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Authors

Harrington, Deborah L
Haaland, Kathleen York

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HEMISPHERIC SPECIALIZATION FOR MOTOR SEQUENCING: ABNORMALITIES IN LEVELS OF PROGRAMMING*

DEBORAH L. HARRINGTON†‡ and KATHLEEN YORK HAALAND†§

†Veterans Administration Medical Center and Departments of Psychology and Neurology, University of New Mexico, Albuquerque, NM, U.S.A.; and §Department of Psychiatry, University of New Mexico, Albuquerque, NM, U.S.A.

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Abstract—Left and right hemisphere stroke patients and control subjects performed sequences of hand postures which varied in complexity (repetitive and heterogeneous) and length (one to five). Performance in the hand ipsilateral to the stroke was compared to a control group using the same hand. Neither stroke group had problems preprogramming sequences prior to movement.

The only deficit seen for the right hemisphere group was a greater difference in movement time (MT) between heterogeneous and repetitive sequences relative to controls, regardless of sequence length. This suggested right hemisphere damage results in subtle timing but not error deficits on more complex movements, perhaps due to increased external spatial demands.

The left hemisphere group was slower to execute single postures, and had difficulty scheduling motor programs for repetitive and heterogeneous movements such that inter-response times (IRTs) were more affected by sequence length than for controls. Left hemisphere patients also made more errors on heterogeneous sequences as they increased in length, and the difference in MTs between repetitive and heterogeneous sequences increased more with increasing length relative to their control group. These results suggested the left hemisphere plays a role in controlling single postures, in scheduling motor programs during repetitive and heterogeneous movements, and in processes related to sequential ordering.

INTRODUCTION

LEFT HEMISPHERE specialization for controlling many movements in *both* arms has been widely documented [9]. Sequencing of arm and hand postures appears to be especially dependent on the integrity of the left hemisphere [3, 13–17, 20, 27], but the precise cognitive mechansims have been disputed.

Some work [13–16] has attributed the greater sequencing deficits in left relative to right hemisphere damaged patients primarily to memory. When memory factors were controlled in a task where subjects imitated each hand position in a sequence immediately after it was demonstrated, sequencing was slower in all patient groups (left and right frontal and temporal) relative to the controls [16]. However, the procedure for eliminating memory factors also emphasized speed, which may be particularly crucial as slowed sequential tapping rates and a trend for slowed repetitive tapping rates have been reported after damage to the left or right hemisphere [22]. As speeded tasks likely involve different cognitive

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‡Address all correspondence to: D. L. Harrington, Psychology Service (116B), VAMC, 2100 Ridgecrest Drive SE, Albuquerque, NM 87108, U.S.A.

abilities, patients with damage to many different areas of the cerebral cortex may show motor sequencing problems, but perhaps for different reasons.

Others [17, 18] have proposed that the left hemisphere is specialized for controlling changes in hand postures as the performance of repetitive movements is not typically impaired. The presence of greater perseverative but not sequence order errors in left hemisphere damaged groups has also been used to support the hand posture transition hypothesis [17, 18, 27], but it is difficult to infer cognitive mechanisms from error data alone especially in the absence of manipulations designed to affect specific processes. Errors may reflect many processing deficits such as generating or retrieving an internal motor program, failure to monitor movement, forgetting, or inattention.

The present study combined error measures with reaction time (RT), inter-response time (IRT) and total movement time (MT) data from correct trials to examine the roles of the hemispheres as they relate to specific cognitive deficits in motor sequencing. Performance was examined on sequences of hand postures that varied in length and the number of different hand postures while memory factors were minimized. The effect of sequence complexity on left or right hemisphere stroke patients' ability to plan sequences prior to movement was examined by analyzing the effects of sequence length on RT performance for sequences containing different hand postures (heterogeneous), and those containing repetitions of the same posture. For repetitive sequences, normal controls show no effect of sequence length on RT suggesting they are able to use the redundancy of the repetitive movements to plan them as a unit [10]. As patients with left hemisphere damage show no performance deficits on repetitive movements [17, 18], we predicted their RTs should be similar to controls regardless of variations in sequence length. As for heterogeneous sequences, RT increases with sequence length for controls as they must assemble a motor program containing different subprograms, one for each response in the sequence [10, 11]. If the left hemisphere stroke patients' sequencing deficits are related to impaired preprogramming [4, 12, 17], their RTs should vary as a function of sequence length in a different way than for the control group. Sequence length could have less of an effect on their RT in comparison to controls which would imply they do not preprogram information about all responses in the sequence, or RT could increase more with sequence length which would suggest their rate of preprogramming is slower. As deficits in motor sequencing typically have not been reported in patients with right hemisphere damage, except in studies of speeded performance [13–16, 22], right hemisphere stroke patients were expected to show RT functions similar to their controls for both types of sequences.

Difficulty using motor programs to control the execution of hand posture sequences was examined by comparing groups on the pattern of IRTs and MT. The IRT analyses examined the effect of sequence length on the execution of a single posture within a sequence. These analyses should be sensitive to whether subjects engage in programming processes during movements that pertain to the number of responses within a sequence, not simply to an individual posture. If left and right hemisphere stroke patients plan repetitive and/or heterogeneous sequences normally and optimally utilize the output from the motor plan, IRTs should be affected by sequence length in the same way as for their respective control groups. Alternatively, if hemispheric damage produces deficits using motor programs to control sequencing, the time to execute an individual posture should be more affected, relative to control subjects, by the number of other responses contained within the sequence. At a more macro level, the MT analyses, which summed across all IRTs within a sequence, focused on the execution of the entire sequence by examining the relative difficulty of sequencing repetitive postures vs different postures. These analyses are sensitive to whether motor sequencing deficits are more related to programming and execution processes that control sequential movements involving posture changes. If left hemisphere patients have difficulty controlling sequences containing posture changes but not those containing repetitive postures [17], the difference in MT between repetitive and heterogeneous sequences should be greater relative to their control group. A second issue addressed through the MT analyses was whether sequencing deficits could be explained by problems executing a single movement. If left hemisphere damage produces deficits largely associated with executing single postures [2, 3, 19], the left stroke group's MTs should be longer for both single and sequences of postures; when MTs are adjusted to control the time it takes to execute a single posture, the amount of increase in MT with sequence length will be similar to their control group. Finally, if both patient groups are simply slower initiating and executing movements, RTs, IRTs and MTs will be longer but the pattern of sequence type or length effects should be similar to their control group.

