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Motor and non-motor sequence learning in patients with basal ganglia lesions: the case of serial reaction time (SRT)

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Abstract

In order to address the question of whether the basal ganglia are involved exclusively in regulation of motor sequence learning, or if they are involved in non-motor sequence learning as well, two versions of the serial reaction time (SRT) task were administered: First is the standard version of the SRT task in which the sequence is executed motorically, and the second is a non-motor version of the task which requires response only to a particular position of the sequence. Sixteen patients with damage restricted to the region of the basal ganglia and 16 matched control subjects participated in this study. In addition to the motor and non-motor SRT tasks, two declarative memory tests (Visual Paired Associates and Rey Auditory-Verbal Learning Test) were administered to the participants. Results indicate that the two groups did not differ either on learning rate of the two declarative tasks, or on the declarative component of the SRT tasks (i.e., 'generate'). However, the control group was significantly superior to the basal ganglia (BG) group in learning a specific sequence in the motor and non-motor SRT tasks. Results suggest that the basal ganglia are involved in the regulation of non- motor as well as motor sequence learning.

1. Introduction

It is well established that the learning and memory of some forms of knowledge are preserved in amnesic patients [19]. Based on this notion, Cohen and Squire [2] have introduced the distinction between two forms of memory—'declarative' and 'procedural' memory. The former is memory for facts and events, while the latter is the ability to acquire and retain new skills. Declarative memory, which is impaired in amnesics, is typically tested by methods of recall and recognition. Procedural memory, which is preserved in amnesics, is tested by using a wide variety of tasks such as the Tower of Hanoi puzzle [3], mirror reading [2], and serial reaction time (SRT) [14].

While the role of the medial temporal and diencephalic structures in declarative memory is well documented, the brain structures subserving procedural memory are not yet as clear [20]. Some researchers have pointed to the basal ganglia as the crucial area for processing of procedural information [18]. In animal studies, damage to the basal ganglia has been found to affect procedural memory [12], but studies of patients suffering from degenerative diseases of the basal ganglia such as Parkinson's disease (PD) and Huntington's disease (HD), are less conclusive. PD patients were found to be impaired in a variety of skill learning tasks, such as complex tracking [5], SRT [4,9] and the Tower of Toronto [17]. However, other studies do not support the basal ganglia hypothesis of procedural memory. Heindel, et al. [7] tested two groups of PD patients, one demented and the other not demented, with no difference between groups in terms of motor symptoms; they found that the patients' impairment on learning the pursuit-rotor task was correlated with the degree of dementia but not with the

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Table 1
Demographic and clinical information of the BG patient group

Patient	Sex	Age	Education	Side	Lesion location[a]	Etiology	Clinic[b]
1	M	71	12	Right	GP + Put	Infarct	Hemiparesis
2	M	61	10	Right	GP + Put	Hemorrh	Hemiparesis
3	F	52	12	Left	GP + CN + Put	Hemorrh	Hemiparesis + Neglect
4	M	60	10	Right	CN + Put	Infarct	Asymptom
5	M	45	14	Right	GP + Put	Infarct	Asymptom
6	F	50	14	Right	G + Put	Infarct	Asymptom
7	M	48	15	Left	GP + Put + TCN	Hemorrh	Hemiparesi + Dysphasia
8	M	65	10	Left	GP + Put	Infarct	Asymptom
9	M	71	12	Right	Put	Infarct	Asymptom
10	M	68	11	Left	CN	Infarct	Asymptom
11	F	50	16	Left	CN	Infarct	Asymptom
12	F	36	12	Right	CN + GP	Infarct	Asymptom
13	F	70	7	Right	CN + Put + GP	Infarct	Asymptom
14	M	65	9	Right	Put + GP	Infarct	Asymptom
15	M	52	8	Right	CN + Put + GP	Infarct	Asymptom
16	M	74	8	Right	CN + Put	Infarct	Asymptom

[a] GP = Globus pallidum; Put = Putamen; CN = Caudate nucleus; TCN = Tail of the Caudate nucleus.
[b] Initial clinical symptoms.

severity of motor symptoms. Contrary to findings by Saint-Cyr et al. [17], in two other studies PD patients' performance on a Tower puzzle did not differ from normal controls [1,13].

Several attempts have been made in the literature to resolve these conflicting findings. Owen et al. [15] showed that PD patients' performance is a function of clinical disability and precise index of performance (i.e., accuracy vs latency). Some researchers raised the possibility that the heterogeneity of PD patients has further contributed to inconsistent reports in the literature. Vakil and Herishanu-Naaman [23] found that the PD patients with bradykinesia, but not those patients with tremor as the predominant symptom, demonstrated impaired procedural learning. Other researchers have emphasized the heterogeneity of the procedural tasks. Harrington et al. [6] found that PD patients were impaired in the acquisition of a motor (i.e., rotary pursuit) task but not in the visual-perceptual (i.e., mirror reading) task.

