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Impairment of beat-based rhythm discrimination in Parkinson's disease

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ABSTRACT

Humans often synchronize movements to the beat, indicating that motor areas may be involved in detecting or generating a beat. The basal ganglia have been shown to be preferentially activated by perception of rhythms with a regular beat (Grahn and Brett, 2007), but their necessity for beat-based rhythm processing has not been proven. Previous research has shown that Parkinson's disease (PD) patients are impaired in timing of isochronous intervals (Harrington et al., 1998a; O'Boyle et al., 1996), but little work has tested more complex rhythms. In healthy volunteers, behavioural performance is better for rhythms with a beat than without a beat (Essens, 1986). We tested PD patients and controls on a rhythm discrimination task to determine if basal ganglia dysfunction results in an impairment of processing rhythms that have a beat. Unlike rhythm reproduction, discrimination has no motor requirements that are problematic for patients. Half the rhythms had a beat-based structure, and half did not. Subjects heard a rhythm twice and then indicated if a third presentation of the rhythm was the same or different. We predicted that PD patients would benefit less from beat structure than controls, resulting in a group by rhythm-type interaction, with reduced relative performance for the beat-based sequences in the PD group. Indeed this was the pattern of the results. In the control group, a significant advantage was observed for discrimination of rhythms with a beat compared to those without a beat. This advantage was greatly reduced in the PD group. Discrimination of beat-based rhythms was significantly impaired in PD patients compared to controls, whereas discrimination of non-beat-based rhythms did not differ significantly. This suggests that the basal ganglia are part of a system involved in detecting or generating an internal beat, and that this system is compromised in patients with Parkinson's disease.

1. Introduction

A connection between perception of musical rhythm and induced movement can be observed frequently in daily life. Toe- or finger-tapping to the rhythm occurs spontaneously, in people of all ages. In fact, motor areas of the brain have been shown to be active in many neuroimaging studies of rhythm and timing, in particular the premotor and supplementary motor areas, cerebellum, and basal ganglia (Lewis et al., 2004; Penhune et al., 1998; Ramnani and Passingham, 2001;

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Schubotz and von Cramon, 2001; Coull et al., 2004; Ferrandez et al., 2003; Nenadic et al., 2003; Pastor et al., 2004; Rao et al., 2001; Dhamala et al., 2003). Studies that have examined temporal processing in neuropsychological patients highlight a similar network of cortical and subcortical motor areas to that revealed by neuroimaging (Halsband et al., 1993; Harrington et al., 1998b; Artieda et al., 1992; Rammsayer and Classen, 1997; Molinari et al., 2003; Ivry et al., 1988; Ivry and Keele, 1989; Mangels et al., 1998; Nichelli et al., 1996). Thus, evidence from multiple methodologies highlights the connection between musical rhythm and movement, and the importance of motor areas in music processing, in particular for rhythm (for a review, see Zatorre et al., 2007).

On the other hand, deficits in temporal processing have also been found after damage to non-motor areas, including the prefrontal cortex (Nichelli et al., 1995; Mangels et al., 1998; Harrington et al., 1998b) and the inferior parietal lobule (Harrington et al., 1998b). However, these areas are most likely involved in working memory and sustained attention processes that are present in the tasks used to test temporal processing. For example, two of the studies find that patients with prefrontal damage were also impaired on control tasks (Nichelli et al., 1995; Mangels et al., 1998), suggesting that the observed deficits in timing tasks for prefrontal patients may be due to a more general impairment that is not specific to timing. In addition, the choice of control tasks is crucial for any neuropsychological study. For example, frequency discrimination is often used as a control condition for duration discrimination (Harrington et al., 1998b; Mangels et al., 1998), even though frequency discrimination can occur within the first few-hundred milliseconds after stimulus onset, whereas duration discrimination requires sustained attention to the entire duration. Further, in healthy volunteers, dual-task conditions do not impair frequency discrimination, but do impair duration discrimination (Casini and Ivry, 1999). Thus, it is critical that appropriate control tasks are used when examining temporal deficits in any neuropsychological patients, in order to be confident that observed deficits are not just due to increased difficulty.

Not all temporal sequences induce spontaneous movement in listeners: perception of an underlying tactus, or beat, is generally required. A beat is a perceived pulse that marks equally spaced points in time (Large and Palmer, 2002). When a beat is perceived, humans can (and often do) synchronize movements to the beat perceived in the rhythm (e.g., Drake et al., 2000). Humans can often synchronize at rates that are integer multiples or fractions of the beat, suggesting that we have access to several distinct levels of periodicity (Drake et al., 2000; Parncutt, 1994). It is not entirely clear why humans do this, as there are no examples of this behaviour occurring spontaneously in other animals. It is possible that the function is to improve timing or memory for temporal sequences. Detection of the beat structure enables one to encode the temporal intervals of the rhythm in terms of the beat, instead of as an unrelated series of durations in time. When a regular beat can be perceived, behavioural measures of performance such as rhythm reproduction are improved (Povel, 1981; Patel et al., 2005). Thus, detection of a beat structure does appear to improve timing. This mechanism may be analogous to 'chunking', a way of reducing complex patterns to simpler components.

