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Motor sequence chunking is impaired by basal ganglia stroke

L.A. Boyd [a,b,c,d,*], J.D. Edwards [e], C.S. Siengsukon [c], E.D. Vidoni [f], B.D. Wessel [a], M.A. Linsdell [d]

[a] Department of Physical Therapy, University of British Columbia, Vancouver, British Columbia, Canada
[b] Brain Research Centre, University of British Columbia, Vancouver, British Columbia, Canada
[c] Department of Physical Therapy and Rehabilitation Sciences, University of Kansas Medical Center, Kansas City, KS, United States
[d] Graduate Program in Rehabilitation Sciences, University of British Columbia, Vancouver, British Columbia, Canada
[e] Graduate Program in Epidemiology, University of British Columbia, Vancouver, British Columbia, Canada
[f] Department of Neurology, University of Kansas Medical Center, Kansas City, KS, United States

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ABSTRACT

Our main aim was to determine whether individuals with stroke that affected the basal ganglia, organized movement sequences into chunks in the same fashion as neurologically intact individuals. To address this question, we compared motor response times during the performance of repeated sequences that were learned, and thus may be planned in advance, with random sequences where there is minimal if any advance preparation or organization of responses. The pattern of responses illustrated that, after basal ganglia stroke, individuals do not chunk elements of the repeated sequence into functional subsequences of movement to the same extent as neurologically intact age-matched people. Limited chunking of learned movements after stroke may explain past findings that show overall slower responses even when sequences of action are learned by this population. Further, our data in combination with other work, suggest that chunking may be a function of the basal ganglia.

1. Introduction

Motor learning is preserved after numerous types of brain damage and disease, including stroke (Boyd, Quaney, Pohl, & Winstein, 2007a; Boyd & Winstein, 2003, 2004a, 2004b), amnesia (Knowlton, Mangels, & Squire, 1996), brain injury (Gomez-Beldarrain, Grafman, Ruiz de Velasco, Pascual-Leone, & Garcia-Monco, 2002), Parkinson's disease (Harrington, Haaland, Yeo, & Marder, 1990), and Alzheimer's disease (Knopman & Ryberg, 1989). The maintenance of the ability to acquire new motor skills despite brain damage and disease has been attributed to the distributed nature of the neuroanatomic regions that support this form of learning (Poldrack & Packard, 2003; Poldrack et al., 2005; Reber, Stark, & Squire, 1998; Squire, 1987, 1992). These include the cerebellum, basal ganglia, and motor cortical areas (ie., primary motor cortex, supplementary motor area, premotor cortex) (Squire, 1987). Disruption of one portion of the neural network that supports motor learning is not without penalty (Boyd & Winstein, 2003, 2004a, 2004b; Boyd et al., 2007a), but the ability to acquire new motor skills is rarely abolished by brain damage.

Learned motor sequences are performed with specific patterns of timing that are considered to reflect the processes of organizing the individual movements within the brain (Nissen & Bullemer, 1987; Rosenbaum, 1983; Sakai, Kitaguchi, & Hikosaka, 2003). The organization of individual motor elements within a larger sequence illustrates that one feature of learned movements is the chunking of elements into sub-sequences (Miller, 1956). This hierarchical organizational of learned responses facilitates efficient production of sequential movements, as processing for all but the first response can be completed before the movement begins (Rosenbaum, Kenny, & Derr, 1983).

In neurologically intact individuals, motor learning is indexed as faster or more accurate movements at a delayed retention test that is separate from practice (Boyd, Vidoni, & Siengsukon, 2008; Nissen & Bullemer, 1987). Individuals with stroke also demonstrate improved response timing (Boyd & Winstein, 2003, 2006; Boyd et al., 2007a), error rates (Boyd & Winstein, 2006) and movement accuracy (Boyd & Winstein, 2006, 2004a, 2004b) associated with motor learning. However, learned motor responses are never as fast or accurate after stroke when comparisons are made to age-matched healthy individuals (Boyd & Winstein, 2003, 2004a, 2004b; Pohl & Winstein, 1999; Pohl, Winstein, & OnlaOr, 1997; Velicki, Winstein, & Pohl, 2000; Winstein, Merians, & Sullivan, 1999). Slower and less accurate learned responses are not solely related to impaired motor execution after stroke; these differences are apparent even when individuals with stroke use their non-

* Corresponding author. Address: Neurobiology of Motor Learning, University of British Columbia, 217-2277 Wesbrook Mall, Vancouver, British Columbia, Canada V6T 2B5. Fax: +1 604 822 1860.
E-mail address: lara.boyd@ubc.ca (L.A. Boyd).

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hemiparetic arm for responses (Pohl et al., 1997). One possible explanation for the difference in response characteristics between individuals with stroke and age-matched neurologically intact people may be how the two groups organize and plan learned movements.

The concept that individual memory items may be grouped into larger, single processing units or "chunks" was first proposed by Miller (Miller, 1956). Since then, numerous investigations have demonstrated that learning sequences of individual movements involves chunking or clustering sets of responses (Sakai et al., 2003; Shea, Park, & Braden, 2006). Chunking representations of movements into fewer, yet larger, responses allows the respondent to overcome the limitations of working memory by forming a hierarchical structure for multiple memory items (Sakai et al., 2003). The use of chunks in serial behavior is noted when a structure is externally imposed (Koch & Hoffmann, 2000; Povel & Collard, 1982; Stadler, 1993) and also emerges spontaneously through task practice (Sakai et al., 2003; Shea et al., 2006). Critically, chunking makes processing of visuomotor sequences more efficient; each chunk is treated as a single memory unit which allows longer or more complex sequences to be learned, and their expression to be optimized (e.g., faster, fewer errors), through the linking of individual chunks (Sakai et al., 2003). Taken together, it appears that chunking facilitates faster, more efficient movements during the execution of learned visuomotor sequences.