Sequence learning as measured by the SRT task has been consistently shown to be impaired in PD patients [4,9,16] and in HD patients [10,26]. These results were interpreted as support for the hypothesis that the basal ganglia are involved in the regulation of procedural memory or at least in sequence learning. In light of the findings by Harrington et al. [6], it could be argued that the impaired performance on the SRT task in PD and HD patients is due primarily to the fact that this task requires motor sequence learning. Thus, impaired performance on the SRT task could not be interpreted as reflecting impaired procedural or even sequence learning in general, but only motor sequence learning.

In order to address the question whether the basal ganglia are involved exclusively in the regulation of motor sequence learning, or in non-motor sequence learning as well, two versions of the SRT task were administered. The first is the standard version of the SRT task which requires continual response to all the stimuli presented. In this task, each sequence of motor responses (pressing a sequence of buttons) corresponds to a sequence of lights presented in different spatial locations. For the second task, we modified the original task so that it did not require the motor performance of the sequence. This task requires a selective response to a particular stimulus. Here the sequence of lights presented does not require a continual response to the sequence, but just to a particular location. Therefore, in the standard motor version of the SRT (SRTm) task, the sequence is learned by continuous motor reproduction. The reduced reaction time to all components of the sequence indicates the learning of the sequence. However, in the non-motor version of the SRT task (SRTnm), the sequence is not reproduced motorically but is only presented repeatedly, and thus reduced reaction time to a particular location indicates learning of the sequence. These tasks will be described in more detail in section 2.

In all the studies that tested the basal ganglia hypothesis of procedural memory in humans, participants were either PD or HD patients. The problem with testing these types of patient groups is that several studies have demonstrated that the pathology in PD [22] and HD [21] patients may extend beyond the basal ganglia region. For this reason, in this study we tested patients with cerebrovascular accident circumscribed to the basal ganglia. The goal of this study is twofold: First, to test patients with lesions restricted to the area of

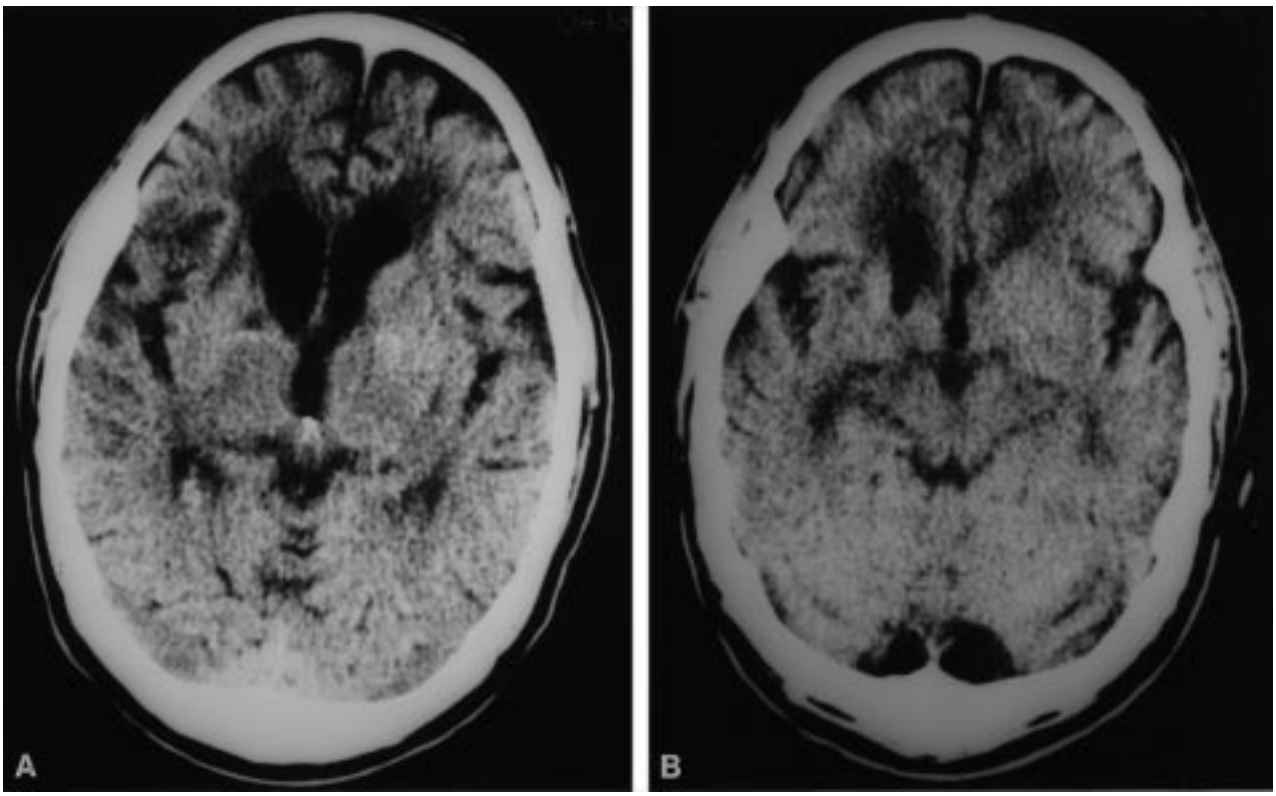

Fig. 1. Computerized tomography of patient 12, showing an old infarction in the caudate nucleus that includes a very small part of the globus pallidum, on the right side.

