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MOTOR SEQUENCING WITH LEFT HEMISPHERE DAMAGE

ARE SOME COGNITIVE DEFICITS SPECIFIC TO LIMB APRAXIA?

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SUMMARY

Sixteen left-hemisphere stroke patients, who were apraxic or nonapraxic, and 17 control subjects performed sequences of hand postures that varied in the number of different postures (repetitive and heterogeneous) and sequence length (one to five). Performance of the left hand (ipsilateral to stroke) was compared with a control group using the left hand.

All stroke patients had slower reaction times and were slower to execute single hand postures, but the apraxic group was not slower than the nonapraxic group. Both the apraxic and the nonapraxic groups had similar problems scheduling or timing motor programs for both sequence types such that inter-response times were more affected by sequence length than the control group. However, only the apraxic group showed abnormalities in preprogramming heterogeneous sequences. The apraxic group also made more errors and had longer movement times (MTs) than for the other groups, but only for heterogeneous sequences containing more than three hand postures. The nonapraxic group did not show slower MTs or greater errors, regardless of the type or the length of sequences. These results suggested deficits in encoding, generating single movements and in scheduling or timing a series of actions which generally attributable to left hemisphere damage. However, abnormalities in temporal organization processes prior to and during movement were specific to apraxia. The dissociation between the two stroke groups on some but not all aspects of sequencing has implications for different cognitive mechanisms supporting motor sequencing.

INTRODUCTION

Left hemisphere damage is frequently accompanied by ideomotor limb apraxia, a disorder of skilled movement that cannot be attributed to weakness, sensory loss, language comprehension deficits or general intellectual deterioration. Clinical assessment of limb apraxia is based on an examination of gesture performance to command and/or imitation (e.g. brush teeth, salute, put finger on ear). Although apraxia and aphasia frequently coexist, apraxia is considered a cognitive-motor disorder because the degree of gestural disruption can be dissociated from aphasia severity or type (Goodglass and Kaplan, 1972; Lehmkuhl *et al.*, 1983; Rothi and Heilman, 1984), and severe apraxia has been reported in patients without language disturbances (Heilman *et al.*, 1973). Gestural disturbances in apraxia have been attributed to a variety of problems including difficulties integrating memory representations of intra- and extrapersonal space (Haaland and Flaherty, 1984), a loss or disruption in spatiotemporal memory codes (Heilman *et al.*, 1982; Rothi *et al.*, 1988; Poizner *et al.*, 1990) and encoding deficits (Faglioni *et al.*, 1990).

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The cognitive mechanisms of this disorder have been disputed, in part, because most investigations of gesture performance are based on clinical descriptions which rely heavily upon the performance of familiar movements and error analyses. Other characteristics of movement which may be disrupted are ignored. In particular, clinical descriptions of ideomotor apraxia do not specifically point to a sequencing deficit, yet many individual gestures require sequencing of several component movements.

Abnormalities in sequencing with left hemisphere damage have been examined most thoroughly in studies of largely unfamiliar movements, which when combined into sequences do not represent meaningful gestures. While many studies have reported greater sequencing deficits with left than right hemisphere damage (Kimura and Archibald, 1974; Kimura, 1982), others have shown that left hemisphere damage produces deficits in the performance of isolated movements (Kolb and Milner, 1981; Kimura, 1982; De Renzi *et al.*, 1983; Harrington and Haaland, 1991*a*). This latter finding suggests the possibility that sequencing deficits may be due to the cumulative effects of deficits in programming single movements, but when this problem was controlled, impaired sequencing was still evident (Harrington and Haaland, 1991*a*). Others have suggested that memory factors can explain left hemisphere specialization for sequencing (Roy, 1981; Jason, 1986; Roy and Square-Storer, 1990) whereas sequencing deficits with left but not right hemisphere damage even when memory was not required have also been reported (Harrington and Haaland, 1991*a*).

Few studies have directly examined whether cognitive deficits in limb sequencing with left hemisphere damage are specific to the disorder of apraxia or more general to the role of the left hemisphere in controlling a wide variety of movements (*see* Haaland and Harrington, 1990). The present study compared apraxic and nonapraxic patients with left hemisphere damage. Performance was examined on sequences of hand postures that varied in length and the number of different hand postures. Although most studies have been restricted to analyses of errors, the present study also examined reaction times (RTs) for correct movements to determine whether the cognitive operations utilized to carry out the action were completely normal.

Previously we reported that generating a motor plan prior to movement was intact with left hemisphere damage as sequence length had a similar effect on RTs of both patients and normal control subjects, regardless of sequence complexity (i.e. sequences containing repetitive vs different responses) (Harrington and Haaland, 1991*a*). However, if apraxia produces a deficit in identifying or recognizing the to-be-performed actions (Heilman *et al.*, 1982) or in the rate of retrieving subprograms for each response to assemble a motor plan (Harrington and Haaland, 1987), RTs should increase more with sequence length in the apraxic than the nonapraxic patients.

Programming difficulties during movement were examined by comparing apraxic and nonapraxic patients on inter-response times (IRTs) and movement times (MTs). The IRT analyses examined the effect of sequence length on the execution of a single posture within a sequence to determine whether programming during movement was influenced by the number of other responses within a sequence, not simply the individual hand posture. Inter-response times of patients with left hemisphere damage were more affected than those of control subjects by the number of other responses in a sequence, suggesting they engaged in more programming concerning the sequence while executing a single posture (Harrington and Haaland, 1991*a*). If this deficit is specific to apraxia, only the

IRTs of apraxic patients should vary with sequence length. At a different level of enquiry, the MT analyses summed across all IRTs within a sequence, and compared the difficulty of sequencing repetitions of a posture vs different postures (i.e. heterogeneous sequences) to examine programming processes related to sequencing movements with a more complex structure. Previously we found error rates and MTs for heterogeneous but not repetitive sequences increased as sequence length increased more in the left hemisphere-damaged patients, implicating deficits in some aspect of temporal organization. If these deficits are specific to the disorder of apraxia, only the apraxic patients will show this pattern of errors and MTs.

METHODS

Subjects

Seventeen normal controls and 16 left hemisphere-damaged stroke patients were tested at the Albuquerque Veterans Affairs and Lovelace Medical Centers. All subjects were right-handed males and performed the task with their left hand. The arm ipsilateral to the lesion was examined in the stroke group to avoid biasing the sample by excluding hemiplegic patients and to minimize factors that were purely motoric or sensory in nature.