Multiple brain regions have been identified for learning motor sequencing tasks. To date, only a few studies have considered the neural substrates associated with chunking of these responses. The performance of well-learned sequences is impaired by inactivation of the posterior putamen (Miyachi, Hikosaka, Miyashita, Karadi, & Rand, 1997). Similarly, individuals with Parkinson's disease show poor motor sequence production, (Harrington & Haaland, 1991) and abnormal reaction time costs on tasks involving switching between perceptual domains (Hayes, Davidson, Keele, & Rafal, 1998; Shook, Franz, Higginson, Wheelock, & Sigvardt, 2005). Motor sequence deficits have also been observed in individuals with basal ganglia stroke (Boyd & Winstein, 2003; Boyd et al., 2007a; Vakil, Blachstein, & Soroker, 2005; Vakil, Kahan, Huberman, & Osimani, 2000). Failure to express and/or form chunked responses may explain motor learning deficits that become apparent after basal ganglia damage (Graybiel, 1998). Blocking striatal type-2 dopamine receptors with the drug raclopride significantly affects new sequence learning in monkeys (Levesque et al., 2007) inducing fluctuations in performance across individual elements (Tremblay et al., 2008). Specifically, raclopride-induced performance fluctuations appear to be related to the inability to cluster individual movements into larger chunks. These data suggest that dopamine is integral to motor sequence learning, perhaps via the linking of individual learned movements. Because basal ganglia function is reliant on dopamine (Cavada & Goldman-Rakic, 1989), in the current study, we tested the premise that this region is integral for chunking of learned motor sequences by examining a group of individuals with stroke that affected the basal ganglia.

The present study investigated whether impaired ability to group or "chunk" individual elements of a sequence of movements during learned motor sequences explains the slower responses that are shown by individuals with stroke when they use their non-hemiparetic arm. Our main goal was to determine whether individuals with stroke involving the basal ganglia organized movement sequences with the same efficiency as age-matched neurologically intact healthy controls. We capitalized on the definition of a chunked response from past work (Sakai et al., 2003; Shea et al., 2006) that identified a chunk as a cluster of significantly faster responses (i.e., shorter response times (RT)) that follow a longer response. Presumably, the longer RTs associated with the first response in a chunk reflects the time to plan both the first and subsequent movements (Shea et al., 2006). The following faster responses are therefore pre-planned, and thus their RTs index time to execute the movement but not to prepare for it. We expected that contrasting chunking during learned repeated sequences of responses with responses from random sequences, which cannot be predicted, pre-planned or chunked, would reveal differences in the organization of learned movements between individuals with basal ganglia stroke and age-matched healthy control participants.

2. Methods

2.1. Participants

Thirteen individuals with chronic (>6 months post onset) middle cerebral artery (MCA) stroke (ST) involving the basal ganglia and 13 age-matched healthy controls (HC) participated in this study. The chronic phase of stroke is typically defined as 6+ months after onset, when cerebral edema and inflammation have subsided (Jorgensen, Nakayama, Raaschou, & Olsen, 1995a; Jorgensen et al., 1995b, 1995c). All participants in the HC group were free from neurological damage; subject demographics are presented in Table 1. 12 of 13 participants in each group were right-hand dominant, one in each group was left-hand dominant. To minimize the effect of motor execution deficits on response speed, all testing was completed with the non-hemiparetic hand; owing to lesion location 12 of the 13 participants (11 right-hand dominant and one left-hand dominant) in each group used their dominant hand to complete testing. Each individual provided institutionally approved informed consent; all participants were also screened for dementia using the Mini-Mental State Exam (MMSE) and hand dominance using the Edinburgh Inventory (EI). Participants were not enrolled if (1) they scored below the 25th percentile on the MMSE using age adjusted norms (Crum, Anthony, Bassett, & Folstein, 1993), (2) they were in the HC group and exhibited any frank or clinically evident signs of neurological impairment or disease (Lundy-Ekman, 1998), or (3) they had any orthopedic condition or color blindness that would impair response ability. In total, twenty-six individuals were recruited from the University of British Columbia, the local community and the Brain Behavior Lab database.

Table 1
Participant demographics.

	Age	Sex	Hand used[a]	MMSE	Digits backwards	Digit symbol-coding	Time post stroke	Fugl-Meyer	Orpington score
HC	59.6	8 F	2 L	29.8	6.2	66.7	–	–	–
	(15.5)	5 M	11 R	(.6)	(1.4)	(11.8)			
ST	59.4	5 F	2 L	28.3	5.7	47.0[b]	59.6	33.5	2.8
	(15.9)	8 M	11 R	(2.0)	(1.8)	(12.7)	(52.9)	(17.6)	(.67)

F=Female, M=Male. L=Left, R=Right. MMSE=mini-mental status exam. Upper extremity Fugl-Meyer motor score are for the hemiparetic arm. Range 0–66; higher scores denote less arm motor impairment. Orpington score < 3.2 indicates mild stroke. Data are mean (standard deviation) and time is in months.

[a] 12 of 13 participants in each group were right-hand dominant, one in each group was left-hand dominant; owing to lesion location 12 of 13 used their dominant hand to complete testing.

[b] Digit symbol-coding was significantly different between groups $p = .001$.

2.2. Lesion location

To verify that the basal ganglia comprised a primary and common area of damage in the stroke group, we obtained diagnostic images for the majority of individuals with stroke in this study (11 of 13). Owing to contraindications to MR in some individuals (e.g., metal clips, claustrophobia) 5 of the 11 brain scans were performed using CT; the other six were MRI scans. Using MRIcro (Rorden, 2003) masks of each clinical lesion were drawn to illustrate the extent and location of brain damage (Fig. 1). One patient (Subject 4) was excluded from the figure due to poor image resolution that resulted from head motion during scanning. However, chart data for this individual indicated damage to the subcortex. Images for two other patients (Subjects 5 and 10) could not be obtained and these individuals could not tolerate scanning owing to contraindications. However, individual medical records identified the caudate as site of the lesion location for Subject 5, and the subcortical MCA territory for Subject 10. Further, a board certified neurologist (RH) reviewed our images and chart histories, and confirmed basal ganglia involvement in each participant in the stroke group.

