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Temporal Processing in the Basal Ganglia

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This study investigated the role of the basal ganglia in timing operations. Nondemented, medicated Parkinson's disease (PD) patients and controls were tested on 2 motor-timing tasks (paced finger tapping at a 300- or 600-ms target interval), 2 time perception tasks (duration perception wherein the interval between the standard tone pair was 300 or 600 ms), and 2 tasks that controlled for the auditory processing (frequency perception) demands of the time perception task and the movement rate (rapid tapping) in the motor-timing task. Using A.M. Wing and A.B. Kristofferson's (1973) model, the total variability in motor timing was partitioned into a clock component, which reflects central timekeeping operations, and a motor delay component, which estimates random variability due to response implementation processes. The PD group was impaired at both target intervals of the time perception and motor-timing tasks. Impaired motor timing was due to elevated clock but not motor delay variability. The findings implicate the basal ganglia and its thalamocortical connections in timing operations.

It has become increasing apparent that the traditional view of the basal ganglia as a motor system is far too restrictive. There is now mounting evidence that dopamine activity in the basal ganglia–thalamocortical pathways is related to some cognitive processes that underlie actions as well as to behaviors that are less dependent on the motor system. Investigations into the role of the basal ganglia in explicit timing operations parallel the historical focus on the motor system, wherein motor timing has received far more attention than time perception. The present study used individuals with Parkinson's disease (PD) to determine if the basal ganglia and its dopaminergic-dependent thalamocortical pathways (Alexander, DeLong, & Strick, 1986) play a more general role in controlling processes that govern explicit timing, both in perception and in movement.

The basal ganglia have been a focus of investigations into the neural control of timing, in part, because there are disturbances in rhythmic movement in PD (Freeman, Cody, & Schady, 1993; Nakamura, Nagasaki, & Narabayashi, 1978; Narabayashi & Nakamura, 1985). In addition, pharma-

cological manipulations of dopamine, which is depleted in PD, have shown that time perception in animals is altered when dopamine is reduced (Maricq, Roberts, & Church, 1981; Meck, 1983). It has also been suggested that time perception and motor timing engage a common timekeeping operation (Keele, Ivry, & Pokorny, 1987; Keele, Pokorny, Corcos, & Ivry, 1985), in which case both forms of timing should be disrupted in individuals with PD, if the basal ganglia controls timing operations. Empirical findings in PD are controversial, however, because time perception was impaired in PD in one study (Artieda, Pastor, Lacruz, & Obeso, 1992) but not in another (Ivry & Keele, 1989). Similarly, some studies have found motor-timing deficits in PD (O'Boyle, Freeman, & Cody, 1996; Pastor, Artieda, Jahanshahi, & Obeso, 1992; Wing, Keele, & Margolin, 1984) and others have not (Duchek, Balota, & Ferraro, 1994; Ivry & Keele, 1989).

Time perception has been studied using tasks that have no motor requirements, so that ostensibly the task is a relatively pure reflection of timing processes. Only two studies have investigated the role of the basal ganglia in time perception, and discrepant results have been reported. Ivry and Keele (1989) found no impairments in medicated PD patients when they made judgments about the relative duration of two tone intervals. In contrast, Artieda and colleagues (1992) reported that temporal perception was diminished in PD patients, who were withdrawn from medication, when they were tested for their ability to discriminate two stimuli that were separated by small intervals of time. In this study, performance improved significantly after PD patients received dopaminergic replacement therapy, but it is not known whether their performance actually returned to normal levels, because comparisons were not made with the control group and the medication status of the patients was confounded with practice effects on the perception tasks. Although the medication status of PD patients is an important factor, dopaminergic functioning is not fully restored by

medication (Jankovic & Marsden, 1988), so that if the basal ganglia controls time perception, deficits could still emerge, even in patients receiving dopaminergic replacement therapy. The discrepant findings between the two studies also could be due to the use of different tasks, which may vary in their dependence on time perception.

Although the role of the basal ganglia in motor timing has received more attention, the assessment of timekeeping operations is complicated by the involvement of motor planning and implementation processes that are impaired in PD (Harrington & Haaland, 1991). Motor-timing competency is commonly assessed under conditions in which participants reproduce intervals of a constant duration. Participants tap with their index finger in synchrony to a series of tones, after which the tones stop, and they continue to tap at the same pace. Timing competency is assessed when the tone is absent, because during this phase, participants must maintain an internal representation of the target interval duration. Early observations in healthy adults showed that the variability of interresponse intervals (IRIs) increased with the duration of the target interval and that adjacent IRIs tended to be negatively correlated (Wing, 1980; Wing & Kristofferson, 1973). These observations were captured in a model that assumes that time is represented explicitly in the brain by a pacemaker or a clock (Wing & Kristofferson, 1973). The model proposes that the total variability of the IRIs can be partitioned into two independent sources. One source is the clock component of variability, which represents the operation of a central timekeeping mechanism. The other source is the motor delay component, which estimates the random variability due to the delay in the triggering of the response implementation process. The computation of this component rests on the assumption that adjacent IRIs will correlate negatively and nonadjacent IRIs will not correlate. Therefore, the motor delay variance is calculated from the negative Lag-1 covariance. The clock variance is then estimated by subtracting the motor delay variance from the total variance. These sources of variability appear to have some functional specificity, because they have been dissociated in patients with neurological disorders (Ivry & Keele, 1989; Wing et al., 1984) and in healthy individuals by manipulating variables that alter one, but not the other, variance source (Sergent, Hellige, & Cherry, 1993).

