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RESEARCH ARTICLE

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Evidence for effector independent and dependent representations and their differential time course of acquisition during motor sequence learning

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Abstract To investigate the representation of motor sequence, we tested transfer effects in a motor sequence learning paradigm. We hypothesize that there are two sequence representations, effector independent and dependent. Further, we postulate that the effector independent representation is in visual/spatial coordinates, that the effector dependent representation is in motor coordinates, and that their time courses of acquisition during learning are different. Twelve subjects were tested in a modified 2×10 task. Subjects learned to press two keys (called a set) successively on a keypad in response to two lighted squares on a 3×3 display. The complete sequence to be learned was composed of ten such sets, called a hyperset. Training was given in the *normal* condition and sequence recall was assessed in the early, intermediate, and late stages in three conditions, *normal*, *visual*, and *motor*. In the *visual* condition, finger–keypad mapping was rotated 90° while the keypad–display mapping was kept identical to *normal*. In the *motor* condition, the keypad–display mapping was also rotated 90°, resulting in an identical finger–display mapping as in *normal*. Subjects formed two groups with each group using a different *normal* condition. One group learned the sequence in a standard keypad–hand setting and subsequently recalled the sequence using a rotated keypad–hand setting in the test conditions. The second group learned the sequence with a rotated keypad–hand setting and subsequently recalled the sequence with a standard keypad–hand setting in the test conditions. Response time (RT) and sequencing errors during recall were recorded. Although subjects committed more sequencing errors in both testing conditions, *visual* and *motor*, as compared to the *normal* condition, the errors were below chance level. Sequencing errors did not differ significantly between *visual* and *motor* conditions. Further, the sequence recall accuracy was over 70% even by the early stage when the subjects performed the sequence for the first time with the altered conditions, *visual* and *motor*. There were parallel improvements thereafter in all the conditions. These results of positive transfer of sequence knowledge across conditions that use dissimilar finger movements point to an effector independent sequence representation, possibly in visual/spatial coordinates. Initially the RTs were similar in the *visual* and the *motor* conditions, but with training RTs in the *motor* condition became significantly shorter than in the *visual* condition, as revealed by significant interaction for the testing stage and condition term in the repeated measures ANOVA. Moreover, using RTs for single key pressing in the three conditions as baseline indices, it was again observed that RTs in the *visual* and *motor* conditions were not significantly different in the early stage, but *motor* RTs became significantly shorter by the late testing stage. These results support the hypothesis that the *motor* condition benefits more than the *visual* because it uses identical effector movements to the *normal* condition. Further, these results argue for the existence of effector dependent sequence representation, in motor coordinates, which is acquired relatively slowly. The difference in the time course of learning of these two representations may account for the differential involvement of brain areas in early and late learning phases found in lesion and imaging studies.

Key words Sequence representation · Effector dependence · Effector independence · Skill learning · Transfer of sequence knowledge · Time course of sequence learning

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Introduction

It is a common observation that when a skill is being acquired the subject needs to be more attentive in the initial phase; however, during the later, more automatic phase, attention can be engaged in other tasks (Fitts 1964). After mastering a skill, it appears as if the effector knows what to do and hence no overt attention is needed. Another common sense observation is that once a skill is acquired its memory is robust and lasts for a long time. In this context it is tempting to ask if the representation of skill memory is different at various stages of learning and if the corresponding neural bases are also distinct. In this study we use a finger movement sequence learning paradigm to present evidence for the existence of an effector dependent sequence representation apart from an effector independent sequence representation. We also show that the time course of development of these two representations is different and hypothesize about the possible neural bases for these representations.

In the following, we review previous studies that inspired our thinking on sequence representations and their neural loci. Hikosaka and colleagues studied various aspects of skill learning in monkeys using a 2×5 sequence learning paradigm (summarized in Hikosaka et al. 1995, 1996b; Rand et al. 1998) in which a sequence of ten button presses is learned by trial and error. They observed that, as training progressed, monkeys improved on two measures of performance: errors, monkeys made fewer errors before attaining a success criterion, and response time (RT), the time taken to perform a sequence decreased with training. However, the time course of improvement on these two measures was different: errors reached an asymptotic minimum level within a shorter period of training, but RTs continued to improve over longer periods (Hikosaka et al. 1995, 1996b). This result pointed out that acquisition of sequence knowledge (as measured by errors) may take place quickly but long-term motor sequence memory (as measured by RT) may take longer to establish. In another experiment, Rand et al. (1998) found that when monkeys used the opposite hand on well-learned sequences, error and RT measures deteriorated compared to those with the trained hand, indicating a possible storage of motor sequence memory in hand-specific representation. Further, during the well-learned stage, monkeys exhibited a higher proportion of anticipatory hand and eye movements (Miyashita et al. 1996) and these anticipatory responses broke down when monkeys performed the same sequence but with their opposite hand. These results reflect a specific kind of memory, motor sequence memory, which is optimized for specific body parts, as opposed to general or pure sequence knowledge which can be used to control a variety of body parts. Again, these results point to the possibility that sequence knowledge is acquired faster and earlier than RT (speed) improvements in skill acquisition. Miyachi et al. (1997) observed that muscimol (a GABA agonist) injection in the anterior striatum affected learning of new sequences and blockade of the posterior striatum affected recall of well-learned sequences in monkeys. In a similar experimental paradigm using functional MRI (fMRI) on human subjects, Hikosaka et al. (1996a) compared the activation of presupplementary motor area (pre-SMA) and supplementary motor area (SMA) and observed that pre-SMA was particularly active in learning new sequences while SMA was active in sequential movements, but not learning. Karni et al. (1995) asked human subjects to practice finger-to-thumb opposition sequences and performed fMRI scanning at regular intervals over a period of 5 weeks. They observed that performance of a well-practiced motor sequence elicited enhanced activation in the hand area of primary motor cortex (M1) as opposed to an unpracticed sequence consisting of the same component movements. They argued that a specific representation of practiced motor sequence evolves during long-term practice and that the M1 may constitute a site for the long-term memory of motor skills. Based on all these findings, it can be suggested that sequence learning is possibly mediated by different representations at different stages and the corresponding neural bases may also be distinct.

Based on the above evidence and the computational constraints in sequence learning, Nakahara and colleagues (Nakahara 1997; Nakahara et al. 1997, 1998; see also Hikosaka et al. 1999) made a specific hypothesis, that a sequence representation in visual coordinates develops faster than the one in motor coordinates, while representations in both coordinates are learned concurrently. In the current context, this hypothesis can be reformulated in a general way as follows: ‘during sequence learning an effector independent representation develops faster than an effector dependent representation, although both are learned simultaneously’. To date there has been no direct experimental verification of this proposal. We therefore attempt to test this hypothesis here, and, in general, we would like to address the question of neural representation of skills and how it changes in different stages of learning. Recently several researchers have started to address these questions (Keele and Curran 1995; Clegg et al. 1998; Grafton et al. 1998).

In the current experiment, subjects are presented with a series of visual stimuli on a display grid. They discover the correct sequence of key presses on a keypad corresponding to the visual stimuli. During different stages of learning, subjects are tested on the same visual sequence but in altered keypad and hand configurations. In one condition, the keypad stays the same but subjects use different finger movements than the original learning condition. In another condition, the keypad is rotated but subjects use identical finger movements as in the learning condition. In this finger movement sequence learning paradigm, we now state the hypothesis more explicitly as follows.

If, after sufficient learning, sequence recall is mediated by effector dependent representation (i.e., in motor coordinates, say, in the finger/arm coordinates), then performance with the keypad–hand conditions that retain the learned effector (finger) movements is faster than in

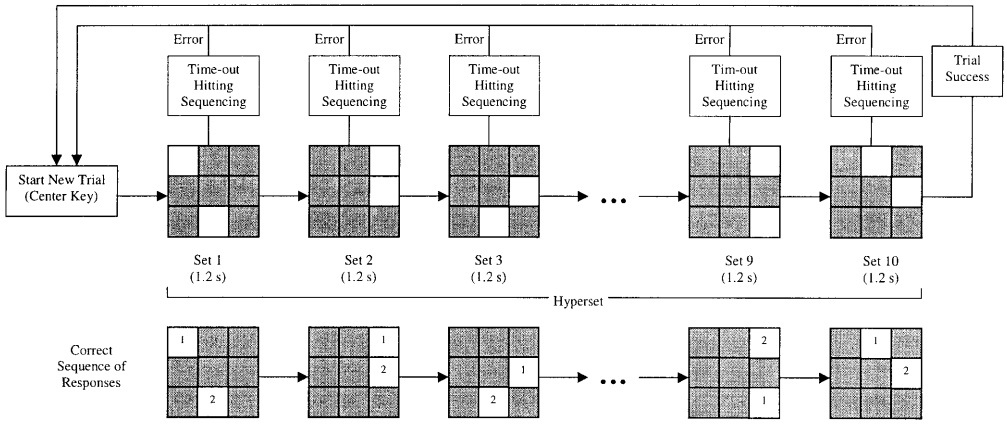

Fig. 1 The 2×10 sequence task procedure. Time-out errors are caused if a set is not completed within 1.2 s and hitting errors are caused if irrelevant keys are pressed. Sequencing errors are caused if keys are not pressed in the correct order shown in the *lower part* of the figure (figure modified from Hikosaka et al. 1996a). During test blocks sequencing errors do not cause reset of a trial as in training blocks

the conditions that do not preserve the learned finger movements. Further, this advantage will be seen only after sufficient learning and not during the initial stages of learning. However, if after learning, sequence recall is *not* mediated by effector dependent representation, then all the keypad and hand configurations yield similar performance results.