All subjects were administered a 15-item apraxia battery (Haaland and Flaherty, 1984) consisting of five transitive (representational gestures with pretended object use), five intransitive (representational gestures without pretended object use) and five nonrepresentational gestures. Subjects were videotaped as they imitated unilateral limb movements and their performance was scored from the videotape. Errors were scored relative to the examiner's performance and consisted of six categories, described in detail by Haaland and Flaherty (1984): (i) perseveration; (ii) orientation; (iii) position of hand; (iv) body-part-as-object; (v) target; (vi) undue hesitations. Subjects who made any of these errors on five or more items were classified as apraxic. Table 1 shows seven of the patients who were classified as apraxic and nine of the patients who were nonapraxic. All of the control subjects scored within the normal range. There were no significant differences among the three groups in age or education level. Mann-Whitney U tests (Siegel, 1956) showed no significant differences between the apraxic and the nonapraxic groups in the mean number of months post-stroke (apraxic: mean = 40, SD = 42; nonapraxic: mean = 30, SD = 55). Two of the apraxic but none of the nonapraxic 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 the neuropsychological tests summarized in Table 1 to describe their visuospatial and language skills. Comparisons between groups used the Mann-Whitney U statistic. On the Block Design subtest of the Wechsler Adult Intelligence Scale-Revised Form (WAIS-R) (Wechsler, 1981), visuospatial organization skills in the apraxic group were significantly ($P < 0.025$) poorer than the nonapraxic group, the members of which were not impaired relative to those of the control group. Two of the apraxic patients and one nonapraxic patient scored below the lowest score of the control group on this test. Both the apraxic and the nonapraxic groups were similarly impaired relative to the control group ($P < 0.025$) on verbal fluency from the Cookie Theft picture of the Boston Diagnostic Examination of Aphasia (BDEA) (Goodglass and Kaplan, 1972). Comparisons between the two stroke groups on auditory comprehension from Part V of the Token Test (De Renzi and Vignolo, 1962) showed performance was significantly ($P < 0.05$) worse for the apraxic than the nonapraxic group which was not impaired relative to the control group. Two of the apraxic patients had moderate (9 errors) and two had severe (21 errors) auditory comprehension deficits, whereas the remaining patients scored within normal limits. The latter two apraxic patients also were severely dysfluent. In contrast, only one nonapraxic patient had severe auditory comprehension deficits (18 errors), but was only mildly dysfluent (5.8). The remaining patients had normal auditory comprehension.

Apparatus

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

TABLE 1. DEMOGRAPHIC AND NEUROPSYCHOLOGICAL PROFILE OF SUBJECTS

	Apraxic group (n = 7)			*Nonapraxic group (n = 9)*			*Control group (n = 17)*		
	Mean	*(SD)*	*Range*	*Mean*	*(SD)*	*Range*	*Mean*	*(SD)*	*Range*
Age	63	7.5	55–76	63	6.9	51–76	63	6.5	56–75
Education	12	3.4	8–16	12	1.9	8–15	13	0.8	12–14
Apraxia severity[1]	7.4	2.4	4–10	13.3	1.4	11–15	13.6	1.3	11–15
Visuospatial organization[2]	6.0	1.4	4–8	9.1	2.5	5–14	10.7	2.8	6–14
Auditory comprehension[3]	10.4	7.8	0–21	4.1	5.5	0–18	1.8	2.0	0–7
Verbal fluency[4]	5.1	2.3	1.0–6.5	6.3	0.5	5.3–6.8	6.8	0.2	6.3–7.0

[1]Number of items correct out of 15 (Haaland and Flaherty, 1984).
[2]Scale scores from the Block Design subtest of the WAIS-R (Wechsler, 1981).
[3]Number of errors on Part V of the Token Test (De Renzi and Vignolo, 1962).
[4]Fluency rating based on the description of the Cookie Theft picture from the BDEA (Goodglass and Kaplan, 1972). Scores range from 0 to 7.

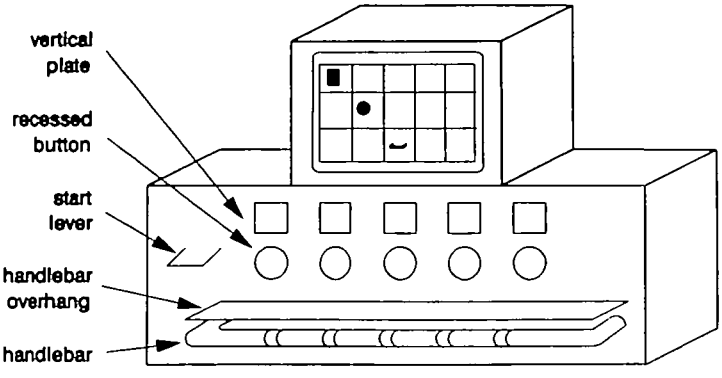

FIG. 1. Diagram of the hand-posture sequencing apparatus. The monitor situated above the apparatus depicts an example of a sequence.

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. The start plate was located to the left of the manipulanda, and subjects always moved from the left to the right. When a change in hand posture was made, subjects moved to the right diagonally (up or down) to the next manipulandum. A monitor presented pictorial displays of the entire motor sequence (*see* Fig. 1).

Procedure

Subjects began 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 s to 2 s, a tone signalled subjects to begin the sequence. Upon completion of the last response in the sequence, the visual display terminated. Reaction time was measured from the onset of the tone 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. Movement time 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 ms 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).

Design

Two types of sequences, repetitive and heterogeneous, were presented. Repetitive sequences varied in length from one to five responses with each length consisting of repetitions of plate (P), button (B), or

handlebar (H) responses (i.e. P, PP, PPP, PPPP, PPPPP, B, BB, BBB, BBBB, BBBBB, H, HH, HHH, HHHH, HHHHH). Heterogeneous sequences varied in length from two to five responses and were constructed so that the first two responses were the same for all sequence lengths with the remaining response(s) consisting of the addition of the first response (i.e. PB, PBP, PBPP, PBPPP, HB, HBH, HBHH, HBHHH). Sequence type was blocked and 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.

Computerized tomography scan quantification

Computerized tomography scans were available on all stroke patients. Computerized procedures were used to quantify lesion size and location (anterior vs posterior) (Harrington and Haaland, 1991*a*). Lesion size was expressed as a ratio of lesion volume to brain volume. Lesion location was expressed as both volumetric and linear measures. The volumetric measures were the proportion of the total lesion volume that was located anterior and posterior to a line halfway between the frontal and occipital poles. The linear measures were the distance of the lesion from frontal and occipital poles divided by 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

The analyses focused on the comparisons of the apraxic group with the nonapraxic and control groups. All RT and IRT analyses were based on a mixed model design with group (i.e. control, apraxic and nonapraxic) as the between-subject factor and sequence length as the repeated factor. Planned comparisons contrasted the performance of the apraxic, the nonapraxic and the control groups. Separate analyses of variance (ANOVAs) were conducted for each measure. Repetitive and heterogeneous sequences were analysed separately.

Movement times and errors during movement were analysed using a mixed model design with group as the between-subject factor and sequence length (two to five hand postures) and sequence type (i.e. repetitive vs heterogeneous) as the repeated factors. Because errors before movement were low and averaged 5% for all three groups, regardless of the length or the type of sequence, these data will not be discussed further. The sample of apraxic and nonapraxic patients was small. Thus, statistical tests exceeding the 0.05 experiment-wise α level were reported when there were clear trends for group differences (i.e. $P = 0.10$).

Cognitive processing prior to movement: reaction times

Repetitive sequences. To examine the apraxic and the nonapraxic patients' ability to preprogram repetitive sequences, the effect of sequence length on RT was analysed. In earlier studies (Harrington and Haaland, 1987, 1991*a*,*b*) it was shown that sequence length has little or no effect on RTs for repetitive movements, perhaps, because subjects impose an organization on the sequence such that they plan it as a single unit, regardless of the number of responses. Figure 2A shows the apraxic and the nonapraxic groups preprogrammed repetitive sequences similar to the control group, regardless of length ($F < 1.0$). For all subjects, sequence length had no effect on RTs. There was a trend for the mean RT of the entire left stroke group to be longer than the control group ($P < 0.06$), but there was no difference between the apraxic and the nonapraxic patients.

