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Spatial Bias and Right Hemisphere Function: Sex-Specific Changes with Aging

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Abstract

Patterns of cerebral asymmetry related to visuospatial functions may change with age. The typical leftward bias on a line bisection task may reflect cerebral asymmetry. With age, such leftward bias decreases. This study demonstrated that the age-related decrease of leftward bias may actually be sex-specific. In addition, previous research suggests that young adults' deviation in line bisection may reflect asymmetric hemispheric activation of perceptual–attentional "where" spatial systems, rather than motor-intentional "aiming" spatial systems; thus, we specifically fractionated "where" and "aiming" bias of men and women ranging in age from 22 to 93 years old. We observed that older men produced greater rightward line bisection errors, of primarily "where" spatial character. However, women's errors remained leftward biased, and did not significantly change with age. "Where" spatial systems may be linked to cortico-cortical processing networks involving the posterior part of the dorsal visuospatial processing stream. Thus, the current results are consistent with the conclusion that reduced right dorsal spatial activity in aging may occur in the male, but not female, adult spatial system development. (*JINS*, 2011, *17*, 455–462)

Keywords: Attention, Perception, Adult development, Hemispheric asymmetry, Pseudoneglect, Brain lateralization, Right hemisphere, Aging, Gender differences

INTRODUCTION

Previous research demonstrated that patterns of cerebral asymmetry observed in the task performance and functional brain images of younger adults differs from that of older adults. These differences have been used to infer neuromorphological changes that may occur with increasing age. Recent work suggests that some of these age-related changes in cerebral asymmetry may be sex-specific (e.g., Barrett & Craver-Lemley, 2008). However, sex-specific changes associated with aging could reflect differential aging of distinct cognitive and neural systems. Thus, we designed the current study to fractionate the contributions of posterior perceptual–attentional and anterior motor–intentional systems to sex-specific, age-related changes in the lateralized spatial bias observed in a line bisection task.

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Cognitive Aging in Spatial Functions

Several researchers observed that older adults do not produce the systematic leftward error that young adults produce while bisecting horizontal lines, a task that appears to critically rely on right hemisphere (RH) spatial systems, especially the dorsal visuospatial system for locating and interacting with stimuli (Bisiach, Capitani, Colombo, & Spinnler, 1976; Bjoertomt, Cowey, & Walsh, 2002; Cicek, Nalcaci, & Kalaycioglu, 2007; Foxe, McCourt, & Javitt, 2003; Ungerleider & Mishkin, 1982). Increasing age in healthy adults correlates with reduced leftward line bisection error (Failla, Sheppard, & Bradshaw, 2003) or even rightward errors (Fujii, Fukatsu, Yamadori, & Kimura, 1995). These results suggest that aging is associated with reduced RH dominance in spatial attention, or with a decline of RH visuospatial function (Cherry, Adamson, Duclos, & Hellige, 2005; Goldstein & Shelly, 1981). In addition to line bisection errors, Barrett and Craver-Lemley (2008) examined the degree of error in aged *versus* young adults on several visuospatial motor tasks, and found results consistent with age differences in dorsal spatial brain function. In their study, aged participants made less leftward line bisection error than young adults. Reduced left bias also occurred on a spatial-syntactic drawing task in aged compared with young adults. This spatial–syntactic drawing task required participants to make a drawing to depict the action of a sentence. While young adults more often drew the subject of the sentence to the left of the object, aged adults placed the subject relatively to the right of the object. Since aged participants demonstrated less leftward bias on both types of tasks, this supports a change in fundamental organization of dorsal spatial function, rather than a change specific to task parameters or factors affecting task accuracy.

Performing a visuospatial motor task, such as manually bisecting a line, requires accurate representations at many stages of information processing (e.g., space perception, space representation, spatial motor planning and initiation). At the outset, visual spatial processes must supply veridical information about the three-dimensional location of an object. Information about the object's location in external space will then be supplied to spatial motor representational and motor planning systems. Accurate action on the object requires that these motor systems make use of a veridical spatial representation of the body and limbs. Asymmetric or dysfunctional activity occurring at any of these stages may lead to systematic spatial errors.