Materials and methods

Our study used 12 right-handed subjects, 11 males and one female, with ages in the range of 20 to 33 years and with a mean of 24.5 years.

Apparatus and behavioral paradigm

The 2×10 sequence task

Subjects were tested in a "modified 2×10 task" (see Fig. 1) which was originally devised to test sequence learning in monkeys (Hikosaka et al. 1995) and in humans (Hikosaka et al. 1996a; Sakai et al. 1998). The aim of the current experiment was to evaluate transfer of sequence learning from a trained condition to novel untrained conditions. Visual stimuli consisting of two illuminated squares on a 3×3 grid were displayed on a computer monitor placed at a distance of 60 cm in front of the subject and the center of the grid display on the monitor was adjusted to eye level. Subjects learned to press two corresponding keys (called a *set*) successively on a keypad in response to the visual stimuli. The order of key presses had to be discovered by trial and error. Ten such sets constituted a *hyperset*. The same hyperset was used in an experiment. Each subject performed two such experiments with two different hypersets. A hyperset was generated randomly with a condition that there were no repeated sets within the hyperset. Subjects were instructed to respond as quickly as they could throughout the experiment. Sets were presented at an even pace. If subjects did not complete two key presses within 1.2 s after presentation of visual stimuli, a *time-out error* was flagged and the trial was terminated and presentation was reset to the beginning. If subjects completed responses before 1.2 s, the subsequent set was presented after an appropriate delay. In the rotated testing conditions subjects had a tendency to hit irrelevant keys and upon such a *hitting error*, the trial was reset. There is a third kind of error, called a *sequencing error*, which occurs when keys are pressed in an incorrect order and leads to a trial reset during training blocks, as shown in Fig. 1. For example, as shown in the lower part of Fig. 1, the key labeled '1' is to be pressed first and then the one labeled '2' for a successful completion of set 1.

Subjects were instructed to use their index, middle, and ring fingers, with the middle finger aligned on the center key. They were further instructed to use each finger for the respective column/row of keys only. For example, the middle finger is used only for the middle column of keys in the *normal* condition (Fig. 2a). To encourage subjects to follow the alignment, we asked them to press the center key with their middle finger to start a trial. If a set was performed correctly, they moved to the next set, as shown in Fig. 1. The main difference between a training block and a test block was that during a test block a trial was not reset upon a sequencing error. This was done in order to facilitate assessing only the recall performance (sequencing errors and RT) and also to prevent any sequence learning during test blocks. Thus a trial in a training block is classified as *complete* when the subject correctly performed all ten sets (hyperset) in a row without any errors while a trial in a test block is deemed *complete* as long as there are no hitting or time-out errors.

Training was given in the *normal* condition and sequence recall was assessed during test blocks in three conditions, *normal*, *visual*, and *motor* (see Fig. 2). In the *normal* condition for group 1, both the keypad-to-display mapping and the access of hand to the keypad were in natural settings. As shown in Fig. 2a, in the *visual* condition access of the arm to keypad was rotated 90° while the keypad-to-display mapping was kept identical to the *normal* condition. Thus in the *visual* condition, spatial targets on the keypad were the same as in *normal*, although the actual finger movements were different. In the *motor* condition the keypad-to-display mapping was also rotated 90°, resulting in an identical finger-to-display mapping to the *normal* condition. Thus in the *motor* condition finger movements were the same as in *normal*. Subjects rested their right hand on a rotatable arm rest. A mask covered the hand and keypad. This was done to prevent subjects from using direct visual/spatial cues during training and testing and also to facilitate formation of a robust finger-to-display mapping. In order to ensure that our results hold good even for unconventional learning situations, we used the *visual* condition in group 1 as the *normal* setting to learn 2×10 sequences for group 2. As shown in Fig. 2b, appropriate *visual* and *motor* conditions were determined for group 2 using the same principles as described above, keeping the spatial targets the same for the *visual* condition and keeping the finger movements identical for the *motor* setting.

In the following, we describe various mappings that subjects may use while performing the 1×9 and 2×10 tasks. Visuo-spatial mapping specifies the target position on the keypad corresponding to a given visual stimulus on the display. For example, if the visual stimulus is on the top left corner square on the display, then the corresponding spatial target is the left key in the upper row on the keypad both in the *normal* and the *visual* conditions in group 1 (see Fig. 2a). Thus it can be seen that *normal* and *visual* conditions use an identical visuo-spatial mapping. Spatial-motor mapping specifies the required finger movement corresponding to a given spatial target on the keypad. For example, if the given spatial target is the center key in the lower row on the keypad, the index finger needs to be depressed for correct key press in both the *visual* and the *motor* conditions in group 1 (see Fig. 2a). Thus the

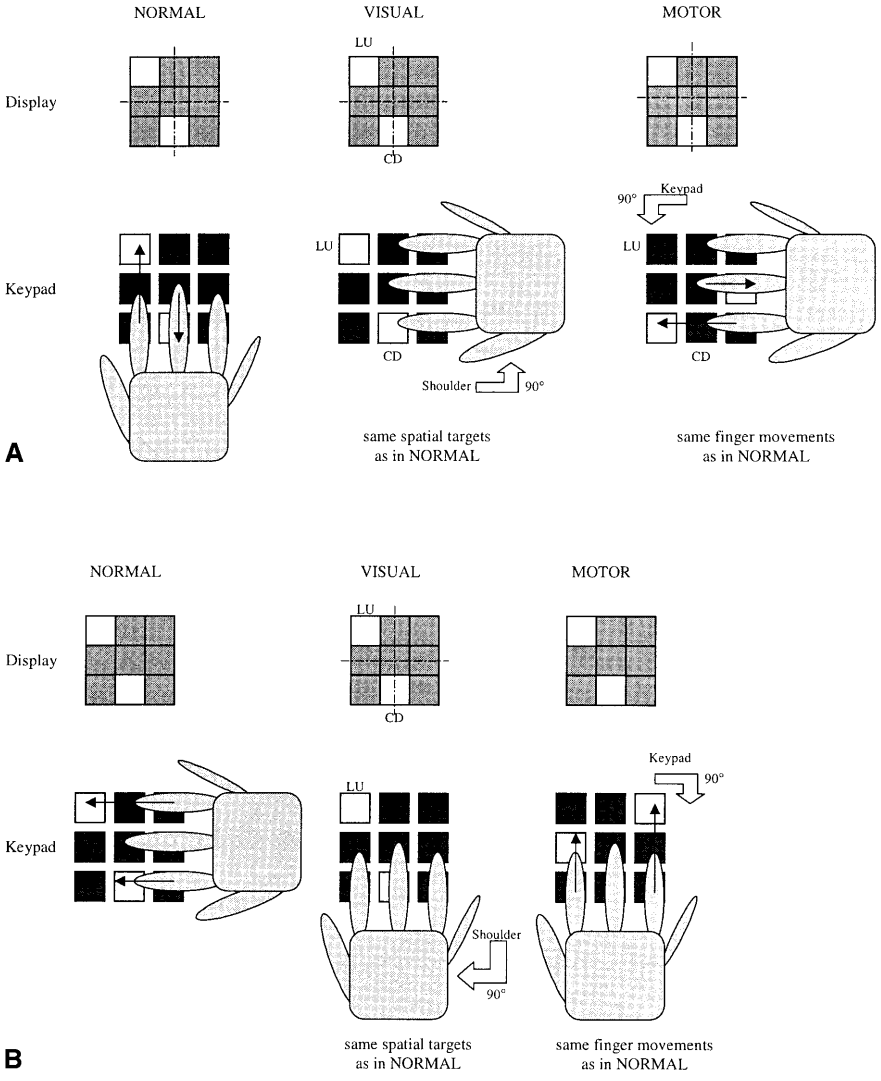

Fig. 2a,b Testing conditions for groups 1 and 2: *normal*, *visual*, and *motor*. Hand is rotated 90° in the *visual* condition and keypad is also rotated 90° in the *motor* condition. *Visual* condition uses the same spatial targets whereas *motor* condition uses identical finger movements to the *normal* condition. **a** Testing conditions for group 1. **b** Testing conditions for group 2. *LU* Left-and-up, *CD* center-and-down

visual and the *motor* conditions use an identical spatial-motor mapping. Visuo-motor mapping specifies the effector movement corresponding to a given visual stimulus on the display. For example, if the visual stimulus is on the top left corner square on the display, the index finger needs to be extended to reach the correct target in both the *normal* and the *motor* conditions in group 1 (see Fig. 2a). Thus the *normal* and the *motor* conditions use an identical visuo-motor mapping.