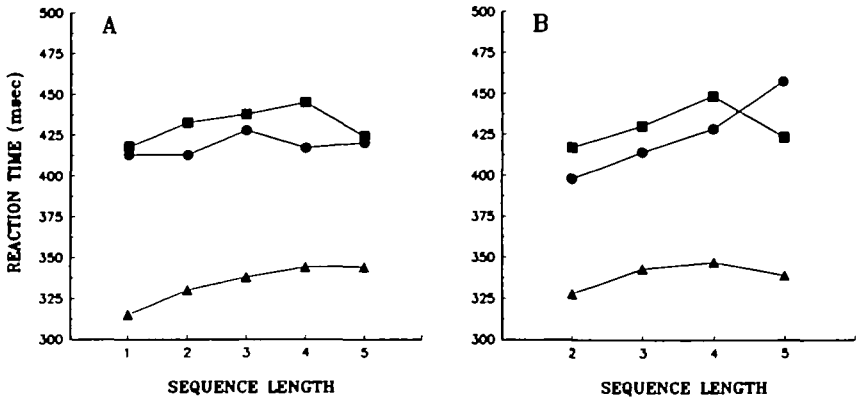

FIG. 2. Mean reaction times for repetitive (A) and heterogeneous (B) sequences. For repetitive sequences, standard errors of the mean averaged 55, 59 and 22 in the apraxic (●), nonapraxic (■) and control (▲) groups, respectively. For heterogeneous sequences, standard errors of the mean averaged 72, 51 and 20 in the apraxic, nonapraxic and control groups, respectively.

Heterogeneous sequences. Reaction times typically increase with sequence length when sequences consist of different movements because subjects construct a motor plan consisting of subprograms, one for each response in the sequence. However, because subjects may chunk or group a series of responses or complete some of the programming prior to the RT interval, nonlinear effects of sequence length on RT are often reported (Harrington and Haaland, 1987, 1991*a*,*b*). Figure 2B suggests that, for sequences containing different hand postures, RT increased more with increasing sequence length for the apraxic than the nonapraxic and the control groups. The supporting statistical analyses showed a group×length interaction [$F(6,90) = 2.26$, $P < 0.05$]. Follow-up analyses comparing the apraxic and the control groups revealed a significant group×length effect [$F(3,66) = 3.37$, $P < 0.025$], whereas no such interaction was found when comparing the nonapraxic and control groups. Trend analyses showed that sequence length had a linear effect on RTs in the apraxic group [$F(1,6) = 6.38$, $P < 0.05$]. By comparison, for both the nonapraxic and control subjects sequence length had a nonlinear affect on RTs [$F(1,25) = 3.85$, $P < 0.06$] such that RTs increase with length up to $n = 4$ and asymptote thereafter. Averaging across sequence length, mean RT of the entire left stroke group was longer than the control group ($P = 0.052$) but there was no difference between the apraxic and the nonapraxic patients.

Cognitive processing during movement

Repetitive sequences: inter-response times. To determine whether the execution of a single movement was more affected in the apraxic patients by the number of other responses within a sequence, not simply an individual hand posture, the effect of sequence length on each IRT was analysed. The difference between the shortest and longest sequence length was analysed for each IRT. Figure 3 displays the means for each IRT as a function of sequence length. There was a trend for the first IRT (IRT_1) to be slower for the entire left stroke group than for the control group ($P = 0.052$) and all IRTs for subsequent responses were significantly slower ($P < 0.025$). However, as

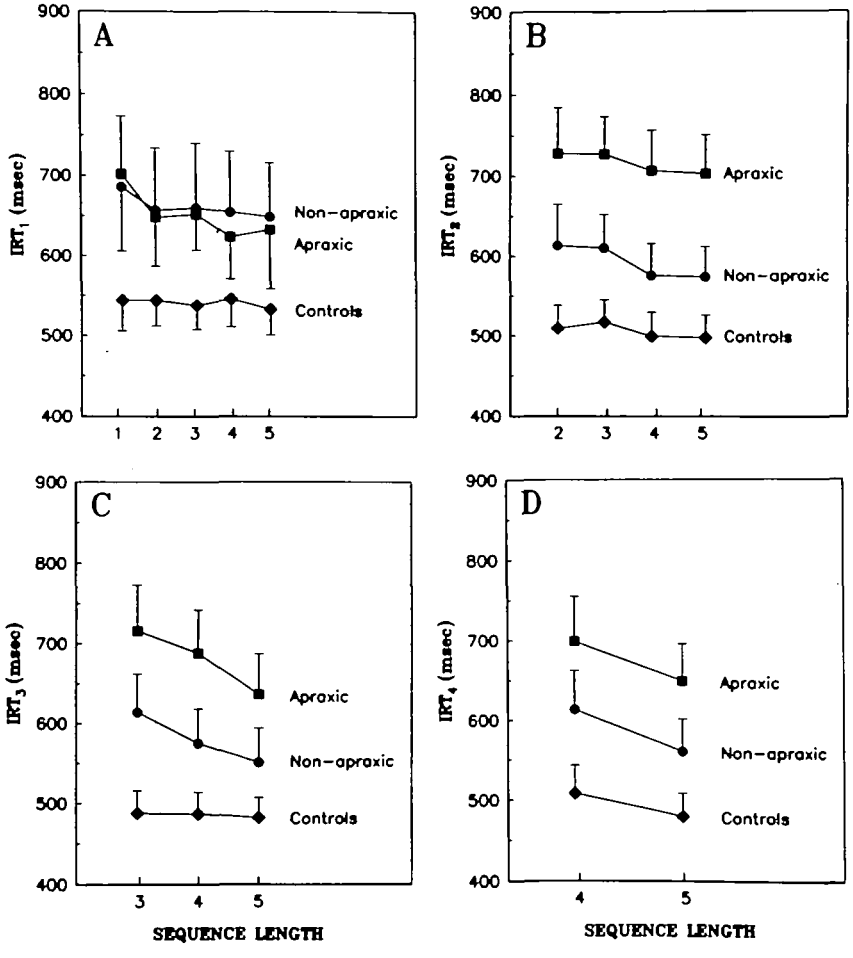

FIG. 3. Inter-response times (IRTs) for repetitive sequences as a function of sequence length. A, B, C, D represent the mean IRTs (plus standard error bars) for IRT_1, IRT_2, IRT_3 and IRT_4, respectively.

can be seen in Fig. 3, the apraxic patients were not significantly slower than the nonapraxic patients. Figure 3A,C,D shows that IRTs changed with sequence length more for the two left stroke groups than for the control group. The supporting statistical analyses showed a group×length interaction for IRT_1 [$F(2,30) = 11.92$, $P < 0.01$] and IRT_3 [$F(2,30) = 11.13$, $P < 0.001$], and there was a trend for an interaction for IRT_4 [$F(2,30) = 2.01$, $P = 0.15$]. The pattern of sequence-length effects on IRTs was similar, however, for the apraxic and the nonapraxic patients. This observation was confirmed by the nonsignificant interactions of group (i.e. apraxic vs nonapraxic)×sequence length for each IRT ($F < 1.0$ for all IRTs). Thus, the execution of a single movement within a sequence was generally more affected by the number of other responses in a sequence for the apraxic and the nonapraxic patients than for the control subjects, suggesting both stroke groups engaged in more programming during movement.

