Implicit Motor Learning in Patients with Parkinson’s and Alzheimer’s Disease: Differences in Learning Abilities?

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Experimental studies show intact implicit motor learning in patients with Alzheimer’s disease (AD) but the results for patients with Parkinson’s disease (PD) are inconclusive. This study tests implicit sequence learning in AD and PD patients, and healthy controls, using the classical Serial Reaction Time Task (SRTT), and a somewhat similar Pattern Learning Task (PLT), which involves stylus movements in different directions, and which allows detailed movement analysis. As expected, the time measures showed less implicit motor learning in the PD patients relative to the other groups in both tasks, but their error percentages increased when the sequence changed from a fixed to a random order, which is indicative of implicit learning. The AD patients showed a reversed pattern of results. Arguably, errors and time measures may reflect the involvement of separate processes, e.g., spatial and motor components, which could be differently affected in AD and PD.

Keywords: Alzheimer’s disease, Parkinson’s disease, implicit learning, motor skill learning, sequence learning

The ability to learn and produce sequential motor actions such as involved in shifting gear, serving in tennis, using a microwave or typing letters is a remarkable capacity of humans (Cohen, Ivry, & Keele, 1990), but in patients with brain damage and degenerative diseases this ability can be diminished. Therapists are often confronted with questions concerning the patients’ (remaining) abilities to acquire new motor skills such as walking with a walking aid. However, the test batteries used in the clinical neuropsychological practice to answer these questions assess explicit memory only (Spaan, Raaijmakers, & Jonker, 2003). Since experimental studies have demonstrated that implicit processes are also relevant in motor skill learning, they consequently yield little or no information about a patient’s ability to (re)learn motor skills. Implicit learning is also important in the context of rehabilitation because explicit learning instructions are not always appropriate for certain groups of people. People suffering from a degenerative disease like Alzheimer’s disease...
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(AD), for example, show diminished explicit learning (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984) but may profit from implicit learning (Van Halteren-Van Tilborg, Scherder, & Hulstijn, 2007).

The learning of motor skills involves changes in a number of quite distinct processes. Willingham (1998, 1999) distinguishes four processes: (1) the strategic process of learning to select new or more effective environmental goals (e.g., picking up a cup of tea), (2) a perceptual-motor integration process that is directed at learning new relationships between environmental stimuli and motor responses (e.g., the mapping of mouse and cursor locations in a computer task), (3) a sequencing process that is directed at learning the order of the submovements of an act (e.g., the movements of a dance routine), and (4) a dynamic process that is based on learning representations of muscle activation patterns that translate the spatial targets into appropriate muscle commands. The dorsolateral frontal cortex has been implicated in the strategic process, while the perceptual-motor integration process has been localized to the posterior parietal cortex and premotor cortex. Motor sequence learning appears to rely on the basal ganglia and supplementary motor cortex, and the neural basis of the dynamic process seems to lie in the cerebellum (Hikosaka, Nakamura, Sakai, & Nakahara, 2002) and in pools of interneurons in the spinal cord (Willingham, 1999).

Learning occurs when one or more of the processes are adjusted to a particular task, improving the efficiency of its performance. Except for the strategic process, modifications may either come about in a conscious or an unconscious mode (Willingham, 1998). The strategic process is closely related to executive functioning; both refer to the processes that support the conscious planning of movements. In this study we investigate mechanisms underlying implicit/unconscious motor learning and therefore Willingham's second process of perceptual-motor integration is involved but our main focus is on sequence learning, the third process Willingham distinguishes in his model. The fourth, dynamic process refers to the force and timing of muscle activity, which we will not address in this study.

The Serial Reaction Time Task (SRTT) developed by Nissen and Bullemer (1987) is one of the most widely used tasks to study implicit unconscious sequence learning in experimental research. In this task participants are presented with successive visual stimuli that appear at different screen locations, to which they are asked to respond by pressing spatially corresponding keys. Initially, the stimuli are presented in a random order, but at some point in time, and unknown to the participants, they are presented in a fixed sequence. In the standard procedure, after several fixed-sequence blocks, in which the sequence can be learned implicitly, the fixed sequence switches to a random stimulus order to test if sequence learning has occurred in the preceding trial blocks. The task hence entails the identification and reproduction of the associations between the stimuli and the required motor responses (visuomotor learning) as well as the recognition and reproduction of a specific sequential pattern (sequence-specific learning; Werheid, Ziessler, Nattkemper, & von Cramon, 2003). A decrement in the reaction times during the execution of the fixed-sequence blocks is due to both visuomotor and sequence-specific learning. Increases in reaction times that are typically observed when participants are required to switch from the fixed to the random sequence reflect sequence-specific learning. Sequences can be learned in the order in which the stimuli appear, i.e., a visuospatial representation, or in the order in which the associated movements
are made, e.g., the sequence of keypresses (Keele & Curran, 1995). For a more recent account of their view, see Keele, Ivry, Mayr, Hazeltine, and Heuer (2003).