METHODS

Subjects

Thirty-seven normal controls, 16 left hemisphere stroke (CVA) patients, and 18 right hemisphere stroke patients were tested at the Albuquerque Veterans Administration and Lovelace Medical Centers. All subjects were right-handed males. Patients performed the task with the hand ipsilateral to the lesion, 20 controls performed with their right hand and 17 with their left hand. The arm ipsilateral to the lesion was examined to avoid biasing the sample by excluding hemiplegic patients and to minimize factors that are purely motoric or sensory in nature (i.e. hemiparesis or hemianesthesia), allowing for a more accurate account of the anatomical correlates of central control processes.

There were no reliable differences among groups, in age or education level. The right hand control group had a mean age of 65 (SD = 4.6) and an average of 13 (SD = 1.7) years of education. The left hand controls had a mean age of 63 (SD = 6.5) and an average of 13 (SD = 0.8) years of education. The left hemisphere stroke patients had a mean age of 63 (SD = 6.9) and an average of 12 (SD = 2.5) years of education. The right hemisphere stroke patients had a mean age of 63 (SD = 12.5) and an average of 11 (SD = 4.0) years of education. Mann–Whitney U Tests showed no significant differences between patient groups in the mean number of months post-stroke (Mean = 27.4, SD = 26.3 for the right hemisphere stroke group; Mean = 34.4, SD = 48.6 for the left hemisphere stroke group) or in the average number of weeks after the stroke in which CT scans were performed (Mean = 42, SD = 91 for the right hemisphere stroke group; Mean = 48, SD = 142 for the left hemisphere stroke group). Four right and two left hemisphere stroke patients were classified as hemiplegic with hemiplegia defined as contralateral grip strength more than two standard deviations below ipsilateral grip strength, which was greater than zero.

All subjects were given neuropsychological tests to describe their cognitive functioning more broadly. Comparisons between groups were carried out using the Mann–Whitney U statistic. On both auditory comprehension (Part V of the Token Test) [1] and fluency (Cookie Theft subtest of the Boston Diagnostic Examination of Aphasia) [5], only the left hemisphere group (Token: 6.9 errors $\pm$ 7.1; Fluency: 5.8 $\pm$ 1.6) showed significant deficits ($P < 0.025$) relative to their control group (Token: 1.8 errors $\pm$ 2.0; Fluency: 6.8 $\pm$ 0.2). Right hemisphere stroke patients performed more poorly on the Block Design subtest of the Wechsler Adult Intelligence Scale—Revised [29] (Scale Score Mean = 6.2, SD = 2.8) than controls (Scale Score Mean = 8.9, SD = 1.7) ($P < 0.001$); left hemisphere stroke patients performed worse (Scale Score Mean = 7.9, SD = 2.6) than their controls (Scale Score Mean = 10.7, SD = 2.8) ($P < 0.01$) although performance was better for the left than the right stroke group ($P < 0.05$).

Apparatus and procedure

Subjects executed sequences of hand postures on the apparatus depicted in Fig. 1. The apparatus was interfaced with a computer, and contained a row of five vertical plates which required contact with the lateral side of the hand, a row of five recessed buttons which required contact with the index finger with the forearm pronated, and a row of five handlebars which required the four fingers to wrap around the bar from underneath with the forearm supinated. Subjects wore gloves equipped with metal contacts. For subjects using their left hand, the start plate was located to the left of the manipulanda, and subjects always moved from the left to the right. For those using their right hand, the start plate was located to the right of the manipulanda, and subjects always moved from the right to the left. This procedure was adopted so that stroke patients would always begin movement in the ipsilateral hemispace. When a change in hand posture was made, subjects moved to the right or the left diagonally (up or down) to the next manipulandum. A monitor presented pictorial displays of the motor sequences (see Fig. 1).

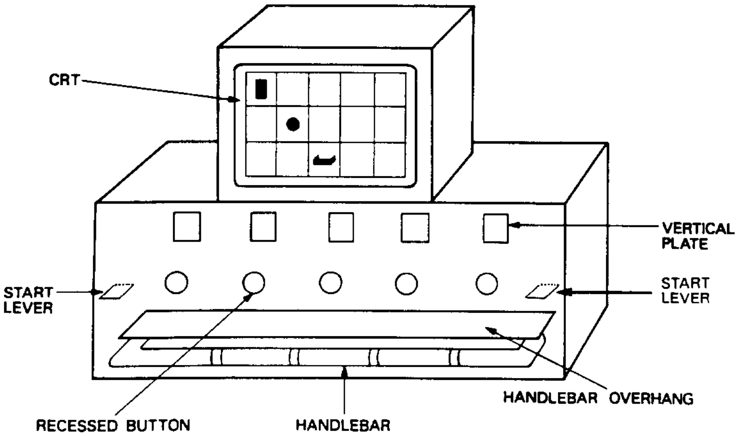

Fig. 1. Diagram of the hand posture sequencing apparatus.

Subjects started each trial by resting their index finger on the start plate, which caused a pictorial display of the sequence to appear on the monitor. After a random delay ranging from 1 to 2 sec, a tone signaled subjects to begin the sequence. Upon completion of the last response in the sequence, the visual display terminated. RT was measured from the onset of the imperative stimulus to when subjects lifted their finger from the start plate. The first IRT was measured from when subjects left the start plate (i.e. the end of the RT interval) to the completion of the first response (i.e. contact with the manipulandum), and subsequent IRTs were measured from the completion of one response to the completion of the next. MT was measured from the end of RT to the completion of the last response in the sequence. An error trial was recorded when subjects took longer than 2000 msec to initiate the movement during the RT interval (i.e. error before movement) or to execute a single hand posture (i.e. error during movement), or if they executed the wrong hand posture (i.e. error during movement).