In particular, research suggests that spatial biases on the line bisection task may originate primarily from either a perceptual–attentional "where" spatial system that is strongly dependent upon visual input, or from a motor-intentional "aiming" spatial system that is strongly dependent upon stored motor representations and relatively insensitive to visual feedback when initiating an action (e.g., Bisiach, Geminiani, Berti, & Rusconi, 1990; Schwartz, Adair, Na, Williamson, & Heilman, 1997). Both types of systems contribute to a visuospatial motor response, and thus to spatial bias, which is almost always implicit, inaccessible to consciousness monitoring (Milner & Goodale, 1995). Spatial bias originating primarily from "where" systems may result in relative unawareness of left or right hemispace, or result in an abnormal propensity to spatially perceive, represent, or attend to the preferred hemispace (McCourt & Jewell, 1999; Porac, Searleman, & Karagiannakis, 2006; Reuter-Lorenz, Kinsbourne, & Moscovitch, 1990). Motor-intentional "aiming" spatial bias may induce erroneous ballistic motor responses toward or in the preferred hemispace, or induce slower or absent initiation of motor responses toward or in the less-attended hemispace (Luh, 1995; Schwartz et al., 1997).

Lesion studies suggest that perceptual–attentional "where" systems may be closely tied to cortico-cortical processing networks involving the posterior part of the dorsal stream for visuospatial functions, that is, temporo-parietal cortical areas. "Aiming" spatial systems may conversely be linked to the subcortico-cortical processing networks involving the anterior dorsal stream, that is, fronto-parietal cortical and subcortical areas (Adair, Na, Schwartz, & Heilman, 1998; Barrett & Burkholder, 2006; Barrett, Crucian, Beversdorf, & Heilman, 2001; Barrett, Crucian, Schwartz, & Heilman, 1999; Heilman, Bowers, Coslett, Whelan, & Watson, 1985; Heilman & Van Den Abell, 1980; Laplane & Degos, 1983; Mesulam, 1999; Na et al., 1998; Sapir, Kaplan, He, & Corbetta, 2007). This anatomic dissociation of "where" and "aiming" spatial networks has been demonstrated in young adults (Ghacibeh, Shenker, Winter, Triggs, & Heilman, 2007). Thus, assessing how perceptual–attentional "where" and motor-intentional "aiming" biases contribute to line bisection performance as a function of age and sex may provide insights into potential sex differences in aging of specific posterior and anterior brain systems.

Decoupling "Where" and "Aiming" Biases

When a viewer performs a standard line bisection task, both "where" and "aiming" spatial bias are aligned, and their influences are thus confounded in the observed behavior. It is unclear, therefore, whether an age-related change in line bisection errors (i.e., reduced leftward or even rightward deviation) may reflect changes in "where" or "aiming" spatial systems. Such changes may respectively involve posterior cortico-cortical brain areas or anterior subcortico-cortical networks.

One method of decoupling the two types of error, is to compare an individual's line bisection performance across two conditions: one in which the visual and motor information is aligned (the *Natural viewing condition*) and a second in which available visual feedback is mirror-reversed with respect to real movements, and thus, visual and motor information are incongruent (the *Reversed viewing condition*). To create these conditions, experimenters must hide the participant's view of her hand and provide visual feedback of performance on a video monitor or computer screen. In the Natural viewing condition, when the participant makes leftward movements (e.g., with a mouse or laser pointer) the cursor on the screen also moves leftward (and vice versa). However, in the Reversed viewing condition, when the participant makes leftward movements, the cursor appears to move rightward (and vice versa). Schwartz et al. (1997) observed that inspection of line bisection errors in the Natural and Reversed viewing conditions can reveal information about the source of a participant's bias. If a participant errs toward the same side (for example, moving toward the left side of the workspace) in both Natural and Reversed viewing conditions, this suggests that the participant has a primary motor–intentional or "aiming" bias—since this type of bias may be relatively insensitive to visual feedback. If a participant's error changes direction between the Natural and Reversed viewing conditions (e.g., the participant made leftward motor responses in the Natural viewing condition, but rightward motor responses in the Reversed viewing condition), this suggests that the bias is dependent on visual feedback, and thus the participant may demonstrate a primarily perceptual–attentional or "where" spatial bias (Schwartz et al., 1997). In a sample of young to middle-aged healthy adults, Schwarz et al. reported that the majority

(75%) of the participants' bisection errors were primarily consistent with "where" spatial bias.