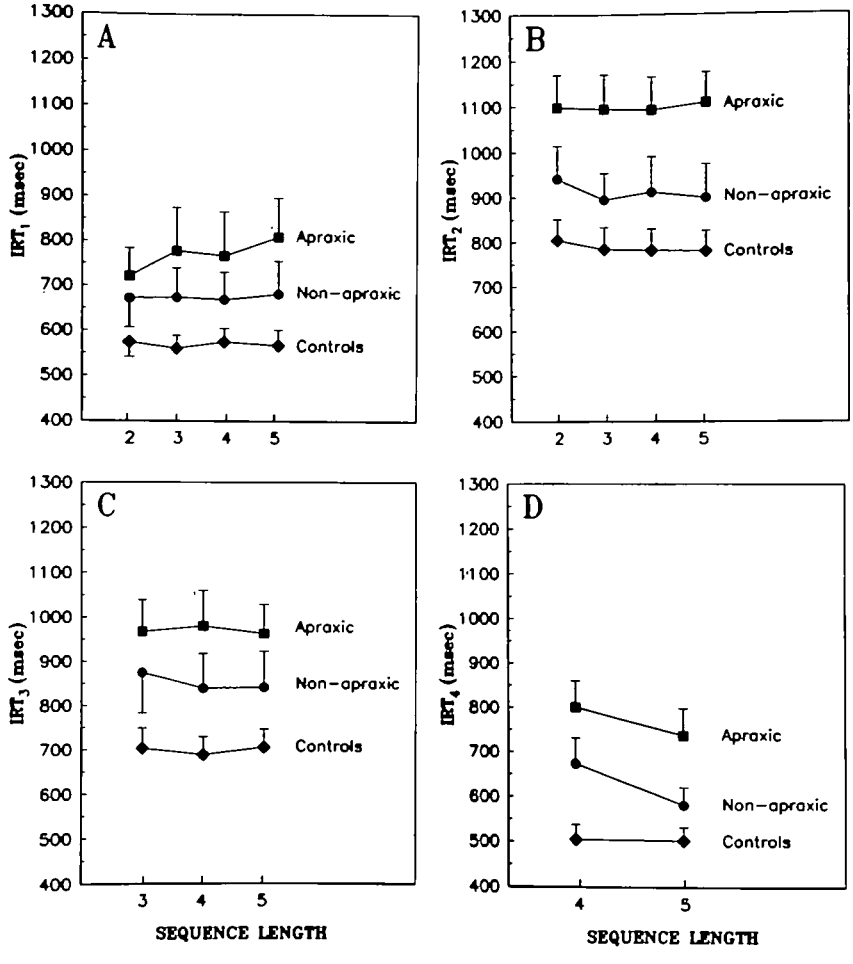

FIG. 4. Inter-response times (IRTs) for heterogeneous sequences as a function of sequence length. A, B, C, D represent the mean IRTs (plus standard error bars) for IRT_1, IRT_2, IRT_3 and IRT_4, respectively.

Heterogeneous sequences: inter-response times. For all IRTs, both left stroke groups were significantly slower than the control subjects regardless of sequence length ($P < 0.025$), but Fig. 4 shows the apraxic patients were not slower than the nonapraxic patients. Figure 4 also suggests that sometimes the pattern of IRTs varied with sequence length in a different way for the stroke patients than for controls. Sequence length had no reliable effect on IRT_2 or IRT_3 for any of the groups (Fig. 4B,C). However, there were significant interactions of group×sequence length for IRT_1 [$F(2,30) = 5.38$, $P < 0.01$] and IRT_4 [$F(2,30) = 9.08$, $P < 0.01$]. In Fig. 4A it appears that IRT_1 increased with sequence length but only for the apraxic group. Follow-up analyses comparing the apraxic and the control groups revealed a group×length interaction [$F(1,22) = 11.27$, $P < 0.01$], indicating that the duration of IRT_1 increased linearly as sequence length increased for the apraxic [$F(1,6) = 5.86$, $P = 0.052$] but not the control group

($F < 1$). No such differences were found when comparing the nonapraxic and the control groups. For IRT_4 (Fig. 4D) the pattern of sequence length effects on IRTs was comparable in the apraxic and the nonapraxic groups. The different pattern of sequence length effects found for IRT_1 and IRT_4 most likely reflects the type of programming ongoing during sequencing. The IRT_1 increased with sequence length only in the apraxic group because programming that began during the RT interval was ongoing. This explanation is consistent with the finding of a greater increase in RT as a function of sequence length for the apraxic group. As for IRT_4, the fourth response was a repetition of a previous hand posture which explains why this pattern of findings was similar to those reported for repetitive sequences.

Movement time. The MT analyses, which focused on the execution time for the entire sequence, examined the relative difficulty of sequencing repetitive vs different hand postures as a function of sequence length. The time to execute a single hand posture was not significantly different between the apraxic (mean = 702, SEM = 71) and the nonapraxic patients (mean = 686, SEM = 80), but MT for a single hand posture was significantly longer for the entire left stroke group relative to the control group (mean = 544, SEM = 38) [$F(1,31) = 5.4$, $P < 0.05$]. Similarly, although MTs for sequences of hand postures were not significantly slower in the apraxic (repetitive: mean = 2377, SEM = 168; heterogeneous: mean = 3167, SEM = 214) than the nonapraxic patients (repetitive: mean = 2119, SEM = 178; heterogeneous: mean = 2694, SEM = 221), the entire left stroke group executed sequences more slowly than the control group (repetitive: mean = 1783, SEM = 97; heterogeneous: mean = 2257, SEM = 127) ($P < 0.01$).