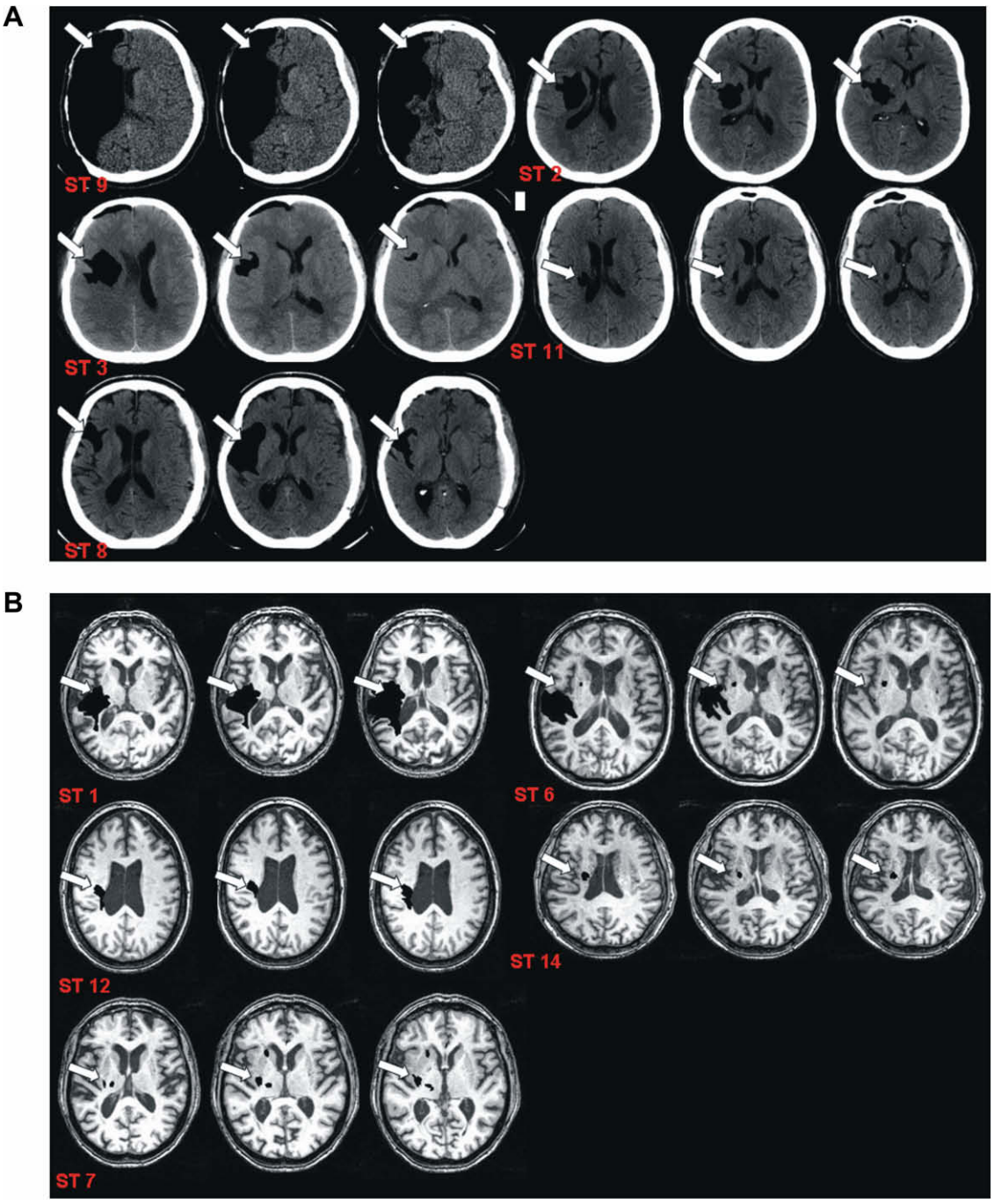

Fig. 1. Lesion location for 10 of 13 members of the ST group; three central images illustrating location are shown for each participant. Distance between slices was 5 mm. Lesions are outlined in black and highlighted with white arrows. (A) CT scans ($n = 5$). (B) MRI scans ($n = 5$).

2.3. Neuropsychological and physical impairment testing

To evaluate whether slowed response times in individuals with stroke resulted from impairments in working memory or information processing speed, and to rule out individuals with disorders of cognition, all participants underwent a series of neuropsychological tests. These included a dementia rating scale, the MMSE (see above); a working memory assessment, digits backwards; and a digit symbol-coding test assessing information processing speed. Participants' physical impairment level was determined via the Fugl-Meyer upper extremity motor scale. Finally to evaluate stroke severity, the Orpington Prognostic scale was completed.

2.4. Task

Participants were instructed to watch the computer screen for a color to appear and respond as quickly and as accurately as possible by pressing the like-colored key. Stimuli were presented one at a time within six circles arranged equidistant from each other and from a centered fixation-cross (Fig. 2). At predetermined intervals, one circle would fill with a color (red, yellow, blue, or green), prompting the participant to respond with the appropriate key press. The number of presentations for each of the positions and colors was the same across trial blocks. Stimuli appeared after a variable inter-stimulus interval period that ranged unpredictably from 250–1000 ms, or after 2500 ms if no response occurred. Individuals with stroke used their non-hemiparetic arm (11 right, 2 left); those in the HC group were matched for arm use (11 right, 2 left). To prevent chunking between the end of one sequence and the beginning of another the sequence was clearly marked; following completion of a 12 stimuli set, a fixation-cross flashed on the screen for 250 ms before the next set of responses began.

Participants completed two days of task practice and returned on a third day for retention testing; each day of testing took approximately 30 minutes. Participants received $90 total to offset the travel and parking costs associated with their participation in this research. The position and color of the stimuli were determined as follows. Days 1 and 2 were identical; all participants completed 6 blocks of 120 responses each. The first block consisted of 120 pseudo-random stimuli (i.e., no consecutively repeated colors or positions). Blocks 2 through 6 were comprised of a 12-element sequence repeated 10 times in each block. The sequence was designed to contain no more than one trill (e.g., Red, Green, and Red), have no repeating positions or colors, and had an arrhythmic stimulus onset that repeated across sequence trials. The repeated sequence followed the same motor (i.e., finger movements) and spatial (i.e., monitor position) pattern over each 12-element trial and a fixation-cross-appeared between each trial. Participants were not made explicitly aware of the presence of a repeating sequence in their responses prior to practice. All participants practiced the same 12-element repeating sequence for all repeating sequence trials.