Although the SRTT is widely used in experimental studies on implicit motor learning, also Maze learning, Rotor Pursuit and Mirror Tracing tasks have been frequently applied, with each providing different perspectives of the ability of patient groups to learn new tasks implicitly (Van Halteren-Van Tilborg et al., 2007). The SRTT is an implicit learning task in which sequences of four different finger responses are learned and thus closely resembles learning to type frequent words or practicing playing runs on the piano. However, it accordingly assesses only one type of sequential motor action. The other experimental tasks involve learning how to correctly manipulate an object (a stylus, pen or computer mouse) via a series of movements in different directions, which is more comparable to learning to serve in tennis or shift gear while driving a car. To compare these different types of implicit sequence learning, in the current study we used Nissen and Bullemer’s SRTT (1987) and the Pattern Learning Task (PLT), a task we devised based on the SRTT paradigm but now requires the manipulation of a hand-held stylus (like in a maze or pursuit task). In the PLT participants need to produce pen-cursor movements toward different targets that are presented in a specific pattern. Accordingly, spatial aspects play a more dominant role in this task. Because in the PLT all movement trajectories are recorded over time, separate movement components such as reaction time (RT), movement time (MT), directional errors (DEs), and the occurrence and timing of corrective movements can be adequately analyzed separately.

Several studies demonstrated that healthy individuals can indeed learn the SRTT sequence implicitly (Cohen, et al., 1990; Curran & Keele, 1993; Nissen & Bullemer, 1987; Willingham, Nissen, & Bullemer, 1989), in other words, without explicit learning instructions and without being consciously aware that part of the trial sequence could be learned and without being able to explicitly report (part of) the fixed sequence afterward. Although Alzheimer (AD) patients are known to have explicit learning disabilities, their implicit learning seems intact. Most AD studies also report intact implicit learning in the SRTT (Grafman et al., 1990; Knopman & Nissen, 1987; Knopman, 1991; Willingham, Peterson, Manning, & Brashear, 1997), although Ferraro, Balota, and Connor (1993) only found preserved implicit learning in the early stages of the dementia (i.e., mild AD). The AD studies that used other experimental tasks likewise provided clear evidence of preserved implicit motor learning abilities in their patient cohorts (for a review, see Van Halteren-Van Tilborg, et al., 2007).

Since these studies involve implicit motor learning, the abilities of patients with Parkinson’s disease (PD) have also been the topic of several experimental studies. However, the results are more inconsistent than those reported in the AD studies (Roncacci, Troisi, Carlesimo, Nocentini, & Caltagirone, 1996; Siegert, Taylor, Weatherall, & Abernethy, 2006). Numerous studies using the conventional SRTT reported PD patients to have problems with the implicit acquisition of the sequences (Doyon et al., 1997; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995; Laforce & Doyon, 2001; Sommer, Grafman, Clark, & Hallett, 1999; Stefanova, Kostic, Ziropadjja, Markovic, & Ocic, 2000; Thomas-Ollivier et al., 1999; Werheid,
Zysset, Müller, Reuter, & von Cramon, 2003; Westwater, McDowall, Siegert, Mossman, & Abernethy, 1998), and this was also the conclusion of a more recent meta-analysis (Siegert, et al., 2006).

In contrast, several studies that used modified versions of the SRTT did report intact implicit learning in PD patients in some task conditions. The SRTT Helmuth, Mayer, and Daum (2000) used in their PD study required two types of sequences to be produced: a “number sequence” where the numbers 1 through 4 appeared in a fixed sequence with the location of the numbers being random, and a “spatial sequence” in which the order of the locations was fixed but the numbers appeared in random order. The patients were found to have learning deficits in the number sequence but not in the spatial sequence. Another recent PD study also found preserved implicit spatial sequence learning in their patients in an SRT task with reduced motor demands (Smith & McDowall, 2006). Werheid, Ziessler, Nattkemper, and von Cramon (2003), on the other hand, reported reduced sequence learning in their PD patients when stimuli and responses were spatially compatibly aligned (e.g., in the classical SRTT), but intact learning when the spatial component was removed (i.e., stimuli were presented centrally). They explained this sequence learning deficit by a predominance of automatic response activation over learning-based stimulus anticipations during the learning phase, not by a deficit in spatial learning.