To determine the neural substrates of this mechanism, we previously compared behavioural reproduction and neural activity for three different types of rhythms, termed metric simple, metric complex, and nonmetric (Grahn and Brett, 2007). The metric simple and metric complex rhythms were composed of intervals that were all rated by integer-ratios (1:2:3:4), and could be written using standard Western musical notation. However, the metric simple rhythms had a regular grouping of intervals, such that we predicted a regular 'beat' or pulse would be perceived. The metric complex rhythms used the same intervals, but arranged such that we predicted no regular beat would be perceived in the rhythm. They were both termed metric, as they both exhibited periodicity (at the level of the smallest interval: 220–270 msec). However, the metric simple condition also exhibited periodicity at rates known to be more salient (Drake et al., 2000; Parncutt, 1994; Noorden and Moelants, 1999) for human beat perception: 440–1080 msec (two or four times the smallest interval of the metric sequences). One question of interest was whether the presence of simple integer-ratios in the rhythm was enough for participants to perceive a beat (in which case a beat would be perceived in both the metric simple and metric complex conditions), or whether the regular grouping that provided higher level periodicities was also required (in which case, a beat would only be perceived in the metric simple condition). The third condition, termed nonmetric, used noninteger ratios (1:1.4:3.5:4.5), and had no periodicities, nor any regular grouping, thus no potential for beat perception. Therefore, if no beat was perceived in the metric complex rhythms, performance accuracy for metric complex rhythms should have been similar to that of nonmetric rhythms, not metric simple rhythms. If a beat was perceived, performance should have been similar to metric simple rhythms. Importantly, these rhythms are matched for all other temporal processing requirements (sequence length, number and length of individual intervals), apart from whether or not a beat can be perceived.

Behaviourally, the metric simple rhythms were reproduced more accurately than the metric complex or nonmetric rhythms (which did not significantly differ from each other) (Grahn and Brett, 2007), suggesting no beat was perceived in the metric complex rhythms. In addition, the metric simple rhythms elicited increased activity (compared to the metric complex and nonmetric rhythms) in a subset of motor areas: the basal ganglia and supplementary motor area/pre-supplementary motor area (pre-SMA/SMA) (Grahn and Brett, 2007). There were no differences in activity between the metric complex and nonmetric conditions. Together, these results suggested that simple integer-ratios are not necessarily enough for humans to perceive a regular beat, and that the timing system engaged by beat perception may be mediated by the basal ganglia and pre-SMA/SMA, a set of neural structures connected via striato-thalamo-cortical loops (Leh et al., 2007; Hoover and Strick, 1993; Tokuno et al., 1992; Schell and Strick, 1984).

However, neuroimaging of healthy volunteers cannot tell us if the basal ganglia system is *necessary* for this process to occur. Here we examine whether the basal ganglia are critical for beat processing by testing patients with disruption of normal functioning in this system due to Parkinson's disease (Agid et al., 1993).

Parkinson's disease (PD) is characterised by progressive cell death in the substantia nigra that decreases dopamine release by the striatum, affecting excitatory input to the posterolateral putamen (Jellinger, 2001). Previous behavioural studies in patients with PD have shown deficits in simple timing tasks (Harrington et al., 1998a; Artieda et al., 1992; O'Boyle et al., 1996). These are likely due to the decreased dopamine levels in the striatum. For example, in PD patients, dopaminergic treatment improves motor timing (O'Boyle, 1997; Pastor et al., 1992; O'Boyle et al., 1996) and time perception (Malapani et al., 1998). In addition, administration of haloperidol (a dopamine receptor antagonist) to healthy adults impairs timing of both 50 msec and 1000 msec intervals (Rammsayer, 1999). The exact role of the basal ganglia in temporal processing is not thoroughly clear, however: some behavioural work has shown no temporal performance impairment in PD patients (Shin and Ivry, 2003; Duchek et al., 1994).

Neuroimaging studies conducted with PD patients confirm dysfunction of the basal ganglia: hypoactivity is observed during movement-related tasks, particularly those involving internal generation or self-initiation as opposed to external cues (Jahanshahi et al., 1995; Lewis et al., 2007; Yu et al., 2007). Neural structures that receive basal ganglia output, such as the SMA/pre-SMA, are also reported to be underactive, though not in all studies (Rascol et al., 1994; Haslinger et al., 2001; Jahanshahi et al., 1995; cf. Catalan et al., 1998). Dopaminergic treatment at least partially normalises activation in the basal ganglia and SMA/pre-SMA (Haslinger et al., 2001; Rascol et al., 1994; Elsinger et al., 2003; Lewis et al., 2007). When scanning PD patients completing temporal tasks, the pattern is not as clear. Underactivation in the basal ganglia and SMA/pre-SMA, normalized following dopaminergic treatment, has been reported in one study using paced finger-tapping (Elsinger et al., 2003), but not in another that used internally versus externally guided timed movement. (Cerasa et al., 2006). Overall, disruption of basal ganglia function is manifest in PD, though the consequences of this disruption for blood-oxygenation-level dependent or cerebral blood flow measures appear to be varied.

