



Hand-centered attentional and motor asymmetries in unilateral neglect

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Received 3 July 2000; received in revised form 4 January 2001; accepted 10 January 2001

Abstract

On several accounts of ‘selection for action’, acting on a target object among distractors requires that irrelevant inputs and responses to these inputs are inhibited, and relevant inputs and responses selected. In unilateral neglect associated with right-hemisphere lesions, selection processes may be biased toward stimuli on the right, as right is usually defined by head and body hemispace. In normal subjects performing reaching-to-target tasks, selection may be ‘hand-centered’ (*Journal of Experimental Psychology: Human Perception and Performance* 18(4) (1992) 891–905) in that distractor stimuli close to the hand compete strongly with the target for the control of action, causing greater interference than distractors far from the hand. We reasoned that in the context of a reaching task, a left–right asymmetry in unilateral neglect may be defined with respect to the position of the hand. This predicts that target and distractor stimuli to the left of hand (i.e. requiring leftward movements for contact) should compete less strongly for the control of action than stimuli to the right of the hand. We tested this hypothesis by asking eight patients with unilateral neglect (and 12 healthy controls) to reach to central targets presented alone and with surrounding distractors from left or right start positions. Patients with neglect, but not controls, were slower to initiate reaches from right start as compared to left start positions. In this context, patients showed interference from distractors to the right of the hand and facilitation from distractors to the left of the hand. This indicates that a left–right selection asymmetry in neglect may be hand-centered. These data can be explained on a model of damage to the portion of a distributed neuronal population coding movement vectors to stimuli in relatively leftward locations. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Unilateral neglect; Hemispatial neglect; Hand-centered; Action-centered; Selection for action; Premotor theory; Distractor interference; Distractor inhibition; Spatial; Motor; Reaching; Attention; Spatial summation; Co-activation; Redundant signals; Frontal lobe; Parietal lobe

According to a prominent theory of attention, the purpose of spatial attention is the selection of a specific action directed toward a target object [1]. To this end, irrelevant inputs from distractor objects (and potential responses to these inputs) must be inhibited, and relevant inputs and responses selected. A related account, known as the premotor theory of attention, suggests that facilitation of processing due to attention is a consequence of activation of neural circuits involved in motor preparation. Thus, attention en-

hances that which is intended as a target for action [21,22]. On both accounts, action can be construed as the primary goal of the organism. Because the number of actions that can be selected at any time is limited (by the number of effectors available to perform the actions, for example), competition arises both between potential targets of action and between potential actions.

Patients with unilateral left neglect fail to report or act on stimuli on the left side of body-centered (egocentric) space, as well as stimuli to the relative (allocentric) left of other stimuli. There are a number of accounts of the disorder. For example, neglect phenomena have been attributed to a failure of representation of the left side of space e.g. [5] and a right–left gradient of spatial attention e.g. [14]. On

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the 'selection for action' and 'premotor theory of attention' accounts just described, unilateral neglect is attributable to an asymmetry in action selection processes. Selection and motor preparation for action are biased toward stimuli on the right (or relative right), and stimuli further to the left exert less influence on selection processes [16]. The notion of competition between rival perceptual and motor processes vying for selection distinguishes the 'selection for action' and 'premotor' accounts of neglect from others.

There are at least two neglect-related phenomena consistent with a putative competitive bias to select right-sided stimuli and rightward actions. The first is visual extinction. In this common syndrome, subjects respond adequately to a left-sided visual or tactile stimulus when it is presented in isolation, but fail to report or respond to the same stimulus when it is paired with another stimulus to the relative right. The second phenomenon is that many patients with neglect are significantly slower both to initiate and perform leftward as compared to rightward limb movements; i.e. they exhibit directional hypokinesia [12,15]. Even when a relatively leftward movement is selected, the movement may be influenced by objects to the relative right. Thus, the reach trajectories of patients with neglect may deviate toward a distractor object presented on the ipsilesional (right) side of a target [9]. These data are consistent with a deficit in selecting responses requiring leftward movements.

In the neglect studies described above, as well as in many other related studies, 'left' and 'right' have been defined in egocentric (body-centered) and allocentric (stimulus-centered) coordinates, and it is with reference to these frames that attention and action are frequently said to be biased. In other words, 'left' neglect has referred to neglect of stimuli on the left side of the subject and/or to the left of other stimuli. However, the definition of 'left' and 'right' need not be limited in this manner. Physiologic studies with monkeys e.g. [2,11] and experimental work with humans e.g. [24] indicate that visual information can be represented with respect to a number of reference frames, including retinotopic, head-centered, shoulder-centered, and hand-centered frames. In other words, stimulus location may be defined in terms of the position of the stimulus relative to a reference system with its origin at the locus of the effector (eye, head, shoulder, hand) used to 'acquire' the target.

Consistent with this possibility, an important paper by Tipper, Lortie and Baylis [25] demonstrated that stimulus and response selection processes in healthy subjects may be referenced to hand-centered frames in the context of a reaching task. The investigators reasoned that evidence for hand-centered coding of target and distractor locations would take the form of

relatively greater competition for selection by distractor stimuli close to the hand, and relatively less competition from distractors far from the hand, irrespective of where these distractors were located in retinotopic, body-centered, or allocentric coordinates. They asked subjects to reach to a red target light presented near the center of a board, ignoring a yellow distractor light which appeared with the target on some trials. Distractors appeared at one of several locations on the board, which was angled away from the subjects so that distractors appearing at the top of the board were 'far' and those at the bottom of the board 'near' in egocentric coordinates. Because of the board's angle and the effect of visual foreshortening, 'far' distractors were closer to central targets in retinotopic coordinates than were 'close' distractors.