Subjects practiced the hyperset during a trial. The trial was terminated if subjects committed an error and a new one was initiated. A block consisting of several trials was continued until the success criterion for the block was achieved. Then subjects advanced to the next block of trials after a brief rest period of approximately 30 s. In this fashion, subjects completed a total of 25 blocks consisting of 11 training blocks, 12 test blocks (4 each in the in early, intermediate, and late stages), a speed test block, and a dual-task test block, as shown in Fig. 3. Subjects took about 1 h to complete an experiment. Training in the 2×10 sequence was given in block 1 (with a criterion of four complete trials) and performance in the early stage was assessed in blocks 2–5 (criterion = 2). Further training was given in block 6 (criterion = 4) and the intermediate stage performance was measured in blocks 7–10 (criterion = 2). After extensive training in blocks 11–19 (criterion = 8), the late stage performance was examined in blocks 20–25 (criterion = 2). Each testing stage consisted of 4 blocks with one condition per block arranged as follows: *normal*, *visual*, *normal*, and *motor*. The testing order was counterbalanced across experiments and across subjects. In a speed test block (24th block, N_S in Fig. 3, criterion = 2), subjects were asked to perform sequences at a faster pace (sets paced at 0.8 s). In a dual-task test block (25th block, N_D in Fig. 3, criterion = 2), subjects were asked to count digits backward while performing the sequence recall. N_S and N_D blocks tested whether the subjects achieved a fair level of automaticity in the sequence task.

The 1×9 single-key task

At the beginning and end of the sequence experiment, subjects performed a single-key pressing task (1×9 task). This task enabled us to get baseline measures of RT to press a key in each condition and facilitated the estimation of time-saving in sequence performance as a result of learning. In the task, subjects pressed one key corresponding to an illuminated square on the 3×3 display grid and the hyperset consisted of nine such non-repeating single-key sets. A new hyperset was generated for every trial and hence subjects were not allowed to memorize the sequence. They performed three blocks as shown in Fig. 3, one in each condition (*normal*, *visual*, and *motor*) and the criterion was to attain one complete trial per block. The order of presentation of novel conditions was counterbalanced across experiments. Before beginning any of the experiments, subjects were given a brief practice session with the 1×9 task to familiarize them with the experimental procedure and various testing conditions.

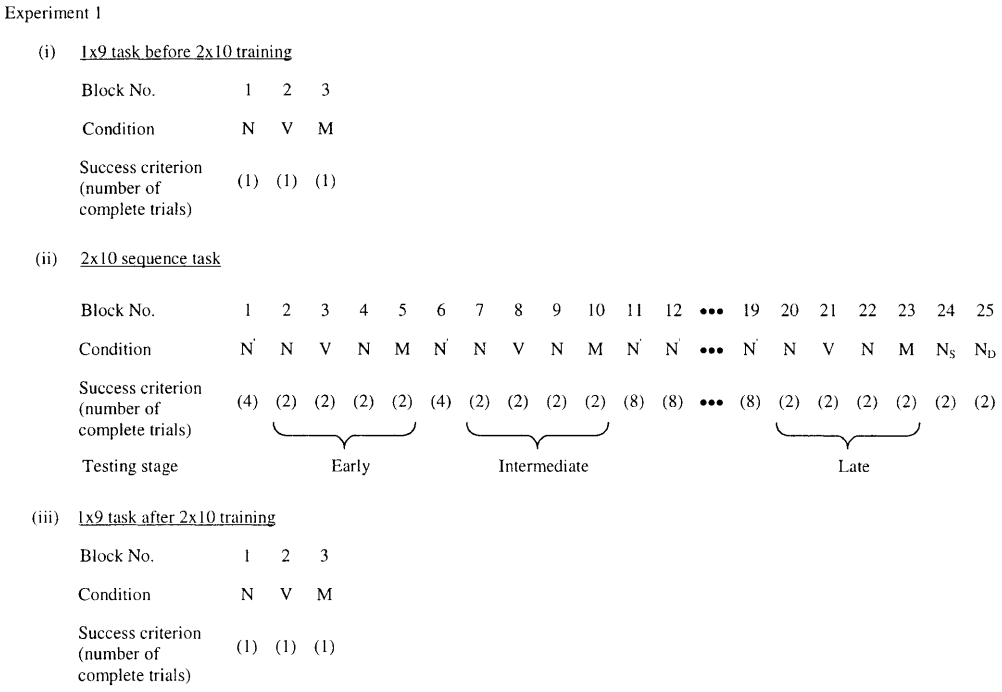

Fig. 3 Schedule of events during an experiment. Each experiment consists of three parts, a single-key (1×9) task, a sequencing (2×10) task, followed by a single-key (1×9) task. Subjects performed two such experiments (exp 1 and exp 2) in which the order of novel conditions (*visual* and *motor*) is counterbalanced. *N′* Training block in *normal* condition, *N* test block in *normal* condition, *V* test block in *visual* condition, *M* test block in *motor* condition, N_S speed test block, N_D dual-task test block

Data analysis

Measurements from the 1×9 task and test blocks of the 2×10 task are considered for analysis. In this study, RT is defined as the time elapsed from presentation of the visual stimuli to the completion of key presses corresponding to one set. Thus in the 1×9 single-key task, total RT corresponds to the total time taken for nine key presses. In the 2×10 task, RT corresponds to the time taken for two key presses and total RT measures the sum of RTs during two complete trials (40 key presses). Errors in the 2×10 test blocks are defined as the total number of sets with sequencing errors (incorrect sets) in the two complete trials, with a possible maximum of 10 errors in each trial, thus giving a total of 20 possible errors per test block. In every test block in the 2×10 task, apart from total RT and errors, the number of trials required to finish a test block was also recorded which reflects the number of hitting or time-out errors.

For the 2×10 task, a repeated measures ANOVA was performed considering testing stages (early, intermediate, and late), testing conditions (*normal*, *visual*, and *motor*), experiment number (exp 1 and exp 2), measurements (total RT and errors) as within-subject repeated measures variables, and the group number (group 1 and group 2) as the between-subject factor. Since there were two test blocks in the *normal* condition in each testing stage, total RT and error values were averaged over these two blocks.

For the 1×9 task a repeated measures ANOVA was also performed considering testing stages (before 2×10 training and after 2×10 training), testing conditions (*normal*, *visual*, and *motor*), experiment number (exp 1 and exp 2), total RT as within-subject repeated measures variables, and the group number (group 1 and group 2) as the between-subject factor. There were no sequencing errors to be considered for analysis in the 1×9 task.