Directly comparing performance in Natural and Reversed viewing conditions (Na et al., 1998; Schwartz et al., 1997) may identify whether spatial errors are primarily of "where" or "aiming" spatial character. However, both "where" and "aiming" systems may be expected to affect spatial performance, and the procedure of Schwartz et al. (1997) does not separately and simultaneously quantify "where" *versus* "aiming" spatial bias. In previous work, we used a video-based apparatus similar to that of Schwartz et al. to decouple "where" and "aiming" spatial bias (Barrett & Burkholder, 2006; Barrett et al., 1999, 2001; Chen, Erdahl, & Barrett, 2009; Garza, Eslinger, & Barrett, 2008). We algebraically fractionated "where" and "aiming" errors (see Equations 1 & 2), and confirmed that line bisection errors in healthy young adults may be primarily of the "where," feedback-dependent spatial type. In these experiments, we further demonstrated that pathological spatial bias in persons with spatial neglect may occur primarily from either "where" or "aiming" errors, or a combination of both error types.

Sex-Specific Changes in Where *versus* Aiming Bias Across the Life-Span?

Although there is a general shift from a leftward bias to either more accurate performance or a rightward bias with aging, relatively few studies systematically investigated whether these changes may be sex-specific (Beste, Hamm, & Hausmann, 2006; Varnava & Halligan, 2007). Right hemisphere (RH) visuospatial systems may be more lateralized and dominant in men compared to women (Gur et al., 1999; Hiscock, Israelian, Inch, Jacek, & Hiscockkalil, 1995; Iachini, Sergi, Ruggiero, & Gnisci, 2005). If declining RH dominance for visuospatial computations occurs with aging, decreased leftward line bisection bias might be more evident in aged men than aged women. We observed this to be the case when we compared line bisection in young and aged people of both sexes (Barrett & Craver-Lemley, 2008).

In the current study, we investigated whether sex-specific changes occur in "where" and "aiming" line bisection bias of a group of adults aged from 22 to 93 years. Based on previous evidence that aged men erred more rightward in a line bisection task than women and placed drawings of objects more rightward than women and young men (Barrett & Craver-Lemley, 2008), we predicted that line bisection errors of older men should be rightward of those in younger men. We further proposed that line bisection error in older women might be comparable to that in young women. However, the primary purpose of this study was to determine whether this sex-specific difference (i.e., men show more age-related change than women) in line bisection performance could be primarily attributed to changes in "where" bias or changes in "aiming" bias. This question has implications for the potential differential aging of anterior and posterior visuomotor systems in men and women. Previous studies suggested that line bisection errors in young adults primarily originate from "where" spatial systems (Barrett, Crosson, Crucian, & Heilman, 2002; Garza et al., 2008); thus, we examined the hypothesis that age may relatively affect processing in "where" systems rather in "aiming" systems. However, since aging is associated with motor perseverative errors (Potter & Grealy, 2006), it is also possible that emerging "aiming" spatial errors might be primarily responsible for a performance change in older *versus* younger adults.

Others reported that line bisection biases are affected by viewing distance, and that leftward errors are lesser in magnitude in far space (Dellatolas, Vanluchene, & Coutin, 1996; Varnava, McCarthy, & Beaumont, 2002). Thus, a secondary objective of this study was to examine whether viewing distance has a robust effect on "where" and "aiming" biases across adulthood.

METHODS

Participants

Participants were recruited via solicitation flyers posted in facilities of the Kessler Institute for Rehabilitation and through flyers and emails in the Kessler Foundation. Forty-four community-dwelling healthy adults (22 females; age range = 22–93 years, mean = 58.8 ± 16.4 years; education years = 14.8 ± 2.7) participated in the study. Data were obtained in compliance with IRB regulations of the Kessler Foundation Research Center. All participants were right-handed, as determined by a 17-item handedness questionnaire (Raczkowski, Kalat, & Nebes, 1974), and had bilateral normal or corrected-to-normal (20/40) vision. All participants reported that they had no history of neurological or psychiatric disorders. Participants were only included if they performed in a normal, unimpaired range on a brief cognitive and depression screening that included the Behavioral Inattention Test (>129/146; Halligan, Cockburn, & Wilson, 1991; Wilson, Cockburn, & Halligan, 1987), Mini-Mental State Examination (≥24/30; Folstein, Folstein, & McHugh, 1975), and Geriatric Depression Scale (<10/30; Yesavage et al., 1983).