In one condition, subjects began each reaching trial with the hand at the bottom of the board. In this case, distractors at the bottom caused the most interference (slowing) on latencies to reach to the central targets. In a second condition, subjects began each reaching trial with the hand resting at the top, 'far' end of the board. In this condition, distractors at the top of the board, 'far' from the subject, interfered the most with central target detection. In other words, the pattern of interference was sensitive to the hand's starting position, and was thus hand-centered, not retinotopic or body-centered.

In a subsequent paper, Tipper, Howard and Jackson [27] provided data demonstrating that when subjects reach for a target presented with a distractor, hand path trajectories deviate away from the distractor object (note that this finding is opposite to that reported in neglect patients by Chieffi, Gentilucci, Allport, Sasso, and Rizzolatti [9]; we will return to this point below). Both the hand-centered pattern of interference by distractors on reaching latencies and the effect of distractors on deviations in hand path trajectories can be explained, according to Tipper and colleagues [26,27], if one assumes that potential actions to target and distractor locations are encoded in parallel by a distributed and partially overlapping neuronal population programming movement vectors to these potential destinations. Interference by distractors is an index of the cost of uncoupling target locations from the control of action and inhibiting responses to distractor locations.

For example, when a distractor is located to the right of the target, and the distractor location is 'deselected' and uncoupled from action control, neurons coding movement toward it are inhibited below baseline. Since there is overlap in the neurons coding reaches to the right-sided distractor and left-sided target, this means that a portion of the 'right-directional' neurons coding reaches to the target are also

inhibited below baseline. As a result, the reach trajectory is programmed by the remaining population of neurons, which program relatively 'left-directional' movement vectors. Consequently, the reach that is programmed veers away from the right-sided distractor, toward the left.

Given the evidence of hand-centered location coding in healthy subjects, we reasoned that neglect may be defined with respect to the acting hand in the context of action tasks. Consistent with this possibility, we previously reported a case study of a parietal-lesioned patient whose neglect dyslexia was influenced by the position of his acting hand [7,8]. In several studies, the subject (AM) was asked to tap on or near the site of words using the right hand, and we examined effects of tapping location on reading accuracy. There was a location effect that was spatially precise: when AM tapped immediately adjacent to the left end of the words his performance was 60% correct, and only 16% of his reading errors involved neglect of initial letters. In contrast, when he tapped immediately adjacent to the words' right end, his performance dropped to 29% correct, and 53% of his errors involved neglect of initial letters (e.g. fact → act). These as well as data from other tapping locations indicated that there was a left–right gradient of accuracy as a function of whether AM tapped on the far left, left, near right, or far right of stimuli. The benefit of tapping could not be attributed to visual cueing, as when the examiner provided such a cue by tapping at the site of the words, performance was as impaired as in a baseline condition in which AM read with his hands resting in his lap (32% correct). Finally, there was evidence that recruitment of the action system was necessary for the beneficial effect, as when AM rested his hand passively at the left end of words, his performance was also as impaired as in the baseline condition. Thus, left neglect may be defined in part by spatiomotor coordinates of hand activity.

Within the framework of the 'selection for action' and 'premotor' accounts, these data suggest that stimuli to the left of the hand (i.e. requiring leftward movements for contact) should compete less strongly for the control of action than stimuli to the right of the hand (i.e. requiring rightward movements for contact). In the present study, we tested this possibility by asking patients with neglect to reach to central targets presented alone or with distractors from right or left start positions. Two specific predictions emerge from the hypothesis that neglect in action tasks may result, at least in part, from a hand-centered selection asymmetry. The first is that the selection and programming of hand and arm movements to leftward locations should be relatively impaired. Thus, there

should be an asymmetry in the initiation and performance of reaching movements to left as compared to right targets (i.e. directional hypokinesia). The second prediction is that there should be a competitive bias between targets and distractors which favors stimuli to the right, as 'right' is defined with respect to hand position. Thus, distractor interference should be relatively great when the distractor is to the relative right of the hand, as when the hand begins reaching movements from the left of the visual array. In contrast, we expect distractors in the *same allocentric and egocentric locations* to be neglected (and thus cause very little or no interference) when they are to the relative left of the hand, as when the hand starts reaching from the right of the array. As the position of stimuli with respect to the head, body, and target is unaffected by the start position manipulation, any such observed left–right asymmetries in distractor interference would be attributable to neglect defined with respect to hand-centered coordinates.

1. Methods

1.1. Subjects

From a population of MossRehab inpatients and outpatients with unilateral right-hemisphere stroke, we studied eight consecutive patients with evidence of neglect on neurologic examination and in daily activities who met study criteria (arousal, visual acuity, and hearing sufficient to participate; absence of prior neurologic history). Twelve right-handed healthy age-matched adult subjects (nine females and three males) were also enrolled. All subjects provided informed consent to participate. Table 1 shows lesion localization for patients and demographics for all subjects. All subjects had normal (or corrected-to-normal) visual acuity, and normal color vision. Patients all had normal strength and dexterity of the ipsilesional (right) arm and hand. Details of patients' medical histories are provided below.

N1 was an 86 year-old right-handed retired electrical engineer who suffered a right-hemisphere cerebro-vascular accident (CVA) during carotid endarterectomy. On neurologic examination, there was tongue deviation to the left, facial asymmetry, and left facial droop. Tactile sensation was diminished on the left, and there was a left-sided flaccid hemiparesis. There was left-sided visual extinction. Left hemineglect was noted in daily activities.