Results

The 1×9 task: single-key RTs similar in *normal*, *visual*, and *motor* conditions

There were no overall differences across groups in the average RT among the three conditions (see Fig. 4a) as indicated by the lack of main effect for testing condition [$F(2,20)=0.032$]. However, there were groupwise differences as revealed by a significant interaction for the testing condition vs group number [$F(2,20)=9.033$, $P<0.01$]. In group 1, the average RT in the *visual* condition, in which a non-standard visuo-motor mapping was required (Fig. 2a), was significantly longer than those in the *normal* and *motor* conditions (Fig. 4a). In group 2, RTs in the *visual* condition, in which subjects used a standard visuo-motor mapping (Fig. 2b), were shorter as shown in Fig. 4b. Further, RTs for single-key performance in the *normal* and *motor* conditions were not statistically different in the means comparison contrast test [group 1: $F(1,5)=0.009$; group 2: $F(1,5)=0.067$], but there were significant differences between *normal* and *visual* [group 1: $F(1,5)=6.9$, $P<0.05$; group 2: $F(1,5)=7.1$, $P<0.05$] and *motor* and *visual* conditions [group 1: $F(1,5)=7.4$, $P<0.05$; group 2: $F(1,5)=5.799$, $P<0.05$]. We also observed that while the *normal* condition had a marginally significant decrease in RT [$F(1,10)=3.4$, $P=0.08$] and the *motor* condition had a significant decrease in RTs [$F(1,10)=4.7$, $P<0.05$] after 2×10 training compared to before 2×10 training, we did not see any significant differences in the single-key RTs in the *visual* condition [$F(1,10)=0.243$] between the two stages. However, as shown in Fig. 4c, the testing conditions did not differ statistically from one another at any testing stage. Means comparison contrasts before 2×10 training revealed the following: *normal* and *visual* [$F(1,10)=1.6$], *normal* and *motor* [$F(1,10)=0.0002$], and *visual* and *motor* [$F(1,10)=1.5$]. Contrasts after 2×10 training were: *normal* and *visual* [$F(1,10)=1.1$], *normal* and *motor* [$F(1,10)=0.1$], and *visual* and *motor* [$F(1,10)=2$]. Thus, although there seems to be some improvement in the single-key RTs in the *motor* condition as a result of practice

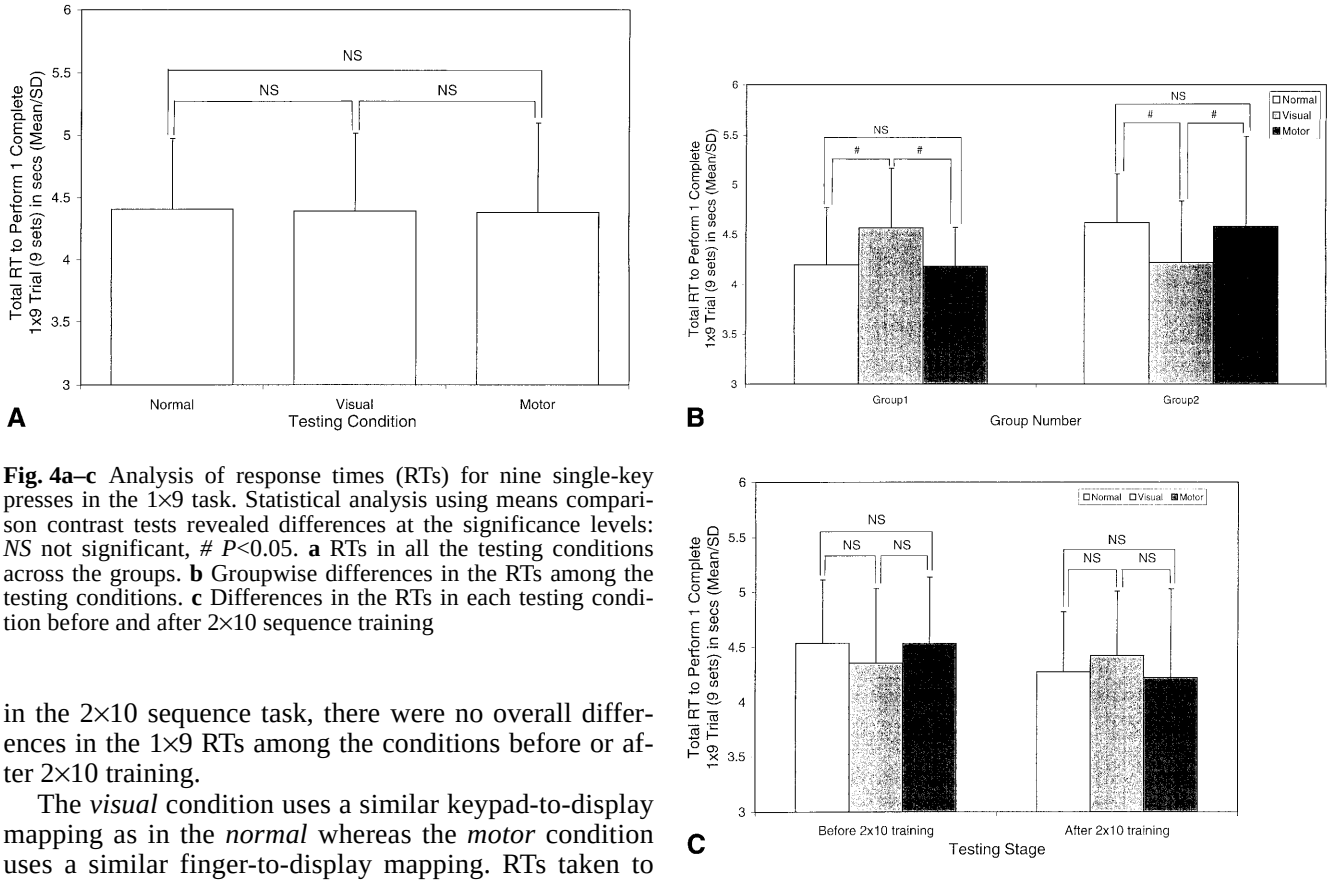

Fig. 4a–c Analysis of response times (RTs) for nine single-key presses in the 1×9 task. Statistical analysis using means comparison contrast tests revealed differences at the significance levels: *NS* not significant, # $P<0.05$. **a** RTs in all the testing conditions across the groups. **b** Groupwise differences in the RTs among the testing conditions. **c** Differences in the RTs in each testing condition before and after 2×10 sequence training

in the 2×10 sequence task, there were no overall differences in the 1×9 RTs among the conditions before or after 2×10 training.

The *visual* condition uses a similar keypad-to-display mapping as in the *normal* whereas the *motor* condition uses a similar finger-to-display mapping. RTs taken to press single keys in various conditions would reflect any mapping-related differences among the conditions. While *visual* was slower and *normal* and *motor* were faster in group 1, *visual* was faster and *normal* and *motor* were slower in group 2, resulting in the three conditions having similar average single-key RTs as shown in Fig. 4a. Thus any difficulties due to mapping-related differences among the conditions were balanced across groups.

The 2×10 task

Figure 5a shows the average number of trials taken by the subjects as they progressed through the 2×10 task. As shown in the figure, the block completion criterion was four complete trials in the early and intermediate training periods but increased to eight trials during the later training period. During the testing period at all the stages, the criterion was two complete trials without committing hitting or time-out errors. With training, subjects required fewer trials to attain the block completion criterion. All the subjects could perform the speed test block (N_S in Fig. 5a) and the dual-test block (N_D in Fig. 5a) well, which indicated that they attained a fair level of automaticity in the sequence performance task. These blocks were not analyzed further. It was observed that subjects needed more trials in the testing periods while performing in the novel conditions, *visual* and *motor*, than in the *normal* training condition. This observation is in general agreement with the results from the other two variables, namely, sequencing errors and total RT.

A trial during the testing period was flagged as an error trial and aborted if subjects committed either a time-out or a hitting error. Error trials during the testing periods were analyzed separately to see if there were any significant differences among the testing conditions, especially between the *visual* and *motor* conditions. It was observed that the variance was not homogeneous among the testing conditions: while the variance in *normal* was 1.2, that in *visual* and *motor* was 31.3 and 810.7, respectively. In order to homogenize the variance (see Winer et al. 1991), a fourth root transformation was applied to the error trial data.[1] Then a repeated measures ANOVA was performed on the transformed error trial data. We considered testing stages (early, intermediate, and late), testing conditions (*normal*, *visual*, and *motor*), experiment number (exp 1 and exp 2), error type (time-out and hitting) as within-subject repeated measures variables, and the group number (group 1 and group 2) as the between-sub-

[1] We found a relation between the mean and standard deviation in the error trial data, large variance at higher means. In such a situation, Winer et al. (1991) recommended root-transformation of the data in order to obtain homogeneous variance. Further, Thut et al. (1996), in a transfer-of-learning study, used third root transformation to bring the variance in the performance accuracy data within a factor of four. In our case, we subjected the error trial data to square root, third root, and fourth root transformations. Fourth root transformation yielded the best results, but similar results were observed with any of these transformations.