To evaluate motor learning associated with repeated sequence practice, all participants completed a sequence retention test on the third day. The retention block employed the same repeated sequence that was practiced on Days 1 and 2. Throughout this study, if participants inquired or commented about the presence of a repeating sequence no direct response was provided; subjects were told only to use whatever task characteristics she/he felt improved their response time.

A custom computer software program (Boyd, 2006, Presentation software platform, NeuroBehavioral Systems Inc., v9.51[1]) controlled the presentation of stimuli and recorded RT.

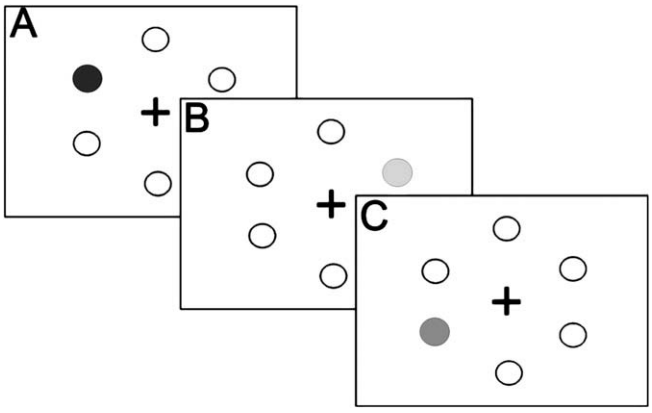

Fig. 2. Schematic of the experimental task. Stimuli for movement were indicated by a color filling one of six circles; in this schematic the colors are represented in grayscale. Responses were made by pressing the corresponding colored key. (A) Element 1 of the repeating sequence, (B) element 2, and (C) element 3, etc.

2.5. Assessment of explicit knowledge

After the conclusion of retention testing, three levels of explicit knowledge were tested: subjective awareness of the existence and composition of the sequence, recognition memory, and recall memory. Asking participants if they noticed anything about the task tested subjective memory. Recognition memory tests determined if participants were able to correctly identify the repeated sequence after watching it played on the screen. A color recall test was given by separately showing fragments (i.e., 4 of the 12 elements of the repeated sequence) of the repeated sequence. Participants were asked to predict which element of the repeated sequence would come next. Table 2 provides the instructions and details of explicit knowledge tests.

2.6. Outcome measures

Response time (reaction time + movement time; RT) is the time from stimulus onset to key press, and was measured and stored for each trial. As is standard procedure in serial reaction time (SRT) task data analyses (Boyd & Winstein, 2003; Boyd et al., 2007a; Nissen & Bullemer, 1987), we calculated the median RT for each 12-element sequence trial. Calculation of median RT values for each sequence trial reduces the sensitivity of this measure to very large or small values. Because RT data can be highly variable, the use of median RT as an outcome measure reflects a more conservative approach to data management (Rosen, 2000). Response times were summarized by calculating the mean and median for each block of 12 trials (Boyd, Quaney, Pohl, & Winstein, 2007b; Nissen & Bullemer, 1987). This procedure was performed for both random and repeated sequences. Trials exceeding two standard deviations from the mean were excluded from analyses (Keppel, 1991). Premature and absent responses constituted less than 1% of total responses and were not dependent on practice and were excluded performance measures.

Based on past work investigating chunking responses during motor learning, we defined a chunk as a cluster of significantly faster responses (i.e., shorter RTs) that followed a longer response (Sakai et al., 2003; Shea et al., 2006). Presumably, the longer RT associated with the first response in a chunk reflects the time to plan the entire response (Shea et al., 2006). The subsequent faster responses that follow are therefore pre-planned, and thus their RTs index time to execute the movement but not to prepare for it. Be-

[1] Neurobehavioral Systems, Inc., 828 San Pablo Avenue, Suite 216, Albany, CA 94706.

Table 2
Explicit knowledge test conditions and questions.

Explicit test condition	Explicit test questions	
Subjective awareness	"Did you notice anything about the task?"	If yes, "What was it?" If no, "There was a repeating sequence. Can you tell me what it was?"
Recognition memory	Watch 10 sequences:3 True 7 False	"Is this a sequence that you recognize?"
Color recall memory	Display 10 separate 4-element sequence fragments (i.e., response 6, 3, 5, 1-?)	"Which element comes next?" (forced choice)

cause random responses cannot be chunked due to the inability to predict and then plan ahead for the next response, RTs from individual elements derived from our random sequences were compared to the elements of our repeated sequence to illustrate chunked sub-sequences as they emerged.

2.7. Statistical analyses

2.7.1. Acquisition practice

Performance of the repeated sequence during practice was examined using a two-factor (Group [HC, ST] X Block [2–6, 8–12]) repeated measures ANOVA with absolute RT as the dependent variable. Only data from the first two days of acquisition practice were included in this analysis; retention test data were considered separately (see below). Random sequence performance was assessed in the same way (Group [HC, ST] X Random Blocks [1, 7] repeated measures ANOVA). Baseline motor demands of the two sequence types were evaluated with a two-factor Group [HC, ST] X Block [Random Block 1, Repeated Block 2] repeated measures ANOVA.

2.7.2. Retention

Motor learning at retention was examined via a Group [ST, HC] by Sequence [Random, Repeated] repeated ANOVA.