The current study used the metric simple and metric complex rhythmic stimuli from the experiment described above (Grahn and Brett, 2007). The nonmetric condition was not included in order to keep the experimental session suitably short, and as performance of the metric complex and nonmetric conditions did not differ in the previous experiment, the current experiment retains the 2 most closely matched conditions. Thus half the sequences give rise to perception of a regular beat, in the other half, no regular beat is perceived. As the metric simple rhythms activated the basal ganglia and SMA, we predicted that PD patients would be impaired when asked to discriminate changes in the metric simple rhythms, due to the dopaminergic deficiency that compromises basal ganglia function. We restricted our sample to PD patients that were in earlier stages of the disease progression (Hoehn and Yahr Stage 1 or 2), when pathology is relatively restricted to dopamine depletion in the putamen and dorsal caudate nucleus (Dauer and Przedborski, 2003; Kish et al., 1988). In addition, we used a discrimination task to prevent any overt motor performance difficulties for PD patients from affecting the results.

Importantly, a deficit was predicted in the condition that healthy volunteers find *easier* (that is, the condition in which healthy volunteers perform more accurately). If a specific deficit in the easier condition was observed, one can rule out explanations due to general difficulty effects or working memory deficits [the latter is particularly important, as working memory is known to be compromised in Parkinson's disease (Gotham et al., 1986; Owen et al., 1992)]. In addition, the rhythms are constructed such that beat is not emphasized externally by changes in timbre, pitch, or volume, which are some of the additional cues to the beat in music. This was intentional, as we do not know of PD patients reporting a complete inability to feel the beat in music. This may be due to the presence of multiple, redundant beat cues present in music, therefore we used rhythms where the temporal structure itself is the only way in which the beat can be perceived.

2. Methods

2.1. *Participants*

The PD patients were recruited by letter from the Parkinson's disease Research Clinic at the Cambridge Centre for Brain Repair, in Cambridge, UK. Written informed consent was obtained from all participants. Fifteen patients (6 female, 9 male) participated. They ranged in age from 57 to 80. The average age was 67 (SD = 8.5). The patients were all at Hoehn and Yahr Stage 1 or 2 (Hoehn and Yahr, 1967), with the mean = 1.9 (SD = .28). All were right-handed, and on their 130 standard L-dopa medication regimen. The mean Universal Parkinson's Disease Rating Scale (UPDRS) score was 30 (SD = 12.5). Disease duration as measured from diagnosis date ranged from 3 to 25 years (mean 8.0, SD = 6.0). All patients satisfied UK Parkinson's Disease Society Brain Bank criteria (Gibb and Lees, 1988). Fifteen controls (7 female, 8 male) were recruited from the Cambridge area by letter and email. They were also right-handed, and ranged in age from 45 to 79 (mean 57, SD = 8.7). Participants in both groups were excluded if they had any significant history of psychiatric or neurological disorder (not related to diagnosis of PD). No participants reported any substantial non-Western musical experience, and all were native to the UK or Western Europe.

2.2. *Materials and stimuli*

Subjects were administered the National Adult Reading Test (NART) (Nelson and Willison, 1991) which has been shown to provide a valid pre-morbid estimate of IQ (Crawford et al., 2001; Bright et al., 2002).

2.2.1. *Stimuli*

Rhythmic stimuli were a subset of those described in a previous fMRI study (Grahn and Brett, 2007), and are listed in Table 1. Sequences were constructed from sets of five, six, or seven intervals. The intervals in the rhythms were related by ratios of 1:2:3:4. The stimuli were of two types: simple (beat-based) and complex (non-beat-based).

There were 30 sequences in each condition. The length of the "1" interval was chosen randomly from 220 to 270 msec (in 10 msec steps) on each trial to prevent subjects from using

Table 1 – Table of standard and deviant rhythm sequences used.

	Metric simple		Metric complex	
	Standard	Deviant	Standard	Deviant
5 intervals	22413	22431	11343	13143
	31413	31431	13242	31242
	31422	13422	23241	23214
	41331	43131	33141	31341
	43113	41313	41133	14133
	43122	41322	41232	42132
6 intervals	112314	112134	121233	122133
	112422	211422	122142	212142
	211134	211314	124113	214113
	211224	112224	132321	312321
	211413	211431	214221	214212
	221331	221313	214311	124311
	222114	221124	221241	221214
	223113	223131	231123	213123
	311322	313122	321411	324111
	312213	312231	323211	323121
	411231	411213	412212	412221
	422112	422211	421311	412311
7 intervals	1111431	1111413	1112412	1121412
	1122114	1121124	1132131	1131231
	1123113	1123131	1132212	1132122
	1123122	1121322	1314111	1311411
	2112231	2112213	1411311	1141311
	2113113	2113131	2123211	1223211
	2211114	2112114	2141211	2142111
	3121113	3121131	2331111	2313111
	3122112	1322112	3113121	3131121
	3141111	1341111	3114111	1314111
	4111131	4111113	3221112	3212112
	4221111	4211211	4111221	4112121

1 = 220–270 msec (in steps of 10 msec), chosen at random for each trial. All other intervals in that sequence are multiplied by length chosen for the 1 interval.