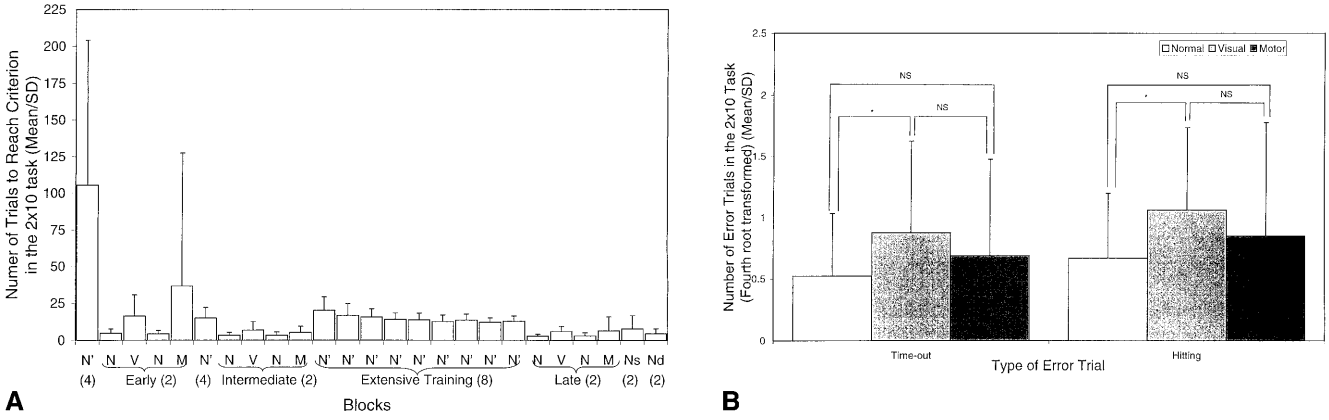

Fig. 5a,b Progress of subjects from the 1st to the 25th block and analysis of error trials. The block completion criterion is shown below the block notation symbols. Notations for blocks are as in Fig. 3. **a** Number of trials taken to attain the completion criterion at various stages in the 2×10 sequence task. **b** Summary of ANOVA on time-out and hitting error trials. Error trial data were transformed using a fourth root transformation in order to homogenize variances. Significance levels: *NS* not significant, * $P<0.01$

ject factor. Significant main effects were found for the testing stage [$F(2,20)=21.5$, $P<0.0001$] and the testing condition [$F(2,20)=6$, $P<0.01$]. There were fewer error trials in the late testing stage compared to the early stage and there were significantly fewer error trials in the *normal* condition as compared to the *visual* and *motor* conditions. To further study the differences based on the error type, time-out and hitting error trials were analyzed separately. Again testing time and condition came out as the main effects. Results are summarized in Fig. 5b. There were fewer time-out and hitting error trials in the *normal* condition as compared to the other conditions, however they reached significance only when compared to the *visual* condition {time-out: *normal* vs *visual* [$F(1,10)=9.1$, $P<0.01$], *normal* vs *motor* [$F(1,10)=2$]; hitting: *normal* vs *visual* [$F(1,10)=10.2$, $P<0.01$], *normal* vs *motor* [$F(1,10)=2.1$]}. Further, subjects committed fewer errors in the *motor* condition compared to the *visual* condition but they did not reach statistical significance: time-out [$F(1,10)=2.6$] and hitting [$F(1,10)=3$]. Possible sources of the time-out and hitting errors, especially in the *visual* condition, are described in the Discussion. The number of trials was not considered for further analysis and only sequencing errors were considered for analysis as they reflected the accuracy of recall of sequence knowledge.

The factors of main interest in the 2×10 task were testing stage and condition because we expected to see differential transfer across conditions and that these differences will be revealed more in later testing stages. Repeated measures ANOVA revealed significant main effects for testing stage [$F(2,20)=43.9$, $P<0.0001$] and testing condition [$F(2,20)=14.4$, $P<0.0001$]. Thus these results suggested that both testing stage and condition affected the performance. To study the relationship in more detail, errors and RT were analyzed individually.

Recall accuracy of the sequence knowledge is high despite differences in the effector movements used for performance

ANOVA on errors revealed a main effect for testing stage [$F(2,20)=17.8$, $P<0.0001$], testing condition [$F(2,20)=6$, $P<.01$], and for group number [$F(1,10)=5.8$, $P<0.05$]. The interaction between testing stage and condition was not significant [$F(4,40)=0.3$] indicating that the sequencing error profile among the various testing conditions did not differ significantly based on the testing stage. Overall, group 2 committed more errors (mean/SD: 4.3/3.5) than group 1 (mean/SD: 2.6/3). This may possibly be due to the use of an unconventional *normal* condition during training in group 2. It was observed that the subjects made relatively fewer errors in all the testing conditions during the late testing stage compared to the early stage {early vs late: *normal* [$F(1,10)=15.8$, $P<0.001$], *visual* [$F(1,10)=23.4$, $P<0.0001$], and *motor* [$F(1,10)=27.2$, $P<0.0001$]}. This suggests that the accuracy of sequence recall had improved with training in all the conditions. Figure 6 shows the number of errors made at each testing stage in all the test conditions. Subjects made more errors in the novel testing conditions than in the *normal* condition at all the testing stages {*normal* vs *visual*: early [$F(1,10)=24.2$, $P<0.0001$], intermediate [$F(1,10)=21.6$, $P<0.0001$], and late [$F(1,10)=16.4$, $P<0.001$]; *normal* vs *motor*: early [$F(1,10)=15.5$, $P<0.001$], intermediate [$F(1,10)=7.6$, $P<0.01$], and late [$F(1,10)=7.2$, $P<.001$]}. Figure 6 also shows that although subjects committed fewer errors in the *motor* condition than in the *visual* condition, the differences did not reach statistical significance at any testing stage {*visual* vs *motor*: early [$F(1,10)=0.97$], intermediate [$F(1,10)=3.6$, $P=0.07$], and late [$F(1,10)=1.8$]}. If subjects did not have any knowledge of the sequence and merely pressed keys in a random fashion, there is a 50% chance of getting a set correct. Thus about 10 sets ('errors at chance level') out of 20 may be correct by chance. It can be observed in Fig. 6 that sequencing errors were below chance level at all stages and in all the testing conditions. This observation suggests that both *visual* and *motor* conditions benefited from the sequence knowledge acquired in the *normal* condition.

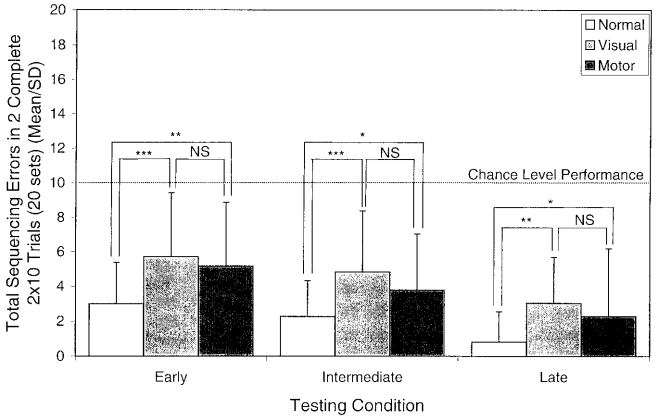

Fig. 6 Analysis of 2×10 sequencing errors committed in each testing condition at various testing stages. Significance levels: *NS* not significant, * $P<0.01$, ** $P<0.001$, *** $P<0.0001$

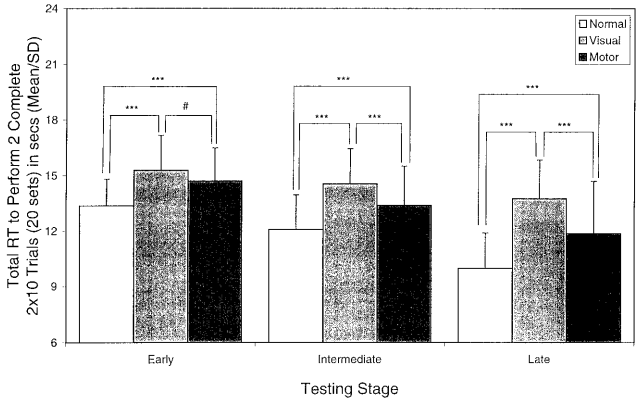

Fig. 7 Analysis of RTs in the 2×10 task in each testing condition at various testing stages. Significance levels: # $P<0.05$, *** $P<0.0001$