Table 1 presents the two types of sequences (repetitive and heterogeneous) which were blocked. Block order was randomized across subjects. Each of the 23 different motor sequences was presented eight times across blocks in a random order. If subjects made an error, the trial was repeated randomly at the end of the block of trials. Subjects were required to correctly complete two practice trials of each of the 23 sequences.

Table 1. Hand posture sequences for Experiment 1

	Sequence length				
Sequence type	1	2	3	4	5
Repetitive	P	PP	PPP	PPPP	PPPPP
	B	BB	BBB	BBBB	BBBBB
	H	HH	HHH	HHHH	HHHHH
Heterogeneous		PB	PBP	PBPP	PBPPP
		HB	HBH	HBHH	HBHHH

Note. The letters P, B and H designate plate, button and handlebar responses.

CT scan quantification

CT scans were available on all stroke patients. Computerized procedures were used to quantify lesion size and location (anterior vs posterior) [32]. Lesion size was expressed as a ratio of lesion volume to brain volume. Lesion location was quantified in two ways: (1) the proportion of the total lesion volume that was located anterior and posterior to a line halfway between the frontal and occipital poles, and (2) the distance of the lesion from frontal and occipital poles divided by the total distance so as to represent a proportion of the slice length. Computations of anterior and posterior distance were weighted by the lesion volume of each slice.

RESULTS

Preliminary analyses of variance (ANOVAs) with repeated measures comparing the two control groups on all measures showed that the control group (left or right) did not interact with sequence length or sequence type. This indicates that both control groups performed the task similarly, although there were nonsignificant trends (see Figs 2 and 3) for the right controls to perform more slowly than the left controls, which is likely due to the direction of movement rather than the hand used. Specifically, perceptual-motor sequences that proceed from right to left are less familiar because highly practiced sequential skills, such as reading and writing, proceed from left to right. Despite the similarity between the two control groups, the data were analyzed separately for the right and the left hemisphere stroke groups using ANOVAs with repeated measures, which compared each stroke group to their respective control group. This approach was adopted because it is likely that with brain damage, hand preference effects in combination with movement direction effects could emerge, influencing the performance of the two stroke groups but for different reasons. This possibility was confirmed in preliminary ANOVAs with brain damage (control vs stroke) and hand (left vs right) as between subject factors and sequence length as the repeated measure. While approximately half of the analyses showed significant brain damage × hand × sequence length interactions, most of the remaining analyses showed significant hand × length interactions ($P < 0.05$), indicating that the effects of hand often varied differently as a function of sequence length, independent of brain damage. The statistical approach adopted in this study does not allow for direct comparisons between the two stroke groups so that our conclusions are limited to describing the presence or the absence of certain deficits in each stroke group relative to their respective control group. However, given our limited knowledge of hand and movement direction factors in complex, perceptual-motor skills, presently, we consider this to be the most valid method for specifying deficits in patients with unilateral hemispheric damage.

All analyses were based on a mixed model design with group (i.e. control vs stroke) as the between subject factor and posture and sequence length as the repeated factors. Trend analyses were performed on effects involving sequence length. The tests of interest were those comparing groups and the interaction of group with sequence length or sequence type. Separate ANOVAs were conducted for each measure. Repetitive and heterogeneous sequences were first analyzed separately, and then MTs were compared between sequence types.

Repetitive sequences

Errors. There was no difference between left or right hemisphere stroke patients and their control groups in errors before or during movement. For all groups, errors before movement averaged 5% and errors during movement averaged 2%.

Reaction time. To examine stroke patients' ability to preprogram repetitive sequences, the effect of sequence length on RT was analyzed. The analyses showed that the left and right hemisphere groups preprogrammed repetitive sequences similar to their respective control group. For all subjects, sequence length had little or no effect on RTs. RT did not vary with sequence length for the right control and right hemisphere stroke groups, but did vary with sequence length for the left control and left hemisphere stroke groups [$F(1, 31) = 6.3$, $P < 0.025$ for the linear trend; $F(1, 31) = 4.8$, $P < 0.05$ for the quadratic trend] such that single movements were programmed approximately 18 msec faster than sequences of movements (regardless of length) [F (1, 31) = 8.0, $P < 0.01$], which has been shown in other studies [10, 11]. There was also a trend for RTs of the left hemisphere group (Mean = 426 msec) to be longer than their controls (Mean = 334 msec) ($P < 0.06$), regardless of sequence length, but no such trend was observed for the right hemisphere group (Mean = 427 msec) and their controls (Mean = 391 msec).

Inter-response times. While there was only a trend for the first IRT (IRT_1) to be slower for left hemisphere stroke patients than controls ($P = 0.052$), all IRTs for subsequent responses were significantly slower ($P < 0.025$). IRTs of right hemisphere stroke patients were not significantly slower than their controls ($P > 0.05$).