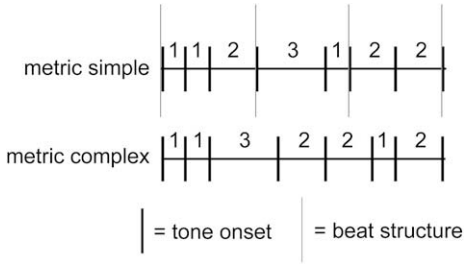

Fig. 1 – Schematic example of the two types of rhythmic sequence stimuli used. Numbers denote relative length of intervals in each sequence. 1 = 220–270 msec (value chosen at random on each trial), in steps of 10 msec.

a beat perceived in the previous trial. The rest of the intervals in each sequence were multiples of the 1 interval. For example, with a 1 interval of 250 msec, the metric complex sequence 321411 has intervals of length 750 500 250 1000 167250 250 (msec). Sine tones (rise/fall times of 8 msec) sounded for the duration of each interval, ending 40 msec before the specified interval length to create a silent gap that demarcated the intervals. A PC with an integrated SoundMAX digital audio soundcard (manufactured by Analog Devices, Inc) was used to produce the sounds, which were played over Dell Altec A215 computer speakers. One of six pitches (varying from 294 to 587 Hz) was picked at random for each trial, and held constant for that trial. The pitch differences between trials helped cue subjects to each new trial.

In the metric simple condition the intervals were regularly arranged into groups of 4 units. The interval arrangements were chosen to induce the perception of a regular beat (every 4 units) in accordance with the model of Povel and Essens (Essens and Povel, 1985). Thus the perception of a regular beat can occur with the onset of each group of four units (as shown in Fig. 1). Other work suggests that participants' representation of the beat agrees with the model's beat predictions. Pilot data reveal that when participants are asked to listen to rhythmic sequences and decide if a beat is present, a beat is felt 90% of the time for metric simple sequences (Grahn and Brett, 2005b). Increased finger tap velocity or force on particular taps during reproduction can also indicate where participants feel the beat. When tap velocity was measured during a reproduction task similar to the one outlined here, the velocity was significantly higher for taps coinciding with the induced beat at the onset of each group of four units when compared to other taps in each sequence (Grahn and Brett, 2005a). In the metric complex condition, the intervals were identical to those in the metric simple condition, but rearranged so as not to be regularly grouped, and therefore had no regular occurrence of a beat.

On half the trials, the third sequence was different from the previous two presentations. The deviant sequences contained a transposition of intervals in the sequence. For example, 211413 has as a possible deviant sequence 211431, in which the 3 interval and the 1 interval have been transposed. Only deviant sequences that were in the same category as the standard sequences were allowed. That is, a metric simple standard sequence could not have a metric complex deviant sequence, and a metric complex standard sequence could not have a metric simple deviant sequence. For example, 43122 would not have 43212 as a possible deviant sequence, because the onsets would no longer be grouped in units of four, and would violate the regular beat structure of the sequence. If these types of deviants were present, subjects could accomplish the task by detecting that onsets in deviant sequences either no longer aligned with the beat (in the metric simple condition), or now aligned with the beat (in the metric complex condition). Another restriction on the deviants for the metric simple condition involved the 112 and 211 patterns. These patterns in metric simple sequences could only be changed from 112 to 211, or 211 to 112. This prevents an accent from being heard off the beat, as a transposition resulting in 121 would put an accent on the 2 interval (Povel and Okkerman, 1981). Other than interval order, all characteristics of the deviant sequences were the same as the standard sequences.

2.3. *Procedure*

Participants were tested on a discrimination paradigm. They listened to two identical presentations of a rhythm, to which they compared a subsequent third presentation. The third

presentation could be the same rhythm or a different rhythm (the different rhythms were the deviant rhythms described above). To indicate whether the third rhythm was the same or different, participants pressed "s" for same, or "d" for different on a computer keyboard. PD patients displaying tremor severe enough to interfere with a button-press response stated their responses aloud ("same" or "different") and the experimenter recorded the response. For this reason, reaction times were not included in the data analysis. Each rhythm presentation was separated by 1100 msec. Participants practised four trials, then completed two blocks of 30 trials each. There were 30 trials of each rhythm type (metric simple and metric complex), presented in random order in each half. Participants adjusted the volume using a volume knob on the speakers such that the sounds were presented at a comfortable level.

Percent correct and d' scores (Macmillan and Creelman, 1991) were calculated for the metric simple and the metric complex conditions, for each subject. D' scores are a purer measure of sensitivity in same/different tasks, as they are less affected by response bias than other measures, such as percent correct, hit rate, false alarm rate, and hit rate minus the false alarm rate (Stanislaw and Todorov, 1999). We predicted that the PD patients would benefit less from the beat structure than the controls. We therefore predicted a sequence-type by group interaction, with reduced relative performance for the beat-based sequences in the PD group.