Different versions of the SRTT thus seem to yield different results on the ability of PD patients to master implicit motor sequences. Differences in task demands causing differences in the relative involvement of spatially and motor-sequence-oriented processes might explain some of the differences in the results. As already mentioned, Keele and Curran (1995) state that one can either learn the visuospatial representation or the sequence of movements. Studies report that patients with damage to the striatum (the input station to the basal ganglia), as seen in PD, have difficulty producing and learning motor sequences (Willingham 1998). On the other hand, the studies mentioned above support the evidence of intact visuospatial learning in PD patients, which conflicts with the visuospatial problems PD patients regularly report during neuropsychological assessments (Cronin-Golomb & Braun, 1997). However, this visuospatial deficit is localized to specific visuospatial tasks and hence not a generalized deficit in PD patients (Brown & Marsden, 1990).

Given the disparity in paradigms and findings, in this study we directly compare AD patients, who in most studies showed intact implicit learning on a variety of experimental tasks, with PD patients, for whom results are inconsistent, both relative to healthy controls, using two implicit learning tasks that require different types of sequential motor actions: the classical SRTT and the newly developed, more spatially demanding PLT. We expected the AD patients to show implicit learning in both tasks similar to the matched, unimpaired controls but also that implicit learning would be compromised in the PD patients on the SRTT. Our expectations as to the results on the PLT were less straightforward. Based on earlier findings and because the spatial component in the PLT is more prominent than it is in the SRTT, we assumed that the PD patients would be better able to learn its spatial sequences than the AD patients, and that therefore their implicit learning on the PLT would be superior to that recorded for the SRTT.
Methods

Participants

Participants were 12 patients with Parkinson’s disease (PD; 7 men), 8 with Alzheimer’s disease (AD; 3 men) and 12 healthy controls (6 men). The patients were recruited from a regional Dutch general hospital. The healthy controls, all without a history of neurological or psychiatric disease, were hospital staff or members of the public recruited via the patients’ spouses. All eligible candidates gave their informed consent before their participation.

A neurologist or geriatrician established the clinical diagnoses. The severity of PD symptoms was rated on the Hoehn-and-Yahr scale of disability (1967), resulting in six PD patients being classified as stage I, five as stage II and one as stage III. At the time of testing six of the PD patients were taking oral medication (four Madopar, one Permax, and one Requip) to alleviate their symptoms. None of the PD patients had dementia as established by neuropsychological testing.

The AD patients were diagnosed in accordance with the NINSDS-ADRDA criteria (McKhann et al., 1984). The MMSE (see next section) was used to determine the severity of the dementia. Patients with an MMSE score < 17 were excluded. Five patients used Rivastigmine and Memantine during the test period.

Table 1 lists the participant demographics per group. The subjects were matched for age and estimated intelligence as closely as possible. General intelligence level was measured using the NLV (Schmand, Lindeboom, & Van Harskamp, 1992), the Dutch equivalent of the National Adult Reading Test (NART; Nelson & O’Connell, 1978), which did not reveal any significant differences between the patient and control groups. The Mini-Mental State Examination (MMSE; Folstein, Folstein & McHugh, 1975) was administered to assess overall cognitive functioning. To optimize the age match for the Alzheimer group, we used a subgroup of the total control group for our AD analyses.

Tasks and Procedure

For the SRTT the participants were seated in front of a computer monitor with a four-key response box placed directly below it. Four horizontally aligned squares, reflecting the alignment of the response keys, were continually displayed at the bottom of the screen. Each trial a stimulus (an asterisk) would appear in any of

