with the findings of visuospatial difficulties following lesions in the RH only, imply that specialization of the RH for *certain* cognitive functions occurs very early in brain development and may be hardwired earlier than LH functions. Perhaps highly specified functions, such as visuospatial processing and spatial attention, cannot be supported by alternative parts of the brain, resulting in persisting deficits following very early brain injury.

Children in both lesion groups required significantly more time to complete each of the visual cancellation tasks than did the controls. It is likely that impaired organizational search strategies contributed to the increased time seen in both lesion groups. Interestingly, although LH children performed more poorly than RH children in the number of target omissions on the cancellation tasks, there was no significant difference in the time to complete the tasks between the two groups. This raised the possibility that visual field deficits could be affecting our results. However, there was an absence of effect of visual field deficits in all variables measured in the visual and manual exploration task, including the number of omissions on the left and right sides, the time required to complete the cancellation tasks, and the average time to locate the target on the left and right sides of the board. Another explanation for the prolonged times seen in children with focal brain injury is that these children may have persisting spatial analytic deficits. Interestingly, the literature on the effect of early focal brain injury on the development of spatial analytic processing shows that children with LH damage are more impaired in defining the parts of a spatial pattern while children with RH damage demonstrate impaired pattern integration (Stiles, 1998, Stiles *et al.*, 2003). Exploration of this hypothesis, however, is beyond the scope of this study and should be further considered and evaluated in future studies. Finally, we cannot rule out the possibility that the children with focal brain damage might have motor deficits that slowed their performance. We believe this is unlikely, however, in that they were using their dominant hand. Furthermore, the tasks used in the current study were not tests of motor speed and did not require particularly adept fine motor skills to be successfully accomplished.

Although some studies have reported dissociations in spatial neglect according to modality (Chokron *et al.*, 2002, Cubelli *et al.*, 1991, Marsh and Hillis, 2008, Villardita, 1987) we did not reach the same conclusions. The patterns of deficits in children with either LH or RH focal lesions were the same in visual and tactile domains. Children with RH damage had deficits suggestive of primarily contralateral neglect in both the visual cancellation and manual exploration tasks, whereas subjects with LH lesions demonstrated bilateral difficulties in both tasks with slightly poorer performance on the right. However, since children with LH damage also performed more poorly on both sides of extra-personal space, it is difficult to determine whether the pattern seen in LH children is related solely to a generalized spatial inattention problem or to some other deficit that we did not identify in the current study. Our results from the two studies lend support to the theory that unilateral spatial neglect may be a “supramodal” disruption of spatial attention (De Renzi, 1970). Other studies have also demonstrated the co-occurrence of visual and tactile neglect in adults (Caneman *et al.*, 1992, Vallar *et al.*, 1991). It is alternatively possible that our findings only reflect group differences and that those differences might not co-occur at the individual level. Further studies would be required to determine whether there is a true supramodal spatial attention deficit.

There are important theoretical implications to be derived from this study. Early unilateral brain damage results in very different patterns of spatial attention and neglect than are found in adults after stroke, suggesting that the developing brain uses different neural substrates and strategies to develop spatial awareness than to maintain it once fully developed. The results also suggest potential limitations to plasticity in the developing brain, in that there may be long-lasting spatial attention deficits in children with early focal brain damage. In addition to the theoretical implications of the present study in regards to the limitations of the immature brain's capacity to compensate for early damage in the left or right hemisphere, the findings presented may also have important therapeutic implications for the development and implementation of appropriate interventions for children with early brain damage. It may be helpful, for example, to give a child with a RH lesion a worksheet with problems that are organized in a structured manner to reduce or eliminate any subtle

contralateral neglect. In addition, children with perinatal unilateral brain damage may require longer times to complete school tests. It may also be beneficial for these children to be seated on the side of the classroom ipsilateral to the side of their lesion to allow for better attention processing. Further research must be done to elucidate the various determinants of how children with early focal brain lesions fare over time. A better understanding of their prognosis will allow clinicians and therapists to provide targeted rehabilitative therapy at early stages for remediation.

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Abbreviations

RH	Right Hemisphere
LH	Left Hemisphere

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Highlights

- There are persisting spatial attention deficits after perinatal stroke.
- LH lesion subjects demonstrate bilateral difficulties on visual and tactile search tasks.
- RH lesion subjects demonstrate contralateral neglect in visual and tactile search tasks.
- There are differences in functional lateralization for spatial attention between the developing brain and adult brain.