3. Results

Preliminary analyses were conducted to determine if age or NART scores influenced discrimination performance. No significant effects of age were found ($F < 1$), so this was not included as a covariate. Number of NART errors, however, was predictive of performance [d': $F(1,27) = 10.06$, $p = .004$; percent correct: $F(1,27) = 9.08$, $p = .006$], so this was included as a covariate (control mean = 10 NART errors, SD = 6.7, PD mean = 13 NART errors, SD = 4.3). Thus, a between-subjects repeated measures ANCOVA was conducted, with group (patient, control) as the between-subjects factor, rhythm type as the within-subjects factor, and NART scores as a covariate on d' scores and percent correct. Controls were significantly more accurate at deviant discrimination than PD patients overall [d': $F(1,27) = 20.42$, $p = .01$; percent correct: $F(1,27) = 4.18$, $p = .05$]. See Figs. 2 and 3 for accuracy measures in both groups. The effect of rhythm type did not reach significance [$F(1,27) = 2.84$, $p = .10$], however, the main effects must be interpreted in light of a significant interaction between group and rhythm type [d': $F(1,27) = 3.99$, $p = .028$, one-tailed; percent correct: $F(1,27) = 2.94$, $p = .049$, one-tailed], confirming our hypothesis. Simple effects testing showed that PD patients were impaired compared to controls on only the metric simple condition [d': $F(1,27) = 7.99$, $p = .009$; percent correct: $F(1,27) = 5.96$, $p = .02$], but not the metric complex condition [d': $F(1,27) = 1.90$, $p = .18$; percent correct: $F(1,27) = 1.2$, $p = .28$]. Further, the improvement in performance for PD patients on the metric simple condition compared to the metric complex condition was smaller than for controls (d': .35 difference for PD patients, .85 difference for controls; percent correct: 4.8% difference for PD patients, 11.5% difference for controls), though for d' scores, this was significant [for PD patients, d': $t(1,14) = 2.14$, $p = .05$; percent correct: $t(1,14) = 2.04$, $p = .06$; for controls, d': $t(1,14) = 4.86$, $p < .001$; percent correct: $t(1,14) = 4.15$, $p = .001$]. A partial correlation analysis was performed between the UPDRS measure of disease severity and discrimination performance (controlling for NART scores), but no significant correlations were found.

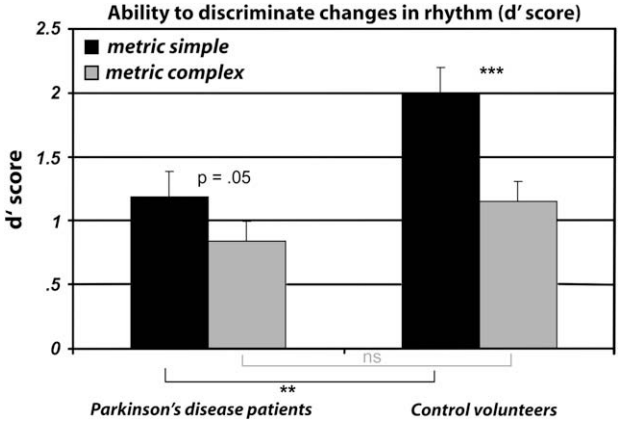

Fig. 2 – D' scores (adjusted for NART performance) for patients and controls on beat-based and non-beat-based in the deviant discrimination task. ns = not significant, ** $p < .01$, *** $p < .001$.

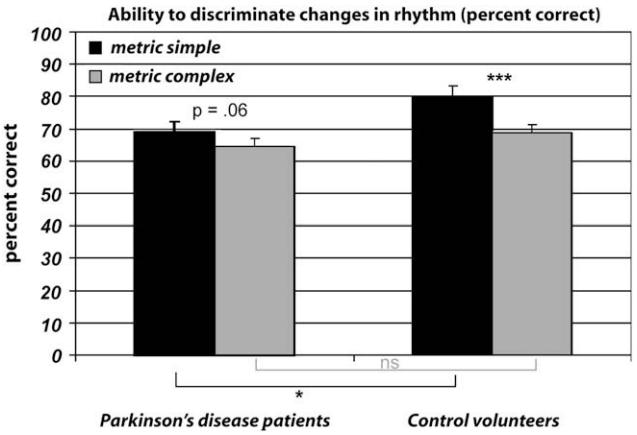

Fig. 3 – Percent correct scores (adjusted for NART performance) for patients and controls on beat-based and non-beat-based rhythms in the deviant discrimination task. ns = not significant, * $p < .05$, *** $p < .001$.

4. Discussion

In controls, the condition with a beat-based structure (metric simple) was discriminated correctly significantly more often than the condition without a beat-based structure (metric complex). In PD patients, the benefit for beat-based rhythms was much less (5% benefit as opposed to a 12% benefit for controls), and only marginally significant. A significant

interaction between group and condition was found, as predicted: PD patients did not show the same benefit as controls for the beat-based condition. PD patients' discrimination was significantly worse than controls only in the beat-based condition. In the non-beat-based condition, their discrimination performance did not significantly differ from controls. These data suggest that PD patients are either impaired at extracting the beat structure when initially listening to the rhythms, or that they are less able to use the beat structure to improve their performance during the subsequent comparison of the rhythms.

It is important to acknowledge that other pathological factors may contribute to general PD deficits. For example, some noradrenergic, serotoninergic and cholinergic deafferentation of the cortex occurs in PD (Agid et al., 1987), and cortical Lewy bodies could also be a factor (Byrne et al., 1989; Gibb et al., 1989). Patients with PD may also have compromised function in frontal cortex (Scatton et al., 1983). However, we feel that the observed deficit for the PD patients in this study is unlikely to be related to non-specific effects of Parkinson disease. The patients were all at early stages of PD (Hoehn and Yahr stages 1–2 at the time of testing), at which time dopamine depletion is more circumscribed and focused principally on the basal ganglia (Kish et al., 1988; Dauer and Przedborski, 2003). In addition, unlike rhythm reproduction or beat synchronization tasks, the discrimination task did not require any motor responding and therefore our results are unlikely to be explained by a motor deficit. More importantly, the patients are significantly impaired on the *easier* condition. Any non-specific timing impairment would be expected to be present across all conditions, and if anything to a *greater* extent in the more difficult condition. As the PD patients are not significantly impaired in the non-beat-based condition, the deficit appears to be specific to sequences that involve beat processing. As rhythms in the beat-based condition are comparable to simple musical rhythms in a 4/4 meter, common in Western and popular music, it is perhaps not surprising that healthy volunteers find this condition easier. Although our rhythms were not taken from musical extracts, they are similar to those found in music to which many people, non-musicians and children included, can tap along (Drake, 1993).