In order to emphasize the fact that there was positive transfer of sequence knowledge to both *visual* and the *motor* conditions leading to accuracy in recall, we computed (from Fig. 6) the percentage accuracy in sequence recall across the testing stages using the formula 100×[1–(sequencing errors/20)]. Thus accuracy is 100% if all the 20 sets were performed without sequencing errors. Calculations showed that at the early stage accuracy was 85, 71, and 74%, in the intermediate stage it was 89, 76, and 81%, and by the late stage it improved to 96, 85, and 89%, in *normal*, *visual*, and *motor*, respectively. An important observation is that even at the early testing stage when subjects performed the novel conditions for the first time, recall accuracy was over 70% in both *visual* and *motor*. Given that *visual* and *normal* conditions used different finger movements, sequence encoding at the level of finger movements in the *normal* condition could not possibly lead to accuracy in the *visual* condition. They both, however, share the same display-to-keypad (visuo-spatial) mapping. Hence, if subjects memorized the sequence of visual stimuli to be turned off (sequence encoding in visual coordinates), they could figure out the corresponding targets on the keypad using the same visuo-spatial mapping as in the *normal* condition. In the *motor* condition also they could rely on the sequence representation in visual coordinates but use a rotated visuo-spatial mapping to figure out targets on the keypad. The other possibility is that subjects memorized the sequence of key-press locations in the keypad frame of reference (sequence encoding in spatial coordinates). By relying on the sequence representation in spatial coordinates, subjects could perform successfully in both *visual* and *motor* conditions without depending on the sequence encoding in finger movements. Overall, these results suggest that sequence knowledge could be recalled with similar accuracy in both the *visual* and *motor* conditions despite the fact that they required dissimilar finger movements. Thus results on sequencing errors point to the possibility of storage of sequence knowledge without regard to the type of effector movements used for recall.

Motor condition has significant gains in RT than *visual* condition

Analysis of RTs by ANOVA revealed significant main effects for testing stage [$F(2,20)=57.9$, $P<0.0001$] and condition [$F(2,20)=34.8$, $P<0.0001$]. The interaction term, stage vs condition, was also significant [$F(4,40)=7$, $P<0.001$]. Thus the main effects were that RTs improved with training and that they were different depending on the testing condition. RTs improved significantly in all the testing conditions by the late testing stage as compared to the early stage {early vs late: *normal* [$F(1,10)=165$, $P<0.0001$], *visual* [$F(1,10)=33.2$, $P<0.0001$], and *motor* [$F(1,10)=116.6$, $P<.0001$]}. Figure 7 shows the RTs at various stages across all the testing conditions. Both the *visual* and *motor* conditions were significantly slower than the *normal* condition at any testing stage {*normal* vs *visual*: early [$F(1,10)=52.4$, $P<0.0001$], intermediate [$F(1,10)=86.5$, $P<0.0001$], and late [$F(1,10)=205.1$, $P<.0001$]; *normal* vs *motor*: early [$F(1,10)=25.7$, $P<0.0001$], intermediate [$F(1,10)=24.3$, $P<0.0001$], and late [$F(1,10)=50.7$, $P<0.0001$]}. More importantly, the *visual* condition was slower than the *motor* condition at all the testing stages {*visual* vs *motor*: early [$F(1,10)=4.7$, $P<0.05$], intermediate [$F(1,10)=19.1$, $P<0.0001$], and late [$F(1,10)=51.9$, $P<0.0001$]}.

RTs in the 1×9 single-key task include the time taken for mapping and movement-related processes and does not have any sequencing component. We wanted to assess the improvements in RTs in the 2×10 sequence task after taking the time taken for extra sequencing processes in the 1×9 task into consideration. Hence we used the average RTs in the in 1×9 task to estimate the time taken to complete 40 key presses in each testing condition. Because of the learning of sequential prediction, the total RT for 40 button presses in the 2×10 task would be shorter compared to the estimated value from the single-key task. Using the 1×9 task RT measures as baseline indices, we then computed percentage improvements using the formula 100×[1–(2×10RT/1×9RT)], in each condi-

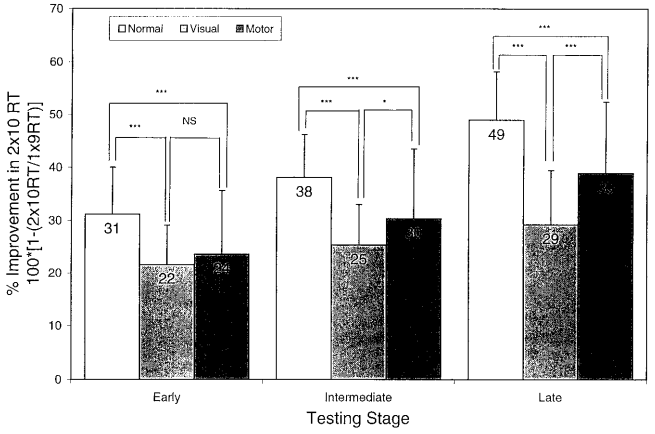

Fig. 8 Percentage improvement in RTs in the 2×10 sequence task at each testing stage and across all the testing conditions using 1×9 single-key RTs as baseline. Significance levels: *NS* not significant, * $P<0.01$, *** $P<0.0001$

tion in the 2×10 task at every testing stage and for each subject. Repeated measures ANOVA on the improvement scores revealed main effects for the testing stage [$F(2,20)=54.1$, $P<.0001$] and condition [$F(2,20)=22.7$, $P<0.0001$], along with a significant interaction term [$F(4,40)=6.9$, $P<0.001$]. Results are summarized in Fig. 8. In the early stage, 2×10 RTs in both *visual* and *motor* were significantly less improved than in *normal* {*normal* vs *visual* [$F(1,10)=44.2$, $P<0.0001$] and *normal* vs *motor* [$F(1,10)=27.8$, $P<.0001$]}. Furthermore, *visual* and *motor* were not significantly different at the early stage [$F(1,10)=1.9$]. In the intermediate stage, *normal* remained significantly more improved than *visual* and *motor*, but now *motor* seemed to have improved more than *visual* {*normal* vs *visual* [$F(1,10)=78.3$, $P<0.0001$], *normal* vs *motor* [$F(1,10)=28.8$, $P<0.0001$], and *visual* vs *motor* [$F(1,10)=12.1$, $P<.01$]}. By the late stage, while *normal* remained significantly more improved, *motor* also became quite significantly improved than *visual* {*normal* vs *visual* [$F(1,10)=185.2$, $P<0.0001$], *normal* vs *motor* [$F(1,10)=48.2$, $P<0.0001$], and *visual* vs *motor* [$F(1,10)=44.5$, $P<.0001$]}. In summary, although during the early stage the *visual* and *motor* conditions had similar percentage improvements, the results in the intermediate and late stages indicated more improvement in the *motor* condition than in the *visual* condition. It may be possible that subjects did not acquire facility with finger movement sequencing in the early stage and hence RTs in the *motor* condition were similar to those in the *visual* condition. In contrast, after long practice in the *normal* condition, facility with finger movements might have enabled shorter RTs in the *motor* condition compared to the *visual* condition. Taken together, results on RTs support the view that training in the *normal* condition benefits the *motor* condition significantly more than the *visual* condition. Further, the *motor* condition may have benefited because of the use of identical effector movements as in the *normal* condition.

Discussion

Effector independent sequence representation in visual coordinates

Although in our experiment subjects never practiced a sequence in novel conditions, *visual* and *motor*, except during testing stages, analysis of errors revealed that the performance was above chance level (cf Fig. 6). Subjects committed more sequencing errors in the untrained testing conditions than in the trained *normal* condition, but the accuracy of recall by the late testing stage was over 80% in both *visual* and *motor*. This transfer, although not perfect, is remarkable by considering the fact that we did not provide any feedback about the sequencing errors during the test period; even if subjects committed a sequencing error, the trial was not terminated. There are several other possible reasons why the errors in the *visual* and *motor* conditions did not diminish as much as in the *normal* condition, especially in the *visual* condition.

Limitations imposed by time-out

If subjects did not complete the two button presses corresponding to a set within 1.2 s, the trial was timed out flagging a time-out error. It is possible that sequence recall in testing conditions with rotated mapping, as in the *visual* and *motor* conditions, requires additional time leading to longer RTs and/or errors. During the *motor* condition, subjects could eventually overcome this limitation by taking advantage of the finger movements practiced in the *normal* condition. In contrast, in the *visual* condition subjects would have to rely on the sequence knowledge in visual coordinates, figure out spatial targets using visuo-spatial mapping, and then direct movements using a rotated spatial-motor mapping. This chain of events might take longer than the limit of 1.2 s, thereby leading to more time-out errors in the *visual* condition.

