



Attentional grasp in far extrapersonal space after thalamic infarction

Anna M. Barrett^{a, b, *}, Ronald L. Schwartz^c, Gregory P. Crucian^{a, b}, Manho Kim^d,
Kenneth M. Heilman^{a, b}

^aDepartment of Neurology, University of Florida College of Medicine, Florida, USA

^bVA Medical Center, Gainesville, FL, USA

^cDepartment of Neurology, University of Florida Health Science Center, Jacksonville, FL, USA

^dDepartment of Neurology, Massachusetts General Hospital, Boston, MA, USA

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Abstract

Studies of animals and humans with focal brain damage suggest that attention in near and far extrapersonal space may be mediated by anatomically separate systems. Thalamic lesions have been associated with spatial neglect, but whether asymmetric attention specific to near or far space occur after thalamic damage has not been explored. It is also unclear if thalamic injury can induce contralesional defective response inhibition.

We tested a woman with a left thalamic infarction who reported that, when driving, she had a tendency to veer towards people or objects on the right side of the road. Our patient and four controls performed a line bisection task with a laser pointer in near and far extrapersonal space. The experimenter marked each bisection either from the right of the presented line (right-distractor, RD) or the left (left-distractor, LD). RD and LD trials were pseudo-randomized.

Our patient performed similarly to controls (mean -0.7 mm, controls -0.6 mm) on the line bisection task in near space. In far space she erred significantly rightward compared to her performance in near space ($p < 0.001$). Controls performed similarly in near and far space. The experimenter position did not affect our patient's performance on near line bisections, nor did controls demonstrate a distractor effect for the near condition. In the far condition, however, our patient showed a significant distractor effect (LD -3.3 mm, RD 35.3 mm, $p < 0.001$). Controls also demonstrated a distractor effect in the far condition (LD -6.4 mm, RD 0.7 mm, $p < 0.01$), though of much smaller magnitude.

Our results suggest that frontal-thalamic systems regulating visual attention may be disrupted by thalamic infarction. Such damage may produce an attentional grasp specific to far extrapersonal space. Published by Elsevier Science Ltd.

Keywords: Thalamus; Attention; Stroke

1. Introduction

Attention and action in near extrapersonal space may be mediated by an anatomically separate brain system from attention and action in far extrapersonal space. Holmes and Horrax [22] and Brain [3] reported

a patient whose ability to reach for and localize objects differed within and outside arms' length.

Rizzolatti and colleagues [35] found in primates that the neglect of different regions of extrapersonal space appear to be related to different frontal anatomic areas. Using selective frontal resections, they showed that unilateral damage to area 6 produced deficits in near space (the peribuccal region) whereas damage to the frontal eye fields (area 8) produced deficits with more distant objects. The near/far dissociation can also be produced by subcortical damage in areas pro-

* Corresponding author. Section of Neurology, PO Box 850, Pennsylvania State University College of Medicine, Hershey, PA 17033, USA. Tel.: +1-352-392-3491; fax: +1-352-392-6893.

E-mail address: abarrett@psghs.edu (A.M. Barrett).