N2 was a 54 year-old right-handed steel worker admitted to hospital with a large right middle cerebral artery (MCA) infarction. There was a tongue deviation, facial droop, flaccid hemiparesis, Babinski

Table 1
Subject demographics

	Age	Education	Handedness	Gender	Time since stroke	Lesion location (all right hemisphere) ^a
<i>Neglect patients</i>						
N1	86	16	R	M	9 weeks	IP, DPF
N2	55	12	R	M	9 months	SP, IP, DLF, ST, IT, BG, IC/CS
N3	66	12	R	M	5 months	ST, BG, IC/CS
N4	49	18	R	M	7 months	IP, ST, AT, PT, EC
N5	70	21	R	M	8 weeks	IP, SP, DLF, PT, IT, BG
N6	78	12	R	M	6 weeks	IP, DLF, ST, IT, O
N7	61	12	R	M	6 weeks	IP, DLF, ST, AT, PT, BG
N8	69	18	L	M	8 weeks	SP, BG, IC/CS
Mean	66.8	15.1				
SD	11.9	3.6				
<i>Control subjects</i>						
C1	45	16	R	F		
C2	56	18	R	M		
C3	53	12	R	F		
C4	45	16	R	F		
C5	69	16	R	F		
C6	51	16	R	F		
C7	70	18	R	M		
C8	71	12	R	F		
C9	81	12	R	M		
C10	71	12	R	F		
C11	44	12	R	M		
C12	66	14	R	M		
Mean	60.2	14.5				
SD	12.6	2.4				

^a IP, inferior parietal; SP, superior parietal; DPF, dorsal prefrontal; DLF, dorsolateral frontal; AT, anterior temporal; IT, inferior temporal; PT, posterior temporal; O, occipital; BG, basal ganglia; EC, external capsule; IC/CS, internal capsule/centrum semiovale.

reflex, and loss of tactile sensation on the left. There was evidence of left hemineglect.

N3 was a 66 year-old right-handed retired janitor with a history of a hemorrhagic right-hemisphere CVA with facial asymmetry, dense left-hemiparesis and left hemisensory loss. There was a left upper quadrantanopsia as well as left visual neglect.

N4 was a 47 year-old right-handed high school teacher who suffered a right-hemisphere hemorrhagic CVA with left hemiplegia. A craniotomy and evacuation of the hematoma was performed. Subsequent to the evacuation, there was a left central facial weakness, decreased left tactile sensation, and left hemiparesis. There was a rightward gaze deviation and left hemineglect in daily activities.

N5 was a 70 year-old right-handed retired physician who underwent cardiac surgery which was complicated by a right MCA infarction with left facial droop and dense left-sided hemiplegia. There was a right gaze preference and left hemineglect.

N6 was a 78 year-old right-handed retired construction manager with past medical history of a right occipital temporal parietal infarction who was admitted to the hospital with a new right MCA stroke with

dense left hemiparesis and left Babinski reflex. There was evidence of a right gaze preference, left hemineglect, and anosognosia.

N7 was a 67 year-old right-handed retired machinist admitted to the hospital with a right CVA with dense left hemiparesis. There was evidence of tongue deviation to the left. Sensation was intact to light touch and proprioception. There was a right gaze preference and left hemineglect in daily activities. There was left auditory, visual, and tactile extinction.

N8 was a 68 year-old right-handed retired school superintendent who suffered a right CVA during cardiac surgery. Postoperatively, there was a dense left hemiplegia, left tongue deviation, and left facial weakness. There was evidence of left hemineglect.

1.2. Background testing

All neglect patients underwent background paper and pencil testing with line, letter, and star cancellation and line bisection tests from the Rivermead Behavioral Inattention Test [28] to confirm the presence of neglect. Additionally, patients were assessed for

visual field deficits and visual extinction.¹ Only subject N3 exhibited visual field deficits (left upper quadrantanopsia). Subject N4 had inconsistent left-sided extinction on bilateral simultaneous stimulation. All patients exhibited left neglect on the tasks of the Rivermead Behavioral Inattention Test, as defined by a disparity of at least 20% in the mean number of items canceled on the left versus right of the line, letter, and star cancellation tasks, and/or mean deviation of at least 2 cm to the right on the three lines of the line bisection task.

1.3. Experimental apparatus

The experimental apparatus was modeled on the one used by Tipper, Lortie and Baylis [25]. Subjects sat before a 45.5 cm × 60.8 cm board that rested on a table-top. The board sloped away from the subjects at an angle of 11°.² There were five 2.0 cm² square stimulus buttons arranged in a 'cross' shape (a central vertical column of top, center, and bottom buttons; left and right buttons horizontally flanking the center button) with a distance of 11.3 cm separating each row and column. Two circular start buttons 2.3 cm in diameter were positioned directly below the left and right center-row stimulus buttons at a distance of 22.6 cm. The left and right start buttons were thus equidistant from the center stimulus button.

¹ We also tested seven of the patients (one patient was discharged prior to test administration) with two computerized tasks included to determine whether neglect was predominantly of the perceptual (attentional) type, comprising primary deficits in detecting left-sided targets, or the motor (intentional) subtype, consisting of primary deficits with leftward movements [10,12]. In the 'perceptual' background task, lateralized targets were displayed, and subjects were required to respond as rapidly as possible upon target detection with a central button press response. In the 'motor' task, central targets were displayed which signaled the response to be produced, and subjects were required to move from a central start position as rapidly as possible to produce a lateralized response. Procedure and apparatus for the computerized testing were highly similar to those reported by Bartolomeo, D'Erme, Perri, and Gainotti [3]. Neglect was defined by significant difference in latency to respond to left versus right targets or response keys and/or $\geq 10\%$ difference in left versus right 'missed' trials (failures to respond within 5000 ms). By these criteria, subjects N1, N4, N6, and N8 exhibited both perceptual and motor neglect. N2 appeared to exhibit motor neglect only. N3 showed perceptual neglect as evidenced by more left-sided errors on the lateralized target task. N7 failed to exhibit significant lateralized differences on either task. Subsequent statistical analyses aimed at assessing patterns of association between these tasks, on the one hand, and measures of hemihypokinesia and hand-centered neglect from the main experimental task, on the other, failed to reveal any relationships between the tasks. Consequently, we will not present these data here.