Figure 1.

Manual Exploration Task. Examples of search strategies. O, Origin; P, Progression; R, Organization; N/S, Not Scorable; System, Systematic; Unsystem, Unsystematic; System-P, Systematic-Patting.

Color preference for Figure 1: Web only (black and white version attached).

Figure 2.

Visual Cancellation Task. Mean number of omissions made by control ($n = 50$), left hemisphere (LH) lesion ($n = 19$), and right hemisphere (RH) lesion ($n = 19$) participants summed across the four trials; * $p < .05$ for lesion vs. control group comparisons; ** $p < .05$ for LH vs. RH group comparisons. Error bars represent standard error of the mean. Color preference for Figure 2: Web only (black and white version attached).

Figure 3.

Sample of structured letters cancellation task in a patient with a RH lesion demonstrating subtle contralateral neglect. Target stimuli: the letter “A”. Target omissions are marked by scorer with a red arrow. Colored pencil order: 1st orange, 2nd green, 3rd brown, 4th red. Color preference for Figure 3: Web only (black and white version attached).

Figure 4. Visual Cancellation Task. Mean time required by control (n = 50), left hemisphere (LH) lesion (n = 19), and right hemisphere (RH) lesion (n = 19) participants for each trial; *p < .05 for lesion vs. control group comparisons. Error bars represent standard error of the mean. Color preference for Figure 4: Web only (black and white version attached).

Table 1

Visual cancellation test results for LH lesion (n = 19), RH lesion (n = 19), and control children (n = 50). Mean (SD) number of target omissions on the left and right halves of the page on each trial and summed across all four trials; lower scores reflect better performance on that half of the page. Mean (SD) number of seconds needed on each trial and summed across all four trials. Independent t-tests were used for statistical analyses.

Task	Control Children	LH Lesion Children	RH Lesion Children	
<i>Random Letters</i>				
Mean Time to Completion (s)	192.73 (85.73)	256.0 (99.12) $\dagger p = .011$	275.8 (102.86) $\dagger p = .001$	$\ddagger p = .550, ns$
Mean Number of Omissions on Left	1.17 (1.49)	4.32 (5.46) $\dagger p < .000$	1.74 (2.00) $\dagger p = .206, ns$	$\ddagger p = .061, ns$
Mean Number of Omissions on Right	1.35 (1.76)	5.89 (6.06) $\dagger p < .000$	1.74 (1.79) $\dagger p = .427, ns$	$\ddagger p = .007$
<i>Random Shapes</i>				
Mean Time to Completion (s)	155.04 (72.17)	240.74 (96.22) $\dagger p < .000$	213.26 (80.14) $\dagger p = .005$	$\ddagger p = .345, ns$
Mean Number of Omissions on Left	0.59 (1.10)	2.63 (3.68) $\dagger p = .001$	2.79 (3.61) $\dagger p < .000$	$\ddagger p = .895, ns$
Mean Number of Omissions on Right	0.80 (1.04)	2.89 (4.53) $\dagger p = .003$	2.05 (2.46) $\dagger p = .004$	$\ddagger p = .481, ns$
<i>Structured Letters</i>				
Mean Time to Completion (s)	155.73 (68.88)	246.1 (111.82) $\dagger p < .000$	225.0 (92.90) $\dagger p = .001$	$\ddagger p = .531, ns$
Mean Number of Omissions on Left	1.06 (1.77)	3.58 (4.40) $\dagger p = .001$	2.74 (4.31) $\dagger p = .025$	$\ddagger p = .555, ns$
Mean Number of Omissions on Right	1.41 (2.00)	5.11 (5.80) $\dagger p < .000$	2.05 (2.20) $\dagger p = .250, ns$	$\ddagger p = .039$
<i>Structured Shapes</i>				
Mean Time to Completion (s)	138.96 (55.50)	190.47 (87.88) $\dagger p = .005$	214.84 (89.79) $\dagger p < .000$	$\ddagger p = .403, ns$
Mean Number of Omissions on Left	0.58 (1.31)	3.26 (3.66) $\dagger p < .000$	1.79 (2.82) $\dagger p = .018$	$\ddagger p = .173, ns$
Mean Number of Omissions on Right	0.72 (1.16)	3.74 (4.72) $\dagger p < .000$	1.42 (1.61) $\dagger p = .049$	$\ddagger p = .051, ns$
<i>Summed Across All Four Trials</i>				
Mean Time to Completion (s)	630.49 (255.30)	933.32 (344.9) $\dagger p < .000$	928.89 (328.8) $\dagger p < .000$	$\ddagger p = .968, ns$
Mean Number of Omissions on Left	2.92 (3.07)	13.79 (14.71) $\dagger p < .000$	9.05 (11.19) $\dagger p = .001$	$\ddagger p = .271, ns$
Mean Number of Omissions on Right	3.94 (3.34)	17.63 (17.70) $\dagger p < .000$	7.26 (6.00) $\dagger p = .005$	$\ddagger p = .021$