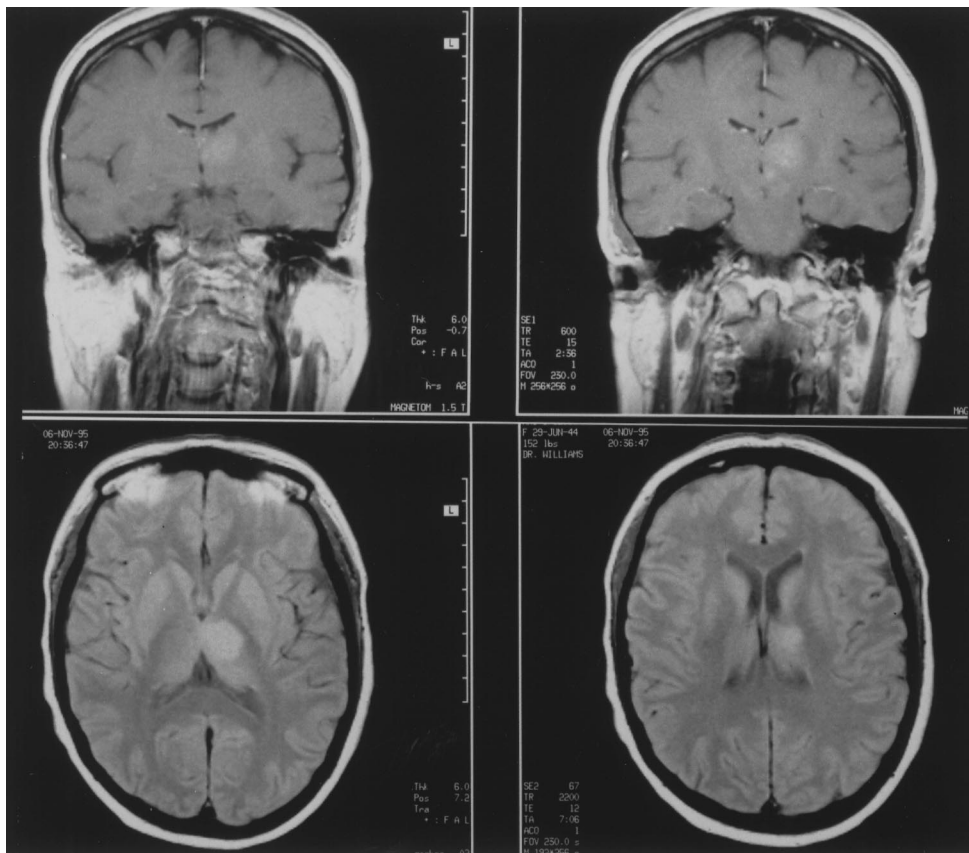


Fig. 1. Magnetic resonance imaging of the brain for patient KH. Increased signal consistent with infarction can be seen on these proton-weighted (balanced) images affecting the left anterior dorsal thalamus (right side of image) on coronal (top images) and axial views (bottom images). See text for further details.

jecting to the dorsolateral frontal cortex [30,31]. This damage produces sensorimotor inattention in rats resembling the neglect syndrome and affects rostral or snout regions less than caudal body regions.

In humans, Halligan and Marshall [18] and Menemeyer and coworkers [32] described patients who neglected near space, and Shelton et al. [37] described a patient with neglect for far extrapersonal space. Subsequently there have been additional reports of patients with spatial neglect of near or far space [8,9,17,32]. All of these patients with spatial neglect had cortical lesions.

We recently evaluated a patient with a left medial thalamic lesion who reported that when driving she had a tendency to veer towards people and objects on the right side of the road. Tests for neglect in peripersonal space were normal but in extrapersonal space she showed a right-sided attentional bias.

2. Methods

2.1. Case report

KH, a right-handed woman with 13 years of edu-

cation, a history of hypertension and hypercholesterolemia, was 52 when she sought evaluation at the Memory Disorders Clinic at the University of Florida Health Center. One month before being seen in clinic, at a local hospital she reported the sudden onset of dizziness and confusion. She had a normal general neurological exam, including eye movements, and serum chemistries, blood count, and serologic workup for vasculitic causes of stroke and dementia were normal. Her husband reported that she was intermittently quite drowsy as if “suddenly sleeping deeply”. She was admitted to a psychiatric service, but when a CT scan followed by an MRI scan of her brain were obtained, they revealed left thalamic infarction, probably injuring the anterior, ventral anterior, anterior dorsal median nuclei and perhaps the anterior intralaminar nuclei as well [12] (Fig. 1). The locus and appearance of her lesion suggested an infarction in the territory of the paramedian thalamic artery [7].

At the time of Memory Clinic evaluation, she complained of memory and concentration problems. She also reported that when driving she had a disturbing tendency to veer to the right towards people or objects present on that side of the road. Her general neurological examination was normal except for mild motor

Table 1
Results of line bisection task for KH and control subjects

Line length (cm)		Near space (laser pen) error in mm (SD)		Far space (laser pen) error in mm (SD)	
Near	Far	KH	Controls	KH	Controls
22	123	0.08 (2.93)	−0.10 (3.61)	16.56 (18.32)	−1.29 (12.73)
24	134.2	−1.50 (2.78)	−1.18 (3.10)	15.42 (30.78)	−4.44 (20.2)
Mean for both line lengths		−0.7 (2.94) ^a	−0.6 (3.4) ^b	15.99 (25.07) ^a	−2.9 (16.93) ^b

^a $t = -4.717$, $df = 47$, $p < 0.001$.