| Table 1 Basic Demographics for All Patients and Healthy Controls |
|-------------------|---|-------|-------|-------|
| Group             | N  | Sex   | Mean age (SD) | Mean Nart-IQ (SD) | Mean MMSE (SD) |
| Alzheimer’s disease | 8  | 5m/3f | 79.5 (10.1) | 96 (12.6) | 19.6 (2.0) |
| Parkinson’s disease | 12 | 7m/5f | 67.5 (9.7) | 108 (7.9) | 28.3 (2.3) |
| Alzheimer controls (age-matched subgroup) | 8  | 4m/4f | 78.3 (6.4) | 90 (13.1) | 26.8 (1.6) |
| Parkinson controls (full group) | 12 | 6m/6f | 69.6 (13.9) | 97 (15.2) | 27.5 (1.8) |
the four positions, but never in the same position twice in succession. The participants were instructed to press the key that corresponded to the square in which the asterisk appeared as fast but also as accurately as possible to prevent mistakes. The asterisk remained on the screen until the correct button had been hit, after which it disappeared. Following a 500-msec delay, the next stimulus appeared. All participants received the task instructions before the test session and performed a ten-trial practice session. The actual test comprised six trial blocks each consisting of 100 trials. In the first block (R1) the stimuli were presented in a pseudo-random order. In the next four blocks (L1-L4) a fixed ten-trial sequence (D-B-C-A-C-B-D-C-B-A) was repeated ten times and in the sixth block (R2) the stimuli were again presented in a pseudo-random order. The participants were not informed about the repeated sequence.

Again seated in front of a computer monitor, the participants performed the Pattern Learning Task on a sheet of paper that was fixed to a digitizer (WACOM) using a normal-looking, noninking pen to control the cursor on the screen. The position of the pen tip on and up to 5 mm above the digitizer was recorded. Four dots (2.6 cm in diameter) were continuously displayed on the screen, one of which turned red (see Figure 1).

![Figure 1](image-url) — An example of the pen movements in one fixed ten-trial sequence (A-D-B-C-A-C-B-D-C-B) of the Pattern Learning Task (PLT). The four possible target locations (A, B, C and D) are shown as open black circles. At the start of the first movement (from A to D) the cursor is depicted and the colored target. The fifth trial (from A to B) started in a direction (determined at the periphery, i.e., at the point where the pen trajectory crossed the dotted circle around A), which deviated more than 22.5 degrees from the direction of the ideal A to C line, and is therefore marked as a directional error. The display seen by the participants consisted only of the four black circles, positioned in the middle of the PC screen, one of which was filled with red as the target, and the dark blue pen cursor.
Participants were instructed to move the cursor (a blue dot with a 0.9-cm diameter) toward the red target by means of the pen as quickly as possible. After the cursor had been inside the target for a period of 200 ms, a beep lasting 200 ms was sounded. Immediately after the beep the next trial started with another circle turning red. Participants familiarized themselves with the task with a practice block consisting of four blocks of 24 trials using two stimulus positions only. The actual test comprised six blocks of 100 trials each, with a short break (several minutes) in between the blocks. A first pseudo-random trial block (R1) was followed by four blocks (L1-L4) with a fixed sequence that was repeated ten times, after which in the sixth block (R2) another pseudo-random sequence of stimuli was presented. Again, the participants were not informed about the repeated sequence. Two versions of the task were used with the short version consisting of a less burdening four-item sequence (A-B-D-C) and the longer version of a ten-item sequence (A-D-B-C-A-C-B-D-C-B) that most closely resembled the SRTT. Overall, both versions produced similar results and were completed by all participants. Since the long version can be best compared with the SRTT, and to restrict the number of data to be accounted for, we will not report the results on the short task.

All participants were examined individually. They always performed the MMSE as the second and the NLV as the fourth component in the test session, with the SRTT and the PLT being administered alternately, albeit that the two PLT task versions were always presented in succession.

After the test session all participants were asked if they had noticed anything with respect to the tasks to establish whether they had become aware of the tasks’ fixed sequences. As in our experimental design (two implicit sequence learning tests) the participants needed to remain naive with regards to the fixed sequence till the end of the test session, inquiries about explicit sequence knowledge could not be made after each of the tests.

**Data Analysis**

As explained, learning in the SRTT and the PLT involves both visuo-motor learning and sequence-specific learning. Accordingly, it is generally acknowledged in implicit learning studies that the general decrease observed across learning trials—in this study from block R1 to block L4—must be interpreted as the combined result of these two learning components. However, from block L4 to block R2, the effect of task-specific sensory-motor learning will be minimal compared with the disruption caused by the change of a fixed target sequence to a random sequence. It, consequently, is general practice in implicit learning studies to take the difference between the second random block (R2) and the previous fixed-sequence block (L4) as a measure for the amount of sequence learning (Knopman & Nissen, 1987). A second indication of sequence learning might be found in the increase of errors when the order of the stimuli changes from fixed (in block L4) to random (in block R2). Therefore, for the SRTT we took the increases in reaction time (RT) and in the percentage of errors recorded in the second random block (R2) relative to the fourth fixed-sequence block (L4) as measures of implicit sequence learning. Trials in which an incorrect button was pushed were excluded from the RT analysis.