2.7.3. Chunking

To assess the chunking of elements, we first conducted an exploratory cluster analysis (Everitt, 1993), to identify groups of elements (i.e., chunks) within the sequence that were similar to one another based on the response time variable. First, subtracting RTs of individual elements in random sequences from the elements in repeated sequences for each participant derived a change score variable. Since we had no a priori estimate of the number of clusters that would be present in each sequence (HC vs. ST), we employed a hierarchical approach to these analyses (Everitt, 1993). We applied a hierarchical agglomerative clustering algorithm to iteratively merge smaller clusters into larger clusters, based on a specified measure of proximity (Fukuoka, Lindgren, Rankin, Cooper, & Carroll, 2007). As the element variable was the unit of analysis, variable clusters were identified using absolute values of the Pearson correlation coefficient as the measure of similarity. With 12 elements in the sequence, the range of clusters was defined as a minimum of 2 to a maximum of 12 (i.e., one for each element). To combine clusters at each stage, we used Ward's Method (Ward, 1963), which first calculates the means for all variables and then generates and sums the squared Euclidean distance to the cluster means. At each stage, clusters with the smallest increase in summed distance are merged. This analysis yielded a number of potential variable cluster solutions, ranging from 12 to 2 groups of variables. Although one of the limitations of cluster analysis is the subjective selection of the optimal solution (Overall & Magee, 1992), we used a combination of the distance between the values of coefficients in the agglomeration schedule (Mojena & Wishart, 1980) and inspection of the icicle plot for the variable cluster that appeared to be the most consistent across all clustering stages, to identify the optimal solution for our analysis.

To determine if these clusters represented significant groupings of elements (i.e., chunks), we next conducted paired *t*-tests to pinpoint the locus of significant differences in individual elements for the two response types. Because random sequences cannot be chunked, significant differences between the two response types revealed elements of the repeated sequence that were grouped together. Paired *t*-tests were performed between an average random measure for each element (Day 1 random + Day 2 random + Day 3 random/3) and mean RTs from each of the 12 sequence elements from the first practice block and the retention block. To account for multiple *t*-tests in this procedure we employed a Bonferroni correction, resulting in a corrected critical *p*-value of $p = .004$.

Once significant chunks were identified, we then sought to confirm that the basal ganglia played an integral role in the process of chunking during motor sequence learning. As described above, previous work has shown that response times for the first element in a chunk may reflect the time to plan the entire response, while subsequent, faster, responses to elements in the sequence may represent the time to execute the movement (Shea et al., 2006). Thus, we would expect that, if damage to the basal ganglia is associated with differences in the ability to chunk motor sequences, response times would differ for initial vs. final sequence elements in individuals with stroke compared to healthy participants. Due to unequal variances, we conducted a Mann-Whitney test between the groups, to compare reaction times for the initial elements within each "chunk" and we conducted an independent samples *t*-test between groups, examining reaction times for the final elements within each chunk. Importantly, only those individuals with confirmed basal ganglia lesions (from Fig. 1) were included in these analyses.

3. Results

3.1. Acquisition practice: performance related changes in behavior

Both groups demonstrated improved performance for the repeated sequence, with evidence for task practice shown by a reduction in absolute RT across the acquisition period (Main Effect of Block, $F(9,216)=17.454$, $p < .001$; Fig. 3). However, the ST group made less overall change across practice, as shown by a significant Group by Block interaction ($F(9,216)=1.870$, $p = .050$). Response times for random sequences were not different between the two groups ($p = .202$; Fig. 3). Finally, the basic motor demands of the two sequences types (random, repeated) were not statistically significantly different ($p = .192$) as shown by comparison of initial performance (block 1) of random and repeated sequences.

3.2. Retention tests: learning related changes in behavior

Motor learning was shown by a Main Effect of Block (Fig. 4) that confirmed that both groups were faster for repeated as compared to random sequences at retention ($F(1,24)=39.754$; $p = .001$).

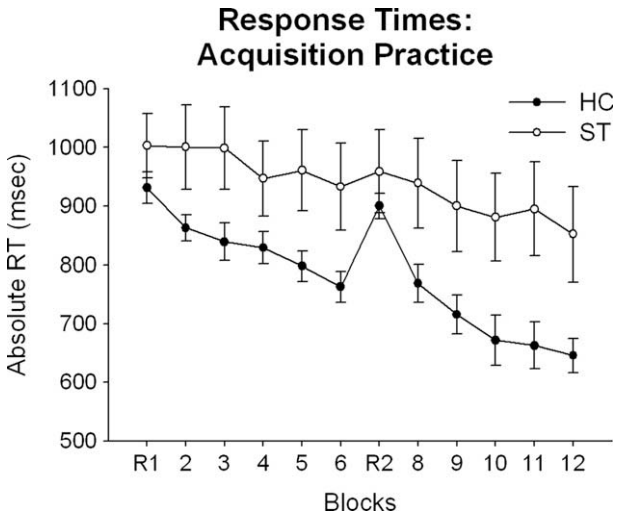

Fig. 3. Absolute RTs across practice for random (R1 performed at Block 1 and R2 performed at Block 7) and repeated sequence blocks (2–6, 8–12). Both groups showed improved performance; however, the HC group was faster for repeated but not random sequences across practice. Error bars are standard error of the mean.

3.3. Chunking: organization of movement sequences

Despite both groups showing sequence-specific learning, individuals in the HC group demonstrated faster sequence RTs at retention as compared to the ST group. To account for this finding, we examined if the ability to chunk or organize individual elements from movement sequences into sub-sequences influenced the speed of responding at retention. The HC group showed minimal chunking in the first practice block (Fig. 5A), with one chunk of information, 2-elements in length emerging at the beginning of the sequence. In contrast, the ST group did not demonstrate chunking of any elements at the first practice block (Fig. 5B). At retention testing, the HC group demonstrated more and longer chunked sub-sequences; 10 of 12 individual responses chunked into four sub-sequences (two 3-elements long, and two 2-elements long; Fig. 5C). Individuals in the ST group demonstrated low levels of response organization; only three small chunks were evident (three 2-elements each; 6 of 12 individual responses chunked; Fig. 5D).

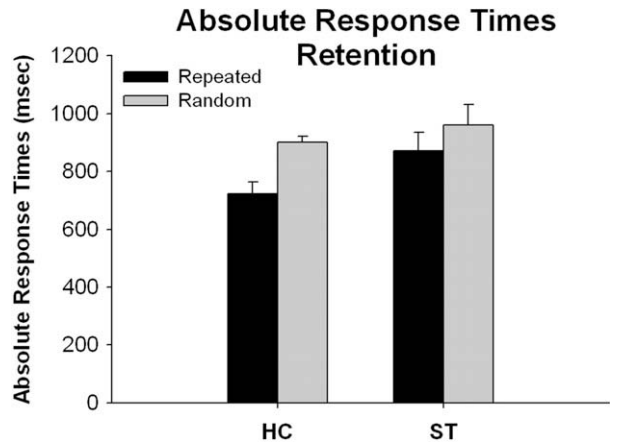

Fig. 4. Absolute RTs for repeated and random sequences at retention for both groups. A main effect of block confirmed faster RTs for repeated sequences for both groups. Despite having learned the repeated sequence, the ST group responded slower during repeated sequences at retention as compared to the HC group. Error bars are standard error of the mean.