Stimuli and Procedure

Participants bisected horizontal lines in both near (within arm's reach) and far (outside of arm's reach) space. They were seated so that their mid-sagittal plane was centrally positioned in front of one of the presentation screens. The room was dimmed, and the experimenter was seated out of the participant's view. In the near condition, a 23-cm black horizontal line was presented on a white screen at a distance of 55 cm from the participant. In the far condition, a 72.8-cm line was presented at a distance of 175 cm from the participant (Figure 1). Therefore, the lines subtended 23.6 degrees of visual angle at both viewing distances. A mouse pad (35.6 × 43.2 cm) and a wireless mouse were centered in front of participants, and this workspace was covered by a box so that the hand and the mouse were not visible. A Dell notebook computer (Microsoft Windows OS) projected horizontal line stimuli and recorded responses with customized

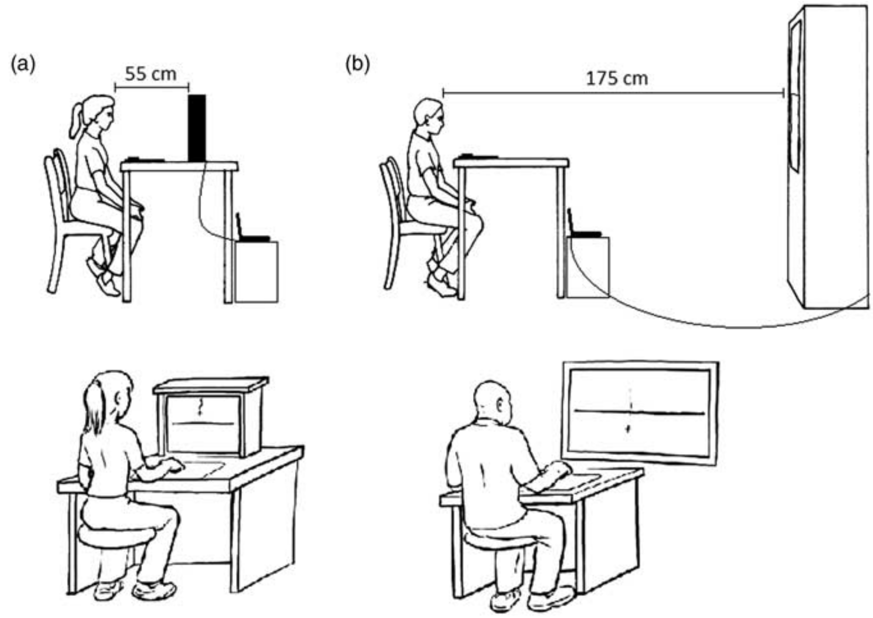

Fig. 1. The video-computerized line bisection task, in the near (a: 55 cm between participants' eyes and the screen), and far space conditions (b: 175 cm). The workspace (i.e., the participant's hand and mouse pad) was covered by a box (not shown). In the Natural viewing condition, the cursor moved in the same direction as the hand, for example, rightward hand movement moved cursor to the right. In the Reversed viewing condition, the cursor moved in the horizontally opposite direction, for example, rightward hand movement moved cursor to the left.

software. A Sony flat-screen computer monitor (40×30 cm) served as the near screen, and a Sony HD projection screen (123×92.5 cm) displayed the horizontal line in far space.

Participants were tested under both Natural and Reversed viewing conditions (see the Introduction section for more historic details). In the Natural viewing condition, the cursor on the video screen moves in tandem with the hand movement, for example, rightward movement of the hand moves the cursor to the right. In the Reversed viewing condition, rightward movement of the hand moves the cursor to the left. Participants bisected lines using the curser with the mouse in the right hand. Half of the trials started with the cursor in the upper right corner, and the other half started with the cursor in the upper left corner. The cursor start location alternated trial by trial. Participants were asked to move the cursor down to the subjective center of the line as quickly as possible, without much hesitation or careful estimation (this procedure was to counterbalance left- and right-sided motor cuing that may affect "aiming" bias; Garza et al., 2008). Iterative corrections were not permitted; rather, participants were encouraged to make a ballistic response. Errors were recorded as mm deviations from true center in the motor workspace, with leftward errors coded as negative and rightward as positive.