PLT performance was recorded and analyzed by means of OASIS software (De Jong, Hulstijn, Kosterman, & Smits-Engelsman, 1996). Also in this task the
increase in total time (TT) in the last random block (R2) relative to that recorded for the last fixed-sequence block (L4) was taken to reflect the measure of implicit learning. We subsequently subdivided TT in the time needed to initiate a movement (RT) and the time needed to cross the distance between the two circles (movement time or MT). We defined RT as the time between the onset of stimulus presentation and the time at which the pen left the start circle and crossed its 0.4-cm periphery (total diameter: 3.4-cm). We opted for this later distance threshold value and not for a velocity criterion (a change from standstill to movement) because a few patients were not able to keeping their pen in one place after reaching the target of the previous movement, and waiting for the next stimulus to appear. A second reason for adopting this distance criterion was that participants were allowed to start moving the pen toward the anticipated next stimulus before it was actually displayed. This instruction stimulated participants to move more or less continuously, with only very short intermittent stops, between successive target movements, but made a definition of reaction time based on a velocity threshold not reliable. We defined MT as the time taken to cross the distance between the start-circle’s periphery and the periphery of the target circle. The TT, RT, and MT analyses excluded trials in which a directional error had been made.

For the PLT we analyzed directional errors (DE; see Figure 1), which were defined as movements that left the start circle at the wrong angle, i.e., deviations >22.5 degrees from the most optimal angle. In the SRTT an error was the end result of pressing the wrong button. It should be emphasized that the errors for the two tasks were hence not of the same caliber. In the PLT an error only reflects the choice of a nonoptimal movement direction in the first phase of the movement toward the target that can be corrected during the later stages of the movement. None of the participants actually hit a noncolored target after making a directional error. Note that if participants were fast and started moving the pen in the anticipated direction without waiting for the next target stimulus to turn red, they were more likely to make errors, particularly in the second random block (R2), because here the previously learned sequence of directions did no longer apply. Therefore, an increment in error rate in block R2 relative to that recorded for L4 was taken to indicate effects of implicit sequence learning.

When asked at the end of the test session, none of the participants expressed explicit knowledge of the sequence in the PLT. The two participants (both PD patients) that did indicate such an awareness for the SRTT were subsequently eliminated from the SRTT analyses. Furthermore, one patient was eliminated because of extremely slow RTs.

**Statistical Analysis**

Repeated-measures ANOVAs (GLM) were conducted with one within-subject factor (Block) and one between-subjects factor (Group) to test learning effects. Simple group differences (in average scores across learning blocks and in R2-L4 differences) were tested with an independent samples t test, and are reported with 1-tailed significance values in case of predictions of the direction of the difference. The Parkinson group was compared with the total control group, while the AD patients were compared with an equally large number of age-matched controls that were selected from the total control group. Alpha was set at 0.05 throughout the study.
Results

SRTT Performance Scores

The mean RTs for the three groups on each of the six SRTT blocks are presented in Figure 2. The two patient groups and their controls showed some learning in the task, which was evident from a significant decrement in RT across blocks R1 through to L4 (PD/C: $F_{(4,16)} = 7.91, p = .001$; Linear contrast: $F_{(1,19)} = 33.08, p < .0001$; AD/C: $F_{(4,11)} = 12.26, p < .0005$; Linear contrast: $F_{(1,14)} = 12.26, p = .001$). As expected, the PD and the AD groups had slightly longer RTs than their respective control groups (PD/C: $t_{(19)} = 1.765, p = .047$; AD/C: $t_{(14)} = 1.78, p = .049$). More importantly given this study’s focus on sequence learning, we found that the L4-R2 increase in RT was significant in the PD/C and the AD/C comparisons.