the basal ganglia and second, to test motor and non-motor versions of the same procedural learning task (i.e., SRTm and SRTnm) in addition to declarative memory tests.

2. Method

2.1. Participants

The subject population consisted of two groups, basal ganglia (BG) patients and normal controls. The subjects in the BG group sample consisted of 18 patients selected from the data base of a general neurology clinic, on the basis of discrete lesions in the basal ganglia as seen in computerized tomography (CT). Exclusion criteria were as follows: previous neurological disease, head trauma, endocrine diseases and the use of any drug that could affect cognitive performance. They were also required to have a full command of oral and written Hebrew. In order to rule out other brain lesions outside the basal ganglia, every CT was independently evaluated by an expert neurologist and an expert neuroradiologist. A detailed description of the extent of patients' lesions is presented in Table 1. Fig. 1 presents a CT scan of a typical BG patient.

All of the patients underwent a behavioral neurology examination, as described below. One patient was excluded because she had concentration problems, and a second patient because mental status examination evinced an incipient dementia. The remaining sample consisted of 11 men and 5 women, whose ages ranged from 36 to 74 years (M = 58.63), and their education ranged from 7 to 16 years of schooling (M = 11.25). They were all right handed. Based on the behavioral neurology examination, all were at the normal range for age and education.

2.2. Behavioral neurology examination

We initially interviewed the patient and a close member of the family for a complete medical history, looking in particular for any decrease in daily functioning, either at home or at work, or any signs of depression (e.g., apathy, insomnia). In addition affective state was assessed with the Hamilton scale for depression.

Motor sensory examination was mainly aimed to detect any minimal weakness of the limbs, rigidity, coordination deficits or bradykinesia. None of them showed any motor impairment at the time of testing. The mental status examination consisted of the following cognitive domains (and tests used): attention and concentration (Serial 7s, Digit span, and Digit Symbol,

subtest of the WAIS-R), language (spontaneous speech, Boston Naming Test, and automatic speech), praxis (pantomime to command and complex actions), visuo-spatial performance (drawing to command and drawing to copy), executive functions (comprehension and similarities subtest of the WAIS-R). Declarative memory was assessed as a part of the procedure in the present study (see tests and procedure section). In the case of one patient who initially had aphasia, we also included the subtests of understanding and repetition from our aphasia battery. In the case of another patient who initially had had neglect, we extended testing to more specific tests for neglect, as line bisection, line cancellation and tests for extinction. Clinical examination was completed by routine laboratory tests: CBC, ERS, liver, kidney and thyroid function, and levels of Vitamin B12 and folic acid. All patients were asymptomatic by the time they entered the study. The behavioral neurology study and the tests for procedural memory were performed between 9 and 25 months ($M = 16.33$) from the onset of clinical symptoms, where present. Patients were informed about the study and gave their written consent.

The control group consisted of 16 normal subjects, matched with the BG group for age and education level. The sample consisted of 7 males and 9 females, whose ages ranged from 42 to 72 years ($M = 57.75$), and education ranged from 7 to 17 years of schooling ($M = 12.0$). The groups did not differ significantly either on age, $t(30) = 0.23$, $P > 0.05$, or educational level, $t(30) = 0.79$, $P > 0.05$.

2.3. Tests and procedure

Participants were tested individually in two separate sessions, one day apart. Two tests were used to assess declarative memory: Visual Paired Associates (VPA)—a subtest of WMS-R [25] and the Rey Auditory-Verbal Learning Test (AVLT) [11]. Two considerations were involved in choosing these tests. First, these are standard tests of visual (i.e., VPA) and verbal memory (i.e., Rey AVLT), and second, these tests provide memory measures that are parallel to those measured by the procedural task (i.e., baseline and learning rate). Two versions of the serial reaction time task (SRT) [14] were employed in order to test procedural learning. The first is the standard version of the SRT task which requires continual motor execution of all elements of the sequence (SRTm). The second is a modification of the task that requires selective response to a particular element of the sequence (SRTnm).