The results of the hierarchical cluster analyses and paired *t*-tests provided additional support for the existence of chunking in the HC group (Table 3). In the HC group, the agglomeration schedule showed a sharp decrease in the value of coefficients from the 5th to the 4th stage of clustering (2.024–1.756) and the icicle plot revealed the consistent clustering of similar variables across several clustering stages, identifying 4 main groups of elements (i.e., chunks). We thus determined that the optimal cluster solution involved 4-element clusters. Results of the cluster membership and icicle plot revealed that, consistent with the individual element response time data in Fig. 5A–D, a clear pattern of clusters emerged (Table 4). By contrast, results of the cluster membership and icicle plot in the ST group showed no evidence of patterns of element clusters.

Paired *t*-tests revealed that healthy controls showed observable grouping of elements during the retention block, with significant differences observed for elements 1–3 and 5, and elements 9, 11, 12 at retention (Table 3). These results are consistent with the clusters identified in the cluster analysis and suggest that the groups of elements showing a longer response time followed by one or more significantly faster response times represent functional sub-sequences of movement. In contrast, individuals in the ST group appeared to chunk some elements into sub-sequences during retention, although to a much lesser extent, with significant differences observed only for elements 3, 6, and 11. Taken together, these results suggest that healthy participants employed a chunking strategy, organizing elements into chunks to optimize task efficiency during a learned visuomotor sequence, while individuals in the ST group displayed a reduced ability to organize or 'chunk' individual elements from a movement sequence into functional sub-sequences.

Results of the independent samples *t*-test indicated that individuals with stroke involving the basal ganglia displayed significantly slower response times for the final elements within motor sequence chunks ($t(73) = -3.46$, $p = .001$), but the Mann-Whitney test indicated that no difference in response times occurred between the groups for the initial chunk elements ($Z = -.65$, $p > .05$). These data offer support for a relationship between the basal ganglia and the chunking of elements involved in the execution of motor sequences.

3.4. Neuropsychological testing

The ST group performed significantly worse on digit symbol-coding than the HC group ($t(23) = -4.164$, $p = .001$), indicating poorer digit symbol-coding capacity. There was no statistically significant difference between the groups for working memory performance indexed by digits backwards or on the dementia rating scale, MMSE (Table 1). A strong correlation ($r^2 = .60$; $p = .003$) was found between digit symbol-coding ability and absolute RT at retention in the ST group; no relationship was noted between digit symbol-coding and HC group performance ($p = .913$).

3.5. Assessment of explicit knowledge

At the conclusion of testing, 11 of 13 (84.6%) individuals with stroke and 10 of 13 (76.9%) healthy controls subjectively recognized that a pattern was present in the learning task. For recognition testing, participants were deemed to have learned the task if they were explicitly able to correctly identify 2 of the 3 (66%) 'true' motor sequences that they had practiced before and 4 of the 7 (57%) 'false' motor sequences that they had not previously been exposed to. Both groups of participants were able to recognize which sequences were true and which were false with at least 66% accuracy (Table 4; $p = .412$). For the color recall test, there were no significant differences between the groups (Table 4; $p = .241$).