![Figure 2](image_url) — Mean reaction times per group for the random blocks (R1 and R2) and the fixed-sequence blocks (L1-L4) of the Serial Reaction Time Task (SRTT). Error bars reflect standard errors.
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(PD/C: $F_{(1,19)} = 31.37, p < .0001$; AD/C: $F_{(1,14)} = 33.68, p < .0001$). This increment was smaller in the PD group than it was in their control group (PD: 55 ms, Control: 105 ms; $t_{(19)} = 1.765, p = .047$), but not significantly different for the AD group and their controls (AD: 183 ms, Control: 120 ms; $t_{(14)} = 1.21, p = .246$ (2-tailed)).

The SRTT error percentages for the R1 to L4 blocks did not differ significantly between groups (PD: 3.6%; AD: 5.0%; controls 4.0% (with 3.7% for the AD control group)). Implicit learning of the fixed sequence was reflected by a significant increment in error rates in block R2 relative to block L4 in the PD and the control group, with rates increasing from 2.4% to 5.6% and from 4.5% to 5.1% ($F_{(1,19)} = 11.93, p = .003$), respectively. This increase in errors was larger for the PD group than it was for the controls ($t_{(19)} = 2.36, p = .029$ (2-tailed)).

Contrary to expectations, with increases from 5.9% to 6.2% and 5.2–5.5%, respectively, the L4-R2 increments in error percentages for the AD patients and their controls were not significant, nor did they differ between the two groups.

**PLT Performance Scores**

Figure 3 depicts the means and standard errors for the total times (TTs) on the six blocks of the PLT for all participants of each group as none of the participants had explicitly indicated discernment of the PLT sequence following the test session. Further analyses also did not reveal any differences between the two PD patients that had been excluded for the SRTT analyses and the other patients. The controls of the AD group showed the same course in mean TT as the total control group, but overall their TTs were prolonged with approximately 100 ms.

Analogous to the SRTT, patients and controls demonstrated learning, as was reflected by a significant TT reduction across blocks R1 through to L4 (PD/C: $F_{(4,19)} = 19.91, p < .0001$; Linear contrast: $F_{(1,22)} = 84.77, p < .0001$; AD/C: $F_{(4,11)} = 8.08, p = .003$; Linear contrast: $F_{(1,14)} = 37.05, p < .0001$).

As expected and also in line with the SRTT data, the controls showed lower mean TTs than the two patient groups (PD/C: $t_{(22)} = 1.938, p = .033$; AD/C: $t_{(14)} = 1.908, p = .039$). As indicated by the L4-R2 increments in TT, both the AD patients and the controls showed implicit learning of the fixed PLT sequence (AD: 67 ms, Control: 59 ms; $t_{(14)} = 0.359, p = .725$ (2-sided)), whereas the L4-R2 increase in the PD group was significantly smaller than it was in their controls (PD: 12 ms, Control: 55 ms; $t_{(22)} = 2.724, p = .006$).

The two graphs of Figure 4 show the PLT mean reaction (RT) and movement times (MT) for the three groups. Note the contrasts between the increments in RTs and MTs in the L4 and R2 blocks, which we took as possible signs of implicit learning: the figure shows marked increments in RT and no increase in MT in these specific blocks. Figure 4 also shows a small increase in RT for the PD patients, which was overall smaller than the RT increase recorded for the controls, but the significance of this interaction was reduced ($p = .066$) when compared with the strong interaction we found in the TTs of the PD patients and their controls ($p = .006$, as reported in the previous paragraph).

The mean directional error (DE) rates for the six PLT blocks for each of the three groups are presented in Figure 5. What stands out is the significant increase in DEs between blocks L4 and R2 for all groups including the PD patients who had shown no increase in their TTs ($t_{(31)} = 5.014, p < .001$; group differences in L4-R2 increase: PD/C: $t_{(22)} = 0.331, p = .744$; AD/C: $t_{(14)} = 0.07, p = .945$).
As predicted, the Parkinson patients showed less evidence of implicit learning than both the healthy controls and the Alzheimer patients, as was reflected by the time measures in the SRTT and the PLT. However, the increases in the error percentages we noted for the PD patients did indicate some implicit learning in both tasks, while when we took errors into account in the AD group, learning appeared somewhat compromised. Our conjecture that the performance of Parkinson patients would be less affected in the PLT in which spatial demands were more prominent was not confirmed. We will next discuss the findings on performance times and errors for the two tasks separately.

**Figure 3** — Total times for the random blocks (R1 and R2) and the fixed-sequence blocks (L1-L4) per group for the Pattern Learning Task (PLT). Error bars reflect standard errors.