To control for the possibility that MT differences among groups on sequences could

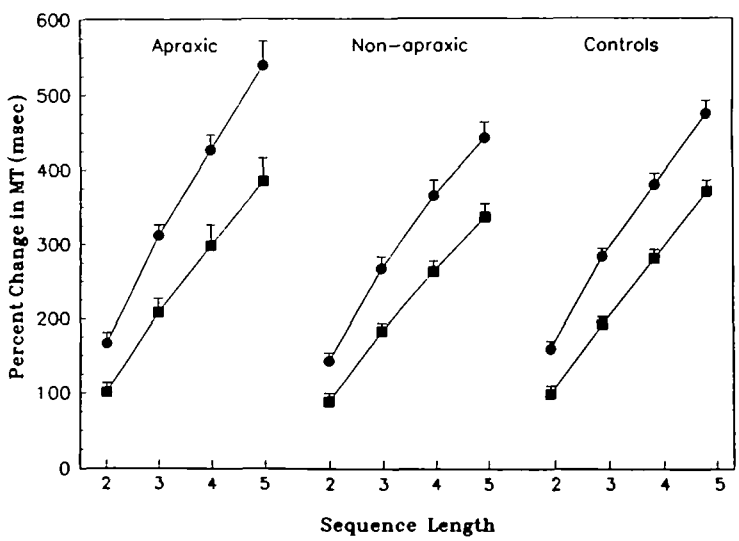

FIG. 5. The mean percentage change (plus standard error bars) in movement time (MT) for repetitive (■) and heterogeneous (●) sequences. Percentage values were calculated using the following formula: $(MT_n - MT_1)/MT_1$ where n represents a particular sequence length and MT_1 is the time to execute a single hand posture.

be due to the cumulative effects of slower execution times for a single posture, the percentage increase in MT for sequences relative to the time to execute a single posture was analysed. When MTs were corrected for baseline performance of single postures there was an interaction of group×sequence type×sequence length [$F(6,90) = 2.62$, $P < 0.025$]. Figure 5 suggests that this interaction was due largely to performance differences in the apraxic group, especially on heterogeneous sequences. The supporting statistical analyses showed that sequence type and sequence length had similar effects on adjusted MTs for the nonapraxic and the control groups. In contrast, for repetitive sequences the apraxic group did not differ from the nonapraxic or the control groups in the percentage change in MT as a function of sequence length. However, for heterogeneous sequences comparisons among the three groups revealed a group×length interaction [$F(6,90) = 3.42$, $P < 0.01$], indicating that MTs increased much more rapidly with sequence length for the apraxic group relative to both the nonapraxic group [$F(1,14) = 9.53$, $P < 0.01$] and the control group [$F(1,22) = 5.78$, $P < 0.05$]. In addition, the apraxic patients showed a greater difference in MT between the two sequence types relative to the nonapraxic patients [$F(1,14) = 5.84$, $P < 0.05$] and the normal control subjects [$F(1,22) = 5.82$, $P < 0.05$]. This effect, however, was specific to longer sequences such that the apraxic group showed greater differences between the two sequence types only when sequences contained four or five postures [apraxic vs nonapraxic group: n = 4 $F(1,14) = 2.62$, $P = 0.12$ and n = 5 $F(1,14) = 9.58$, $P < 0.01$; apraxic vs control group: n = 4 $F(1,22) = 4.48$, $P < 0.05$ and n = 5 $F(1,22) = 8.02$, $P < 0.01$]. These findings demonstrated that only the apraxic group had difficulty executing longer sequences of heterogeneous postures which did not involve additional changes between different hand postures, only a repetition of a preceding posture.

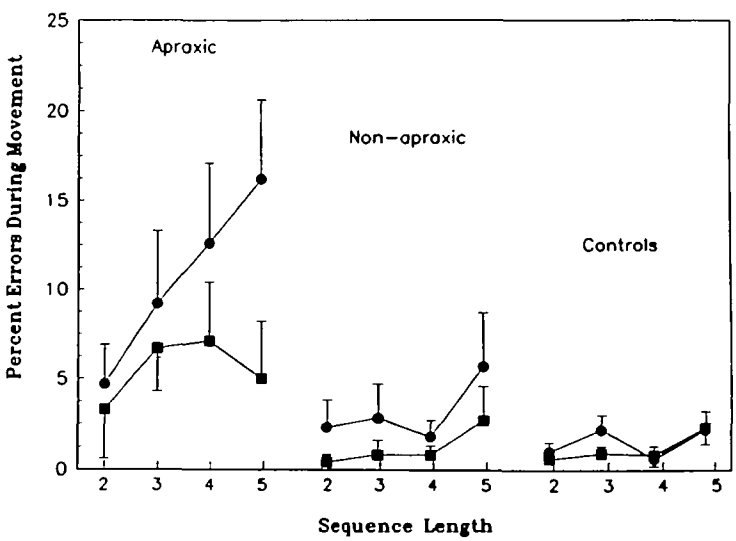

FIG. 6. The mean percentage errors (plus standard error bars) during movement for repetitive (■) and heterogeneous (●) sequences.

Errors during movement. The analyses of the percentage errors during movement compared group differences in error rates and, most importantly, showed whether the group differences varied depending on sequence type or length. Error rates for a single hand posture were not significantly different among the groups (apraxic: mean = 3.5, SEM = 2.3; nonapraxic: mean = 2.4, SEM = 0.8; control: mean = 0.9, SEM = 0.4), although there was a tendency for all of the left stroke patients to make more errors on a single posture than controls ($P < 0.10$). Figure 6 shows that the percentage errors generally increased for all subjects as sequences became longer but primarily for heterogeneous sequences, and especially for the apraxic patients. The supporting statistical analyses showed an interaction of group×sequence type×sequence length [$F(6,90) = 3.65$, $P < 0.01$]. Planned comparisons showed that for repetitive sequences the pattern of errors did not vary among the three groups as a function of sequence length, although Fig. 6 shows there was a trend for errors to increase with length more in the apraxic than the control group [$F(3,66) = 2.63$, $P = 0.057$]. No such trends were found in the nonapraxic group ($F < 1$). For heterogeneous sequences, comparisons among the three groups showed a group×length interaction [$F(6,90) = 4.34$, $P < 0.001$] such that there were no differences between the nonapraxic and the control groups in error rates, regardless of sequence length ($F < 1$). However, errors increased more with increasing sequence length for the apraxic group relative to both the nonapraxic group [$F(3,42) = 2.81$, $P = 0.05$] and the control group [$F(3,66) = 10.05$, $P < 0.001$]. In addition, the apraxic group showed a greater increase in errors for heterogeneous sequences, but only for those containing four [apraxic vs nonapraxic: $F(1,14) = 2.07$, $P = 0.17$; apraxic vs control: $F(1,22) = 6.71$, $P < 0.025$] and five hand postures [apraxic vs nonapraxic: $F(1,14) = 4.73$, $P < 0.05$; apraxic vs control: $F(1,22) = 15.29$, $P < 0.01$]. No such differences between sequence types were found between the nonapraxic and the control groups. These findings parallel the MT results as sequencing was disrupted in the apraxic but not the nonapraxic patients largely on heterogeneous sequences consisting of four or five responses.

Relationship between sequencing and cognitive status

Apraxia severity was correlated with auditory comprehension ($r = -0.64$), verbal fluency ($r = 0.65$) and visuospatial skills ($r = 0.58$), such that poorer language and spatial skills were related to more severe apraxia, accounting for 34–41% of the variance. Although auditory comprehension and verbal fluency were highly correlated ($r = -0.80$), neither of these tests was related to visuospatial skills ($r = -0.09$ and $r = 0.30$ for auditory comprehension and verbal fluency, respectively) indicating a separate underlying visuospatial component to apraxia. These findings raise the question as to whether the pattern of sequencing differences between the apraxic and nonapraxic patients might vary depending upon these measures, especially as the apraxic group was significantly impaired relative to the nonapraxic group on auditory comprehension and visuospatial skills. To examine this, separate regression analyses were conducted, analysing the relationships between the Token Part V, the Cookie Theft and the Block Design subtests and RTs, IRTs, adjusted MTs and errors for repetitive and heterogeneous sequences. The interaction of an ancillary test with group and sequence length was of interest. The results reported in this section are exploratory and preliminary, and should be interpreted with caution as the sample sizes were small, multiple statistical tests were con-

ducted and the majority of patients were not clinically impaired on the ancillary tests.