The technique used in our laboratory to decouple "where" and "aiming" spatial errors has been previously described (Barrett & Burkholder, 2006; Chen et al., 2009; Garza et al., 2008). The novelty of the method is in quantifying "where" and "aiming" spatial bias separately, while tightly controlling the parameters of task performance in a single 30-min testing session, so as to avoid confounds induced by stimulus or task differences.

The logic of this operational definition of spatial bias by quantifying "where" *versus* "aiming" errors is as follows: When a viewer performs line bisection in the Natural viewing condition, both "where" and "aiming" spatial biases are assumed to contribute to spatial errors as they would in life—visual input of the movement and the movement itself are directionally aligned or congruent. This is analyzed algebraically by adding these spatial bias components to obtain the total error in the Natural viewing condition:

$$\textit{Error made in the Natural viewing condition} = \text{``}\textit{where}\text{''}\ \textit{error} + \text{``}\textit{aiming}\text{''}\ \textit{error} \quad (1)$$

In the Reversed viewing condition, as visual feedback is mirror-reversed (i.e., left–right reversed), "where" bias may be 180° reversed in direction, whereas "aiming" bias may remain right–left unchanged. This is expressed algebraically by changing the sign applied to "where" bias when calculating the total error in the reversed viewing condition:

$$\textit{Error made in the reversed viewing condition} = -\text{``}\textit{where}\text{''}\ \textit{error} + \text{``}\textit{aiming}\text{''}\ \textit{error} \quad (2)$$

Collecting averaged performance data (i.e., mean errors) from both the Natural and Reversed viewing conditions allows us to solve for the two variables ("where" and "aiming" bias) by summing across the two equations. Thus, we suggest, we can fractionate "where" and "aiming" bias quantities contributing to performance of a single, functionally integrated task.

Participants bisected lines in Natural and Reversed viewing conditions in a total of four trial blocks (based on a design of 2 viewing conditions × 2 distance conditions), with two practice trials and eight real trials per block, with the order of the trial blocks pseudorandom between participants. "Where" and "aiming" bias components were calculated on the average of these eight trials within each block and then averaged across blocks. Participants were told of the upcoming trial condition (i.e., Natural or Reversed viewing) and encouraged to practice with the mouse during the two practice trials at the beginning of each condition. A brief break was allowed between trial blocks if the participant asked for it.

RESULTS AND DISCUSSION

Line Bisection Error in Natural Viewing Condition

We first assessed line bisection error under the Natural viewing condition. Overall, our participants demonstrated the typical leftward error ($n = 44$; -1.2 ± 3.9 mm; $p = .045$) confirmed by a one-sample one-tailed t test (comparing performance to zero or perfectly accurate). To test the homogeneity of regression slopes across age, we conducted a mixed analysis of covariance (ANCOVA) with viewing distance as the within-participants variable, sex as the between-participants variable, age as the covariate, and customized an interaction factor combining age and sex (we created a customized model in SPSS® 18.0). The ANCOVA revealed a sex by age interaction, $F(2,41) = 12.66$, $p < .001$, $\eta_p^2 = 0.38$, and no other effects. Thus, for the following analyses, errors made in near and far distances were collapsed. The age by sex interaction is depicted in Figure 2. Separate simple linear regression analyses for each sex revealed that men's errors progressively became more rightward with increased age, $F(1,20) = 11.0$, $p = .003$, $\beta = 0.596$ (see the solid line in Figure 2), but women's errors did not significantly change with age, $F(1,20) = 1.9$, $p = .188$, $\beta = -0.292$ (see the dashed line in Figure 2). Thus, we replicated previous findings of altered bias in men compared with women as a function of aging (Barrett & Craver-Lemley, 2008; Varnava & Halligan, 2007). In addition, it may be more likely for women than men regardless of age to show leftward spatial errors. However, an effect of viewing distance on line bisection error did not reach significance. Wilkinson and Halligan (2003) pointed out that on the group level, such effect may not be replicated because of a relatively small effect size. Failure to replicate the effect of viewing distance is consistent with our previous findings as well (Chen et al., 2009).