Wing and Kristofferson's (1973) theoretical framework drove several investigations into the role of the basal ganglia in motor timing. An early case study of 1 medicated PD patient attributed the elevated IRI variability during the continuation phase to a deficiency in the central timekeeper (Wing et al., 1984), because only the clock source of variability was impaired. Two group studies of PD have shown that motor timing is impaired in patients who were withdrawn from dopaminergic replacement therapy (O'Boyle et al., 1996; Pastor et al., 1992), but it improves substantially when medication is reinstated (see Ivry & Keele, 1989, for conflicting results). However, in these studies, both the clock (C) and the motor delay (MD) variability were impaired in unmedicated patients, which raises concerns about whether the timekeeping and the motor implementation processes

were independent, as the model assumes, because the computation of the clock variance depends on the motor delay variance (i.e., var[C] = var[I] − 2var[MD], where I is the total variability). For this reason, it has been more desirable to study medicated PD patients, wherein motor delay variability is typically normal (Duchek et al., 1994; Ivry & Keele, 1989; O'Boyle et al., 1996). In group studies of medicated PD patients, however, the findings are discrepant with one study showing abnormal clock variability (O'Boyle et al., 1996) and two other studies reporting normal clock variability (Duchek et al., 1994; Ivry & Keele, 1989).[1] The reason for these negative findings is not entirely evident. One possibility is that the latter two studies may have tested patients who were predominantly in early stages of the disease (i.e., mild, asymmetric neurological symptoms on medication) and may have neglected to systematically test the most affected hand. In fact, medicated PD patients with asymmetrical symptoms showed normal motor timing when tested on their "better" hand but showed abnormal motor timing when tested on their most affected hand (O'Boyle et al., 1996). This explanation could account for the negative findings of Duchek and colleagues (1994), whose sample consisted of a high percentage of unilateral PD patients, but its bearing on the Ivry and Keele (1989) study is unknown because in the latter study the stage or the severity of the medicated PD group was not documented.

Only one study (Ivry & Keele, 1989) has investigated motor timing and time perception in the same group of medicated PD patients, showing that motor timing and time perception were normal. However, given the conflicting findings in PD, the fact that time perception has not been well studied, and the potential importance of disease severity, it is unclear whether the basal ganglia or its thalamocortical pathways mediate one or both forms of timing in humans.

The role of the basal ganglia in timing was examined in the present study in a control group and in a group of medicated PD patients, the large majority of whom showed bilateral symptoms. Participants were studied in two conditions of a motor-timing and a duration perception task. In both tasks, the interstimulus interval (ISI) between tones was manipulated (300 or 600 ms) to provide a more reliable test of timing competency than previous studies that used a single interval (Duchek et al., 1994; Ivry & Keele, 1989; O'Boyle et al., 1996). The longer ISI was close to the 550-ms ISI used in several studies, and the shorter ISI was twice as fast but did not exceed the maximum tapping speed of the patients. We predicted that if the basal ganglia support timing operations in perception, PD patients will show impaired duration perception. Similarly, if the basal ganglia control motor-timing processes, individuals with PD will

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[1] Although Pastor and colleagues (1992) studied the effect of levodopa medication on motor-timing variability, statistical tests comparing medicated PD patients with control participants were not conducted, because the vast majority of PD patients were excluded due to Lag-1 autocorrelations outside the expected range when tested both on and off medication. The remaining sample of 4 PD patients precluded meaningful statistical analyses of the data.

show greater variability in the clock component of motor timing. Alternatively, if the basal ganglia support a timekeeping operation that underlies both time perception and motor timing, individuals with PD will show impairments on both timing tasks.

A secondary aim of our study was to investigate the relationship between symptom severity and timing competency to determine if the degree of dopaminergic transmission dysfunction[2] could explain some of the discrepant findings in studies of medicated PD patients in which this relationship has not been examined. This issue has been addressed in two studies of unmedicated PD patients, wherein symptom severity was not related to motor-timing variability (Pastor et al., 1992) but was significantly correlated with performance on tests of temporal perception (Artieda et al., 1992). In the present study, the severity of neurological symptoms (i.e., tremor, rigidity, and bradykinesia) was correlated with performance in both timing tasks to determine if this variable could account for some of the controversial findings in the literature.

Method

Participants

Table 1 describes the characteristics of the 24 normal controls and the 34 PD participants. All PD patients were receiving dopaminergic replacement therapy and were tested during their normal medication cycle when they were optimally medicated ("on" state). All participants were right-handed, and independent t tests showed there were no significant differences between the groups in age, education, gender, or scores on the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975). All individuals in the PD group scored at or above 24 on the MMSE, which is within normal limits. However, it is possible that as a group our PD patients may have shown some mild cognitive decline, because the MMSE is not a comprehensive neuropsychological assessment and is insensitive to more subtle impairments in cognitive functioning. Disease severity was assessed by a board-certified neurologist (N.H.) using the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn et al., 1987) and the Hoehn–Yahr scale (Hoehn & Yahr, 1967). All severity ratings were conducted when patients were on medication. Table 2 displays these data and shows that disease severity was mild (Stage 1), affecting only one side of the body, in approximately one fourth of the PD participants and moderate to severe (Stages 2 through 4) in the remaining participants, who showed bilateral symptoms of the disease.