Limitations due to dominant finger movement sequencing

Overall, it was observed that subjects committed slightly more hitting errors in the *visual* condition (see Fig. 5b). The finger movement sequencing practiced in the *normal* condition may have interfered with the responses during the *visual* condition, thereby leading to more hitting errors in the *visual* condition. Similarly, until the movements are practiced well there are chances of hitting errors in the *motor* condition also. It is to be noted that the hand access to the keypad is different in the *normal* and *motor* conditions. Thus, even though the sequence of finger movements is identical in both the *normal* and *motor* conditions, shoulder rotation differences may have resulted in inaccurate landing of fingers on the keypad, thereby leading to hitting errors in the *motor* condition.

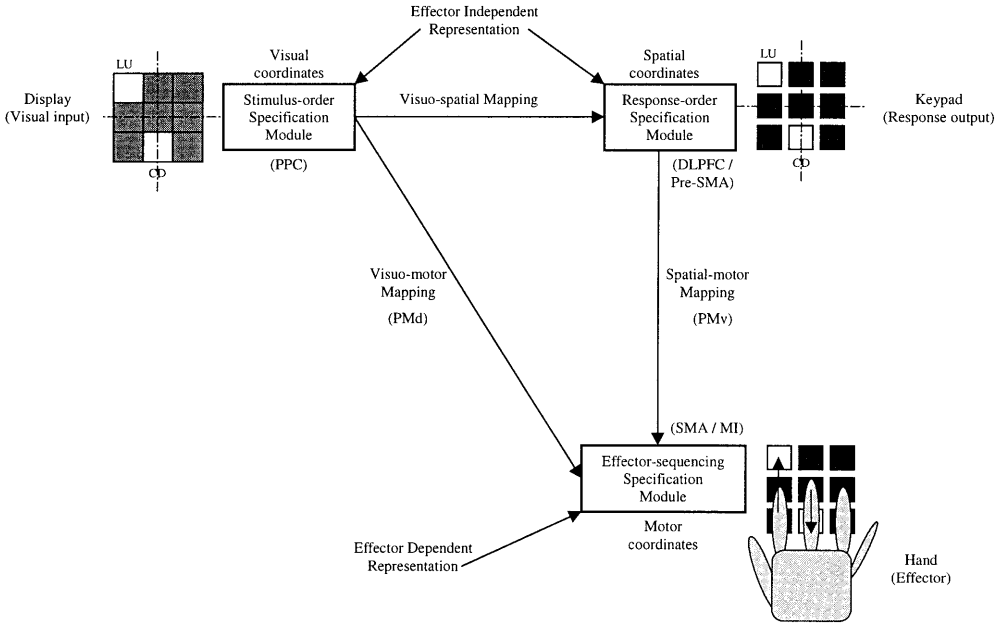

Fig. 9 A modular view of the finger-sequence learning task depicting modules that use effector independent and dependent representations and their possible cortical localization. *LU* Left-and-up, *CD* center-and-down, *PPC* posterior parietal cortex, *DLPFC* dorsolateral prefrontal cortex, *PMd* dorsal premotor cortex, *PMv* ventral premotor cortex, *SMA* supplementary motor area, *MI* primary motor cortex

In spite of these limitations, we did not see any statistically significant differences between the *visual* and *motor* conditions (cf Figs. 5b, 6) on any measure of error, time-out, hitting, or sequencing. There were striking differences in the keypad and hand settings between the novel and the trained conditions. *Visual* and *normal* conditions used the same keypad-to-display mapping but required dissimilar finger (effector) movements, whereas *motor* and *normal* conditions shared an identical finger-to-display mapping (requiring identical effector movements) but used dissimilar keypad-to-display mapping (see Fig. 2). In addition, both the novel testing conditions used rotated shoulder joint compared to the *normal* condition. Thus the proximal muscles at the shoulder joint level, to the extent they are involved in sequence performance, would have been employed differently depending on the testing condition (*normal* vs novel). Thereby successful recall of sequence knowledge in novel testing conditions, as evidenced by high accuracy, suggests effector independence in sequence representation.

Many previous researchers also argued for effector independent representation based on results on positive intermanual skill transfer, finger tapping (Laszlo et al. 1970), abstract figure drawing (Thut et al. 1996), sequential finger movements (Taylor and Heilman 1980), and handwriting with dominant and non-dominant hands (Wright 1990). All these previous results and the current findings support the "effector independent sequence representation hypothesis" as summarized in Keele and Curran (1995). Keele and Curran also termed this characteristic "modularity of representation". The importance of the current study is that we also present evidence, in the next section, for an effector dependent representation and show that there are differences in the time course of development of these two representations. We sketch a modular view of the finger sequence learning task in Fig. 9.

As per the scheme in Fig. 9, sequence knowledge would be represented at an abstract level, say, in visual coordinates (display coordinates) in the stimulus-order specification module. This module interacts via a visuo-spatial mapping with the response-order specification module which specifies the sequence of responses in spatial coordinates (keypad coordinates). According to the effector independence hypothesis, both the stimulus-order and response-order specification modules do not need to care about the type of effector eventually engaged to make an output. The effector-sequencing specification module in this framework does not need to represent sequence knowledge in any way. The effector-configuration required to achieve the target is determined by the appropriate mapping, visuo-motor or spatial-motor. Thus sequence representation is independent of the effector employed for learning and for eventual recall. However, we also argue below for the existence of an effector dependent sequence representation in the current task.

Effector dependent sequence representation in motor coordinates

One of the manifestations of effector dependent representation is in RT improvements. Especially in motor skill learning scenarios, RT improvements point to effective use of the effector muscles. Thus the RT gains seen in *normal* and *motor* conditions as opposed to the *visual* condition in the 2×10 task (Fig. 8) may be ascribed to the acquisition of an effector dependent sequence representation. From the modular view in Fig. 9, we can consider three possible explanations for the dissimilar improvements seen in RTs: (1) due to improved effector independent sequence representation, (2) due to improved spa-

tial-motor and visuo-motor mappings, and (3) due to acquisition of motor sequence representation. We present arguments against possibilities 1 and 2, and supporting 3, and conclude that a sequence representation might have been acquired in motor coordinates.

Possibility 1. Improved effector independent sequence representation

It is not tenable to attribute all improvements solely to improved effector independent (visual/spatial) sequence learning in the stimulus-order or response-order specification modules (Fig. 9). If this is the case then since these modules represent sequences without regard to the effector employed eventually, we should have seen equal improvements in all the conditions. Figures 7 and 8 clearly indicate that the three conditions had differential improvements by the late testing stage, thus arguing against this possibility.

Possibility 2. Improved spatial-motor and visuo-motor mappings

It can be argued that dissimilar improvement is due to the development of differential capabilities in the spatial-motor or visuo-motor mappings. Firstly, since *visual* and *motor* conditions use the same spatial-motor mapping, as described before, this mapping cannot be the source of differences in RTs in these conditions.

Secondly, let us consider visuo-motor mapping. During the initial stages, sequence processing may happen via the longer route (in Fig. 9, from visual-to-spatial-to-motor) and then as training progresses a direct visuo-motor mapping would be established. Since the *normal* and the novel *motor* condition use identical finger movements, the direct mapping may enable subjects to perform at high speeds during the late stages in both these conditions. In fact, results from the 1×9 task point to such a possibility. Although single-key RTs in the *normal* condition decreased marginally significantly, there was a significant decrease in single-key RTs in the *motor* condition between the pre- and post-2×10 testing stages. This indicates that the visuo-motor mapping acquired in the *normal* condition may have transferred to the *motor* condition.

However, effective visuo-motor mapping cannot completely account for the decreased RTs in the *motor* condition in the 2×10 sequence task. Firstly for the *motor* condition, we analyzed whether the improvement in the 2×10 task was significantly more than that in the 1×9 task. For this purpose, we computed the ratio of improvement in the *motor* condition in the 1×9 task from the pre-to-post test periods (mean/SD: 0.06/0.16). Similarly, we computed the ratio of improvement in the *motor* condition in the 2×10 task from the early-to-late testing stages (mean/SD: 0.19/0.16). Repeated measures ANOVA on these two ratio scores revealed that improvement in the 2×10 *motor* condition was significantly more than that in the 1×9 task [$F(1,10)=11.2$, $P<0.01$]. Thus, the significant improvement observed in 2×10 RTs in the *motor* condition cannot be solely due to an improved visuo-motor mapping as revealed by 1×9 RTs. Secondly, since the percentage improvements (shown in Fig. 8) consider single-key RTs in each condition as baseline, any differences in the mapping abilities would have been accounted for. Thus we can turn down the possibility that development of differential mapping capabilities completely accounts for the differences in RTs in *visual* and *motor* conditions in the sequence task.