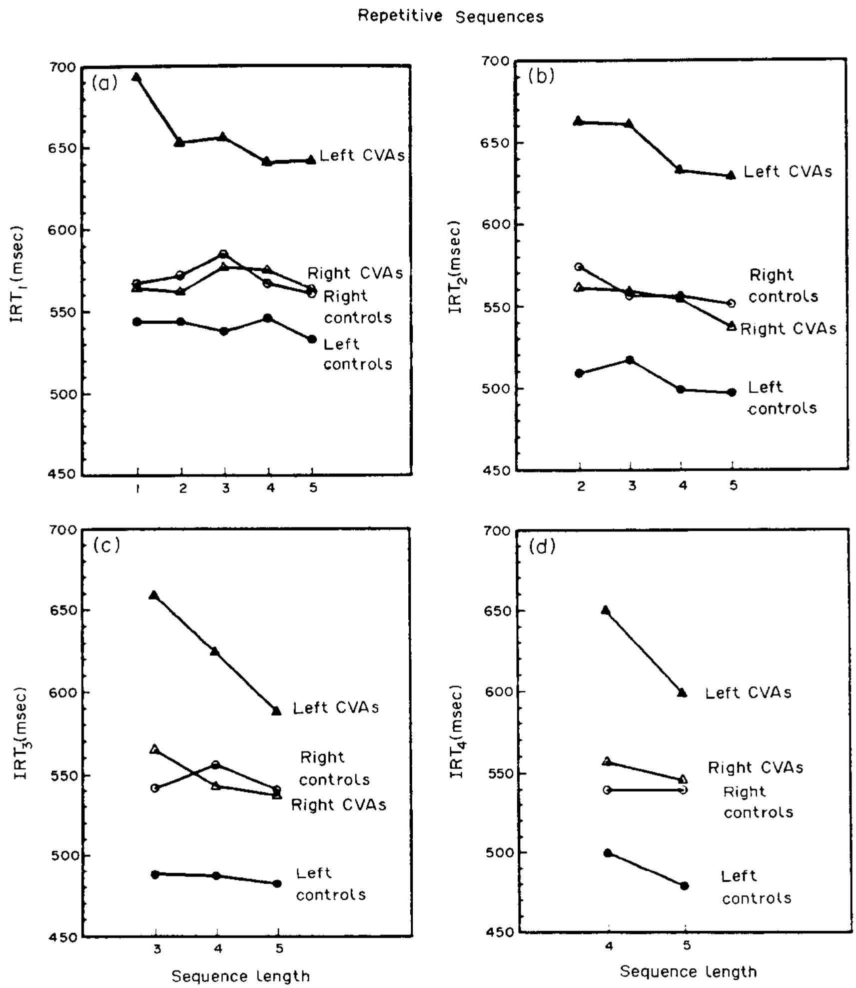

Fig. 2. Inter-response times (IRTs) for repetitive sequences as a function of sequence length. (a), (b), (c) and (d) designate the mean IRTs for IRT_1, IRT_2, IRT_3 and IRT_4, respectively. Data are plotted for the left and right hemisphere stroke (CVA) groups and their respective control groups.

To examine whether the stroke patients continued to engage in programming processes concerning the sequence, not just an individual posture, the effects of sequence length on each IRT were compared between each stroke group and their respective control group. The pattern of IRTs as a function of sequence length generally differed between the left hemisphere stroke group and their controls. Figure 2(a) shows group interacted with sequence length [F (4, 124)=2.6, $P<0.05$] such that IRT_1 varied with sequence length for the left hemisphere group, but not the control group. Left hemisphere stroke patients executed the first hand posture faster as sequence length increased from one to four responses, where IRT_1 becomes asymptotic thereafter [F (1, 15)=9.6, $P<0.01$ for the linear trend; F (1, 15)=5.0, $P<0.05$ for the quadratic trend]. Figures 2(b), 2(c) and 2(d) show a similar pattern of findings except that for the second IRT (IRT_2), group did not interact with sequence length; for both groups IRT_2 decreased from two to four responses and becomes asymptotic thereafter [F (1, 31)=6.7, $P<0.025$ for the linear trend; F (1, 31)=5.9, $P<0.025$ for the quadratic trend]. However, for the third (IRT_3) and fourth IRTs (IRT_4), group interacted with sequence length [F (2, 62)=8.9, $P<0.001$ and F (1, 31)=4.2, $P<0.05$]. For the left hemisphere group but not their controls, IRT_3 decreased as sequence length increased [F (1, 15)=43.6, $P<0.001$]. For both groups IRT_4 decreased with sequence length [F (1, 15)=17.2, $P<0.001$ and F (1, 16)=4.7, $P<0.05$ for the left stroke and control groups, respectively], but Fig. 2(d) shows this effect was more marked for the left stroke group. These findings show that the left hemisphere group is more affected than their controls by the number of other responses in a sequence, suggesting they engage in more programming during movement.

In general, the pattern of sequence length effects on IRTs did not differ between the right hemisphere group and their controls. Figures 2(a) and 2(d) show that sequence length had no effect on IRT_1 or IRT_4 for the right hemisphere stroke patients and right controls, whereas Fig. 2(b) shows that IRT_2 of both groups was somewhat faster for longer sequences [F (1, 36)=11.4, $P<0.01$]. However, Fig. 2(c) suggests that right hemisphere stroke patients may have had some minor programming problems during movement when compared to their controls [F (2, 72)=5.0, $P<0.01$], since IRT_3 decreased slightly with increasing sequence length for the right stroke patients only [F (1, 17)=12.9, $P<0.01$].

Heterogeneous sequences

Errors. The right hemisphere group did not make more errors before or during movement in comparison to their control group. For both groups, errors before movement averaged 5% and during movement, 4%. The left hemisphere group did not make more errors before movement than their controls, but group interacted with sequence length [F (3, 93)=3.6, $P<0.025$] such that the left hemisphere group made increasingly more errors during movement as sequence length increased [F (1, 15)=10.1, $P<0.01$ for the linear trend]; whereas for the controls, there was no effect of sequence length on error rates (Mean=2%). Errors during movement for the left hemisphere group ranged from 3.4 to 10.3% as sequence length increased from one to five responses, but left hemisphere stroke patients had a higher error rate than their controls ($P<0.025$), only for sequences containing four and five responses. These findings suggest that the left hemisphere stroke group has a deficit in some aspect of programming during movement, especially when heterogeneous sequences contain more responses. This is the case even though the additional responses contained in longer sequences were repetitions of a previous posture (see Table 1).

Reaction time. To examine the stroke patients' ability to preprogram heterogeneous sequences, the effect of sequence length on RT was analyzed. These analyses showed that the left and the right hemisphere stroke patients preprogrammed sequences similar to their controls. RTs increased as sequence length increased similarly for the left hemisphere group and their controls [$F(1, 31) = 5.6$, $P < 0.025$ for the linear trend] and the right hemisphere group and their controls [$F(1, 36) = 27.6$, $P < 0.001$ for the linear trend]. Averaging across all groups, RT increased approximately 33 msec between sequences containing two and five responses. There was a trend for the overall RTs of left hemisphere stroke patients (Mean = 427 msec) to be longer than their controls (Mean = 337 msec) ($P = 0.052$), whereas no such trend was observed for right hemisphere stroke patients (Mean = 448 msec) and their controls (Mean = 399 msec).