PD patients did show a small benefit in discrimination of the beat-based rhythms compared to the non-beat-based rhythms, although this only reached significance when comparing d' scores, not percent correct. Their capacity to process the beat appears therefore to not be completely lost (consistent with some residual preserved function in the basal ganglia in PD). However, all patients were in the early stages of PD, and on medication, which may have mitigated any underlying deficit to a certain extent. In addition, as mentioned in the introduction, other brain areas are involved in timing processes, and may provide compensation for any deficits in timing functions normally subserved by the basal ganglia.

The PD deficit was predicted on the basis of fMRI data that shows increased basal ganglia activity for the beat-based condition during a similar discrimination task in healthy volunteers. The current results suggest that the basal ganglia have a direct role in beat-based processing. However, the exact nature of the basal ganglia's role cannot be determined from these studies. The basal ganglia are connected to mesial premotor areas: the SMA and pre-SMA. Activity in these areas is highly associated with basal ganglia function via the basal ganglia–thalamo-premotor loop (Schell and Strick, 1984; Alexander et al., 1990). The dopaminergic deficit in Parkinson's disease is thought to result in an inhibition of projections to these areas. Thus a role in beat processing for the SMA/pre-SMA cannot be ruled out.

Further, additional studies will be required to elucidate the exact nature of the process that the basal ganglia and SMA/pre-SMA are mediating in beat perception. They may be involved in detecting the underlying beat that is present in the metric simple condition, or alternatively, in generating an internal beat to use as a guide during the discrimination phase (a way of organizing the onsets of the different rhythmic intervals with reference to the regular beat). It is likely that when a more obvious beat is present in the auditory stimulus, such as during music listening (when volume, pitch, timbre, harmony, etc. all provide cues to the beat) this deficit may be mitigated. Anecdotally, none of the patients described any reduction in their enjoyment of music or inability to perceive its rhythmic characteristics. Also, as any deficits in motor synchronization to music (the most commonly reported activity in response to rhythm perception) could be due to the motor symptoms of the disease, this would not be a reliable indicator of inability to perceive the beat (hence the perceptual task used here).

In summary, these data show that patients with PD are specifically impaired in processing beat-based sequences compared to non-beat-based sequences. The two types of sequences were matched on all other temporal parameters, and the impairment was present in the condition that healthy volunteers found to be easiest. The basal ganglia and the mesial premotor system therefore appear to be necessary for processing rhythms in which a beat structure is present.

REFERENCES

Agid Y, Javoy-Agid E, and Ruberg M. Biochemistry of neurotransmitters in Parkinson's disease. In Marsden CD, and Fahn S (Eds), *Movement Disorders*. London: Butterworth, 1987: 166–230.

Agid Y, Ruberg M, Javoy-Agid F, Hirsch E, Raisman-Vozari R, Vyas S, et al. Are dopaminergic neurons selectively vulnerable to Parkinson's disease? *Advances in Neurology*, 60: 148–164, 1993.

Alexander GE, Crutcher MD, and DeLong MR. Basal ganglia–thalamocortical circuits: parallel substrates for motor, oculomotor, 'prefrontal' and 'limbic' functions. *Progress in Brain Research*, 85: 119–146, 1990.

Artieda J, Pastor MA, Lacruz F, and Obeso JA. Temporal discrimination is abnormal in Parkinson's disease. *Brain*, 115: 199–210, 1992.

Bright P, Jaldow E, and Kopelman M. The national adult reading test as a measure of premorbid intelligence: a comparison with estimates derived from demographic variables. *Journal of International Neuropsychological Society*, 8: 847–854, 2002.

Byrne EJ, Lennox G, Lowe J, and Godwin-Austen RB. Diffuse Lewy body disease: clinical features in 15 cases. *Journal of Neurology, Neurosurgery, and Psychiatry*, 52: 709–717, 1989.

Casini L and Ivry R. Effects of divided attention on temporal processing in patients with lesions of the cerebellum or frontal lobe. *Neuropsychologia*, 13: 10–21, 1999.

Catalan MJ, Honda M, Weeks RA, Cohen LG, and Hallett M. The functional neuroanatomy of simple and complex sequential finger movements. *Brain*, 121: 253–264, 1998.

Cerasa A, Hagberg GE, Peppe A, Bianciardi M, Gioia MC, Costa A, et al. Functional changes in the activity of cerebellum and frontostriatal regions during externally and internally timed movement in Parkinson's disease. *Brain Research Bulletin*, 71: 259–269, 2006.

Coull JT, Vidal F, Nazarian B, and Macar F. Functional anatomy of the attentional modulation of time estimation. *Science*, 303: 1506–1508, 2004.