^b $t = 1.810$, $df = 191$, $p = 0.072$.

impersistence and bilateral defective response inhibition of lateral eye movements to peripheral stimuli on both sides. Neuropsychological testing, including the Florida Mental Status Exam [13], the Boston Naming Test [23], the Hopkins Verbal Learning Test ([4], a list-learning memory test), identification of body parts, all aspects of speech or language, including reading and writing, praxis, map localization, right/left orientation, and calculations, was normal except for the following findings. She had reduced verbal fluency on the Controlled Oral Word Association Test/FAS [2] with only 19 items total. She was also amnesic, with a total score of 15 on the Hopkins Verbal Learning Test (below the cutoff for her age group), though recognition performance on the Hopkins was normal (11/12). She bisected 20, 22-cm lines held at eye level normally (0.6 mm left of midpoint), and canceled all the targets on a random line cancellation test [1]. She exhibited no extinction to double simultaneous stimulation in any sensory modality.

2.2. Procedures

To investigate whether KHs subjective problem with driving might represent a right-sided attentional bias or defective response inhibition in far extrapersonal space, we tested line bisection with a laser pointer in near and far extrapersonal space. The paradigm was modified from Halligan and Marshall [18]. Four age- and education-matched female controls without neurological disease (mean age 50 years, mean education: 13.75 years) were tested using the same paradigm.

For the *near* condition (near extrapersonal space), 24 lines 22 cm in length and 24 lines 24 cm in length centered on 8.5×11 sheets of white paper were presented 30 cm from the patient at 10° above eye level, to be bisected with a laser pointer held in both hands. In the *far* condition (far extrapersonal space) 24 lines of 123 cm and 134.2 cm, matched to subtend the same visual angle (40.3 and 43.5°), were presented 167.75 cm from the patient at 10° above eye level to be bisected in similar fashion. Line thickness was also matched for subtended visual angle (3 mm for near lines, 17 mm for far lines). The stimuli were presented in four blocks

with near and far condition alternating. After KH indicated she was satisfied with her bisection on each trial, the experimenter marked her chosen bisection point with a small sticker, and the distance was measured and recorded.

KH easily and rapidly performed the experimental task. However, because of motor impersistence, she was unable to keep the laser pointer focused on her selected bisection point for long enough to allow accurate measurement of her error. For this reason, the paradigm was modified so that the experimenter stood closer to the line and to one side in all conditions. For each trial, the experimenter approached quickly from the designated side after KH marked the line. The position of the experimenter (“left-distractor” vs “right-distractor” conditions) was pseudo-randomized in blocks of six trials, KH did not receive any instruction regarding the experimenter’s position, and the exper-

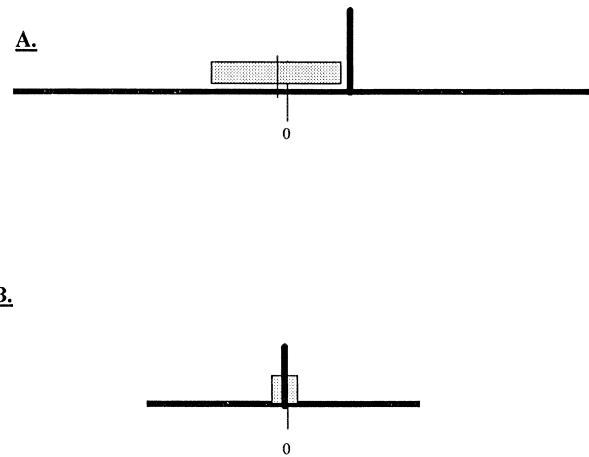


Fig. 2. Performance for patient KH for near and far conditions (see text). For the far condition (A), patient KHs mean performance (heavy vertical line) is shown with the mean for four controls (light vertical line) proportionate to mm deviation from center point (marked “0”). KHs performance falls outside the 95% confidence interval for control performance (shaded rectangle). For the near condition (B), patient KHs mean performance (heavy vertical line) is shown with the mean for four controls (light vertical line, obscured by KHs mean). KHs performance falls within the 95% confidence interval for four controls (shaded rectangle).

Table 2
Results for right- and left-distractor conditions for patient KH and control subjects

Line length (cm)		Near space mean error in mm (SD)		Far space mean error in mm (SD)	
Near	Far	Left-distractor	Right-distractor	Left-distractor	Right distractor
Subject KH					
22	123	0.0 (2.22)	0.17 (3.61)	2.92 (13.73)	30.21 (10.36)
24	134.2	-2.5 (3.00)	-0.5 (2.24)	-9.58 (20.89)	40.42 (13.48)
Mean for both line lengths		-1.25 (2.88) ^a	-0.17 (2.96) ^a	-3.33 (18.43) ^b	35.31(12.86) ^b
Controls					
22	123	-0.02 (3.41)	-0.19 (3.83)	-6.14 (11.97)	3.56 (11.67)
24	134.2	-0.92 (2.95)	-1.44 (3.25)	-6.73 (19.18)	-2.16 (21.19)
Mean for both line lengths		-0.47 (3.20) ^c	-0.81 (3.59) ^c	-6.43 (15.9) ^d	0.7 (17.26) ^d

^a $t = 1.143$, $df = 23$, $p = 0.265$.