"Where" *versus* "Aiming" Errors

We used errors produced in both Natural and Reversed viewing conditions to decouple "where" and "aiming" errors (Equations 1 & 2), and performed a multivariate analysis of covariance (MANCOVA) with "where" and "aiming" error as dependent variables, viewing distance and sex as the independent variables and age as the covariate. This analysis revealed a significant age by sex interaction on "where" errors, $F(1,40) = 9.8$, $p = .003$, $\eta_p^2 = 0.20$, and no other significant effects (Figure 3). Collapsing data across the near and far distances, separate simple linear regressions for each sex revealed that older men's "where" errors were rightward of those in younger men, $F(1,20) = 18.5$, $p < .001$, $\beta = 0.69$, but older women's "where" errors were not significantly different from those in younger women, $F < 1$, $\beta = -0.197$.

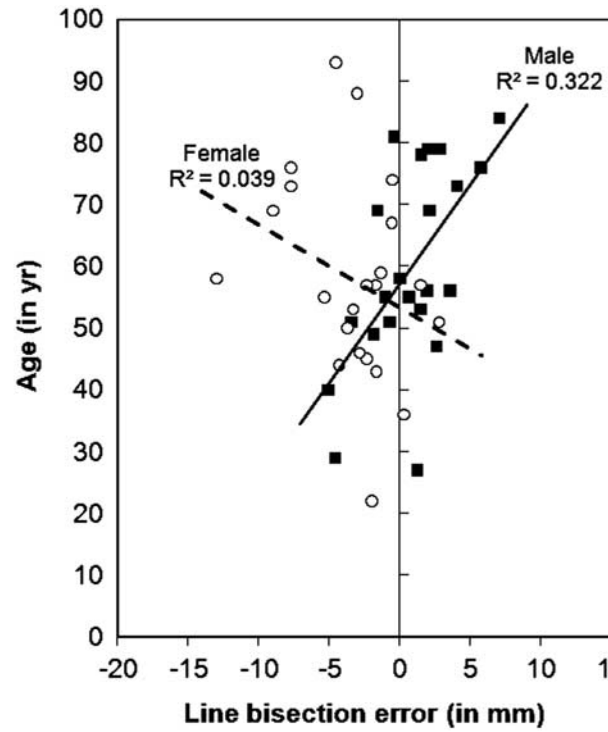

Fig. 2. Line bisection errors in the Natural viewing condition made by males (dark squares and solid trend line) and females (white circles and dashed trend line) with increased age. Adjusted R^2 values are noted. Positive error values denote rightward errors and negative leftward errors. Vertical line at zero indicates accurate performance.

These findings are consistent with the hypothesis that RH dominance in dorsal, cortical–cortical, "where" spatial systems may be reduced with aging specifically in men, but not women.

GENERAL DISCUSSION

The major finding of the present study was that older men produced greater rightward line bisection errors than did younger men, with rightward errors primarily of a perceptual–attentional "where" character. In contrast, women made leftward "where" spatial errors regardless of their age. These results point to sex-specific changes in the function of dorsal, cortical–cortical visuospatial networks in aged men compared to younger men and to women.

Our results are consistent with the preponderance of work on line bisection biases in healthy adults. Typically, young adults err leftward when bisecting horizontal lines