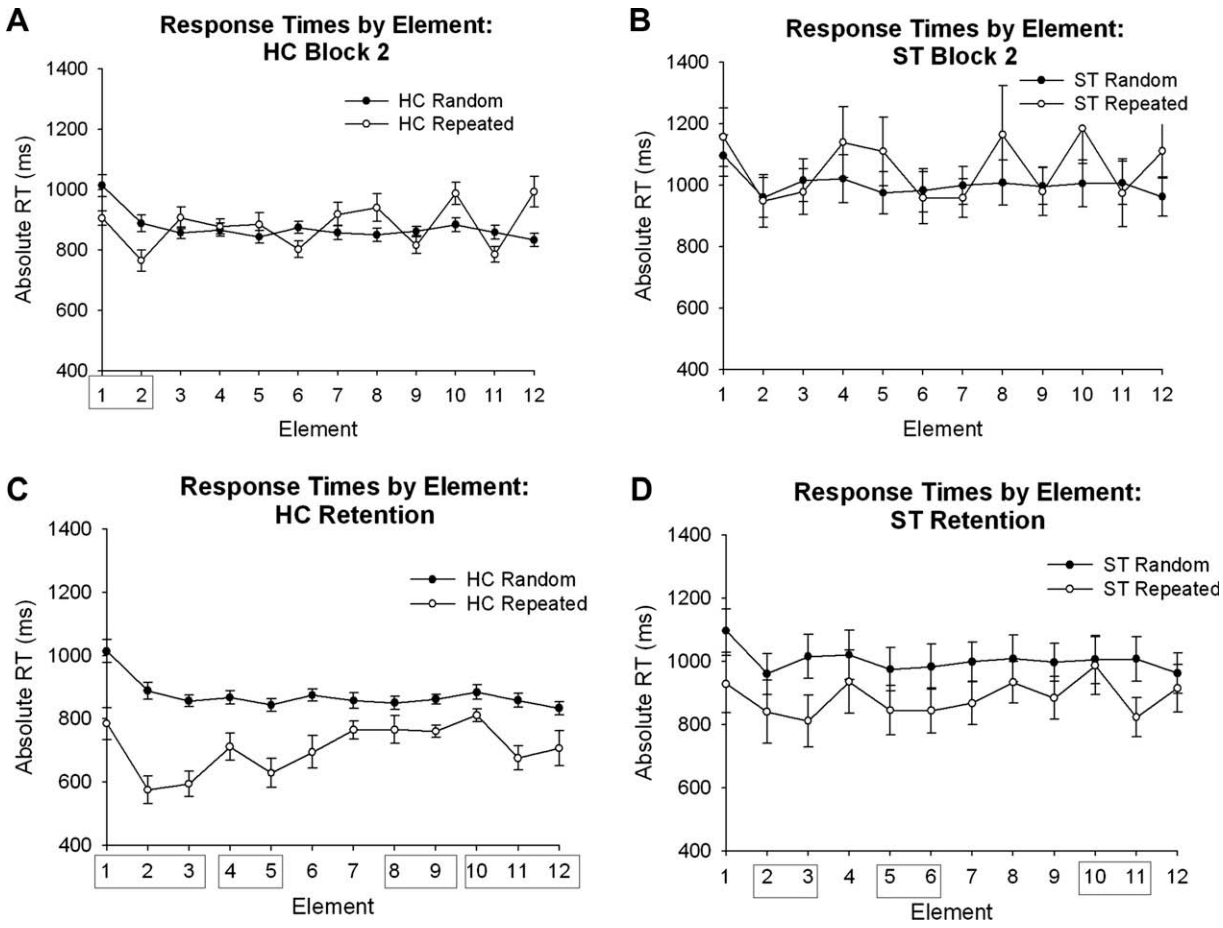

Fig. 5. Element analyses for block 1 of practice and also for retention. Chunked responses are outlined in squares on the *x*-axis. (A) HC repeated and random sequence performance at block 1, (B) ST repeated and random sequence performance at block 1, (C) HC repeated and random sequence performance at retention, and (D) ST repeated and random sequence performance at retention. Error bars are standard error of the mean.

Table 3
Cluster membership identified by cluster analyses and *p*-values from paired *t*-tests for elements in the movement sequence during practice and retention task blocks for HC and ST.

Element	Control			Stroke		
	Cluster membership	*p*-value		Cluster membership	*p*-value	
		Practice	Retention		Practice	Retention
1	1	**.000**	**.001**	1	.444	.026
2	1	**.003**	**.000**	2	.861	.068
3	1	.127	**.000**	3	.376	**.001**
4	2	.619	.005	1	.240	.084
5	1	.147	**.001**	2	.042	.007
6	2	.015	.006	4	.583	**.001**
7	2	.107	.005	3	.459	.005
8	2	.022	.063	1	.169	.102
9	2	.057	**.000**	1	.789	.046
10	4	**.003**	.005	3	.007	.690
11	4	.018	**.001**	4	.657	**.000**
12	4	.036	**.001**	2	.005	.404

Bolded items show tests that survived our corrected *p*-value and are significantly different indicating chunking. Practice data are from the first block of the repeated sequence (block 2) on day 1; retention data are from the retention test on day 3.

4. Discussion

We were interested in determining whether individuals with stroke that affected the basal ganglia organized movement sequences with the same efficiency and manner as age-matched, neurologically intact healthy controls. Our approach was to compare RT performance for repeated sequences that were learned and thus may be planned in advance and effectively organized, with random sequences where there is minimal, if any, advance preparation and organization of responses. Sequential tasks offer an important window into the organization of learned responses as analyses of the transitions between individual elements allows the identification of chunks or sub-sequences of movements (Miller, 1956; Rosenbaum et al., 1983; Sakai et al., 2003). The pattern of

Table 4
Recognition and recall memory scores from explicit testing.

	ST	HC
Recognition memory		
% Correct recognition true	66.7	82.1
	(40.8)	(22.0)
% Recognition false	68.1	83.3
	(30.4)	(20.9)
Color recall memory		
% Recall correct color	51.5	51.6
	(20.4)	(15.9)

There were no significant between group differences for explicit testing. Data are presented as mean (standard deviation).

individual element durations illustrates the organizational structure of the sequence (Povel & Collard, 1982) and the overall reduction in performance time for repeated sequences as compared to random sequences indexes the effectiveness of the structure that has been imposed (Shea et al., 2006). In our analysis, we discovered that after basal ganglia stroke, individuals do not chunk individual elements of their overall response into functional sub-sequences of movement to the same extent as neurologically intact age-matched people. Limited chunking of learned movements after stroke, may explain past findings (Boyd & Winstein, 2003; Boyd et al., 2007a; Pohl & Winstein, 1999; Winstein et al., 1999) that show overall slower responses even when sequences of action are learned.

Importantly, baseline differences in motor execution speed do not explain the disparate performance of individuals in the ST and HC groups in our element analysis. Our data illustrate this point in two ways. First, RT for random sequences was comparable across our experimental groups (Fig. 3). The similarity in random sequence RTs between groups demonstrates that it is sequence organization as opposed to a generalized impairment in motor execution after stroke that explains between group differences at retention. Second, early in practice (i.e., Random Sequence in Block 1 versus Repeated Sequence in Block 2) before learning has taken place, there was no difference between random and repeated sequence RTs. This finding illustrates that the motor execution requirements between the two types of sequences (repeated and random) were alike, and that both groups were similarly capable of meeting these demands.

In addition, several experimental design features further ensured that the between group difference in chunking was not related to impaired motor execution associated with aging or stroke. Because our control participants were age-matched to individuals with stroke in this work, it is unlikely that motor execution differences associated with aging accounts for any of our between group differences (Shea et al., 2006); all participants were older (mean age ST group 59.4, mean age HC group 59.6). In addition, using individual fingers for each individual response ensured that the chunking patterns that emerged were not reliant on the distance to be moved as has been the case in past work (Sakai et al., 2003; Shea et al., 2006). Finally, the use of the non-hemiparetic arm for response selection likely minimized the impact of motor execution deficits associated with stroke on overall response speed. Though we cannot completely rule out the impact of stroke on generalized motor execution as has been reported by others (Pohl et al., 1997; Velicki et al., 2000) the similarity of random RTs between the ST and HC groups suggests a minimal effect on performance during the implicit task employed in the present work.

A difference in the acquisition and/or utilization of explicit knowledge that was gained over practice is another possible explanation for the difference in chunking ability that we noted. However, this account is weakened by our finding that the amount of explicit knowledge gained by ST and HC groups was similar (Table 4). We were surprised by the extent of explicit knowledge gained by all of our participants. The results of our recognition tests demonstrated that participants acquired substantial explicit knowledge and that this knowledge did not differ between ST and HC groups. In sum, even though considerable explicit knowledge was gained for the repeating sequence this awareness did not aid chunking of repeated motor sequences after basal ganglia stroke.