^b $t = 7.681$, $df = 23$, $p < 0.001$.

^c $t = 0.831$, $df = 95$, $p = 0.408$.

^d $t = 3.328$, $df = 95$, $p = 0.001$.

imenter did not speak with, instruct, or interact with the patient while in view. KH was videotaped while bisecting the near and far lines and during several initial attempts to measure her errors in the far line bisection task without the experimenter in view.

3. Results

The results for line bisections in the near and far positions for KH and four age- and education-matched female controls are summarized in Table 1 and illustrated in Fig. 2. Separate results for the right- and left-distractor conditions are presented in Table 2 and Fig. 3. Mean data was compared using paired t -

tests for both KH and controls for near vs far conditions and right- vs left-distractor conditions for near and far conditions separately, and 95% confidence intervals were computed for control performance in the near and far conditions.

KH performed similarly to controls in the near condition (KH mean -0.7 mm, control mean -0.6 mm, within controls' 95% confidence interval) and there was no significant distractor effect (mean -1.25 mm for KHs left- vs -0.17 mm for right-distractor, $p = 0.265$). However, for the far condition, KHs errors fell outside controls' 95% confidence interval (KH mean 15.99 mm, control mean $= -2.9$ mm, outside controls' 95% confidence interval) and were significantly different from her errors in the near condition ($t = -4.717$, $df = 47$, $p < 0.001$). There was a trend toward more leftward bias in controls in the far vs near condition (mean -0.6 mm near, mean -2.9 mm far, $p = 0.072$). However, the mean leftward angle of error in the near and far conditions was similar (-1.15° for near vs -0.99° for far). Since the same angular error would have produced a larger measured error in the far than the near condition, limits on angular accuracy imposed by the apparatus most likely accounted for this control performance difference.

In the far condition, controls exhibited a left-distractor effect, with the left-distractor condition 7.13 mm leftward (mean -6.43 mm) of the right-distractor condition (0.7 mm, $p = 0.001$). However, this effect was small in magnitude compared with the right-distractor effect KH demonstrated in the far condition (mean 35.31 mm), 38.64 mm to the right of the left-distractor condition (mean -3.33 mm, within normal range; left vs right $t = 7.681$, $p < 0.001$).

No quantitative measurement of KHs line bisection performance without distraction is available. Initial attempts to perform the far line bisection task without the experimenter in view were videotaped, however, and

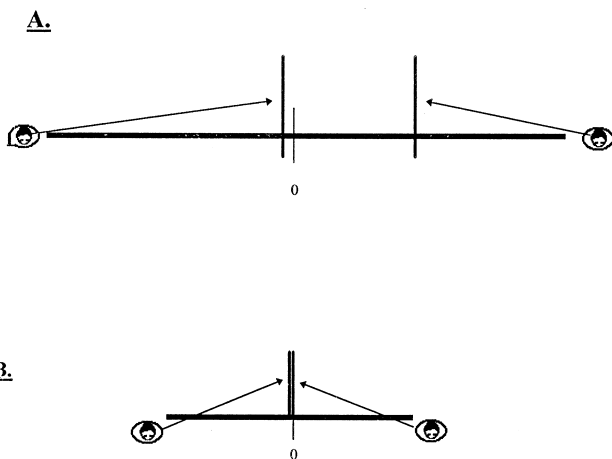


Fig. 3. Mean performance for patient KH for left- and right-distractor conditions, depicted proportionate to mm deviation from center point "O" (see text). In the far condition (A), the mean performance when the examiner is on the right is significantly rightward of the mean performance when the examiner is on the left. In the near condition (B), there is no significant difference in mean performance between the right- and left-distractor conditions.

she appeared to err similarly to her performance in left-distractor trials. This suggests that the rightward error during the right-distractor trials represented a true distraction effect.