Despite the differences between the two stroke groups in auditory comprehension and visuospatial skills, these tests did not interact with group, sequence length or sequence type for any measures, indicating that group differences on these tests could not explain the pattern of findings for the apraxic and the nonapraxic groups. However, there was a significant verbal fluency × group × length interaction [$F(3,36) = 4.13$, $P < 0.025$]. Follow-up analyses showed poorer verbal fluency was correlated with greater increases in error rates for sequences containing two vs five responses for both groups (apraxic $r = -0.65$; nonapraxic $r = -0.66$). However, as sequence length increased from two to five postures, apraxic patients with normal fluency ($n = 3$; fluency $= 6.5 \pm 0$) or impaired fluency ($n = 4$; fluency $= 4.1 \pm 2.7$) showed similar increases in error rates (9.4% and 13.1%, respectively). In contrast, error rates increased more for the nonapraxic patients with impaired fluency ($n = 5$; fluency $= 5.9 \pm 0.4$) than for those with normal fluency ($n = 4$; fluency $= 6.7 \pm 0.2$) (6% and 0%, respectively). These findings show that, while better verbal fluency was associated with smaller changes in error rates with increasing sequence length in both groups, the apraxic group still showed a greater increase in error rates with longer sequences regardless of the fluency rating.

Computerized tomography analyses

Table 2 presents the lesion volume and location measurements for the apraxic and the nonapraxic groups. While Table 2 suggests that the apraxic patients had somewhat larger lesion sizes than the nonapraxic patients, Mann-Whitney U tests showed no significant group differences. Only three of the apraxic patients had lesion sizes greater (4.4%, 6.1%, 12%) than the largest lesion size found in the nonapraxic group, and in the remaining apraxic patients lesions occupied <1.7% of the total brain volume. Also there were no reliable differences between the apraxic and the nonapraxic groups on the linear and volumetric measures of lesion location.

TABLE 2. LESION VOLUME AND LOCATION FOR THE APRAXIC AND THE NONAPRAXIC GROUPS

	Apraxic group			*Nonapraxic group*		
	Mean	*(SD)*	*Range*	*Mean*	*(SD)*	*Range*
Lesion volume[1]	3.8	(4.2)	0.1–12.0	1.3	(1.3)	0.1–3.7
Anterior lesion volume[2]	48.5	(40.4)	0–97	58.1	(45.5)	1–100
Posterior lesion volume[2]	51.5	(40.4)	3–100	41.9	(45.5)	0–100
Anterior distance[3]	41.3	(17.1)	22–68	40.0	(15.5)	14–68
Posterior distance[3]	26.1	(21.4)	1–50	38.2	(20.5)	0–53

[1]Lesion volume is proportional to the total brain volume.

[2]The volumetric measurements 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.

[3]The linear measures are proportional to the total distance from the frontal to the occipital pole. A smaller proportion indicates that the lesion is located closer to the frontal or occipital pole.

DISCUSSION

The results showed deficits in some levels of programming were general to left hemisphere damage, whereas others were specific to the disorder of ideomotor limb apraxia. All patients with left hemisphere damage exhibited deficits in initiating the

sequence (i.e. slower RTs), executing single postures and controlling individual movements during sequencing. Only the apraxic patients showed a disruption in programming heterogeneous sequences prior to and during movement, but only for longer sequences. These findings could not be attributed to motor slowness because there were no differences between the apraxic and the nonapraxic patients in absolute RTs, IRTs or MTs. Also the findings were not related to lesion size, quantified measures of lesion location or auditory comprehension deficits. Although poor verbal fluency was associated with greater increases in error rates with increasing sequence length, these increases were greater in the apraxic group, regardless of whether the patients were fluent or not. Thus, language deficits cannot entirely explain the different pattern of sequencing abnormalities found between the apraxic and the nonapraxic groups. This is consistent with other studies showing poor gesture learning and gesture comprehension deficits in apraxic-aphasic but not nonapraxic-aphasic groups (Rothi and Heilman, 1984; Rothi *et al.*, 1985).

Cognitive deficits general to left hemisphere damage

Encoding deficit. The conceptualization of apraxia as a motor programming disorder has a long tradition, yet the specific nature of the hypothetical programming deficit has been both controversial and elusive. Two studies using the selective reminding method (Buschke and Fuld, 1974) reached different conclusions about the processes underlying gestural learning deficits in apraxia. Faglioni *et al.* (1990) reported that apraxia was a deficit specific to encoding and storage, but not retrieval. In contrast, others have found storage but not encoding or retrieval problems in aphasic-apraxic and aphasic-nonapraxic patients (Rothi and Heilman, 1984). In our study, RTs of the apraxic and the nonapraxic groups were slower (regardless of sequence length or type) than the control group which may point to an encoding deficit with left hemisphere damage, although response initiation deficits cannot be ruled out.

Generating spatiotemporal memory codes. After assembling a motor plan, additional cognitive computations must be engaged to translate the plan into physical movement. These computations most likely involve many levels of programming. Inter-response times of single movements and individual postures within repetitive or heterogeneous sequences were equally slowed in the apraxic and the nonapraxic groups. Spatial orientation and location deficits with left hemisphere damage (Rothi *et al.*, 1988; Poizner *et al.*, 1990) could underlie slowed IRTs for individual movements if a deterioration in spatiotemporal codes results in difficulties generating the motor patterns for individual postures.

Scheduling/timing movements. At a different level of analysis, the negative relationship between IRTs and sequence length for repetitive sequences and for IRT_4 of heterogeneous sequences suggested both stroke groups continued to engage in programming concerning the sequence, not simply an individual hand posture. One possible explanation for this pattern of findings is that left hemisphere damage disrupts the ability to schedule efficiently motor programs for individual movements within a sequence (Harrington and Haaland, 1991*a*). Specifically, before activating the physical parameters of a response other cognitive computations are likely to be required, such as scheduling when to execute a response. For instance, each response in a sequence may be associated with an absolute time at which to execute the movement. When sequences contain

repetitive movements, subjects normally either apply the same timing rule to all responses or time all responses simultaneously so that the length of a sequence has no effect on IRTs. When timing is dysfunctional, it proceeds more serially. Scheduling movements may be postponed to ensure that the computations of when a response will be initiated coincides with the activation of the physical parameters of the response, minimizing as much as possible prolonged delays between individual responses. Thus, patients with left hemisphere damage initiate movements contained in longer sequences faster because they have more time to complete the scheduling of the remaining postures in the sequence while executing the preceding postures. With shorter sequences, response execution is delayed because cognitive operations occur closer in time and must be at least partially completed before the activation of any particular hand posture. The proposed timing deficit is consistent with mounting evidence from studies of brain-damaged adults, language-impaired children, and neurologically intact subjects showing the left hemisphere is superior to the right hemisphere in the efficiency of processing rapid, temporal information (*see* Hammond, 1982; Tallal, 1983; Tzeng and Wang, 1984).