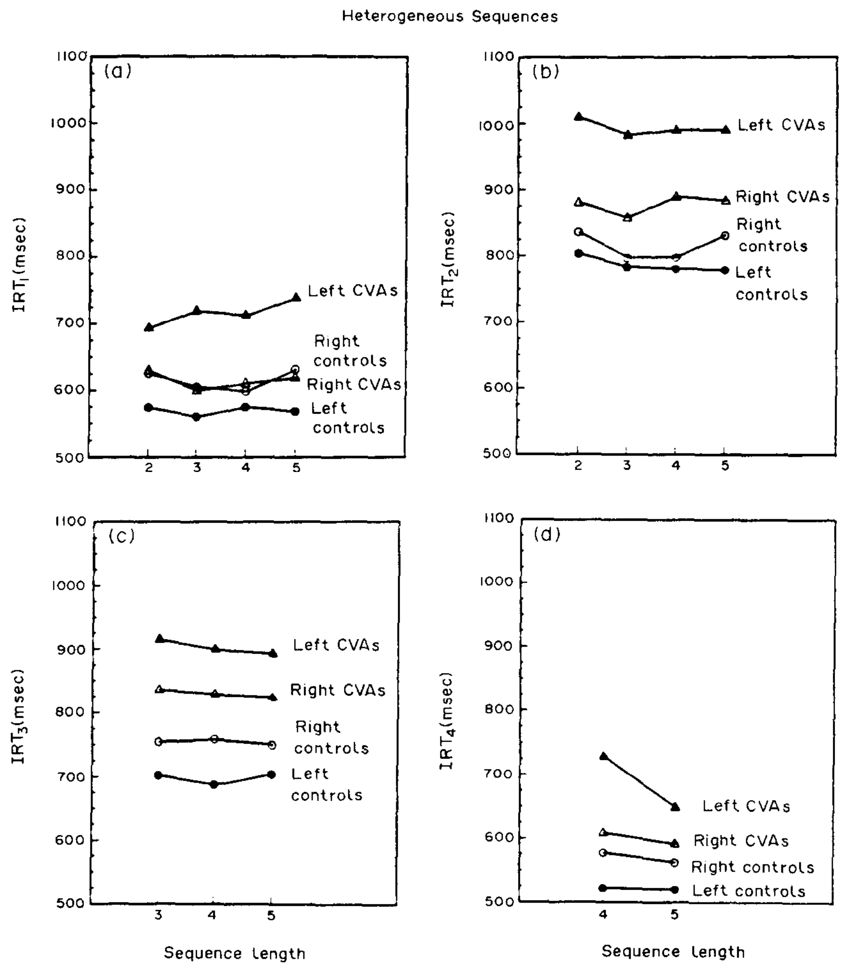

Fig. 3. Inter-response times (IRTs) for heterogeneous sequences as a function of sequence length. (a), (b), (c) and (d) designate the mean IRTs for IRT_1, IRT_2, IRT_3 and IRT_4, respectively. Data are plotted for the left and right hemisphere stroke (CVA) groups and their respective control groups.

Inter-response times. For all IRTs, the left hemisphere group was significantly slower than their controls, regardless of sequence length ($P<0.025$), whereas no such differences were found between the right hemisphere group and their controls. To determine whether the stroke patients were more likely than their controls to engage in programming processes concerning the sequence, not simply a single posture, the effects of length on each IRT were analyzed. Figure 3 indicates that the pattern of IRTs varied with sequence length sometimes differently for left hemisphere stroke patients in comparison to controls. Figure 3(a) shows that sequence length interacted with group [$F\,(1, 31)=4.4$, $P<0.05$] such that while there was no effect of length on IRT_1 for controls, there was a trend for IRT_1 to increase with length for the left stroke group [$F\,(1, 15)=4.0$, $P<0.07$]. This finding suggests that when sequences contained different postures, programming that began during the RT interval was ongoing for left hemisphere stroke patients. However, sequence length had no reliable effect on IRT_2 or IRT_3 for the left hemisphere group or their controls (Figs 3(b) and 3(c)). As for IRT_4, Fig. 3(d) shows an interaction of group with sequence length [$F\,(1, 31)=16.9$, $P<0.001$] such that the duration of the fourth hand posture decreased with sequence length, but only for the left hemisphere group [$F\,(1, 15)=31.2$, $P<0.001$]. Recall that the fourth hand posture is a repetition of the previous one which explains why this pattern of findings is similar to those reported for repetitive sequences. The IRT findings suggest that while controls appear to have completed programming during the RT interval, the left hemisphere stroke patients continue to engage in programming processes that are affected differently by sequence length earlier rather than later in sequencing.

The pattern of sequence length effects on the IRTs for the right hemisphere group did not generally differ from their controls. Figure 3(a) shows that sequence length affected IRT_1 similarly for both groups, but the effect was not linear [$F\,(1, 36)=9.0$, $P<0.01$ for the quadratic trend]. Figure 3(b) shows that for IRT_2, group interacted with sequence length [$F\,(3, 108)=3.1$, $P<0.05$]; however, follow-up analyses showed a similar pattern of length effects for the controls [$F\,(1, 19)=7.9$, $P<0.025$ for the quadratic trend] and the right hemisphere stroke patients [$F\,(1, 17)=6.6$, $P<0.025$ for the quadratic trend], suggesting the interaction may have been spurious. Figures 3(c) and 3(d) show no length effects on IRT_3 for either the right hemisphere group or their controls, whereas IRT_4 was significantly faster for longer sequences [$F\,(1, 36)=4.6$, $P<0.05$] in both groups which is similar to findings for repetitious sequences and suggests both groups are engaged in some programming for longer sequences.