**Discussion**

As predicted, the Parkinson patients showed less evidence of implicit learning than both the healthy controls and the Alzheimer patients, as was reflected by the time measures in the SRTT and the PLT. However, the increases in the error percentages we noted for the PD patients did indicate some implicit learning in both tasks, while when we took errors into account in the AD group, learning appeared somewhat compromised. Our conjecture that the performance of Parkinson patients would be less affected in the PLT in which spatial demands were more prominent was not confirmed. We will next discuss the findings on performance times and errors for the two tasks separately.
Figure 4 — Mean reaction times (left panel) and mean movement times (right panel) for the random blocks (R1 and R2) and the fixed-sequence blocks (L1-L4) per patient group for the Pattern Learning Task (PLT). Error bars reflect standard errors.
The control and AD group both showed a lengthening of their response times on the random trial block of the SRTT relative to the preceding fixed trial block, which increment is taken to reflect implicit sequence learning in this task (Knopman & Nissen, 1987). As was to be expected based on the literature, the RTs of the PD patients increased less than they did in the healthy controls. A meta-analysis of studies that used the SRTT had shown that implicit learning, as reflected in response time, was significantly impaired in Parkinson patients relative to the performance of healthy peers (Siegert et al., 2006). Our study thus confirmed these results but now in a PD group with mild symptoms. Half of our PD patients had been diagnosed as stage 1 on the Hoehn-and-Yahr scale while some of the earlier studies included relatively more stage-2 and stage-3 PD patients (Doyon et al., 1997; Stefanova et al., 2000). However, some studies did not report Hoehn-and-Yahr ratings (Jackson et al., 1995, Sommer, et al., 1999), rendering a sound comparison in terms of disease severity impossible.

**Figure 5** — The group’s mean directional error rates across the random blocks (R1 and R2) and the fixed-sequence blocks (L1-L4) for the Pattern Learning Task (PLT).
In the PLT we took the increase in total performance time (TT) between the fixed and random blocks as the measure of implicit motor-sequence learning. Both the controls and the AD patients showed an increment in their TTs, but the PD patients did not, indicating that in this group implicit learning could not be established. When we subdivided the TT into a response (RT) and a movement component (MT), the RT pattern corresponded with the TT pattern while the MTs were not prolonged in the final random block. The PD and control groups even showed a decrease in the time they needed to move the cursor into the target in the final block. All groups learned to execute the required movements slightly more quickly in the course of all trial blocks (learning phase), but the learning effect was unrelated to sequence presentation. In contrast, the RTs of all groups increased in the final block, which is indicative of implicit sequence learning, although the increment was less pronounced ($p = .066$) in the PD group.

Besides reflecting the time the participants needed to search for the location of the next target, to plan the muscle commands and to initiate the movement, the recorded PLT reaction times may also have included some of the actual movement time as we set the boundary between RT and MT somewhat late, i.e., at the moment the pen left the start circle. Because this choice may have introduced more variance in RTs, it may have resulted in a statistically smaller difference between the PD and control groups’ RTs than we found for their total performance times. Alternatively, the measure of RT has been suggested to be less appropriate in this patient group because Parkinson patients are typically characterized by a slowed reaction and an inability to initiate movements fast, which might thus prevent them from demonstrating sequence learning through a difference in RT (Westwater et al., 1998). However, this cannot explain the increase we found in their RTs in the last random block, an increment we took as evidence of implicit learning.

Overall, we gained additional information by looking at the RT and MT components of the TTs. The performance differences between the PD patients and the controls in the PLT occurred exclusively during the preparation and initiation stages of the action and not during the execution of the sequenced action.