It is possible that with more practice the ST group would have eventually demonstrated chunking that was equivalent to that demonstrated by the HC group. However, given the same exposure to the task, the ST group demonstrated a fundamental difference in their ability to organize sequential responses when compared to age-matched healthy controls. Future work should consider whether increased practice aides chunking after basal ganglia stroke.

Clinical, behavioral, and animal data demonstrate that the basal ganglia are central to implicit motor learning (Bailey & Mair, 2006; Boyd & Winstein, 2004b; Brown, Redondo-Verge, Chacon, Lucas, & Channon, 2001; Levesque et al., 2007) and also to the performance of learned behaviors (Jog, Kubota, Connolly, Hillegaart, & Graybiel, 1999; Miyachi et al., 1997). One function of the basal ganglia appears to be grouping individual movements into functional chunks (Graybiel, 1998; Jog et al., 1999; Levesque et al., 2007; Tremblay et al., 2008). Specifically, blockade of type-2 dopamine receptors disrupts chunk formation (Levesque et al., 2007; Tremblay et al., 2008), but does not prevent motor learning in monkeys. Damage to the medial caudate and putamen in particular, slows the initiation of learned sequential responses, perhaps by impeding advanced planning (Levesque et al., 2007). Convergent evidence for the role of basal ganglia in skill acquisition is furthered by the finding that administration of levadopa in individuals with stroke facilitates faster responses on learned sequences but has no effect on random sequences (Rosser et al., 2008). Similarly, people with Parkinson's disease who are taking dopamine replacement drugs show implicit motor learning; however, when the same participants are off-medication learning deficits emerge (Soliveri, Brown, Jahanshahi, Caraceni, & Marsden, 1997). Our data support these findings and in combination with past work (Berridge & Whishaw, 1992; Levesque et al., 2007; Rosser et al., 2008), suggest that chunking may be a function of the basal ganglia that is reliant on dopamine in the medial striatum.

We cannot rule out the possibility that either direct or indirect damage to other brain regions in the human stroke model employed in the present work contributed to our findings. The basal ganglia are highly interconnected with other regions of the brain with multiple reciprocal connections existing between the cortical regions and striatum (Cavada & Goldman-Rakic, 1989; Middleton & Strick, 2000a, 2000b; Middleton & Strick, 2002; Middleton et al., 1997). In addition, there are at least five neuroanatomically separate, reciprocal basal ganglia-thalamocortical circuits, which allow the basal ganglia to have a widespread affect on function (Alexander, DeLong, & Strick, 1986). Taken together the wide connectivity of the basal ganglia positions them ideally to exert a broad influence on motor skill learning. Our data taken in context with other animal (Levesque et al., 2007; Tremblay et al., 2008) and drug (Rosser et al., 2008; Soliveri et al., 1997) based work, strongly suggest a central role for the basal ganglia in the organization of chunks during motor sequence learning. Future work will have to continue to elaborate and expand the known relationships between basal ganglia function and response organization during motor learning.

We discovered a strong relationship within group between performance on the digit symbol-coding task, a test that illustrates the

relationship between memory and response speed, and absolute RT at the retention test for the ST (R^2 = .60; p = .003) but not the HC (p = .913) group. During digit symbol-coding, participants must remember abstract symbols that are associated with individual letters and record as many as possible over a prescribed period of time. Individuals with faster RTs for the repeated sequence at retention scored higher (i.e., produced more correct symbols) on the digit symbol-coding task. Diminished ability during the digit symbol-coding task may explain some portion of the poor chunking of responses in our ST group. Both speed of responding and memory for digit symbol-coding impact performance of the visual attention task (Joy, Kaplan, & Fein, 2004). However, the two groups in this study performed comparably on the digits backward test of working memory. Similarly, MMSE scores were within the normal range for our ST and HC groups. Thus, we believe it is unlikely that memory deficits severely affected digit symbol-coding task performance. More probably slower processing speed was the main contributor to altered digit symbol-coding performance and perhaps also to slower RTs at retention for individuals with stroke.

It is also possible that the hand used for the digit symbol-coding task influenced response speed; however, we believe that this explanation is unlikely. Only one individual with stroke and their age-matched control used the non-dominant hand to perform the digit symbol-coding task. Because of this experimental control, we believe that slowed digit symbol-coding by individuals in the ST group reflects diminished processing rather than motor execution speed.

Taken together our findings suggest that a particular class of processing of learned sequential movements is impaired after stroke involving the basal ganglia. We identified poorer response organization as shown by less chunking in individuals with stroke that was not solely related to motor execution deficits. A theoretical model proposed by Verwey (1999) is useful in explaining our results. Verwey proposes that a parallel dual-processor model is responsible for the execution of learned sequential responses (Verwey, 1999, 2003). In this conceptualization a cognitive mechanism plans and represents a learned sequence, while a motor mechanism formulates the particular commands necessary to implement movements. Importantly, these two mechanisms are independent and can operate in parallel. This structure allows chunks of a learned sequence to be executed while the planning of the next chunk is carried out. Importantly, the independence of these two processing stages allows for the possibility that one but not the other may be impaired by brain damage. Our data appear to support the notion of organizational and neuroantomical independence of the cognitive and motor operations as proposed in the dual-processor theory. We demonstrate disrupted cognitive operations, specifically speed of processing as demonstrated by our digit symbol-coding task and impaired chunking of learned responses but not of motor responding; random RTs did not differ between our groups.

5. Conclusions

Our data demonstrate that individuals with basal ganglia stroke do not organize movement sequences into chunks in the same fashion as neurologically intact individuals. Limited ability to chunk learned movements helps explain past findings that after stroke responses are slowed even after motor learning has been demonstrated. Critically, we confirm other work with animal and patient models that illustrate an essential role for the basal ganglia in chunking learned movements into functional sub-sequences. Placed in the context of a dual-processor theory of motor learning, we demonstrate that sub-cortical stroke that impacts the basal ganglia impairs cognitive but not motor operations during skill acquisition.

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