Movement time

The MT analyses, which focused on the execution time for the entire sequence, examined the relative difficulty of sequencing repetitive postures vs different postures. For the left stroke and control groups, an ANOVA with sequence type and sequence length as the repeated factors showed an interaction of group × sequence type × sequence length [$F\,(3, 93)=6.2$, $P<0.001$]. Follow-up analyses indicated that MTs for the left hemisphere group increased more than their controls as a function of sequence length for both repetitive [$F\,(3, 93)=5.9$, $P<0.001$ for the group by length interaction] and heterogeneous sequences [$F\,(3, 93)=10.8$, $P<0.001$ for the group by length interaction]. However, MTs for heterogeneous sequences were longer than MTs for repetitive sequences, especially as sequence length increased, and this effect was greater for the left stroke group than their controls [$P>0.05$ for sequences containing two or three postures; $F\,(1, 31)=9.3$, $P<0.01$ and $F\,(1, 31)=10.1$, $P<0.01$ for sequences containing four and five postures, respectively].

In addition, the left hemisphere stroke group was significantly slower than their controls when executing a single hand posture (Means = 693 msec vs 544 msec) [$F(1, 31) = 5.4$, $P < 0.05$] as well as repetitive ($P < 0.025$) and heterogeneous sequences ($P < 0.025$).

For the right hemisphere stroke patients, ANOVAs with sequence type and sequence length as repeated factors showed that group interacted with sequence type [$F(1, 36) = 4.8$, $P < 0.05$] such that heterogeneous MTs were slower relative to repetitive MTs, more for the right stroke group than their controls, but this was true regardless of sequence length. The right hemisphere group's overall MTs for repetitive and heterogeneous sequences were also not significantly slower than their controls, regardless of sequence length. Further, the time to execute a single hand posture was not significantly different between the right stroke group (Mean = 564 msec) and their controls (Mean = 567 msec).

One possible explanation for the MT findings is that because the left hemisphere group evidenced greater difficulty executing single postures, the increasing impairments with longer sequences are due to the cumulative effects of this deficit. To control for this problem, the percentage increase in MT for sequences relative to the time to execute a single posture was analyzed.

Table 2 shows that when MTs were corrected for baseline performance of single postures, the pattern of results was similar. The percentage increase in heterogeneous MTs was greater relative to repetitive MTs, particularly as sequence length increased, but more for the left hemisphere group than their controls. The supporting analysis showed an interaction of group × sequence type × sequence length [$F(3, 93) = 2.8$, $P < 0.05$]. Follow-up analyses showed that the difference between sequence types increased more as a function of sequence length for the left hemisphere group (Mean increase = 68 msec) than the controls (Mean increase = 43 msec) [$F(1, 31) = 4.5$, $P < 0.05$], despite no differences between groups in sequence type ($P > 0.05$). These findings indicate that the greater effects of sequence type on unadjusted MTs were largely due to the slowness of the left stroke patients in executing single postures. However, these patients still showed relatively greater difficulty executing heterogeneous sequences when sequences became longer, even though MT was adjusted for

Table 2. Mean (standard error) percentage increase* in movement time for repetitive and heterogeneous sequences

Sequence	Left controls			Left CVAs			Right controls			Right CVAs		
length	REP†	HET‡	D§	REP†	HET‡	D§	REP†	HET‡	D§	REP†	HET‡	D§
2	98	158	60	94	153	59	103	159	56	105	176	71
	(5)	(6)	(4)	(6)	(9)	(4)	(5)	(5)	(3)	(8)	(8)	(7)
3	191	283	92	193	287	94	198	285	86	211	320	109
	(9)	(10)	(6)	(10)	(12)	(7)	(6)	(9)	(8)	(13)	(15)	(10)
4	280	380	93	278	392	114	294	387	93	309	445	136
	(12)	(15)	(8)	(15)	(16)	(9)	(10)	(10)	(7)	(17)	(26)	(17)
5	370	475	103	358	485	127	386	494	107	402	544	142
	(15)	(17)	(10)	(18)	(22)	(10)	(12)	(14)	(6)	(22)	(28)	(13)

*The percentage increase in movement time relative to the time to execute a single hand posture was calculated using the following: $(MT_N - MT_1)/MT_1$ where N represents a particular sequence length.

†Repetitive sequences.

‡Heterogeneous sequences.

§These values represent the mean difference in the percentage increase in movement time between repetitive and heterogeneous sequences.

the time to execute a single posture. This is consistent with the previously reported error analyses where for heterogeneous sequences, the left stroke group made increasingly more errors than controls as sequence length increased.

For the right hemisphere group and their controls, group interacted with sequence type [$F(1, 36) = 7.0$, $P < 0.025$] such that there was a trend for the percentage increase in heterogeneous MTs [$F(1, 36) = 3.9$, $P = 0.054$], but not repetitive MTs [$F(1, 36) < 1$], to be greater for the right hemisphere group (see Table 2). Although it appears on the basis of mean difference values that the difference between sequence types was relatively greater as sequence length increased for these patients, there was not a significant group × sequence type × length interaction [$F(3, 108) = 2.0$, $P > 0.05$]. The absence of a reliable interaction is likely due to the relatively large variability within the right hemisphere group, especially for longer sequences (see Table 2). This variability could not be attributed to any neurologic characteristics (i.e. neglect, hemiplegia) of these patients.

CT analyses

Table 3 presents the lesion volume and distance measurements for each stroke group. This table suggests that both groups were equivalent in total lesion volume as well as in measures

Table 3. Means (standard deviation) for lesion volume and location measures

	Left CVAs	Range	Right CVAs	Range
Lesion volume*	2.4 (3.1)	0.1–12.0	3.2 (3.4)	0.1–10.3
Anterior lesion volume†	53.9 (42.2)	0–100	58.6 (41.3)	0–100
Posterior lesion volume†	46.1 (42.2)	0–100	41.4 (41.3)	0–100
Anterior distance‡	40.6 (15.7)	14–68	39.2 (19.3)	15–81
Posterior distance‡	32.9 (21.1)	0–53	35.6 (19.3)	1–60

*Lesion volume is proportional to the total brain volume.

†These measures reflect the proportion of the lesion that is located anterior or posterior to the midpoint between the frontal and occipital poles, and are proportional to the total lesion volume.