2.4. Visual Paired Associates (VPA)

This test consists of a set of six different colours paired along with six nonsense shapes. Each card (10×14 cm) contains one pair. The same set was repeated consecutively three times and presented each time in a different order. Following each set of six cards, six testing cards consisting only of shapes are presented. Participants are presented with a folder with eight different colours and are asked to point to the colour pair associated with the presented test card shape. One more matching block was repeated twenty minutes after completion of the first set of trials. This task was administered in the second session.

2.5. Rey Auditory Verbal Learning Test (AVLT)

The Hebrew version of the test [24] was administered in a standard fashion [11] in the second session. The test consists of 15 common nouns that are read to the subject on five consecutive trials (trials 1–5); participants are asked to remember as many words as possible. Each trial is then followed by free recall. In trial 6 an interference list of 15 new common nouns is presented, followed by a free recall of these new nouns. In trial 7 participants are asked again to recall the first list. Twenty minutes later participants are again asked to recall the first list (trial 8). They are then asked to identify the 15 words from the first list out of 50 words presented verbally (also including the 15 words in the second list and 20 new common nouns) (trial 9).

2.6. Serial reaction time—motor (SRTm)

In this task, a red light appears in one of four squares (3.3×3.3 cm) arranged horizontally on the computer screen. Subjects were given the following instructions: "A red light will appear on one of the four positions on the screen. Using the index finger of your dominant hand, your task is to press as fast as possible one of the first four horizontal numerical buttons on the key board that corresponds to the position of the red light. In other words, for the red light appearing from the left most to the right most position, you have to respond with the keys 1 to 4, respectively." The red light position appeared in a 10-trial sequence of repetitions, i.e., 2131431241. Ten repetitions of this sequence (i.e., 100 trials) consisted of one block. Participants were presented with four blocks, with a 1 min rest between blocks. The starting position of the sequence (i.e., '2') was always the same across blocks. As soon as a response was made, or if the participant did not respond within 5s, the next target spatial location appeared on the screen, whether or not the response made was correct. Reaction time was defined as the time from onset of the stimulus to pressing of the response key. Reaction time was recorded automatically by the computer for correct responses only. (Accuracy of measured reaction time was more

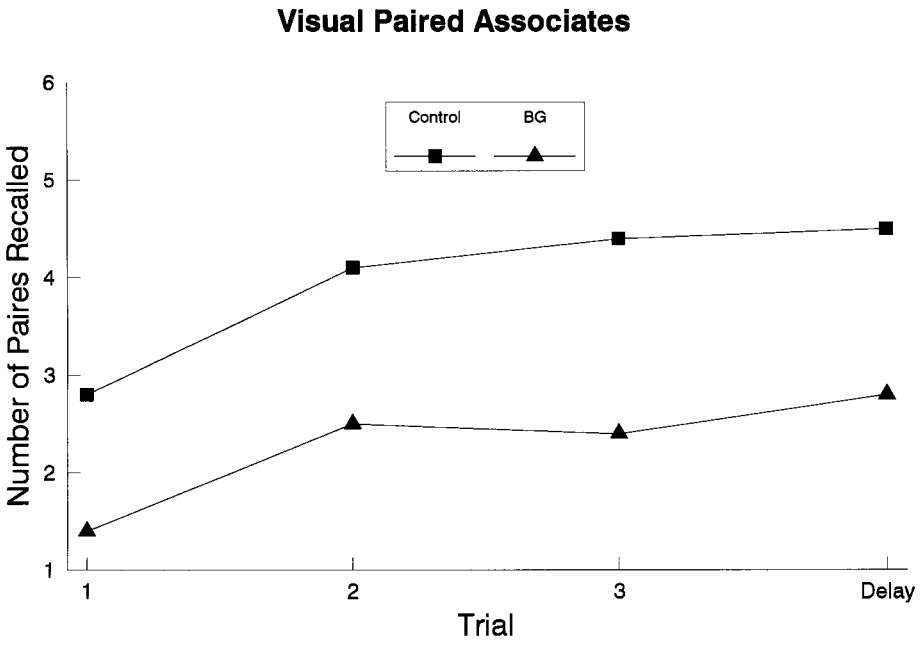

Fig. 2. The mean number of correct answers made by the BG and control groups in the four trials of the VPA task.

reliable in one-hundredth of a second than one-thousandth of a second.) Incorrect responses were recorded as errors. Following the four blocks with repeated sequence, the fifth block was presented with a random sequence. These five blocks were administered in the first session; in the second session on the following day, the sixth block was presented which consisted of the original repeated sequence.

2.7. Serial reaction time—non-motor (SRTnm)

This task was identical to the previous task (i.e., SRTm) except for the instructions given to subjects. In this task subjects were asked to respond as fast as possible by pressing the space bar of the keyboard, only when the red light appeared in position 3. As in the previous task, the red light position appeared in a repetitive 10-trial sequence, which for this task was 1434312413. Notice that the response in the SRTm task is made only with one finger rather than with four fingers, each one corresponding to one of the four stimulus positions, in order to resemble as much as possible the SRTnm in which the response is made with one finger to a single position.