Table 1
Demographic Characteristics

Characteristics	Control (N = 24)		Parkinson's disease (N = 34)	
	M	SD	M	SD
Age	66.8	8.7	69.2	7.6
Education	15.0	3.0	14.9	3.2
Gender (% male)	79		71	
Mini-Mental State Examination[a]	28.5	1.40	27.7	2.2

[a]Folstein et al. (1975).

Table 2
Description of Parkinson's Group

Variable	M	SD
Disease duration[a]	5.50	4.70
UPDRS[b]	29.42	13.56
Tremor[b]	2.09	2.05
Rigidity[b]	1.06	0.89
Bradykinesia[b]	9.18	4.55
Hoehn & Yahr[c]	2.40	0.90

[a]Disease duration is expressed in years and ranged between 1 and 20 years.
[b]Disease severity was assessed by the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn et al., 1987). The total score can range from 0 to 137. The assessments of tremor, rigidity, and bradykinesia are from the UPDRS. Scores can range from 0 to 8 for tremor, 0 to 5 for rigidity, and 0 to 18 for bradykinesia.
[c]Disease severity also was assessed by the Hoehn–Yahr Scale (Hoehn & Yahr, 1967), with 23%, 35%, 35%, and 7% of the patients classified in Stage 1, 2, 3, or 4, respectively.

Procedures

Participants performed all tasks using their right hand. The right hand was tested in the PD group, because the large majority of patients showed bilateral symptoms. Though motor-timing deficits may have been underestimated using this procedure, we report that they are still present, and, thus, the method provides a sufficient test of the hypothesis. The order of tasks was counterbalanced across participants.

Paced finger-tapping task. Participants completed two conditions of a paced finger-tapping or motor-timing task in which they tapped in synchrony to a series of 20 tones (induction phase), after which the tone stopped, and they continued to tap at the same pace for 22 responses (continuation phase). Immediately following the continuation phase, the tones reappeared, and the participants continued to tap at the same pace for 20 additional responses (resynchronization phase). The tones were 50 ms in duration and approximately 75 dB. After the trial terminated, the mean tapping rate during the continuation phase was displayed. The resynchronization phase was included to provide more direct feedback about tapping pace, with the prospect of encouraging participants to minimize extreme deviations from the target interval.

In one condition, the tones were separated by a 300-ms interval; in the other condition, they were separated by 600 ms. Participants completed six consecutive trials at each interval, the order of which was counterbalanced across participants. Error trials were those in which two or more consecutive response intervals fell outside of ±50% of the ISI. This error criterion departs from previous studies that excluded trials if any single response interval fell outside these limits (Ivry & Keele, 1989). Although the intention of this latter criterion was to remove extreme responses due to tremor or alterations in force, the fact that this can result in high rates of repeated trials, especially in neurological patients (Williams, Woollacott, & Ivry, 1992), raised some concern that this procedure may filter out responses that are typical of a particular participant population and that are, therefore, meaningful. Thus, the error criterion adopted in our study was less conservative. Error trials were excluded from the data analyses and were repeated, so that all participants completed six trials at each target interval (see footnote

4 for analyses that excluded trials if any single response fell outside ±50% of the ISI).

Duration perception task. Participants also completed two perception tasks, both of which used the parameter estimation by sequential testing (PEST) procedure to derive a criterion threshold (e.g., for details, see Ivry & Keele, 1989). In the duration perception task, participants judged the relative duration of two tone pairs. As in the finger-tapping task, 75-dB tones were 50 ms in duration. A standard tone pair was presented and followed 1 s later by a comparison tone pair. Participants indicated by pressing a key whether the interval between the comparison tone pair was longer or shorter than the standard.

In one condition, the interval between the two tones in the standard pair was always 300 ms, in the other condition, it was 600 ms. The presentation order of the target intervals was counterbalanced across participants. Ten practice trials were presented followed by 50 experimental trials (i.e., 25 judgments each for the upper and lower thresholds). A difference threshold was computed by taking the difference between the upper and the lower duration thresholds and dividing this value by 2 (i.e., the test threshold was set to equal 1 *SD* from the point of subjective equality [PSE], which is the interval at which participants are equally likely to respond shorter or longer).

Control tasks. A control task, frequency perception, used similar procedures as for the duration perception task. This task was included as a control for the general auditory processing requirements of the time perception task. In addition, because the design of both perceptual tasks is similar, impaired duration perception, but normal frequency perception, would further strengthen the assumption that central timing operations are specifically impaired, rather than other cognitive processes that are required for the performance of both tasks (e.g., auditory discriminations). The interval between the two 50-ms tones in the standard and in the comparison pairs was fixed at 550 ms. The frequency of the standard tones was 1000 Hz, and the comparison tones consisted of higher or lower frequencies. Participants judged whether the pitch of the second tone pair was higher or lower than the standard pair. The 10 practice trials were followed by 50 experimental trials (i.e., 25 judgments each for the upper and lower thresholds). A difference threshold was computed by taking the difference between the upper and lower frequency thresholds and dividing this value by 2.