Cognitive deficits specific to apraxia

Preprogramming sequences. Only the apraxic group showed deficits in assembling a motor plan prior to movement for heterogeneous sequences. This first phase of planning presumably involves identifying and retrieving the subprograms for each response or response unit. Reaction times for heterogeneous sequences increased linearly with sequence length in the apraxic group, whereas in the nonapraxic and control groups there was a nonlinear effect. [In all groups the magnitude of sequence length effects on RT was very small. This was expected because the effect of sequence length diminishes when the interval prior to the imperative stimulus is 1 s or longer (Klapp *et al.*, 1974; Harrington and Haaland, 1991*b*). This is because subjects can plan much of the response before the imperative stimulus.] The first IRT also increased with sequence length, but only in the apraxic group, indicating the apraxic patients continued to engage in preprogramming while executing the first response. Because the form (i.e. linear vs nonlinear), but not the slope, of the RT function differed in the apraxic group a retrieval deficit account of the apraxic group's data is less likely. This is consistent with other studies (Rothi and Heilman, 1984; Faglioni *et al.*, 1990). A more plausible explanation is that the nonlinear effect of length on RT for heterogeneous sequences in the nonapraxic and control groups may reflect organizational strategies. For example, in a sequence of four responses (e.g. PBPP) subjects may treat each response as a unit which explains the linear increase in RT between $n = 2$ and $n = 4$. However, for sequences containing five responses (e.g. PBPPP) subjects may treat each of the first three responses as individual units (e.g. PBP) and the last two as a single unit (e.g. PP), accounting for the asymptote in RT after four postures. Of course, other organizational strategies are possible. In contrast, the linear RT function in the apraxic patients may reflect their tendency to plan each posture in the sequence as a unit, neglecting to chunk or parse the sequence when it is longer. This interpretation may be the most parsimonious account of the RT results as we now consider the pattern of MTs and errors in the apraxic patients.

Temporal organization. Do the proposed abnormalities with left hemisphere damage as inferred through the IRT findings also underlie the MT and error findings in the present study? This does not appear to be the case as only the apraxic group showed

a greater increase in MTs and error rates as heterogeneous sequences increased in length despite showing the same impairments as the nonapraxic group in IRTs. This dissociation suggests a different mechanism supports sequencing skills separate from those linked to timing responses or generating visuospatial memory codes.

We embrace an interpretation of the MT and error results which links it to the RT findings. Specifically, the execution of a sequence is dependent upon the way in which it is organized prior to movement (Rosenbaum *et al.*, 1983). Actions are normally parsed into natural rhythmic or spatial groupings which facilitate the development of skilful behaviours (Povel and Collard, 1982). Apraxia may produce a breakdown in parsing so that organizing principals for grouping responses are disrupted. This may explain why apraxics can normally execute shorter sequences of heterogeneous postures, whereas their performance breaks down on longer sequences, those which could benefit most from a parsing mechanism. In addition, abnormalities in cognitive computations that support parsing should lead to impaired learning which is consistent with deficient learning of hand position sequences or of gestures with left hemisphere damage (Rothi and Heilman, 1984; Jason, 1985; Rothi *et al.*, 1988).

An alternative explanation for the above findings, that apraxia produces a deficit specific to controlling changes in different postures (Kimura, 1977), is not satisfying for two reasons. First, IRTs of the apraxic and nonapraxic groups were slowed equally for repetitive and heterogeneous sequences. Secondly, the apraxic group showed deficits only on heterogeneous sequences containing four or five postures (e.g. PBPP, PBPPP) which consisted of the same number of different hand postures as those containing three postures (e.g. PBP), except for an addition of a repeated posture(s) at the end of the sequence. The MT and error findings, however, cannot rule out the possible role of serial ordering deficits in apraxia. Although little direct evidence exists linking ideomotor limb apraxia to a serial ordering deficit (Kimura and Archibald, 1974; Kimura, 1977; Jason, 1985, 1986), this issue deserves further study as the serial ordering requirements of most tasks, including ours, have been minimal, due to the use of highly practised gestures or sequences containing a limited number of responses.

Summary remarks

The present study, together with previous investigations of sequencing in patients with right hemisphere damage and Parkinson's disease (Harrington and Haaland, 1991*a*,*b*), provide some preliminary clues about several basic and functionally separate cognitive computations that may underlie motor sequencing. In addition, some of these computations appear to be most efficiently carried out by different neural subsystems. This is consistent with MacKay's (1985) theory of action which distinguishes among levels of cognitive-motor function (i.e. representations of actions, timing processes, sequential processes and parsing mechanisms), and predicts apraxia and other motor disorders result from damage to selected neural subsystems.

Prior to movement, encoding of single postures and sequences was slowed in left hemisphere apraxic and nonapraxic patients. Previous sequencing studies have not uncovered such deficits in patients with right hemisphere damage (Harrington and Haaland, 1991*a*) or Parkinson's disease (Harrington and Haaland, 1991*b*), which shows such deficits are not simply general to brain damage.

The apraxic and nonapraxic groups' problems executing single postures or individual

postures contained within a repetitive or a heterogeneous sequence have not been observed in other neurological disorders such as Parkinson's disease (Harrington and Haaland, 1991*b*). Specifically, parkinsonian patients displayed slowed IRTs and greater error rates when executing changes between different hand postures, but generally not when executing repetitions of the same posture (Harrington and Haaland, 1991*b*). This may suggest that processes controlling transitions between different postures (e.g. changes in force production) are regulated more directly by the basal ganglia system, whereas the left hemisphere is specialized for higher level cognitive computations concerned with generating spatiotemporal codes for movements.

The present results emphasized the left hemisphere's efficiency in temporal processing. This is consistent with a large literature examining the perception and production of time in neurologically intact individuals and in patients with damage to the left hemisphere (*see* Hammond, 1982). However, the assertion that timing mechanisms are specific to the cerebral cortex of the left hemisphere is likely to be an oversimplification, as left hemisphere damage resulting from stroke or developmental disabilities typically involves subcortical damage or, at minimum, a disconnection of cortical and subcortical systems. In fact, using a similar sequencing task we found sequence length had negative effects on the IRTs of repetitive sequences in patients with Parkinson's disease (Harrington and Haaland, 1991*b*), which is consistent with other reports of central timing deficits in these patients (Wing *et al.*, 1984; Poizner, 1990). Thus, timing mechanisms for movement may be an emergent property of left cerebral cortex and basal ganglia interactions. The cerebellum, however, is also involved in timing operations, particularly as they concern the measurement or perception of time (Keele and Ivry, 1990). Further research into temporal aspects of movements is needed to determine whether perception of time, reproduction of time intervals and scheduling movements in sequences involve functionally separate cognitive computations which engage different neural subsystems.

Dysfunctional temporal organization processes, as inferred through the RT, MT and error data, were specific to the disorder of apraxia. Interestingly, such deficits have not been observed in patients with Parkinson's disease (Harrington and Haaland, 1991*b*). In these patients, RTs for heterogeneous sequences increased with length up to four responses and then reached an asymptote similar to control subjects. However, the slope of this function is reduced relative to a control group, suggesting that basal ganglia abnormalities affect the ability to preprogram movement sequences completely. In addition, MTs and error rates in parkinsonian patients were normal regardless of sequence length or type. These findings are consistent with the low incidence of apraxia in Parkinson's disease (Sharpe *et al.*, 1983), and further point to the specificity of dysfunctional temporal organization in movement in the disorder of ideomotor limb apraxia. Direct tests of the proposed parsing deficits in these patient groups is one focus of our ongoing investigations in this area.