2.8. Generate

This task was designed to test the declarative memory of the SRT task sequence. In order not to encourage intentional learning of the sequence, the generate tasks were administered only following the two SRT tasks. The SRTm and SRTnm tasks were administered in a counterbalanced order. In order to minimize confusion, subjects were first asked to generate the sequence of the preceding (i.e., second) SRT task, and then to generate the sequence of the first SRT task. Following the sixth trial, subjects were informed that they had been presented with a repeated sequence in the first four blocks and in the sixth block. They were presented with a series of stimuli and were asked to push the response button in the location where they thought the next stimulus would appear. Following the response, whether it was right or wrong, the target moved to the next right position. Subjects were also told that in this task they were not timed and that they should focus on being correct rather than being fast. The number of correct positions selected out of the ten position sequence, were recorded separately for the SRTm and for the SRTnm tasks.

In summary, subjects were tested in two sessions on two consecutive days. In the first session they were tested on the first five blocks of both SRT tasks. The order of presentation of the SRTm and SRTnm was counterbalanced across subjects. In the second session, consistent with the test administration order of the first session, the sixth block of both tasks followed by the generate block of these tasks was administered. The declarative tests (i.e., Rey AVLT and VPA) were always administered in the second session, following the sixth and generate blocks of the SRT tasks.

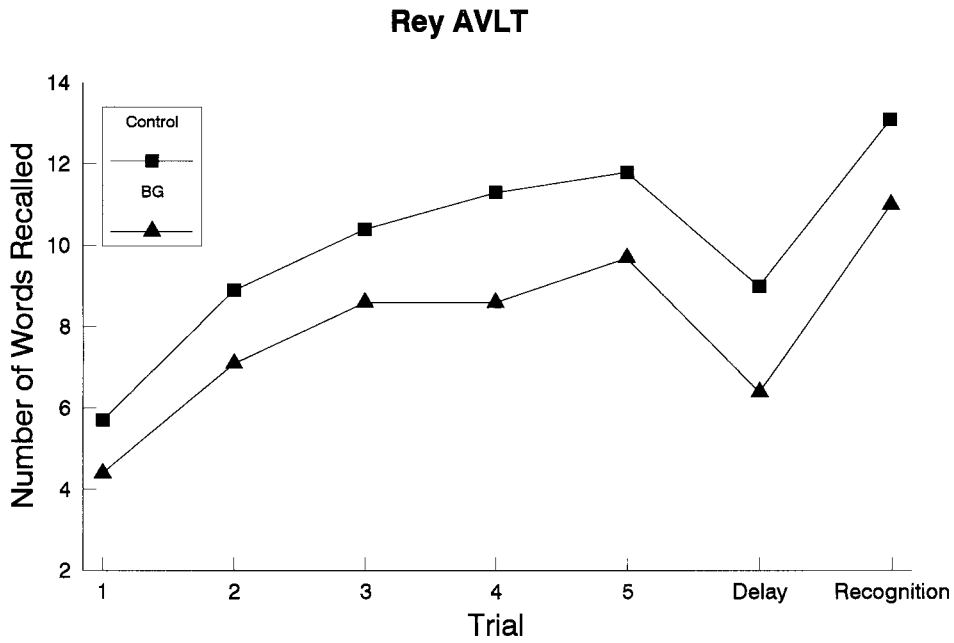

Fig. 3. The mean number of words recalled in the first five trials and the delayed trial of the Rey AVLT by the BG and control groups.

3. Results

3.1. Visual Paired Associates (VPA)

Fig. 2 presents the mean number of correct answers made by the two groups (BG and control) in the four trials of the VPA task. Two separate analyses were conducted. The three trials as a measure of learning and the fourth trial compared with the third trial as a measure of retention over time.

3.1.1. Learning

Performance on the first three trials was submitted to a mixed-design ANOVA in order to analyze the effects of group and learning trials (1 to 3). The former is a between subjects factor and the latter is a within subjects factor. Overall, the number of pairs correctly recognized by the control group was significantly higher than that of the BG group, $F(1,30)=15.65$, $P < 0.001$. There was a significant overall increase in number of pairs learned from trial to trial, $F(2,60)=12.57$, $P < 0.001$. The 'group' × 'learning' trials interaction did not reach significance, indicating that the learning rate of the two groups was not reliably different.

3.1.2. Retention

The groups differ significantly on the number of pairs correctly recognized in the third and the fourth (i.e., delayed) trial of the task, $F(1,30)=12.09$, $P < 0.01$. Neither the delayed effect nor the 'delay' × 'group' interaction reached significance.

3.2. Rey Auditory Verbal Learning Test (AVLT)

Fig. 3 presents the mean number of words recalled in the first five trials and the delayed trial of the Rey AVLT by the two groups. The groups were compared on the learning (i.e., trials 1–5) and retention (i.e., trials 5 and delayed trial) measures of the Rey AVLT.