Another control task, rapid tapping, was included as an additional check to ensure that the base intervals in the paced finger-tapping task did not exceed participants' maximum tapping rate. Participants received six trials in which they tapped as rapidly as possible for 10 s. The mean inter-tap interval across the six trials was taken as a measure of their maximum tapping rate.

Analyses of Paced Finger-Tapping Data

Only the data from the continuation phase of the paced finger-tapping task were analyzed. The first two IRIs of the continuation phase were discarded, and the analyses were performed on the remaining 20 IRIs. On each trial, the following measures were computed and then averaged across the six trials for a particular target interval. The mean IRI was computed as a measure of the extent to which participants achieved the target interval. The untransformed standard deviation of the IRIs was computed and was analyzed because previous studies have reported that a linear transformation of these data has only minimal effects on the standard deviation and the estimates of component sources of variance (Ivry & Keele, 1989; O'Boyle et al., 1996), which was also true of our data (see Results section and Footnote

3). The formal model of Wing and Kristofferson (1973) was applied to the raw data to obtain estimates of the clock and the motor implementation sources of variance. In this model, the total variability (I) of the IRIs is equal to the additive variability of the clock (C) and motor delay (MD) sources. This is expressed as $\text{var}(I) = \text{var}(C) + 2\text{var}(MD)$. According to this model, the clock or internal timekeeper produces a pulse when the target interval passes, and this activates the motor implementation process. The motor delay component is doubled because each IRI includes two implementation processes, one that produces the first response and the other that produces the second response. Var(I) can be computed directly from the data. The estimate of the motor delay variance assumes that participants do not use feedback from a response to affect the timing of the next response, so that the two variance sources are independent. This results in a negative covariance between successive IRIs, and covariances of 0 at lags greater than 1. Thus, the motor implementation component is estimated from the Lag-1 autocovariance, autocov(1) = −var(MD). The clock source of variance can be computed by inserting the I and MD variance terms in the equation and making the appropriate algebraic manipulation.

Results

Separate analyses of variance (ANOVAs) were used to compare the two groups on each dependent measure. ANOVAs with repeated measures were used to test the within-subject effects of interval (300 and 600 ms) in the paced finger-tapping and the duration perception tasks and order (testing order of the 300- and 600-ms conditions) in both of these tasks.

Control Tasks

Frequency perception was not significantly impaired ($p < .20$) in the PD group ($M = 9.9$ Hz, $SD = 6.0$ Hz) relative to the control group ($M = 7.5$ Hz, $SD = 6.8$ Hz), indicating that the PD group's ability to process auditory sensory information, similar to that presented in the duration perception task, was within normal limits. As expected, the mean inter-tap interval in the PD group ($M = 186.6$ ms, $SD = 27.0$ ms) was impaired relative to the control group ($M = 169.1$ ms, $SD = 19.4$ ms), $F(1, 56) = 7.10, p < .01$. Most important, these findings show that the 300-ms target interval in the paced finger-tapping task was considerably longer than all participants' maximum tapping speed.

Duration Perception Task

The duration perception findings are displayed in Figure 1. Figure 1 shows that judgments of duration were less accurate when the interval between the standard tone pair was 600 ms than when it was 300 ms, $F(1, 54) = 37.02, p < .001$. Most important, duration perception was impaired in the PD group relative to the control group for both target intervals, $F(1, 54) = 10.84, p < .01$. This could not be attributed to differences between the groups in the PSE ($M = 308, SD = 31$, and $M = 609, SD = 52$ for the control group; $M = 304, SD = 42$, and $M = 590, SD = 50$ for the PD group). No other significant effects were obtained.
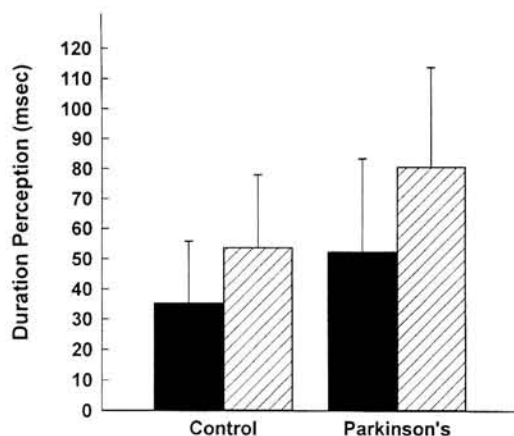
Figure 1. Means (and standard deviations) for duration perception thresholds. The data represent difference thresholds for the 300-ms (solid bars) and the 600-ms (slashed bars) standard intervals. Difference thresholds were obtained using the parameter estimation by sequential testing (PEST) procedure.