Possibility 3. Acquisition of motor sequence representation

We are left with the final possibility that postulates acquisition of sequence representation in motor coordinates in the effector-sequencing specification module (Fig. 9). After having discarded arguments about effectiveness of mapping, faster RTs in *motor* condition may be due to the fact that this condition used identical finger movements to the *normal* condition. Further, since the percentage improvements in Fig. 8 take single-key RTs as baseline indices thus equalizing any mapping-related differences, it can be postulated that some form of sequence knowledge resides in the effector-sequencing specification module. The specification is possibly in an effector-specific coordinate frame (say, in motor coordinates) that affords special advantages to the *motor* condition selectively over the *visual* condition. This representation along with a direct visuo-motor mapping may lead to shorter RTs in the *normal* and *motor* conditions.

Apart from the current study, several previous results (Wright 1990; Jordan 1995) also point to effector dependent representation in sequential skills. However, in the current study we also present results about time course of development of both the effector dependent and independent representations and hypothesize about the possible neural bases for the representations. Wright (1990) studied handwriting with dominant and non-dominant hands. He pointed out that the similarities in handwriting observed across hands at the abstract level of shape of character support an effector independent representation. However, the possibility of effector-specific control strategy might not be ruled out when comparisons across hands were made between well-practiced handwriting such as one's own name and writing of patterns such as equations that are not so well practiced. Jordan (1995) studied transcription typing by switching two keys on a typewriter. Subjects relearned the switched keys in isolation without learning to type whole words on the switched typewriter. They exhibited decreased typing speeds and increased errors with the switched typewriter, more so for prose than for nonsense text. Jordan (1995) concluded that these results go against a strict effector independent representation hypothesis that would predict

equal decrements and supported effector specificity in the representation of motor skills.

Differential time course of learning of the two representations

We hypothesize that the recall accuracy observed in the *visual* condition reflects effective usage of the effector independent representation. Even in the *motor* condition when sufficient facility has not been developed with finger movements, subjects may have had to rely on an effector independent sequence representation. Recall accuracy was over 70% in both *visual* and *motor* conditions even by the early stage, pointing out that a significant amount of effector independent representation may have been acquired even at the early stage. This result suggests that effector independent representation may be acquired relatively quickly. Thereafter, recall accuracy improved in a parallel fashion in all the conditions from the early to the late stage by 11% in *normal*, by 14% in *visual*, and by 15% in *motor*. RT improvements, however, show a different picture. It is hypothesized that RT improvements in the *motor* condition reflect the acquisition of an effector dependent representation. As shown in Fig. 8, *visual* and *motor* conditions had similar improvements in the early stage (22 and 24%, respectively), but started differing in the intermediate stage (25 and 30%, respectively). By the late testing stage, the differences in improvement were very significant (29% in *visual* and 39% in *motor*). This result suggests that effector dependent representation may be acquired relatively slowly, although both the independent and dependent representations are learned concurrently. There are two aspects of effector dependent representation, visuo-motor mapping and motor sequence representation, and especially it is the latter aspect that is assumed to lead to faster RTs in sequence tasks. In other words, motor sequence (effector dependent) representation may develop rather slowly compared to visual sequence (effector independent) representation and affords advantage to conditions that use similar effector movements, thus verifying our hypothesis. In the results reported here, subjects practiced a sequence for about 1 h. We may see more differences in the RTs, if the practice time is extended, say to many days. Overall, the results reported here support the hypothesis proposed by Nakahara et al. (1997).

Differential neural bases for effector independent and dependent representations

The difference in time course of learning of the two representations may account for the differential involvement of brain areas in early and late learning phases observed both in studies on monkeys (Miyashita et al. 1996; Miyachi et al. 1997) and in imaging studies on humans in fMRI (Karni et al. 1995; Hikosaka et al. 1996a; Sakai et al. 1998). There are studies in positron emission tomography (PET; Jenkins et al. 1994; Jueptner et al. 1997a,b) that found differences in the brain areas involved in learning of new sequences as compared to performance of prelearned sequences. Miyachi et al. (1997) observed functional differentiation by injecting muscimol in the anterior and posterior parts of the basal ganglia in monkeys. Blockade of the anterior striatum (caudate head and rostral putamen) significantly affected learning of new sequences while a blockade of posterior striatum affected recall of well-learned sequences. Similarly, a blockade of the pre-SMA significantly affected acquisition of new sequences and that of the SMA mildly affected the performance of well-learned sequences (Miyashita et al. 1996). In an fMRI study on humans, Hikosaka et al. (1996a) observed selective activation of the pre-SMA during acquisition of new sequences and that of the SMA during performance of sequential movements but not in learning. Both Jenkins et al. (1994) and Jueptner et al. (1997a,b) conducted PET studies on humans using a finger-sequence learning paradigm. Jueptner et al. (1997a) observed a shift of activation from the anterior (the dorsolateral prefrontal and the pre-SMA) to the posterior regions (the SMA and the primary motor) of the frontal cortex when new learning is compared with recall of well-learned sequences. Jueptner et al. (1997b) observed similar shifts of activation in the subcortical areas, from the anterior to the posterior basal ganglia. Similarly, Sakai et al. (1998) observed activation of distinct brain areas in different learning stages in a motor sequence learning task. Their results indicated that the dorsolateral prefrontal cortex (DLPFC) is activated in the early stage, the pre-SMA in the early and intermediate stages, the precuneus in the intermediate stage, and the intraparietal sulcus in the intermediate and advanced stages.

Karni et al. (1995, 1998) performed fMRI scanning at regular intervals over a period of 5 weeks while subjects practiced finger-to-thumb opposition sequences. Based on the results, they proposed that skilled motor performance progressed in several stages. The initial stage is characterized by the habituation of the evoked response in M1 with repeated trials. This is followed by a fast learning period in the first session during which the sequence of movements becomes more accurate and the evoked response increases for repeated sequences. Karni et al. (1995, 1998) attributed the change in the processing mode from habituation to fast learning to the changes in inputs received by M1. The enhancement in evoked response continues during the final slow learning stage that ranges over weeks. Eventually, the cortical area responding to a well-practiced sequence becomes more enhanced than for an unpracticed control sequence. Karni et al. (1998) proposed that the neural substrate mediating the initial and later improvements may be different and that M1 might constitute a site for long-term memory of motor skills. Results from our study are in basic agreement with Karni et al.'s (1995, 1998) proposal for the multiple stages of sequence representation and further allow us to consider the nature of those representations in

more detail. By using the same sequence in two different recall settings, effector independent and dependent, we demonstrated that effector independent representation is acquired during the early phase and effector dependent representation in the later phase of skill learning. Thus a switch in processing mode may actually reflect a switch in the type of representation acquired, visuo-spatial vs body-based representation. It remains to be seen whether the representational-switch hypothesis and the neural bases of representations can be verified in fMRI tests using our experimental paradigm. Recently, Grafton et al. (1998) used implicit sequence learning in the serial reaction time paradigm to test transfer of sequence learning from a small keyboard to a large keyboard. Based on the results from PET activation, they argued that while the inferior parietal cortex encoded sequences at an abstract level, the primary sensorimotor cortex encoded in an effector-specific fashion. In the results reported here in the current study, we have studied such representations using an explicit sequence learning paradigm.

We propose here possible cortical localization of various modules and mappings in Fig. 9 and refer to relevant previous studies that inspired our hypotheses. Visual sequence representation is assumed to be in the posterior parietal association cortex (PPC; Jenkins et al. 1994; Jueptner et al. 1997a; Grafton et al. 1998). Response sequence representation is assumed to be in the DLPFC and the pre-SMA (Jenkins et al. 1994; Shima et al. 1996; Jueptner et al. 1997a; Sakai et al. 1998). The cortico-cortical connections (PPC-to-DLPFC and DLPFC-to-pre-SMA) subserve the function of visuo-spatial mapping. The ventral and dorsal premotor cortex are assumed to provide the substrate for spatial-motor and visuo-motor mapping, respectively (Di Pellegrino and Wise 1993). The M1 and the SMA are assumed to be the sites for motor sequence representation (Karni et al. 1995; Tanji 1996; Grafton et al. 1998). The anterior and the posterior basal ganglia (the caudate nucleus and the putamen) participate in visuo-spatial and motor sequence processing, respectively (Jenkins et al. 1994; Jueptner et al. 1997b; Miyachi et al. 1997). Different parts of the cerebellum participate in different mappings depending on their target cortical areas (Jenkins et al. 1994; Lu et al. 1996; Jueptner et al. 1997b). These hypotheses of anatomical localization and time course of activation can be verified directly in fMRI experiments using the current 2×10 paradigm of motor sequence learning and transfer to novel conditions.

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