Crawford JR, Deary IJ, and Starr LJ. The NART as an index of prior intellectual functioning: a retrospective validity study covering a 66-year interval. *Psychological Medicine*, 31: 451–458, 2001.

Dauer W and Przedborski S. Parkinson's disease: mechanisms and models. *Neuron*, 39: 889–909, 2003.

Dhamala M, Pagnoni G, Wiesenfeld K, Zink CF, Martin M, and Berns GS. Neural correlates of the complexity of rhythmic finger tapping. *Neuroimage*, 20: 918–926, 2003.

Drake C. Reproduction of musical rhythms by children, adult musicians, and adult nonmusicians. *Perception and Psychophysics*, 53: 25–33, 1993.

Drake C, Penel A, and Bigand E. Tapping in time with mechanically and expressively performed music. *Music Perception*, 18: 1–24, 2000.

Duchek JM, Balota DA, and Ferraro FR. Component analysis of a rhythmic finger tapping task in individuals with senile dementia of the Alzheimer type and in individuals with Parkinson's disease. *Neuropsychology*, 8: 218–226, 1994.

Elsinger CL, Rao SM, Zimbelman JL, Reynolds NC, Blindauer KA, and Hoffmann RG. Neural basis for impaired time reproduction in Parkinson's disease: an fMRI study. *Journal of the International Neuropsychological Society*, 9: 1088–1098, 2003.

Essens PJ. Hierarchical organization of temporal patterns. *Perception and Psychophysics*, 40: 69–73, 1986.

Essens PJ and Povel DJ. Metrical and nonmetrical representations of temporal patterns. *Perception and Psychophysics*, 37: 1–7, 1985.

Ferrandez AM, Hugueville L, Lehéricy S, Poline JB, Marsault C, and Pouthas V. Basal ganglia and supplementary motor area subtend duration perception: an fMRI study. *Neuroimage*, 19: 1532–1544, 2003.

Gibb WR and Lees AJ. A comparison of clinical and pathological features of young- and old-onset Parkinson's disease. *Neurology*, 38: 1402–1406, 1988.

Gibb WR, Luthert PJ, Janota I, and Lantos PL. Cortical Lewy body dementia: clinical features and classification. *Journal of Neurology, Neurosurgery, and Psychiatry*, 52: 185–192, 1989.

Gotham A-M, Brown RG, and Marsden CD. Levodopa treatment may benefit or impair frontal function in Parkinson's disease. *The Lancet*, 328: 970–971, 1986.

Grahn JA and Brett M. In Avanzini G, Koelsch S, Lopez L, and Majno M (Eds), *Rhythm Processing in Patients with Basal Ganglia Dysfunction*. Secondary Titl, 1060. Leipzig, Germany: The New York Academy of Sciences, 2005a: 490.

Grahn JA and Brett M. The role of the basal ganglia in beat-based rhythm processing. *Journal of Cognitive Neuroscience*, 2005: S202.

Grahn JA and Brett M. Rhythm perception in motor areas of the brain. *Journal of Cognitive Neuroscience*, 19: 893–906, 2007.

Halsband U, Ito N, Tanji J, and Freund HJ. The role of premotor cortex and the supplementary motor area in the temporal control of movement in man. *Brain*, 116: 243–266, 1993.

Harrington DL, Haaland KY, and Hermanowitz N. Temporal processing in the basal ganglia. *Neuropsychology*, 12: 3–12, 1998a.

Harrington DL, Haaland KY, and Knight RT. Cortical networks underlying mechanisms of time perception. *Journal of Neuroscience*, 18: 1085–1095, 1998b.

Haslinger B, Erhard P, Kämpfe N, Boecker H, Rummeny E, Schwaiger M, et al. Event-related functional magnetic resonance imaging in Parkinson's disease before and after levodopa. *Brain*, 124: 558–570, 2001.

Hoehn MM and Yahr MD. Parkinsonism: onset, progression, and mortality. *Neurology*, 17: 427–442, 1967.

Hoover JE and Strick PL. Multiple output channels in the basal ganglia. *Science*, 259: 819–821, 1993.

Ivry R and Keele SW. Timing functions of the cerebellum. *Journal of Cognitive Neuroscience*, 1: 134–150, 1989.

Ivry RB, Keele SW, and Diener HC. Dissociation of the lateral and medial cerebellum in movement timing and movement execution. *Experimental Brain Research*, 73: 167–180, 1988.

Jahanshahi M, Jenkins IH, Brown RG, Marsden CD, Passingham RE, and Brooks DJ. Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. *Brain*, 118: 913–933, 1995.

Jellinger KA. The pathology of Parkinson's disease. *Advances in Neurology*, 86: 55–72, 2001.

Kish SJ, Shannak K, and Hornykiewicz O. Uneven pattern of dopamine loss in the striatum of patients with idiopathic Parkinson's disease. Pathophysiologic and clinical implications. *The New England Journal of Medicine*, 318: 876–880, 1988.

Large EW and Palmer C. Perceiving temporal regularity in music. *Cognitive Science*, 26: 1–37, 2002.

Leh SE, Ptito A, Chakravarty MM, and Strafella AP. Fronto-striatal connections in the human brain: a probabilistic diffusion tractography study. *Neuroscience Letters*, 419: 113–118, 2007.