² The experiment reported here did not exploit the effect of foreshortening afforded by the board's angle (i.e. the retinotopic closeness of back row distractors to center targets). The apparatus was used in a number of other experiments, not reported here, in which this feature of the board was important.

Subjects were positioned so that the start buttons were 16 cm from the torso. Start buttons and stimulus buttons were fitted with touch-sensitive microswitches which were used to measure response times. Fig. 1 shows a schematic of the display apparatus.

The board was interfaced to an IBM microcomputer that controlled the illumination of the stimulus buttons and recorded response times (latency between target appearance and subjects' depression of the target button) and errors.

1.4. Experimental design

Subjects received a practice block of 10 trials prior to the experimental trials. There were six experimental blocks, three of which required subjects to begin each trial by depressing the left start and three the right start button. Left and right start blocks were alternated. Half of the neglect and control subjects began the experiment with a left-start block and the remaining subjects began with a right-start block. There were 120 experimental trials in which a target (a red square) appeared in the center position. In 24 'no distractor' (ND) trials (12 each in left start and right start conditions), the center target appeared alone. These trials provided a baseline for measuring the interference caused by distractors when they were present. There were 96 'distractor' trials in

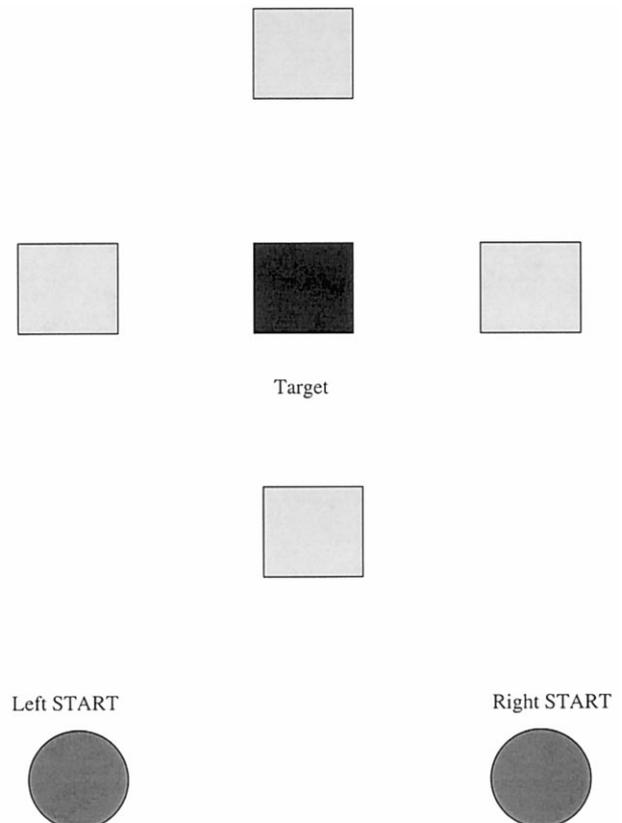


Fig. 1. Schematic drawing of display apparatus (not to scale).

which the center target appeared with a simultaneously-presented distractor (a yellow square) in the top (distractor top, or DT), left (DL), right (DR), or bottom (DB) positions (24 trials with a center target and distractor in each remaining position, 12 each in left start and right start conditions). Finally, to prevent subjects' ability to anticipate target location, there were 160 filler trials in which a red target appeared in the top, left, right, or bottom position (eight ND trials with each of these four target positions and 32 target-distractor trials with each of these four target positions). Trial order was randomized across the experimental blocks.

1.5. Procedure

Room lights were dimmed to maximize detection of the stimuli. Subjects began each trial by fixating on a red dot 1.9 cm in diameter located in the center of the display and depressing the appropriate start button with the right hand. Once the experimenter ascertained subjects' fixation, she initiated the trial. A beep sound of 500 ms duration delivered from the computer provided a warning signal. After a variable delay (500–1000 ms), a target (or target and distractor) appeared. Upon detection of the target (red square), subjects released the start button and depressed the target button as rapidly as possible with the same (right) hand. Targets and distractors were removed when a response was made or after 10,000 ms, whichever came first. Controls performed the experiment in two sessions and neglect patients in four sessions (due to slower response rates) on consecutive days.

Data were recorded in the form of errors (failures to respond within 10,000 ms; responses to incorrect squares), raw initiation times (latencies between target onset and release of the start button) and raw total response times (latencies between target onset and depression of the target button). Interference (or facilitation) attributable to distractors in each position (top, left, right, bottom) was calculated for each subject as the difference in mean response time between the ND trials and trials with distractors in the relevant position.

2. Results

2.1. Errors

No control subject made any errors in any condition. Patients N1, N2, N3, N4, and N6 similarly made no errors. In the left start condition, N5 made four errors and N7 made one error. In the right-start condition, N5 made 18 errors and N8 made one error. Sixteen of N5's errors in the right start condition were failures to respond by deadline. The remaining two errors were responses to distractor (rather than target) location.

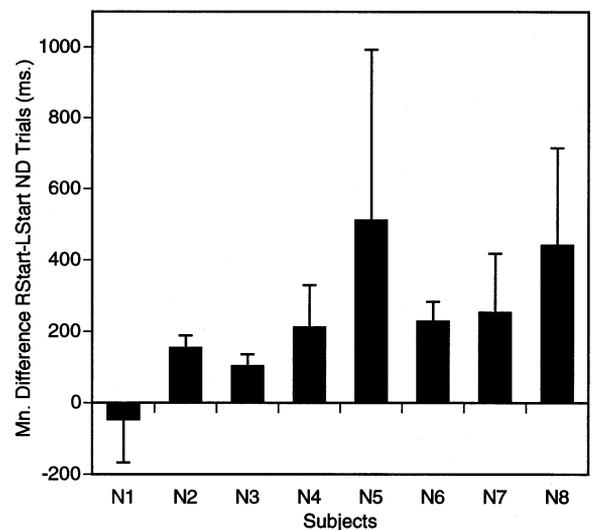


Fig. 2. Mean difference in total raw response time (and S.E.) for each patient's responses to central target in right start versus left start conditions. Positive values indicate that patients were relatively slower in the right as compared to left start condition.