Paced Finger-Tapping Task

As in previous studies (Ivry & Keele, 1989; O'Boyle et al., 1996; Pastor et al., 1992; Williams et al., 1992), we found a similar incidence of violations in the model's assumption of negative Lag-1 covariance (Wing & Kristofferson, 1973). Most of these violations were minimally above 0 (less than .09). When Lag-1 covariances were averaged across the six trials in the 300-ms condition, 13% and 23% of the control and PD groups, respectively, showed mean Lag-1 autocorrelations that were positive. Violations were more frequent in the 600-ms condition with positive mean Lag-1 autocorrelations in 17% and 44% of the control and PD groups, respectively. Some studies have attempted to control for violations in this assumption by setting a positive motor delay estimate to 0 and the clock variance to the total variance (Ivry & Keele, 1989; Williams et al., 1992), but this artificially inflates the clock estimate and eliminates the motor delay estimate. This alteration of the data did not affect the general conclusions relative to when data were analyzed using the positive motor delay estimate (Ivry & Keele, 1989; Williams et al., 1992). In fact, when we reanalyzed our data using the approach of Ivry and Keele (1989), the results remained the same.[3] Still others have adjusted for this violation by removing unusually fast and slow intervals as well as the intervals that precede and follow these intervals (Wing et al., 1984), but this filtering procedure distorts the lag autocorrelation computations. Nonetheless, our results were the same as when we analyzed the data by eliminating intervals that were ±50% of the target interval.[4] This is consistent with the findings of O'Boyle and colleagues (1996) who compared four methods for handling these violations, including the method used in the present study, which was to analyze all data, regardless of violations. Their estimates of the clock components did not vary across the four methods. Although there was some variation in the motor delay estimates, it was small and likely of little or no consequence. This suggests that the

computation of the motor delay and the clock variance sources are relatively robust to violations of the model. Thus, in the present study, the data were analyzed without altering the raw data, subtracting the absolute value of the motor delay variability from the total variability to estimate the clock variability.

Number of Error Trials

The number of error trials (i.e., two or more consecutive IRIs that exceeded 50% of the base interval) was low in both groups. For the 300-ms target interval, 92% and 82% of the control and PD groups, respectively, had no error trials. One participant with PD had four error trials. The remaining participants had three or fewer errors. For the 600-ms target interval, 96% and 79% of the control and PD groups, respectively, had no error trials. Two individuals with PD had three error trials, and the remaining participants had two or fewer error trials. Error trials were repeated and were omitted from all subsequent data analyses.

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[3] We analyzed our motor-timing data using the procedures of Ivry and Keele (1989) in which the data were first corrected for the potential linear drift in the IRIs (i.e., correction for nonstationarity) and then all positive Lag-1 covariances were converted to 0 and the total variability was assigned to the clock component. These analyses showed that total variability was greater in the PD than in the control group, $F(1, 54) = 7.2, p < .025$. (Control group means [with standard deviations in brackets] were 20.4 [4.6] and 31.8 [6.5] for the 300- and 600-ms interval, respectively. PD group means were 24.3 [9.4] and 41.8 [17.5] for the 300- and the 600-ms intervals, respectively.) Clock variability also was greater in the PD than in the control group, $F(1, 54) = 12.8, p < .01$, and there was a trend for a Group × Target Interval interaction, $F(1, 54) = 3.49$, $p = .067$, where clock variability was elevated in the PD group more at the 600-ms than at the 300-ms target interval. (Control group means were 13.6 [4.8] and 23.8 [8.8] for the 300- and 600-ms intervals, respectively. PD group means were 18.9 [10.1] and 35.9 [15.7] for the 300- and 600-ms intervals, respectively.) There was no group difference in motor delay variability, $F(1, 54) < 1.0$. (Control group means were 9.9 [5.0] and 12.2 [7.9] for the 300- and 600-ms intervals, respectively. PD group means were 8.0 [7.0] and 10.8 [12.1] for the 300- and 600-ms intervals, respectively.)

[4] We also analyzed our motor-timing data by excluding intervals that fell outside of ±50% of the target ISI (Wing et al., 1984). These analyses resulted in the same conclusions as those that were carried out on the raw data. Specifically, total variability was greater in the PD than in the control group, $F(1, 54) = 8.73, p < .01$, regardless of the interval. (Control group means [with standard deviations in brackets] were 20.0 [4.2] and 33.0 [6.3] for the 300- and 600-ms intervals, respectively. PD group means were 24.7 [9.3] and 39.9 [11.3] for the 300- and 600-ms intervals, respectively.) Clock variability also was greater in the PD than in the control group, $F(1, 54) = 17.18, p < .001$, regardless of the interval. (Control group means were 11.0 [4.6] and 22.1 [9.1] for the 300- and 600-ms intervals, respectively. PD group means were 18.0 [8.4] and 31.8 [9.9] for the 300- and 600-ms intervals, respectively.) There was no significant difference between the groups in the motor delay variability, $F(1, 54) < 1.0$. (Control group means were 11.4 [4.0] and 15.8 [5.9] for the 300- and 600-ms intervals, respectively. PD group means were 11.2 [5.0] and 16.5 [6.0] for the 300- and 600-ms intervals, respectively.)

Mean IRI

The IRI was close to the target interval for both the PD ($M = 320.6$, $SD = 15.2$, and $M = 604.5$, $SD = 21.7$) and the control groups ($M = 325.9$, $SD = 14.7$, and $M = 617.9$, $SD = 16.4$), although the PD group tapped at a slightly faster pace than the control group at both target intervals, $F(1, 54) = 4.25$, $p < .05$. The mean tapping pace did not vary with order, and there were no interactions of group with order or target interval.