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REFERENCES

BUSCHKE H, FULD PA (1974) Evaluating storage, retention, and retrieval in disordered memory and learning. *Neurology, Minneapolis*, **24**, 1019–1025.

DE RENZI E, VIGNOLO L (1962) The Token Test: a sensitive test to detect receptive disturbances in aphasics. *Brain*, **85**, 665–678.

DE RENZI E, FAGLIONI P, LODESANI M, VECCHI A (1983) Performance of left brain-damaged patients on imitation of single movements and motor sequences. Frontal and parietal-injured patients compared. *Cortex*, **19**, 333–343.

FAGLIONI P, BASSO A, BOTTI C, AGLIOTI S, SAETTI C (1990) Gesture learning and apraxia. In: *Attention and Performance XIII*. Edited by M. Jeannerod. Hillsdale, NJ: Lawrence Erlbaum, pp. 837–856.

GOODGLASS H, KAPLAN E (1972) *The Assessment of Aphasia and Related Disorders*. Philadelphia: Lea and Febiger.

HAALAND KY, FLAHERTY D (1984) The different types of limb apraxia errors made by patients with left vs. right hemisphere damage. *Brain and Cognition*, **3**, 370–384.

HAALAND KY, HARRINGTON DL (1990) Complex movement behavior: toward understanding cortical and subcortical interactions in regulating control processes. In: *Cerebral Control of Speech and Limb Movements*. Edited by G. R. Hammond. Amsterdam: North-Holland, pp. 169–200.

HAMMOND GR (1982) Hemispheric differences in temporal resolution. *Brain and Cognition*, **1**, 95-118.

HARRINGTON DL, HAALAND KY (1987) Programming sequences of hand postures. *Journal of Motor Behavior*, **19**, 77–95.

HARRINGTON DL, HAALAND KY (1991*a*) Hemispheric specialization for motor sequencing: abnormalities in levels of programming. *Neuropsychologia*, **29**, 147–163.

HARRINGTON DL, HAALAND KY (1991*b*) Sequencing in Parkinson's disease: abnormalities in programming and controlling movement. *Brain*, **114**, 99–115.

HEILMAN KM, COYLE JM, GONYEA EF, GESCHWIND N (1973) Apraxia and agraphia in a left-hander. *Brain*, **96**, 21–28.

HEILMAN KM, ROTHI LJ, VALENSTEIN E (1982) Two forms of ideomotor apraxia. *Neurology, New York*, **32**, 342–346.

JASON GW (1985) Manual sequence learning after focal cortical lesions. *Neuropsychologia*, **23**, 483–496.

JASON GW (1986) Performance of manual copying tasks after focal cortical lesions. *Neuropsychologia*, **24**, 181–191.

KEELE SW, IVRY R (1990) Does the cerebellum provide a common computation for diverse tasks? A timing hypothesis. *Annals of the New York Academy of Sciences*, **608**, 179–207.

KIMURA D (1977) Acquisition of a motor skill after left-hemisphere damage. *Brain*, **100**, 527–542.

KIMURA D (1982) Left-hemisphere control of oral and brachial movements and their relation to communication. *Philosophical Transactions of the Royal Society of London, B*, **298**, 135–149.

KIMURA D, ARCHIBALD Y (1974) Motor functions of the left hemisphere. *Brain*, **97**, 337–350.

KLAPP ST, WYATT EP, MACLINGO W (1974) Response programming in simple and choice reactions. *Journal of Motor Behavior*, **6**, 263–271.

KOLB B, MILNER B (1981) Performance of complex arm and facial movements after focal brain lesions. *Neuropsychologia*, **19**, 491–503.

LEHMKUHL G, POECK K, WILLMES K (1983) Ideomotor apraxia and aphasia: an examination of types and manifestations of apraxic symptoms. *Neuropsychologia*, **21**, 199–212.

MACKAY DG (1985) A theory of the representation, organization and timing of action with implications for sequencing disorders. In: *Neuropsychological Studies of Apraxia and Related Disorders*. Edited by E. A. Roy. Amsterdam: North-Holland, pp. 267–308.

POIZNER H (1990) Language and motor disorders in deaf signers. In: *Cerebral Control of Speech and Limb Movements*. Edited by G. E. Hammond. Amsterdam: North-Holland, pp. 303–326.

POIZNER H, MACK L, VERFAELLIE M, ROTHI LJG, HEILMAN KM (1990) Three-dimensional computergraphic analysis of apraxia: neural representations of learned movement. *Brain*, **113**, 85–101.

POVEL D-J, COLLARD R (1982) Structural factors in patterned finger tapping. *Acta Psychologica*, **52**, 107–123.

ROSENBAUM DA, KENNY SB, DERR MA (1983) Hierarchical control of rapid movement sequences. *Journal of Experimental Psychology: Human Perception and Performance*, **9**, 86–102.

ROTHI LJG, HEILMAN KM (1984) Acquisition and retention of gestures by apraxic patients. *Brain and Cognition*, **3**, 426–437.

ROTHI LJG, HEILMAN KM, WATSON RT (1985) Pantomime comprehension and ideomotor apraxia. *Journal of Neurology, Neurosurgery, and Psychiatry*, **48**, 207–210.

ROTHI LJG, MACK L, VERFAELLIE M, BROWN P, HEILMAN KM (1988) Ideomotor apraxia: error pattern analysis. *Aphasiology*, **2**, 381–388.

ROY EA (1981) Action sequencing and lateralized cerebral damage: evidence for asymmetries in control. In: *Attention and Performance IX*. Edited by J. Long and A. Baddeley. Hillsdale, NJ: Lawrence Erlbaum, pp. 487–500.

ROY EA, SQUARE-STORER PA (1990) Evidence for common expressions of apraxia. In: *Cerebral Control of Speech and Limb Movements*. Edited by G. R. Hammond. Amsterdam: North-Holland, pp. 477–502.

SHARPE MH, CERMAK SA, SAX DS (1983) Motor planning in Parkinson patients. *Neuropsychologia*, **21**, 455–462.

SIEGEL S (1956) *Nonparametric Statistics for the Behavioral Sciences* (pp. 116–127). New York: McGraw-Hill.

TALLAL P (1983) A precise timing mechanism may underlie a common speech perception and production area in the peri-sylvian cortex of the dominant hemisphere. *Behavioral and Brain Sciences*, **6**, 219–220.

TZENG OJL, WANG WSY (1984) Search for a common neurocognitive mechanism for language and movements. *American Journal of Physiology*, **246**, R904–R911.

WECHSLER D (1981) *Wechsler Adult Intelligence Scale—Revised*. New York: Psychological Corporation.

WING AM, KEELE S, MARGOLIN DI (1984) Motor disorder and the timing of repetitive movements. *Annals of the New York Academy of Sciences*, **423**, 183–192.

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