2.2. Response latencies

2.2.1. Total time, no-distractor condition

To assess the hypothesis that patients would be slower to reach to the central target from right as compared to left start, a repeated-measures ANOVA with Start Position (left, right) as a within-subjects factor and Group (neglect patients, controls) as the between-subjects factor was run on the data from ND trials with mean total response time as the dependent measure. There were significant effects of Group, $F(1, 18) = 7.9, P = 0.01$ and Start position, $F(1, 8) = 28.5, P = 0.0001$; and a significant interaction of Group and Start Position, $F(1, 18) = 11.9, P = 0.003$. Although both controls and patients were slower to reach to the central target from right as compared to left start (Patients and Controls both $P < 0.01$ by Fisher's PLSD), the Group \times Start Position interaction is attributable to the significant difference in the magnitude of the left versus right disparity in the two groups. For controls, there was a mean difference of 49 ms (7%) between the left start (Mean 733 ms) and right start (Mean 782 ms) conditions. Patients, however, were 232 ms (14%) slower to reach to the target from right start (Mean 1940 ms) as compared to left start (Mean 1708 ms).

Comparisons on the data from individual patients revealed that two of the patients were significantly slower to reach to the target from right start as compared to left start on ND trials (Subjects N2 and N3: $t > 3.1, P < 0.01$), and three others showed trends in the same direction (Subjects N4, N6, N7, N8: $t \geq 1.5, P \leq 0.1$). Subject N5 showed a large mean difference between left start and right start trials in the same direction, but his data were quite variable, resulting in a non-sig-

nificant comparison (Fig. 2). Finally, subject N1 showed no tendency toward a difference between right and left start ND trials.

2.2.2. Initiation time, no-distractor condition

To assess the hypothesis that the difference between right- and left-start trials would be observable even in the stage of response selection (i.e. prior to actual response execution), we carried out a second repeated-measures ANOVA on ND trials with Initiation Time as the dependent measure, Start Position (left, right) as a within-subjects factor, and Group (neglect patients, controls) as a between-subjects factor. There were significant effects of Group $F(1, 18)=4.8$, $P=0.04$; and Start Position, $F(1, 18)=13.1$, $P=0.002$; and a significant Start Position X Group Interaction, $F(1, 18)=11.7$, $P=0.003$. Only the neglect patients were slower to initiate reaches to the central target from right start (Mean, 1255 ms; SD, 1313 ms) as compared to left start (Mean, 1086 ms; SD, 1181 ms; $P < 0.05$ by Fisher's PLSD). For controls, there was no difference between initiation times in the two start positions (right start: Mean, 394 ms; SD, 53 ms; left start: Mean, 389 ms; SD, 50 ms; $P = 0.5$).

2.2.3. Total interference (distractor–no distractor condition)

To test the hypothesis that distractor interference in the neglect group would be influenced by start position, a third repeated-measures ANOVA was run with Start Position (left, right) and Distractor Position (top, left, right, bottom) as within-subjects factors, Group (neglect patients, controls) as a between-subjects factor, and Total Distractor Interference (i.e. difference in Total RT between distractor trials as compared to ND trials) as the dependent measure. There were significant main effects of Group, $F(1, 18) = 4.9$, $P = 0.038$; Start Position, $F(1, 18) = 36.3$, $P = 0.0001$; and Distractor Position, $F(3, 54) = 4.5$, $P = 0.007$. There were also significant interactions of Group and Start Position, $F(1, 18) = 32.6$, $P = 0.0001$; and Group and Distractor Position, $F(3, 54) = 4.04$, $P = 0.01$. The three-way interaction of Group, Start Position, and Distractor Position approached but did not reach significance, $F(3, 54) = 2.18$, $P = 0.1$.

Table 2
Mean interference (SD) in four distractor conditions in patients and controls

Group	Distractor position			
	Top	Bottom	Left	Right
Control	8.6 (26.3)	2.0 (29.5)	-6.8 (19.4)	3.8 (30.3)
Patient	-29.3 (103.6)	-115.0 (242.8)	-91.3 (143.3)	111.7 (330.4)

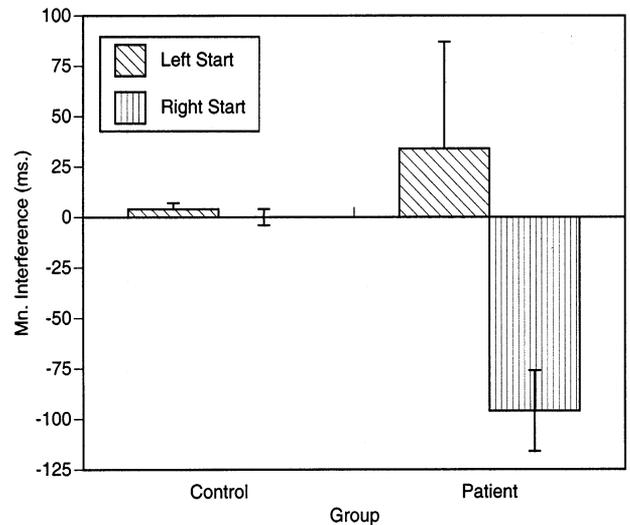


Fig. 3. Mean total interference (and S.E.) by distractors on total response times in right and left start conditions, collapsed across distractor positions.