‡Distance measures are proportional to the total distance from the frontal to the occipital pole. A smaller proportion designates that the lesion is located closer to the frontal or occipital pole.

of lesion location. Mann–Whitney U tests confirmed this observation showing no difference between the left and right hemisphere groups on any of the CT parameters.

To explore whether quantified CT measures of lesion size and location were related to motor sequencing performance, each CT measure was correlated with RT, MT (unadjusted) and the percentage increase in MT (adjusted). The correlations were performed separately for the left and right hemisphere groups. We examined whether the pattern of sequence length effects found for these measures differed depending on lesion size and location. Using separate regression analyses with repeated measures, CT parameters generally did not explain absolute performance level or the pattern of sequence length effects found for left or right hemisphere stroke patients. An exception was the finding that posterior distance was related to the overall difference in MT (unadjusted) between heterogeneous and repetitive sequences for both left hemisphere patients [$F(1, 14) = 5.9$, $P < 0.05$] and right hemisphere patients [$F(1, 16) = 5.2$, $P < 0.05$], accounting for approximately 27% of the variance. Similar findings were obtained for the percentage increase in MT [$F(1, 14) = 9.9$, $P < 0.01$ for the left hemisphere group; $F(1, 16) = 7.2$, $P < 0.025$ for the right hemisphere group], accounting for 41 and 31% of the variance in the left and right hemisphere groups, respectively. These effects showed that more posterior located lesions were associated with greater increases between repetitive and heterogeneous sequences in both unadjusted and adjusted MTs. Lesion size could not explain these findings as it was not correlated with posterior distance for either patient group or with the MT measures.

DISCUSSION

Preprogramming sequences

Prior to movement there was no evidence that patients with left or right hemisphere damage preprogrammed repetitive or heterogeneous sequences differently than the controls. Their rate of preprogramming was also not slower as RT increased with sequence length similarly for all groups. Further, RTs were not slower for either stroke group, although there was a trend for the left hemisphere group to have longer RTs for both sequence types, suggesting some patients likely exhibited such problems.

Single vs repetitive movements

Clues as to the specific nature of programming deficits during movement with left hemisphere damage were suggested by the effects of sequence type and length on the different measures. The IRT and MT data showed that the left hemisphere stroke patients were slower to execute single as well as sequences of hand postures. Deficits executing single postures are consistent with some [2, 3, 19] but not all studies [20]. However, most previous studies have used different movements for the isolated movements rather than the sequences of movements, with some of the isolated movements containing several movement components. Our findings imply that part of the left hemisphere group's deficits may be due to problems accessing the motor engram for a single posture [12], or deficits programming individual movements. This conclusion is consistent with the finding that when MT was adjusted for the speed of executing single postures, the difference between repetitive and heterogeneous sequences was similar for the left hemisphere group and their controls. This finding contrasts with others [20, 21] and indicates that changes in posture transitions do not disrupt performance any more so than repeating a posture in a different spatial location.

However, other results suggested it was also the sequencing requirements of even relatively simple actions which produced deficits with left hemisphere damage. Although the RT data implied the left hemisphere group planned repetitive sequences as a single unit, the IRT data suggested they could not utilize these plans as efficiently as normals to execute successive movements. The IRT data, which showed greater effects of sequence length on individual IRTs for the left hemisphere group than their controls, indicated these patients continued to engage in programming during movement that was otherwise completed by the control group. This cannot be attributed to the motor slowness of these patients as there is no reason why the execution of a single posture should be affected mechanically by the number of other responses contained within a sequence. These findings contrast with other studies which showed greater errors in the left hemisphere group when executing heterogeneous sequences, but no impairment in the speed of executing repetitive movements [17, 20]. Our results, which also showed greater errors only for longer heterogeneous sequences, demonstrate that IRTs are more sensitive than errors for identifying deficits in performing relatively simple movements when factors that should affect higher level control processes, such as sequence length, are manipulated.

Another important factor for uncovering deficits with repetitive movements may be whether sequences have spatial requirements. Previous studies of repetitive finger tapping in one location showed no ipsilateral deficits in right or left hemisphere patients [6], but others [9, 30, 31] have shown left hemisphere deficits in repetitive movements of the arm ipsilateral to the lesion when subjects must alternate movements between two locations.

Deficits performing repetitive, alternating arm movements are also particularly evident after left but not right hemisphere damage when the movement is largely preprogrammed [9]. This finding generalizes to simple aiming movements where left but not right hemisphere stroke patients show greater deficits in the initial, preprogrammed component of the movement [7]. Thus, left hemisphere damage results in problems utilizing motor programs to control a variety of simple movements which are largely preprogrammed in normal subjects.

Sequence length effects: underlying cognitive processes

The analyses of sequence length effects on IRTs were suggestive of programming deficits in patients with left hemisphere damage. There was not a consistent pattern of such effects for the right hemisphere stroke group in comparison to their controls. The IRT analyses are important because they are sensitive to whether subjects continue to engage in programming processes during the execution of an individual posture that concerns the sequence, not just a single posture within the sequence. The sequence length effects on IRTs cannot be attributed to the increasing slowness of MTs for longer sequences because the execution time of any particular posture was actually faster if it was contained within a longer sequence.

The consistent effects of sequence length on IRTs of repetitive postures (i.e. faster IRTs with increasing length) for the left hemisphere group are similar to findings reported for choice RT with normal controls [26]. In this study, the latency of the first key press was faster as the number of responses in a sequence prior to an uncertain response increased, suggesting a model where movement begins before the sequence is entirely programmed. Extending this idea to control processes during movement, left hemisphere damage may disrupt patients' ability to efficiently schedule motor programs. Specifically, these patients may have problems identifying or scheduling subprograms for individual postures before movement begins, such that hand postures contained in longer sequences were more quickly executed because there was more time to identify or schedule the subprograms for the remaining movements. Execution of shorter sequences was delayed to coordinate identification of the subprograms with scheduling the execution of individual postures. For IRT_4 of the heterogeneous sequences, similar problems were observed as this response required repetition of a previously executed hand posture.