3.2.1. Learning

The number of words recalled by the two groups in the first five trials of the Rey AVLT was submitted to a mixed-design ANOVA with group and learning trials as factors; the first effect being a between subjects factor, and the second effect being a within subjects factor. Overall, the control group recalled more words than the BG group in the first five trials of the test, $F(1,30)=10.51$, $P < 0.01$. There was also a significant increase in the number of words recalled from trial to trial, $F(4,120)=126.28$, $P < 0.001$. The interaction between these two main effects did not reach significance.

3.2.2. Retention

The groups significantly differ on the number of words recalled in the fifth and the eighth (i.e., delayed) trial of the task, $F(1,30)=8.09$, $P < 0.01$. Overall, less words were recalled in the delayed trial as compared to the fifth trial, $F(1,30)=100.76$, $P < 0.001$. The 'group' × 'delay' interaction was not significant, indicating that the forgetting rate of the two groups was not reliably different.

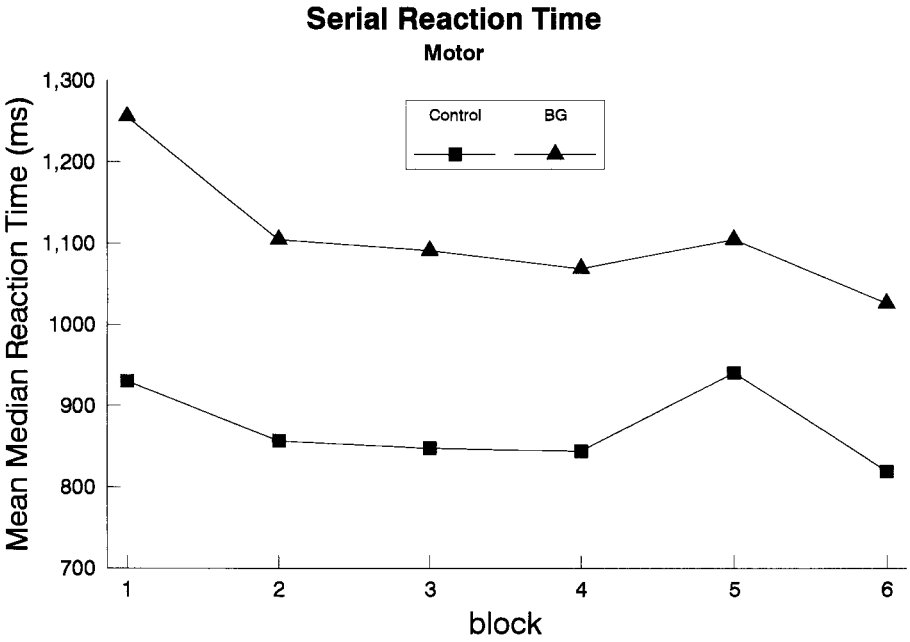

Fig. 4. The mean of the median reaction time of the BG and control groups in the six blocks of trials in the motor SRT task.

3.3. Serial reaction time

Reaction time was the only measure statistically analyzed because the number of errors (i.e., incorrect responses) made by the participants was negligible, and all participants responded within the 5 s time limit. As mentioned above, reaction time was recorded automatically by the computer for correct responses only. Figs. 4 and 5 present the mean of the median reaction time as a function of group and blocks for the SRTm and SRTnm tasks, respectively. The groups (BG and control) were compared on learning, retention, and generate measures of the SRTm and SRTnm tasks. In these tasks learning is expressed in two ways. First as the rate of reduced reaction time over the first four blocks of the repeated sequence, and second as the comparison of the reaction time of the repeated sequence (i.e., fourth block) and the reaction time to a