The Group by Distractor interaction can be seen in Table 2. Post-hoc comparisons demonstrated that for patients, DR caused more interference than DB and DL ($P < 0.03$), and tended to cause more interference than DT ($P = 0.1$). For controls, DL caused less interference than DR and DT ($P < 0.03$), and tended to cause less interference than DB (0.07).

Patients showed greater distractor facilitation than did controls for distractors in bottom ($t = 2.3$, $P = 0.02$) and left ($t = 2.8$, $P = 0.006$) positions, and tended to show more facilitation for top distractors as well ($t = 1.7$, $P = 0.09$). Patients tended to show more interference than did controls from distractors in the right position ($t = -1.6$, $P = 0.1$).

The group by start position interaction is shown in Fig. 3. On left start trials, patients averaged 34.0 ms (SD 302 ms) slower with distractors compared to ND (distractor interference) and on right start trials, averaged 96.0 ms (SD 119 ms) faster with distractors compared to ND (distractor facilitation). The mean 130 ms difference between right and left start trials was significant ($t = 129.9$, $P = 0.001$). Controls, in contrast, showed equal interference in left start (Mean 4 ms, SD 22 ms) and right start (Mean 0 ms, SD 31 ms) conditions (mean difference 4 ms, $t = 3.9$, $P = 0.6$).³

³ Because strategic decisions about when to lift the hand from the start key may affect whether interference effects are exhibited in initiation times, transport times, or both (see [18] for discussion), we limited our formal exploration of interference effects to total time. However, examination of interference effects in the initiation and transport components of the reach indicated that the predominant effects of distractor facilitation from top, left, and bottom distractors in the neglect group in the right start condition was observable largely in the initiation component of the reach (DT, 107 ms; DB, 125 ms; DL, 138 ms. mean facilitation) followed by a more moderate effect of distractor inhibition in the transport component (DT, 11 ms; DB, 21 ms; DL, 13 ms mean interference).

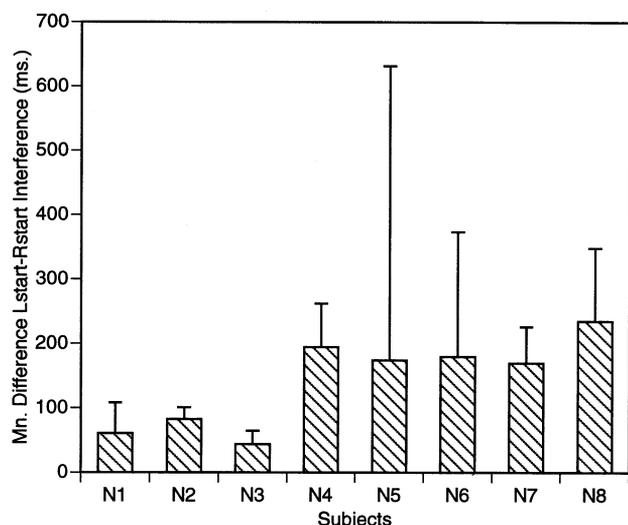


Fig. 4. Mean difference in interference by distractors (and S.E.) for each patient's responses to central target in left start versus right start conditions. Positive values indicate that interference was relatively great in the left start compared to right start condition.

Individual comparisons on the data from each patient revealed that N2, N3, N4, N7, and N8 showed significantly more distractor interference when reaching from left start as compared to right start ($t > 2.1$, $P < 0.05$). Patients N1, N5, and N6 showed non-significant differences in the same direction (Fig. 4).

Although the three-way interaction of Group, Distractor Position, and Start Position merely approached significance, we further explored the possibility of differing patterns in the control and patient data by performing separate two-way ANOVAs for each subject group with Distractor Position and Start Position as within-subjects variables. Table 3 shows the data from the two groups comparing interference for each distractor position in left start and right start conditions. The Distractor Position X Start Position interaction was not significant in the analysis of the data from either group ($P > 0.06$).

3. General discussion

In this study we investigated the hypothesis that a putative asymmetry in selection of targets and responses in neglect may arise with respect to a hand-centered frame of reference in the context of an action task. We assessed the time required for subjects to reach to a central target from right and left start positions, in the presence or absence of distractors. The hypothesis of a hand-centered asymmetry in neglect predicts that patients' performance will have two characteristics. First, it predicts relative slowing in the selection and programming of movements of the hand

in leftward as compared to rightward directions, i.e. slowing of initiation and total reach time to targets at body midline from right as compared to left start positions (directional hypokinesia). Second, the hypothesis predicts relatively greater interference from distractors to the right of the hand (left start) as compared to distractors to the left of the hand (right start).

Both of these predictions were confirmed. First, patients with neglect were significantly slower to initiate and perform reaches to central targets from right start as compared to left start positions.⁴ This replicates findings of other studies e.g. [12,15] indicating that neglect patients may exhibit directional hypokinesia. Consistent with the second prediction, patients showed interference from distractors to the right of the hand (i.e. distractors that would require rightward movements to acquire) and facilitation from distractors to the left of the hand (i.e. distractors that would require leftward movements to acquire). Given that targets and distractors are in the same location with respect to the subjects' bodies and with respect to each other in both start conditions, this suggests that the observed asymmetry in competition between targets and distractors is a function of the locations of targets and distractors with respect to the hand.⁵

Also of interest is the relationship between measures of attentional or perceptual left–right asymmetry and measures of directional hypokinesia. The majority of patients (N2, N3, N4, N7, and N8) exhibited both hand-centered interference as well as at least a trend toward directional hypokinesia asymmetries on the experimental task. While it remains possible that perceptual and motor subtypes of neglect may dissociate, a pattern of association appears to be more prevalent. Below, we discuss a possible account of the hand-centered neglect phenomena which suggests that perceptual and motor neglect might be expected to correlate (and see [16]).