Variability of Tapping Intervals

Figure 2A shows that the total variability (expressed as standard deviations) in the tapping intervals was greater in the PD group than in the control group, regardless of the interval, $F(1, 54) = 5.60$, $p < .025$. Total variability also increased with the duration of the target interval in both participant groups, $F(1, 54) = 17.62$, $p < .001$. No other significant effects were found for this measure of variability.

Figure 2, B and C, shows that this pattern of findings was due entirely to the clock source of variability. As expected, clock variability increased with the duration of the interval, $F(1, 54) = 10.6$, $p < .01$, for the PD and control groups. Most important, clock variability was greater in the PD group than the control group, regardless of the interval, $F(1, 54) = 8.25$, $p < .01$. By contrast, motor delay variability was not significantly different between the groups, $F(1, 54) = 2.15$, $p = .15$, nor was there an interaction of Group × Interval for this variability component, $F(1, 54) = 1.07$, $p = .31$. However, in both participant groups, the variability in the motor delay process increased slightly with the duration of the target interval, $F(1, 54) = 11.07$, $p < .01$. The increase in the motor delay variability between the 300- and 600-ms interval was small (the mean difference between intervals was 5.3 ms), but it is inconsistent with the

predictions of Wing and Kristofferson's model and some (Ivry & Hazeltine, 1995), but not all (Wing & Kristofferson, 1973), empirical findings. There were no other significant effects for the clock or motor delay sources of variability.

Disease Severity

The relationship between disease severity and performance on the control and experimental tasks was examined next. Recall that the PD group showed performance deficits of a similar magnitude at each interval in both timing tasks. Hence, the performance measures from the motor-timing and the time perception tasks were averaged across the 300- and the 600-ms interval conditions to minimize the number of bivariate correlational analyses. In these analyses, only a small adjustment was made for Type I errors ($p = .025$), because they were exploratory. Otherwise, more stringent alpha levels might mask small, but meaningful, relationships between disease severity and performance. Nonetheless, the results should be interpreted cautiously.

Pearson correlations (using one-tailed significance tests) were conducted examining the association between each of the main dependent measures in the aforementioned tasks (total, clock, and motor delay variability; difference thresholds from the duration perception and frequency perception tasks; mean inter-tap interval in the maximum tapping speed task) and five measures of disease severity (total UPDRS score; tremor, rigidity, and bradykinesia from the UPDRS; stage of disease from the Hoehn–Yahr scale). Bradykinesia and stage of disease correlated with paced finger-tapping variability but with none of the other performance measures. Specifically, more severe symptoms of bradykinesia were associated with greater total ($r = .37$, $p < .02$) and clock variability ($r = .36$, $p < .025$). In addition, stage of disease correlated with total ($r = .38$, $p < .02$) and motor delay variability ($r = .50$, $p < .01$).
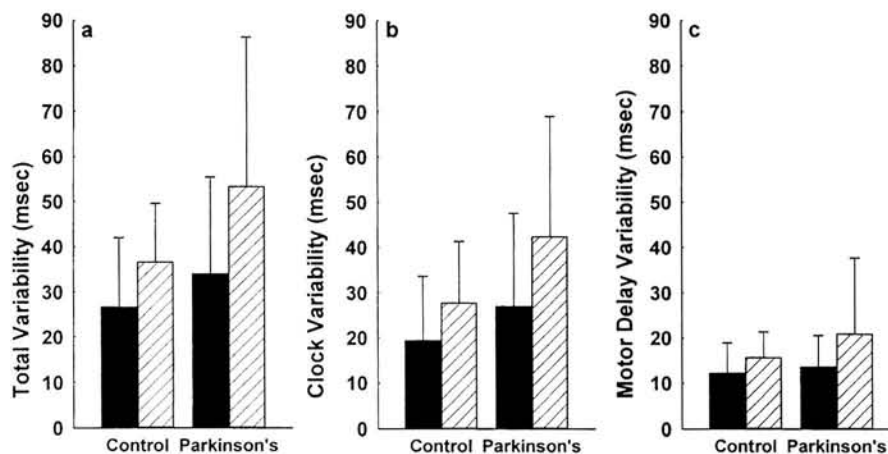

Figure 2. Means (and standard deviations) for variability in paced finger-tapping. Variability is expressed as the standard deviation of interresponse intervals (IRIs) for the 300-ms (solid bars) and the 600-ms (slashed bars) target intervals. A: The total variability in IRIs in the control and Parkinson's disease groups. B and C: The total variability is decomposed using the procedures of Wing and Kristofferson (1973); B and C display the clock and motor delay sources of variability (standard deviations), respectively.

Discussion

The present investigation was inspired by the contradictory empirical findings regarding the role of the basal ganglia in time perception and motor-timing operations. There have been only two previous investigations of time perception in PD, and the findings were contradictory. Similarly, studies of motor timing in medicated PD patients have also reported discrepant results. A catalyst for these studies was Wing and Kristofferson's (1973) two-process model, which assumes that motor-timing variability results from an imprecision in a central clock and in the production of responses that are triggered by the clock. Other closely related empirical and theoretical developments (Keele et al., 1985, 1987) further suggested that time perception and motor timing share a common timekeeper.