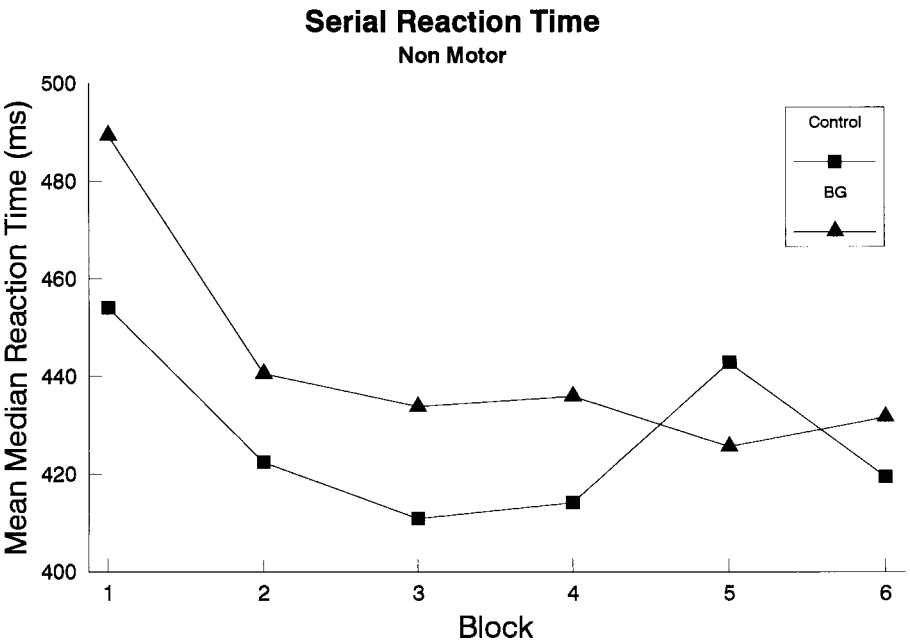

Fig. 5. The mean of the median reaction time of the BG and control groups in the six blocks of trials in the non-motor SRT task.

random sequence (i.e., fifth block). Retention over time (i.e., one day) of the learned sequence is analyzed by comparison of performance on the fourth and sixth blocks. In addition, the groups were compared on the generate task. As in previous studies, the median reaction time per block (i.e., 100 trials) was analyzed [4,14]. Preliminary analyses suggest that the testing order of the SRTm and SRTnm tasks had no significant effect on any of the measures.

3.4. Serial reaction time—motor (SRTm)

3.4.1. Learning—blocks 1–4

The median reaction time of the two groups in the first four blocks of the SRTm task was submitted to a mixed-design ANOVA with group and learning trials as factors; the first effect is a between subjects factor, and the second effect a within subjects factor. Overall, the RT of the control group was faster than that of the BG group, $F(1,30)=10.11$, $P<0.01$. There is also a significant reduction in RT over blocks 1 to 4, $F(3,90)=15.67$, $P<0.001$. The 'group' × 'block' interaction was not significant.

3.4.2. Learning—block 4 vs block 5

As can be see in Fig. 4, the overall reaction time of the control group was faster than that of the BG group, $F(1,30)=6.77$, $P<0.02$. There is an overall increase in the RT to the random sequence (block 5) compared to the repeated sequence (block 4), $F(1,30)=28.05$, $P<0.001$. The 'group' × 'block' interaction reached significance, $F(1,30)=5.96$, $P<0.05$. This interaction indicates that difference between repeated as compared to random sequence is greater for the control group than for the BG group.

3.4.3. Retention—block 4 vs block 6

The group effect, $F(1,30)=8.61$, $P<0.02$ and the block effect, $F(1,30)=8.86$, $P<0.02$, reached significance, but not the interaction between them.

3.5. Generate

The control group ($M=5.38$, $SD=1.89$) and the BG group ($M=6.06$, $SD=1.91$) did not differ significantly in the number of correct sequence positions generated, $t(30)=1.02$, $P>0.05$.

3.6. Serial reaction time—non motor (SRTnm)

The group effect on those measures analyzed in the SRTm task was also analyzed in the SRTnm task.

3.6.1. Learning—blocks 1–4

The only effect to reach significance in this analysis was the learning effect $F(3,90)=12.08$, $P<0.001$, which indicates that overall, there is a decrease in reaction time over blocks in response to the repeated sequence. The group effect and the 'group' × 'learning' interaction did not reach significance.

3.6.2. Learning—blocks 4 vs block 5

Neither main effect for group nor main effect for blocks reached significance. The only effect that reached significance was the 'group' × 'block' interaction, $F(1,30)=9.13$, $P<0.01$. As can be seen in Fig. 5, while the median reaction time for the control group increases from 414.06 ms in the repeated sequence to 442.81 ms in the random sequence, the median reaction time of the BG group decreased from 435.94 ms to 425.63 ms, respectively.

3.6.3. Retention—block 4 vs block 6

In this analysis none of the effects reached significance.

3.7. Generate

The control group ($M=4.56$, $SD=1.93$) and the BG group ($M=5.13$, $SD=2.45$) did not differ significantly in the number of correct sequence positions generated, $t(30)=0.72$, $P>0.05$.

4. Discussion

The basal ganglia hypothesis of procedural learning was evaluated in this study by administering different declarative and procedural tasks to a group of patients with circumscribed damage to the basal ganglia and a matched control group. In both declarative tasks (i.e., Rey AVLT and VPA), although the patient group remembered less items than the control group, their learning rate was not significantly different. Furthermore, the two groups did not differ in the generate tasks (i.e., for the SRTm and SRTnm) which require explicit retrieval of the presentation sequence of the stimuli. This finding indicates that the patients and the controls did not differ in terms of development of explicit awareness of the sequences.