⁴ The reasons for the observed slight differences between leftward versus rightward movements in the total time data of the control subjects are not clear, but may be attributable to the relative ease of performing adductive as compared to abductive movements [6]. This explanation does not accommodate the data from the patients, which showed left–right differences even in initiation time, before movements were launched.

⁵ While we might have expected to observe a hand-centered effect in the control subjects (greater interference from bottom and right distractors than top and left distractors), this was not the case. It is likely that details of the experimental design precluded the emergence of hand-centered effects in the controls. Subjects saw targets in the center position, near fixation, on 120 trials, whereas targets appeared at a particular peripheral locus on only 40 trials. Under these circumstances, it is likely that subjects might covertly attend to the center target, thereby minimizing the likelihood that clear interference effects would be observed.

Table 3
Mean interference (SD) for four distractor conditions in left- and right-start conditions

Group	Distractor Position							
	Top		Bottom		Left		Right	
	Left start	Right start	Left start	Right start	Left start	Right start	Left start	Right start
Control	11.7 (23.7)	5.6 (29.5)	10.0 (18.3)	−6.0 (36.5)	−4.3 (18.1)	−9.3 (21.1)	−1.7 (26.5)	9.5 (33.8)
Patient	39.4 (48.1)	−97.7 (99.6)	−127.0 (332.8)	−103.0 (123.5)	−28.9 (148.6)	−153.8 (114.0)	252.5 (424.9)	−29.0 (90.2)

A related question concerns possible neuroanatomic substrates of the observed hand-centered interference and directional hypokinesia. Several investigations have suggested that directional hypokinesia is associated with frontal lesions e.g. [11], and attentional/perceptual neglect with posterior parietal lesions e.g. [10], but see [13]. While large lesions in many of the present subjects renders it difficult to draw precise conclusions about neuroanatomic correlates of deficit, it can be noted that subject N6, the only subject to exhibit ‘pure’ directional hypokinesia without perceptual neglect on the experimental tasks (i.e. distractor interference effects were asymmetric but not significantly so) had involvement of the inferior parietal lobule. Additionally, several subjects who exhibited both motor and perceptual asymmetries on the experimental tasks had no frontal involvement (N3, N4, and N8). Finally, there was one subject with both perceptual and motor asymmetries who had neither frontal nor parietal involvement (N3). One concern is that with static imaging techniques, it is not always possible to elucidate functional regions of deficit. Frontal, parietal, and subcortical regions are richly interconnected, and damage to one region may impact others in the spatiomotor circuit. Further study with functional imaging techniques may be required to confirm our impression that frontal and posterior parietal involvement are not prerequisites for directional hypokinesia and perceptual neglect, respectively.

There are several theories of neglect which have difficulty accommodating the present findings. Neither the theory that attention is distributed as a left–right egocentric gradient in neglect [14] nor the theory that neglect results from impairment in the left side of a representation of space [5] predict asymmetries in latencies to initiate reaches from right versus left start to a target in a single position at body midline. Moreover, neither theory predicts that interference (or facilitation) from distractors may be a function of the location of the distractors with respect to the hand.

A recent study by Husain, Mattingley, Rorden, Kennard, and Driver [13] bears several similarities to the present study. Patients with neglect were asked to reach to left, central, and right targets, presented

alone or with a distractor, from left, central, and right start positions. The most striking similarity between the two studies is that in a group of three parietal lobe patients, distractor interference effects were large for the left start position (Mean interference, 161 ms) and intermediate for the central start position (Mean interference, 68 ms). Finally, there was a small effect of distractor facilitation for the right start position (a mean of 18 ms faster with a distractor than without). This pattern of results is remarkably similar to those we have reported. Distractor facilitation effects in neglect have not, to our knowledge, been reported prior to the Husain et al. [13] study and the present study (there have, however, been several reports of facilitation from left-sided primes which precede central targets, see below). The convergence of effects in the two studies supports the contention that the pattern of distractor facilitation and interference effects in action tasks may be a function of the start position of the hand.

It might be argued that there is a variant of the ‘attentional gradient’ account which may accommodate our data and that of Husain et al. [13]. It is possible that a left–right egocentric attentional gradient is skewed by the proprioceptive and/or visual cues provided by the hand as it rests on the start button. The hand attracts covert attention to it, leading to reduced neglect of distractors in the left start condition. One shortcoming of this account is that it does not explain the finding that response times are faster with distractors to the left of the hand (in the right start condition) than when targets are presented alone. Additionally, Husain et al. [13] included a control condition suggesting that this account is unlikely to explain the data. In the control experiment, patients were asked to simply press the start key as rapidly as possible when a target was detected. In this case, the same afferent inputs from the hand were present as in conditions in which subjects had to reach for targets, but the directional movement programming was absent. In the control condition, subjects’ response times to left and right targets were not affected by start position. This indicated that the results in the ‘reaching’ conditions were attributable to

the requirement to program a directional motor response.

Our account of the data is consistent with this finding, and unifies the directional hypokinesia, distractor interference, and distractor facilitation effects and see [26,27]. We consider reaching from left start positions and right start positions separately. When reaching from left start, neuronal populations coding rightward movement vectors are activated. The left hemisphere, intact in this patient population, predominates in rightward movement coding. When two locations (target and distractor) are activated, there is initial excitation of an overlapping neural population. This is followed by relatively precise inhibition of the distractor location (and potential movements to this location) once the target has been identified. The inhibitory process exacts a cost on the time to perform reaches to the target. The distractor interference effects seen in the patients in the left start condition are qualitatively similar to the interference effects seen in healthy subjects (i.e. distractors slow response times), suggesting that inhibitory mechanisms for ‘deselecting’ movements toward the incorrect, distractor location are at least approximately normal when the distractor is to the right of the hand.