For heterogeneous sequences, left controls appeared to have programmed the sequence completely prior to movement as sequence length had no effect on IRTs. In contrast, the duration of IRT_1 tended to increase as a function of sequence length for the left hemisphere group, indicating these patients continued to engage in programming processes otherwise completed by controls prior to movement. These findings may also reflect problems scheduling motor programs during sequencing while simultaneously controlling the execution of individual movements.

Sequence type effects: underlying cognitive processes

The entire sequence was the unit of analysis for testing the effect of sequence type and its interaction with sequence length on MT and errors. The relative difficulty of executing heterogeneous vs repetitive sequences was compared, such that programming deficits related to performing sequences that were structurally more complex could be examined. The left hemisphere group's higher error rates during movement for heterogeneous but not repetitive sequences was consistent with reports of greater perseverative errors in these patients [17, 27]. However, error rates of the left hemisphere group also increased with sequence length for heterogeneous sequences, such that they were significantly higher only for those sequences containing four or five postures which contained the same number of hand posture changes as sequences of three postures (see Table 1). This is an important finding and bolsters the observation that when MTs were adjusted to control for the performance of single postures, MT differences between sequence types increased more with sequence length for the left hemisphere group relative to their controls, suggesting the deficits were due to the dual requirements of postural change and sequence length. Taken together, the error data and the adjusted MT data demonstrate that the performance of heterogeneous sequences was impaired in left hemisphere stroke patients but only for longer sequences. Because longer sequences did not contain more changes in different postures than shorter sequences but rather required additional repetitions of a previously performed hand posture, these effects cannot be due solely to response transitions. They may be more reflective of deficits in some aspect of temporal organization such as sequential ordering, which emerges when the structure of a sequence is more complex. Although sequential ordering has been dismissed by some [15, 16] as an explanation for deficits in movement copying, manipulations of ordering difficulty were not robust [15] and sequential ordering was not directly tested by comparing the amount of disruption in performance when transferring from repeated to random sequences [16]. Deficits in various aspects of temporal organization, such as sequential ordering and judgements of recency and frequency, have been reported in patients with frontal lobe damage on non-motor tasks where the number of items to be ordered is considerably larger, and when items are internally [23, 25] or externally ordered [28]. While frontal lesion extent and volume were not related to the sequence length effects in our study, more robust manipulations of ordering difficulty, such as longer, more structurally complex sequences, may show greater sensitivity to intra-hemispheric relationships. There is some suggestion that the number of items to be ordered affects sequential ordering difficulty [25], but this has not been examined in the motor modality, or for both self-ordered and externally ordered conditions within the same experiment.

There was some indication that right hemisphere stroke patients began to evidence programming deficits during movement, but only for heterogeneous sequences. While unadjusted MTs of the right hemisphere group were not significantly slower than their control group for heterogeneous or repetitive sequences, the sequence type $\times$ group interaction showed that the difference in MTs (adjusted and unadjusted) between the two sequence types was greater for right hemisphere stroke patients than their controls. This finding did not significantly vary with sequence length, but there was a trend in the MT mean values to show larger differences between sequence types as length increased relative to their controls. However, the reliability of these trends is questionable given that the variance in mean MTs for the right stroke group increased with sequence length. Further, possible trends for the right hemisphere stroke group to show increasing problems with longer, more complex sequences were not consistent with the error data which did not increase with sequence length for heterogeneous sequences. Thus, the sequence type effect on MTs was the most reliable deficit found in the right hemisphere stroke group. What do these findings suggest? Because the right hemisphere group did not show longer MTs for single postures, longer IRTs for individual movements, or consistent effects of sequence length on IRTs, the effect of sequence type on MT does not appear to be related to problems programming and/or executing single movements or scheduling subprograms for movements during sequencing. The fact that error rates for heterogeneous sequences were also not greater for the right stroke group seems to suggest the sequence type effects were not due to problems performing response transitions. One alternative is that impaired visuospatial skills in right hemisphere stroke patients may affect programming processes, important for mapping responses to the external environment [24] when sequences are spatially more complex. Spatial requirements may have been greater for the right hemisphere and right control groups than the left hemisphere and left control groups as these subjects moved from right to left when executing movements, which is clearly less familiar due to the left–right directional requirements of reading and writing. However, similar findings might also be obtained had these patients moved from left to right as the task itself involves a significant perceptual-motor component. This finding deserves further study.

Motor sequencing and lesion location

For both stroke groups, more posteriorly located lesions were associated with a greater slowing in heterogeneous relative to repetitive MTs, regardless of whether MTs were adjusted for the performance of single postures. This is consistent with greater arm sequencing deficits in left parietal than left frontal patients [19], although the left parietal patients in this study also performed more poorly on single movements. In our study the left hemisphere group performed single movements more slowly, but this was not related to intra-hemispheric lesion location. In a study of lobectomy patients [21], left parietal patients showed the greatest amount of impairment on copying sequential arm movements, but right and left frontal patients were also impaired; whereas no performance abnormalities were found for right parietal patients. This study, however, examined the percentage of correct responses which was not compromised in our right hemisphere stroke patients. All of these studies emphasize the greater importance of the left posterior cortex in regulating movement sequences, which is consistent with findings that left parietal but not anterior apraxics have difficulty recognizing gestures [12]. However, the underlying mechanisms are not known and the specific role of the right parietal cortex has not been carefully examined. One possibility is that greater sequencing deficits with more posterior damage are due to spatial encoding problems which is consistent with monkey data [24], but in humans exactly how the left and right parietal lobes contribute to spatial encoding is not clear.

Summary remarks

The experimental approach adopted in the present study offers a method for isolating motor sequencing deficits. The use of both errors and measures of time together with the manipulation of factors that hypothetically affect certain levels of motor programming revealed that left hemisphere patients had problems scheduling motor programs that were not simply due to their impairments executing a single posture. Their deficits were present even though memory requirements were minimal, and the character of the problem varied as a function of the structural complexity of sequences, which introduced the possibility that sequential ordering problems may be compromised with left hemisphere damage. The right hemisphere group evidenced more subtle deficits associated with executing heterogeneous sequences, possibly due to the external spatial requirements of the task.

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