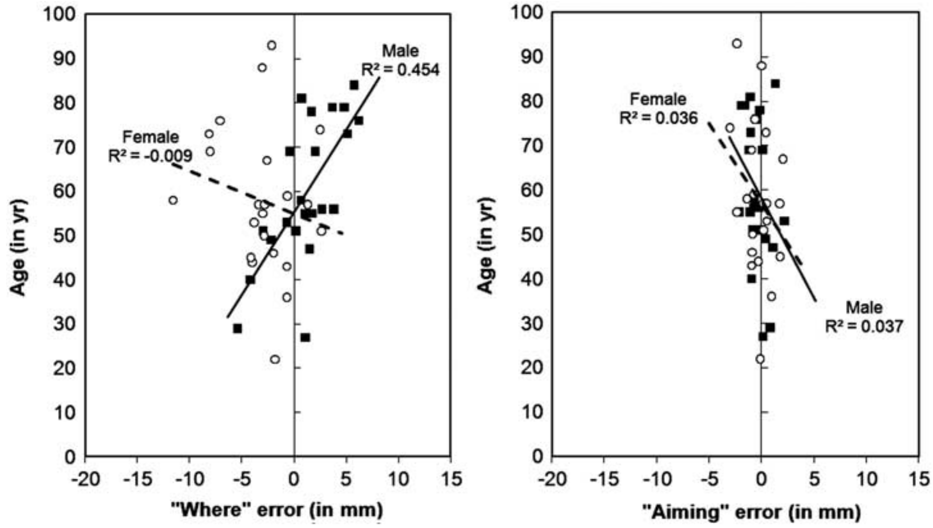

Fig. 3. "Where" and "aiming" errors of males (dark squares and solid trend lines) and females (white circles and dashed trend line) with increased age. Adjusted R^2 values are noted. Positive error values denote rightward errors and negative leftward errors. Vertical line at zero indicates accurate performance.

(Jewell & McCourt, 2000). Previous research reported age-related changes in line bisection errors (Failla et al., 2003; Fujii et al., 1995) and sex-related differences in older populations (Barrett & Craver-Lemley, 2008; Beste et al., 2006; Varnava & Halligan, 2007). In this study, we observed increased rightward spatial errors in older men, but not older women. Both men and women, of all ages, made errors of primarily "where" perceptual–attentional character (replicating Garza et al., 2008). This is consistent with different patterns of dorsal system visuospatial development with aging, occurring in men but not women. Whether this alteration in performance in the older men is pathological is unknown; we did not examine for functional correlates of these errors (Barrett & Burkholder, 2006).

Our findings are also consistent with Varnava and Halligan (2007), who found that from age 14 to 80 years, women erred leftward with their right (dominant) hand, but men's leftward errors reduced or became rightward with age for particular line lengths (180 mm and 100 mm, respectively). Our findings are not consistent, however, with the work of Beste and colleagues (2006), who found a non-linear relation between age and bisection error in women who bisected lines with their left hands. However, Beste et al.'s subject group may have differed from those participating in other studies, since these investigators failed to replicate the previously established observations of leftward bisection error in men and women using their right (dominant) hand to bisect lines. Their data also failed to replicate the finding of a reduction in the leftward error with age (Failla et al., 2003; Fujii et al., 1995). Although the exact nature of these divergent findings is unclear, the effects observed in our current study are consistent with the preponderance of work on line bisection biases.

There are several limitations in this study. Unlike previous research (Garza et al., 2008), we did not observe a distance effect on line bisection errors or "where" *versus* "aiming" spatial bias. However, previous reports of this effect have relied on homogeneously aged samples (Garza et al., 2008; McCourt & Garlinghouse, 2000; Varnava et al., 2002). It is possible, in our current study, that our sample size limited the ability to detect both age-specific and distance-specific line bisection performance differences. In addition, although we demonstrated that "where," dorsal, cortical–cortical spatial systems may be those primarily responsible for sex-specific changes in line bisection performance with aging (Barrett & Craver-Lemley, 2008), we did not attempt in the present study to investigate the neuroanatomic–functional processes responsible for this sex-specific finding.

In conclusion, our results are consistent with the hypothesis that reduced right dorsal spatial activity in aging may reflect the male, not female, adult spatial system development. Aged women may continue to manifest right dorsal brain dominance for visuospatial operations, while men may experience an age-related decline of dorsal, right hemisphere functions. The mechanisms underlying age-related changes in men's spatial processing are not known. This age-related phenomenon in men may be related to a high degree of RH dorsal dominance in early adulthood, or to anatomic hemispheric lateralization. Further work, examining performance on a variety of spatial tasks longitudinally in both sexes over the adult life span, and examining neuroanatomical and ecological correlates of these tasks, is needed to clarify adult development in spatial functions. There is, however, a pragmatic implication of our findings for clinicians: the magnitude of effects in age-related sex-specific spatial bias is quite modest (compared to individuals with brain damage) and may potentially limit the significance of clinical correlates in future studies; however, relatively different patterns of performance observed in aged men and women on this visuospatial task means that an atypical, rightward spatial bias in a subject being evaluated must be considered in the context of normative performance for that subject's age, as well as sex.

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