Although we did not measure reach trajectories in the present study, it is of interest that this model of competition in a distributed neuronal population provides a potential explanation for the deviations toward right distractors seen in a previous study with neglect patients [9]. Recall the mechanism proposed by Tipper, Howard and Houghton [26] to explain control subjects’ reach deviations away from distractors: inhibition of distractor locations was assumed to completely over-ride initial moderate excitation of distractor locations, resulting in below-baseline activation of distractor locations, and thus gross excitation of the neuronal population ‘away’ from the distractors. In neglect, weak initial excitation of targets that would require relatively leftward movements to acquire may be coupled with stronger excitation of distractors that would require relatively rightward movements to reach. Although inhibition of the right distractors is sufficient to prevent frank misreaches to these distractor locations, the inhibition of the right locations is insufficient to completely suppress the strong activation. A slight activation effect remains, resulting in deviation of the reach toward the distractors.

Related mechanisms explain the distractor effects observed in the present study when reaching from a right start in a leftward direction. In this case, the lesioned right hemisphere predominates. Right hemisphere neuronal populations coding leftward movements are weakly excited, resulting in slowing in the selection and programming of leftward movements,

and thus, directional hypokinesia. Location coding is also coarse and more broadly tuned than is normal, and there is greater than normal overlap in the neuronal excitation pattern for target and distractor locations. As a result, the locations of the target and distractor are poorly registered. Since the locations are poorly registered, the excitation from the two locations is in effect summed or ‘pooled’. This summation or pooling of excitation results in the facilitation effects observed with distractors to the left of the hand.

Husain et al. [13] attributed the facilitation effects observed in their study to ‘extra stimulation provided by adding a distractor... to the left of the hand’ which may ‘help to get the hand moving in the problematic direction’ (p. 30), but did not offer a more specific account of how this might occur. We suggest that there are two specific mechanisms by which the facilitatory effects may be observed. The first account, which is based on a race model, situates the effect primarily in perceptual processing stages. In this model, the first stimulus to be detected is sufficient to initiate a response. When there are two stimuli, the probability of rapid detection of either one is greater than the probability of detecting a single stimulus alone (probability summation). In cases in which motor responses are sluggish or difficult to trigger, as when a leftward movement is in preparation, the increased probability of rapid detection also increases the probability that the motor response will be triggered rapidly. The second account is neural summation (also known as co-activation or superposition), in which facilitation results from the pooled activity of the neuronal population see [19,20]. This model accords well with the notion of distributed neuronal populations coding potential reaches in different directions [26,27], and is the account we prefer.

On this model, the reason that the facilitatory effect of left-of-hand distractors should occur solely in the patients, but not in the control subjects can perhaps best be illustrated with a simplified example. Consider a hypothetical spatiomotor nerve cell receiving input from two presynaptic neurons. Imagine, further, that one of the presynaptic neurons normally responds preferentially to stimuli whose acquisition would require movements 10° to the left. Such a stimulus might be located in the central target location when the hand starts reaching from the right. The other presynaptic neuron is normally preferentially tuned to locations and movements to the relative left of this, e.g. stimuli which would require movements 30° to the left. Such a stimulus might be located in the DL (Distractor left) position of our experimental apparatus when the hand starts reaching from the right.

Each presynaptic neuron delivers a certain number of spikes per second to the common postsynaptic

neuron. The contribution of both presynaptic neurons will be added, and when a critical count, c , is reached, the postsynaptic neuron will fire. Imagine that in control subjects, the input from each presynaptic neuron is in fact c , that is, either presynaptic neuron firing alone will trigger a rapid response in the postsynaptic cell. Thus, in controls, there is no benefit to having one input from the cell coding target location and one from the cell coding distractor location. In contrast, consider that in neglect patients the preferential tuning of each neuron to target or distractor location is noisy and coarse (see above), and that the rate of firing of each presynaptic neuron is a diminished $c-1$. Neither of these inputs alone is sufficient to initiate a rapid response in the postsynaptic neuron. Thus, a target appearing alone generates a relatively sluggish response. When the coarsely-tuned activity of the two neurons is pooled, however, as when the target appears with a distractor, the combined count from the two presynaptic neurons is $(2c)-2$, which surpasses the critical threshold necessary for postsynaptic firing. This example can likely be generalized to more complicated neuronal systems [23].

The premotor theory of attention suggests that conscious awareness of an object (a prerequisite for goal-directed action) requires the integrated activity of multiple neural circuits responsible for representation of space and action. Damage to one or some of these circuits in the right hemisphere results in a failure to consciously detect objects on the left. Nevertheless, residual and undamaged circuits may represent the object sufficiently to permit implicit registration of the object. There is indeed evidence that although neglected stimuli are inaccessible to conscious awareness, they may still influence behavior. Berti and Rizzolatti [4], for example, demonstrated that neglected prime stimuli on the left facilitated responses to target stimuli presented in the non-neglected field. The priming effect was observed when the prime and target were physically different but from the same category, and occurred even in some patients who had been unable to report any left stimuli in a preliminary portion of the experiment. Thus, neglected stimuli served to facilitate responses to stimuli in the non-neglected portion of space see also [17]. In combination with data reviewed above suggesting that right-sided stimuli may interfere with the detection of stimuli further to the left, then, there are suggestions of an abnormal asymmetry in priming and interference processes. Undetected stimuli on the left may facilitate responses to stimuli further to the right, whereas stimuli on the relative right may interfere with stimuli to the left. The present data suggest the possibility that in the context of action tasks, such asymmetries in facilitation and interference may be a function of the position of stimuli with respect to the acting hand.

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