In our study, we also analyzed the amount of errors in the two tasks. Both in the SRTT and the PLT the increment in errors we observed in the final random block in both the controls and the PD patients indicated implicit sequence learning. Surprisingly, the SRTT error percentage in the last fixed-sequence block (L4) of the controls was higher than that of the PD patients. This may be explained by a different speed-accuracy trade-off in the two groups during the end of the learning phase: when you respond faster in the fixed-sequence blocks, you are bound to make more errors. Since people with PD are seldom able to react fast or may perhaps have already unlearned the habit to try, they take more time to respond and consequently make fewer mistakes. This seemed to be confirmed by the PLT, where we also recorded higher error percentages during the first part of the learning phase in the control group. Contrary to our expectations, the AD patients showed no increase in the number of errors in the SRTT. Moreover, when examining the PLT data more closely, we found that their DE (directional error) rate had already started to rise in the fourth fixed-sequence block. We hence cannot be sure whether the increase in DEs in the final block is solely explained by implicit sequence learning. Ferraro et al. (1993) mentioned a breakdown of attention in Alzheimer patients. Possibly, also our AD group had more difficulty in keeping their attention focused until the end of the task.
As stated in the methods section, in the PLT a DE reflected the choice of a nonoptimal movement direction in the first phase of the movement toward the target that could be corrected during the later stages of the movement. The DEs could thus reflect both sequence knowledge and a preference for speeded reactions over immediate accuracy (straight-lined trajectories). Because our subjects were allowed to leave the start circle before the new target circle lit up, they indeed favored speed over accuracy, resulting in high DE rates. That in all participants the percentages of DEs in the last random trial block were higher than they were in the first random block can only be explained by their moving more frequently into a direction that they had chosen based on sequence knowledge they had unknowingly acquired in the preceding fixed blocks. An explanation in terms of a sudden change in speed-accuracy trade-off in the final random block is less plausible.

The error results showed evidence of implicit learning in our PD patients but also pointed to a compromised implicit learning in the AD patients, while the patients’ performance times indicated implicit learning in the AD but compromised learning in the PD group. How can this seeming disparity be explained? Possibly, performance times and error measures assess different processes. As already mentioned in the introduction, sequential movement skills are based on several processes and sequences can be represented in the order in which the stimuli occurred, i.e., a visuospatial representation, or the order in which the associated movements are made, e.g., the sequence of keypresses. Hikosaka et al. (1999), and Nakahara, Doya, and Hikosaka (2001) also posited a distinction in the neural networks subserving the learning of sequential procedures. The authors discriminate between a visual loop relying on visual coordinates and a motor loop that depends on motor coordinates, which loops “learn” a sequence in parallel. It is important to note that in Hikosaka’s research the contributions of each of the two mechanisms are assessed by separate measures. Errors are taken as indicators of learning in the visual loop, while reaction or performance times are used as a measure of learning in the motor loop (Bapi, Doya, & Harner, 2000; Hikosaka, Rand, Miyachi, & Miyashita, 1995; Rand et al., 2000). It may be hypothesized that in PD patients mastery of the visual loop is, more or less, intact while mastery of the motor loop is compromised and that the opposite may occur in the AD patients. That learning in the visual loop is compromised in AD is in concurrence with the compromised visuospatial abilities Rascovsky et al. (2002) found and the inferior parietal perfusion Keilp, Alexander, Stern, and Prohovnik (1996) demonstrated in this patient group. It would also explain why studies that used a rotor pursuit test, which according to Willingham (1998) is primarily a motor sequencing task, always reported preserved implicit learning in Alzheimer patients (Van Halteren-Van Tilborg et al., 2007), whereas those using tasks tapping both motor and spatial processes showed diminished learning (Knopman, 1991; Willingham, et al., 1997). However, again, visuospatial functioning has also been found to be compromised in PD patients, while Huang et al. (2007) found metabolic reductions in the patients’ parietal association areas. There is no commonly accepted nosology by which visuospatial disorders are classified and the disorders represent a wide variety of cognitive functions with diverse underlying neuroanatomical mechanisms (Freeman et al., 2000). More research is needed to separate and correlate different visuospatial disorders with motor sequencing disorders.
In sum, we found evidence of implicit sequence learning in our healthy controls and Alzheimer patients on both the SRTT and our PLT, as reflected by the various time measures. However, the tasks’ error rates revealed implicit learning in the Alzheimer group to be impaired. And although the time measures of the Parkinson patients on the SRTT and PLT were indicative of less implicit sequence learning, the error measures of both tests did illustrate that the Parkinson patients had acquired implicit knowledge of the repeated sequences. Although assessing different types of sequential motor actions, the results of the two tasks were similar in this respect.

With our study we have underscored the relevance of discriminating between performance and error measures in experimental research involving Alzheimer and Parkinson patients. The differences in the outcomes of previous studies can at least partly be explained by the differences in the types of tasks and measures used. By looking at the various aspects that underlie our remarkable ability to master sequential motor actions, we can learn more about which processes are deficient in which patient groups. Any proven impairments in a patient’s (remaining) spatial and motor learning abilities may have consequences for the way in which in clinical practice motor skills are (re)trained.

References