The pattern of results for the PD group suggests that internal timing processes are mediated by the basal ganglia, which is contrary to the influential view that only the cerebellum controls timekeeping operations (Ivry & Keele, 1989). The PD group was impaired in their judgments of duration and in the clock component of paced finger tapping, but they showed no deficits in the motor delay component of paced finger tapping or in their judgments of frequency. It is important to note that time perception was dissociated from frequency perception, which demonstrates that, despite the similarities between the two perceptual tasks, time perception deficits in PD were not due to more general impairments in processing sequential auditory information common to both perceptual tasks. In addition, the motor-timing intervals did not exceed the maximum tapping speed of patients, so that this cannot explain the motor-timing variability results.

Our time perception findings extend those of Artieda and colleagues (1992) who reported deficits in somaesthetic, visual, and auditory perceptual timing in PD patients "off" medication. They used a different kind of temporal discrimination task in which participants received pairs of stimuli that were separated in time, and the minimum time interval to perceive the stimuli as distinct was measured. Participants made decisions about whether they perceived one or two stimuli, which arguably may not be a pure measure of timing processes. This contrasts with the duration perception task used in the present study, in which the duration of an interval separating two tones is evaluated (i.e., longer or shorter) relative to a standard tone pair. In both cases, however, perceptual acuity is assessed in terms of the participant's ability to discriminate the least amount of time between two stimuli. Their findings are not easily explained by possible primary sensory deficits in PD, because suprathreshold stimuli were used to control for individual differences in sensory thresholds. In addition, sensory nerve action potentials (from the wrist) and cortical somatosensory evoked potentials (recorded over the contralateral parietal region) were normal in their patients. In contrast to our findings, however, temporal discrimination thresholds in their study were related to disease severity, which may reflect the fact that when patients are off medication, deficits are more apparent.

The finding that the basal ganglia mediates time percep-

tion processes also is consistent with pharmacological manipulations of central timing mechanisms in animals, in which dopaminergic drugs have been shown to alter the internal clock speed (Meck, 1986), whereas cholinergic drugs modify nontemporal aspects (i.e., memory) of duration perception (Meck & Church, 1987). In these studies, however, dopaminergic functioning in the basal ganglia was associated with the operation of an internal clock used to time intervals in the range of seconds to minutes, which may engage different neural systems. Temporal processing of longer durations possibly involves other nontemporal processes including memory and strategic processing. Recordings of cell activity in primates also have linked timing operations to the dopaminergic nigrostriatal inputs (for a review, see Graybiel & Kimura, 1995). In these studies, striatal interneurons have been found to increase their synaptic strength through classical conditioning (CC), in which temporal processing is essential. Others have reported that the timing of a conditioned response (CR) is abnormal in Huntington's disease, despite the normal acquisition of the CR (Woodruff-Pak & Papka, 1996). These findings are intriguing, although their implication for time-dependent operations is uncertain, because the extent to which CC calls upon explicit timing operations is unknown.

Our motor-timing results are consistent with findings of similar impairments in medicated PD patients (O'Boyle et al., 1996) but are contrary to the findings of others (Duchek et al., 1994; Ivry & Keele, 1989). The discrepancies are not likely due to differences in the data analyses, because we and O'Boyle and colleagues demonstrated that different approaches to treating violations of the Wing and Kristofferson model produced very much the same results. Our findings also cannot be explained by the possibility that participants had to switch between timing of two different intervals, because there were no effects of target interval order in any of the analyses. Moreover, O'Boyle and colleagues found significant timing impairments in medicated PD patients when they reproduced only one temporal interval. Rather, we speculated that previous findings of normal motor timing in PD could be due to a preponderance of patients in Stage 1 and 2 of the disease (75%) in one study (Duchek et al., 1994), although no information regarding disease severity was provided by the other study (Ivry & Keele, 1989). This could be crucial because early stage patients show only unilateral involvement (Stage 1). If they have bilateral symptoms (Stage 2), often it is asymmetrical with one side showing only mild symptoms. Hence, these studies may not have systematically tested the impaired hand. In our study, the severity of bradykinesia was correlated with total and clock variability, whereas stage of disease was correlated with total and motor delay variability. Although the magnitude of the associations were relatively small (14% to 25% of the variance) and stage of disease was not significantly correlated with clock variability, disease severity was related to one or more aspects of motor-timing variability and, thus, could account for the negative motor-timing results in the earlier studies. Still, it is possible that other unknown factors might better explain these discrepant findings.