4. Discussion

Based on our results, our patient, who had no spatial neglect when tested in near extrapersonal space, may nevertheless have had a contralesional attentional bias in far extrapersonal space. This deficit may be analogous to those reported in primates after dorsolateral frontal lobe ablation [35]. In our patient, however, a thalamic lesion caused attentional dysfunction. Neglect and defective attention to contralesional extrapersonal space may occur following thalamic infarction [6,16,42]. A contralesional bias to stimuli in far extrapersonal space has not been previously reported, however, related to anterior thalamic damage.

KHs rightward errors in the far condition appeared to be induced by an abnormal attraction to the examiner. This attraction appeared to be asymmetrical. KHs performance when the examiner stood on the left was similar to the mean control performance. Although we were unable to quantify her far line bisections without visual distraction, and, therefore, cannot be sure if she had a rightward bias in the absence of a lateral distractor, her apparently unbiased performance on a few uncued trials and her normal performance in the left-distractor condition support asymmetric distraction in far space. A distractor effect was also observed in far space for controls, but in the opposite direction. Controls were drawn further leftward when the examiner was on the left. This effect was statistically significant, but its magnitude was much smaller than the far right distractibility of our experimental subject.

Dissociation of attention to near and far space has been previously observed in humans in the setting of cortical brain damage [18,32,37]. In animals, however, subcortical lesions can cause near-far segregated deficits in attention or intention [29,30]. After ventral tegmental lesions of the midbrain deplete ascending dopaminergic input, rats recover orientation to touch in a spatially segregated, rostral-to-caudal fashion. This deficit can be pharmacologically manipulated with dopaminergic drugs [31,38]. These observations in animals suggest that visuospatial attention or intention for far extrapersonal space may be mediated via the ascending dopaminergic motor system.

Though our patient had a strong right-sided bias, we were unable to determine if this bias was sensory-attentional or motor-intentional [33,36]. Both types of bias have been associated with asymmetric attraction to visual stimuli. Inappropriate eye movements to contralesional space may occur after a frontal stroke due

to disinhibition of the subcortical structures controlling visual fixation and attentional orienting [5]. Thalamic damage may also indirectly affect the striatal or nigral output to the superior colliculus [14], increasing a tendency toward externally obedient ocular orienting and engagement in the presence of distracting stimuli [10]. The ventral anterior and medial dorsal nuclei of the thalamus, which were injured by KHs stroke, receive striatal input and project extensively to the dorsolateral frontal cortex.

Damage to dorsolateral frontal cortex has also been associated with asymmetric motor-intentional bias. Kwon and Heilman [25] observed a patient with a right dorsolateral frontal stroke who had disinhibited contralateral visual saccades and contralesional bias on the line bisection task. This patient's behavior in near space resembled our patient's deviation to the right in far space. A contralesional performance bias, they suggested, may be mediated by more than a disinhibited collicular system, and may more resemble "externally dependent" grasp and utilization behaviors observed after frontal lobe damage [27,28]. Unilateral seizures [21] and cortical stimulation [36] may also induce a contralesional bias on the line bisection task. These behaviors may occur because avoidance behaviors mediated by the frontal cortex [11] are reduced, or because approach behaviors mediated by parietal cortex are released or functionally unopposed. As subcortical lesions affecting brain areas projecting to dorsolateral frontal cortex can also produce contralesional bias and disinhibited approach behaviors [19,24], this may also explain KHs distractibility.

The retrosplenial cortex may also, however, have an important role in inhibiting visual orienting. Heilman and his coworkers [20] reported a patient who, like KH, told examiners that far stimuli in contralesional space attracted his attention, inducing him to veer when driving. This patient had a unilateral retrosplenial lesion and showed only a mild bias to contralesional near space. Unfortunately, he was not tested in far extrapersonal space. This patient had anterior thalamic hypoperfusion on positron emission tomography (PET) imaging [20]. The dorsolateral frontal lobe, the anterior and dorsal medial thalamus, and the retrosplenial cortex, when ablated, all induce a contralesional bias and are strongly interconnected [15,34,39,40,41]. Animals with retrosplenial cortex lesions show contralesional attentional bias [26]. The dorsolateral frontal lobes, anterior thalamus, and retrosplenial cortex may thus form an inhibitory-avoidance network modulating the approach and orienting systems mediated by the ipsilateral parietal lobe or superior colliculus or both.

The specificity of our patient's defective response inhibition to far extrapersonal space and its presumed relevance to her driving ability suggest that atten-

tional-intentional systems may be spatially segregated for evolutionary reasons. Externally obedient attentional-intentional systems able to induce directional motor preparatory biases may be particularly selective to the far extrapersonal space, as this is the region where threatening or novel relevant stimuli first appear.

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