$\dagger p$ values are for lesion vs. control comparisons

$\ddagger p$ values are for LH vs. RH comparisons

Table 2

Visual cancellation test search strategies employed by LH lesion (n = 19), RH lesion (n = 19), and control children (n = 50) summed across all four trials. Origin: percent of instances of left (L), right (R), and center (C) origin. Initial progression: percent of instances of left-to-right (LR), right-to-left (RL), and undefined (Undef) progression. Organization: percent of instances of systematic (S) and unsystematic (U) organization. Chi-squared tests were used for statistical analyses.

Group	Origin (%)			Initial Progression (%)			Organization (%)	
	L	R	C	LR	RL	Undef	S	U
Control	79.13	7.65	13.22	80.63	14.8	4.6	86.73	13.27
LH Lesion Children	63.15	9.2	27.65	69.72	17.1	13.18	56.6	43.4
	$\chi^2 = 14.32, p = .001$			$\chi^2 = 13.5, p = .001$			$\chi^2 = 60.0, p < .000$	
RH Lesion Children	76.3	17.13	6.57	80.25	18.43	1.33	73.68	26.32
	$\chi^2 = 11.5, p = .003$			$\chi^2 = 2.46, p = .293, ns$			$\chi^2 = 11.24, p = .001$	
	$\chi^2 = 55.82, p < .000$			$\chi^2 = 81.07, p < .000$			$\chi^2 = 11.46, p = .001$	

χ^2 and p values are for lesion vs. control comparisons

χ^2 and p values are for LH vs. RH comparisons

Table 3

Manual exploration test results for LH lesion (n = 21), RH lesion (n = 20), and control (n = 72) children. Mean (SD) number of seconds taken to locate pinhead on left and right side of board. Independent t-tests were used for statistical analyses.

	Control Children	LH Lesion Children	RH Lesion Children	
Mean Time to Locate Target on Left Side (s)	6.72 (4.67)	9.08 (5.07) [†] p = .048	10.17 (9.56) [†] p = .008	[‡] p = .650, <i>ns</i>
Mean Time to Locate Target on Right Side (s)	7.37 (5.42)	10.73 (9.80) [†] p = .044	8.40 (6.28) [†] p = .861, <i>ns</i>	[‡] p = .374, <i>ns</i>

[†]p values are for lesion vs. control comparisons

[‡]p values are for LH vs. RH comparisons

Manual exploration task search strategies employed by LH lesion (n = 9), RH lesion (n = 8), and control children (n = 39) summed across all nine trials. Origin: percent of instances of left (L), right (R), and center (C) origin. Initial progression: percent of instances of left-to-right (LR) and right-to-left (RL) progression. Organization: percent of instances of systematic (S) and unsystematic (U) organization. Chi-squared tests were used for statistical analyses.

Table 4

Group	Origin (%)			Initial Progression (%)			Organization (%)		
	L	R	C	LR	RL		S	U	
Control	2.28	5.69	92.03	37.65	62.35		28.43	71.57	
LH Lesion Children	8.7	0.53	90.77	38.28	61.72		10.52	89.48	
	$\chi^2 = 16.99, p < .000$			$\chi^2 = 0.004, p = .948, ns$			$\chi^2 = 9.0, p = .003$		
RH Lesion Children	6.47	0.55	92.98	51.75	48.25		19.54	80.46	
	$\chi^2 = 12.78, p = .002$			$\chi^2 = 5.2, p = .015$			$\chi^2 = 3.38, p = .066, ns$		
	$\chi^2 = 1.28, p = .528, ns$			$\chi^2 = 5.35, p = .021$			$\chi^2 = 2.95, p = .086, ns$		

χ^2 and p values are for lesion vs. control comparisons

χ^2 and p values are for LH vs. RH comparisons