Knopman and Nissen [10] distinguish between two aspects that are learned in the SRT task. First is 'reaction-time-task learning' which is related to proficiency in execution of the reaction time task; second is the 'sequence-specific learning' which reflects learning of the specific sequence in which stimuli were presented. These two learning aspects are reflected in the learning rate from the first to the fourth block, since in these initial blocks the subject is familiarized with the task and learns the sequence (i.e., implicitly) at the same time. The difference between the fourth block of the repeated sequence, and the fifth block, the random

sequence, reflects only the 'sequence-specific learning'. For this reason all studies using the SRT task viewed the comparison between the fourth and the fifth blocks as reflecting procedural learning, or more specifically, sequence learning [4,9,10,16]. In recent years researchers have drawn attention to the importance of controlling for the probability of each stimulus-response in the repeated and random sequences [9]. Thus, in order to confirm that subjects are learning serial order information, future studies should make sure that the probability of each stimulus-response in all sequences is equal.

The pattern of results in the motor and non-motor sequence learning tasks was basically the same. However, the reaction time for all groups was faster in the non-motor than in the motor task. One possible explanation for this difference between the two tasks is that whereas subjects had to press one of four buttons on the key board in the SRTm task, in the SRTnm task, subjects had to press only on the space bar. Another possible reason for the faster reaction time on the SRTnm task is that while in the motor sequence, each of the four elements (1, 2, 3, and 4) repeated one or more times, in the non-motor sequence, 2 is a unique item with no repetition. It is important to stress that, because the critical comparisons are between the group within each task, in which both groups were administered the same sequence, the overall difference between the tasks is less important.

In the two SRT tasks the learning rate of both groups in the first four learning blocks was not significantly different. However, the difference between block 4 and block 5 was significantly greater for the control group compared to the BG group, indicating better learning of the specific sequence by the control group. Other studies also report a dissociation between 'learning' as expressed in the first learning blocks and the difference between the learned and random sequence. Just like the findings in the present study, Feraro et al. [4] reported that the reduction in RT for PD patients in the first four blocks was not significantly different than that of the control group. However, the difference between the fourth and fifth blocks was significantly larger for the control group. Knopman and Nissen [10] reported that the HD patients had a steeper learning rate than the control group in the first four blocks, but had a smaller increase in RT between blocks 4 and 5 compared to the control group.

The results of the present study are at odds with the conclusion made by Harrington et al. [6] that PD patients are impaired in the acquisition of a motor task (i.e., rotary pursuit) but not of a visuoperceptual task (i.e., mirror reading). It is possible that in addition to the motor aspect, the tasks used by Harrington et al. [6] differ in other aspects (e.g., the non-motor task depends on reading skills) that might have contributed to the difference in performance. In the present study an attempt was made to use tasks that are identical in their cognitive demands (i.e., sequence learning, choice reaction time etc.). These tasks differed only in respect to the execution of the learned sequence. That is, in the standard SRTm task the subject must execute motorically all the elements of the repeated sequence. In the SRTnm task the sequence is only presented visuospatially and a response is expected only to one component of the sequence. Thus, unlike the standard task the sequence is never executed motorically. The most revealing finding in this study is that even under such conditions, the sequence learning of the BG group was impaired. As noted above, because the response in the SRTnm task is made with one finger (to a single position), the response in the SRTm task was also made with one finger only, rather than with four fingers corresponding to each of the four stimulus positions. By doing so we may have reduced the motor element in the motor task. However, this consequence does not concern us, because it further supports our conclusion that the basal ganglia are involved in sequence learning even when the motor component is minimized. It could be claimed that despite the modification we made to the standard SRTm task, the motor component remaining in the SRTnm task is as dominant as in the SRTm task, thereby causing the impairment to the BG group. As stressed above, unlike their performance on the SRTm task, the groups' overall RT on the SRTnm task did not differ significantly, which would argue against such a claim.

An alternative non-motor task might have been the task used by Howard et al. [8]. In their study, one of the groups was required to respond motorically only to the first 10 trials of each block, and just to observe the sequence for the rest of the trials (i.e., 90) of the block. The results indicate that the 'observers' showed the same learning rate of the sequence as the 'performers' that were administered the standard SRT task. However, the 'observers' were more aware of the sequence compared with the 'performers', as reflected by their higher score in the generate task. The authors' interpretation is that the 'observers' had paid more attention to the sequence, and as a consequence, declarative memory processes may have become more involved in their performance of the task compared to the 'performers'. This is one reason why we chose not to use this option as the non-motor task. The other reason is that we were concerned that the participants, particularly the patients, might lose concentration while performing the task in such a passive manner, being required just to observe the sequence.

Finally, the results of the present study support the basal ganglia hypothesis of procedural learning. For the first time, patients with damage restricted to the

basal ganglia region were shown to be impaired in the learning of a non-motor as well as a motor procedural task while declarative learning is preserved. However, further research is required in order to determine whether the impairment observed here with BG patients is unique to sequence learning or whether it reflects procedural/skill learning in general.

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