Our finding of impaired time perception and motor timing

in PD is also consistent with the hypothesis that the basal ganglia regulates a timing operation common to the performance of both tasks. However, it is important to consider an alternative interpretation of these findings. There is some recent evidence that the motor and perceptual tasks used in this study may not engage the same time-dependent computations or that one or both tasks also rely on other unspecified cognitive operations (Ivry & Hazeltine, 1995). In other words, the time-dependent computations may overlap only to a limited extent, so that the basal ganglia may be involved in the explicit representation of time in one task but not another, or may not be involved in time-dependent computations at all. Presently, there is not a definitive method for addressing this possibility, because the component processes underlying the perceptual and motor-timing tasks have not been sufficiently identified. Therefore, correlations among the tasks are of limited value. Nonetheless, it is difficult to see how a deficit in nontemporal processes could account for the PD group's impairment in duration perception, which has been viewed as the strongest evidence for linking time-dependent operations to a neural system (Ivry & Keele, 1989), because it is not confounded by motor factors. Moreover, time perception was dissociated from frequency perception, which, because of the similarities between the two perceptual tasks in nontemporal processes, would appear to point to a specific impairment in time-dependent processes. Although we did not obtain a Group × Target interval interaction for either perceptual or motor timing, this would not necessarily be expected if duration thresholds and clock variability are relatively pure reflections of internal timekeeping processes, which is the prevailing view in the literature.

It is perhaps less certain, however, whether the clock component is uncontaminated by fluctuations in nontemporal processes. This suspicion stems partially from limitations of the Wing and Kristofferson model for decomposing the total variability in motor timing, wherein all sources of variance that cannot be attributed to random fluctuations in motor implementation processes are lumped into the clock component. This is potentially problematic because the clock variance may include variability due to fluctuations in other processes that accompany timing, such as attention (Brown, Stubbs, & West, 1992) or subvocal, nonlinguistic rehearsal (Rao et al., 1997). Moreover, these types of nontemporal processes might be engaged more during longer duration intervals, wherein participants are more likely to engage in strategic processing. If this is the case, an interaction of Group × Target Interval Duration could be due to deficits in nontemporal processes, which play a greater role as the interval duration increases, rather than the competing explanation of a timing deficit, which becomes more pronounced at longer interval durations due to an accumulation over time in the variability of a hypothetical pacemaker. Clearly, more analytic models are needed for sorting out the processes underlying the clock variance, which has been widely associated with timekeeping operations. Nevertheless, given the existing model development and its relative robustness in PD to violations of the underlying assumptions (O'Boyle et al., 1996), our findings

are consistent with a role of the basal ganglia in motor timekeeping operations. Though the time-dependent operations in motor timing may be different from those used during time perception, the basal ganglia appear to play a role in both forms of timing.

Concluding Remarks

The present results suggest that the basal ganglia play a direct role in time perception and motor-timing operations. The former finding is consistent with other studies showing that deficits in PD are not restricted to motor tasks (Pirozzolo, Swihart, Rey, Jankovic, & Mortimer, 1988). However, diminished basal ganglia function in PD is due to the loss of dopaminergic neurons in the substantia nigra, which project to the dorsal putamen (Brooks et al., 1990) and then to the supplementary motor area (SMA; Alexander, DeLong, & Strick, 1986). In later stages of PD, there also is decreased dopamine in the caudate nucleus (Nahmias, Garnett, Firnau, & Lang, 1985), which projects to other areas in the frontal lobe, including the dorsolateral prefrontal cortex (Alexander et al., 1986). Thus, central timing deficits in PD could reflect a dysfunction in dopaminergic-dependent prefrontal cortical areas, which has been found in studies of other cognitive-motor functions (e.g., Jahanshahi et al., 1995; Jenkins et al., 1992; Rascol et al., 1992). In fact, patients with lesions in the premotor cortex or the SMA are impaired in the reproduction of rhythms, in the absence of an auditory cue to guide their performance, despite a normal ability to produce rhythms under auditory guidance (Halsband, Ito, Tanji, & Freund, 1993). Recordings of cortical DC potentials in humans also suggest that the SMA is crucial for carrying out movements that require a precise timing plan (Lang, Obrig, Lindinger, Cheyne, & Deecke, 1990).

These patient studies are consistent with a recent functional magnetic resonance imaging (FMRI) study of motor timing in healthy adults, which showed that the medial premotor system, including the caudal SMA, the putamen, and the ventrolateral thalamus, was specifically activated during the continuation phase of the paced finger-tapping task (Rao et al., 1997). Activation of the lateral cerebellum, however, was not specific to the internal generation of timed movements, which is contrary to the interpretation of the motor-timing deficits that have been reported in patients with focal cerebellar damage (Ivry, Keele, & Diener, 1988). Rather, it appeared that the cerebellum, specifically the dorsal dentate nucleus and its primary output pathway to the sensorimotor cortex, played a more general role in sensorimotor processing.

Even though there is mounting evidence from both patient and functional imaging studies that supports a specialized role of the basal ganglia–thalamocortical system in mediating motor-timing operations, relatively little converging evidence is available that corroborates the neural systems underlying time perception. A recent positron emission tomography (PET) study of time perception showed that, in contrast to motor timing, areas of the frontal lobe were not specifically related to time perception in healthy adults (Jueptner et al., 1995). Rather, time-dependent processing

appeared to be localized within the putamen and thalamus bilaterally, within superior parts of the vermis, and within the cerebellar hemispheres bilaterally. These PET findings are consistent with the interpretation of our time perception results in PD, as well as other findings in patients with cerebellar damage (Ivry & Keele, 1989; Ivry et al., 1988), and suggest that time perception may be mediated by a distributed neural system, including the basal ganglia and the cerebellum. Additional research is still needed to verify these findings.

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