Lewis MM, Slagle CG, Smith AB, Truong Y, Bai P, McKeown MJ, et al. Task specific influences of Parkinson's disease on the striato-thalamo-cortical and cerebello-thalamo-cortical motor circuitries. *Neuroscience*, 147: 224–235, 2007.

Lewis PA, Wing AM, Pope PA, Praamstra P, and Miall RC. Brain activity correlates differentially with increasing temporal complexity of rhythms during initialisation, synchronisation, and continuation phases of paced finger tapping. *Neuropsychologia*, 42: 1301–1312, 2004.

Macmillan NA and Creelman CD. *Detection Theory: A User's Guide*. New York: Cambridge University Press, 1991.

Malapani C, Rakitin B, Levy R, Meck WH, Deweer B, Dubois B, et al. Coupled temporal memories in Parkinson's disease: a dopamine-related dysfunction. *Journal of Cognitive Neuroscience*, 10: 316–331, 1998.

Mangels JA, Ivry RB, and Shimizu N. Dissociable contributions of the prefrontal and neocerebellar cortex to time perception. *Cognitive Brain Research*, 7: 15–39, 1998.

Molinari M, Leggio MG, De Martin M, Cerasa A, and Thaut M. Neurobiology of rhythmic motor entrainment. *Annals of the New York Academy of Sciences*, 999: 313–321, 2003.

Nelson HE and Willison JR. *The Revised National Adult Reading Test–Test Manual*. Windsor, UK: NFER-Nelson, 1991.

Nenadic I, Gaser C, Volz H-P, Rammsayer T, Hager F, and Sauer H. Processing of temporal information and the basal ganglia: new evidence from fMRI. *Experimental Brain Research*, 148: 238–246, 2003.

Nichelli P, Alway D, and Grafman J. Perceptual timing in cerebellar degeneration. *Neuropsychologia*, 34: 863–871, 1996.

Nichelli P, Clark K, Hollnagel C, and Grafman J. Duration processing after frontal lobe lesions. In Grafman J, Holyoak KJ, and Boller F (Eds), *Structure and Function of the Human Prefrontal Cortex*. New York: New York Academy of Sciences, 1995: 183–190.

Noorden Lv and Moelants D. Resonance in the perception of musical pulse. *Journal of New Music Research*, 28: 43–66, 1999.

O'Boyle DJ. On the human neuropsychology of timing of simple, repetitive movements. In Bradshaw CM, and Szabadi E (Eds), *Time and Behaviour: Psychological and Neurobehavioural Analyses*. Amsterdam: Elsevier Science B.V., 1997: 459–516.

O'Boyle DJ, Freeman JS, and Cody FWJ. The accuracy and precision of timing of self-paced, repetitive movements in subjects with Parkinson's disease. *Brain*, 119: 51–70, 1996.

Owen AM, James M, Leigh PN, Summers BA, Marsden CD, and Quinn NP. Fronto-striatal cognitive deficits at different stages of Parkinson's disease. *Brain*, 115: 1727–1751, 1992.

Parncutt R. A perceptual model of pulse salience and metrical accent in musical rhythms. *Music Perception*, 11: 409–464, 1994.

Pastor MA, Artieda J, Jahanshahi M, and Obeso JA. Performance of repetitive wrist movements in Parkinson's disease. *Brain*, 115: 875–891, 1992.

Pastor MA, Day BL, Macaluso E, Friston KJ, and Frackowiak RSJ. The functional neuroanatomy of temporal discrimination. *Journal of Neuroscience*, 24: 2585–2591, 2004.

Patel AD, Iversen JR, Chen Y, and Repp BH. The influence of metricality and modality on synchronization with a beat. *Experimental Brain Research*, 163: 226–238, 2005.

Penhune VB, Zatorre RJ, and Evans AC. Cerebellar contributions to motor timing: a PET study of auditory and visual rhythm reproduction. *Journal of Cognitive Neuroscience*, 10: 752–765, 1998.

Povel DJ. Internal representation of simple temporal patterns. *Journal of Experimental Psychology: Human Perception and Performance*, 7: 3–18, 1981.

Povel D-J and Okkerman H. Accents in equitone sequences. *Perception and Psychophysics*, 30: 565–572, 1981.

Rammsayer T. Neuropharmacological evidence for different timing mechanisms in humans. *Quarterly Journal of Experimental Psychology B: Comparative and Physiological Psychology*, 52B: 273–286, 1999.

Rammsayer T and Classen J. Impaired temporal discrimination in Parkinson's disease: temporal processing of brief durations as an indicator of degeneration of dopaminergic neurons in the basal ganglia. *International Journal of Neuroscience*, 91: 45–55, 1997.

Ramnani N and Passingham RE. Changes in the human brain during rhythm learning. *Journal of Cognitive Neuroscience*, 13: 952–966, 2001.

Rao SM, Mayer AR, and Harrington DL. The evolution of brain activation during temporal processing. *Nature Neuroscience*, 4: 317–323, 2001.

Rascol O, Sabatini U, Chollet F, Fabre N, Senard JM, Montastruc JL, et al. Normal activation of the supplementary motor area in patients with Parkinson's disease undergoing long-term treatment with levodopa. *Journal of Neurology, Neurosurgery, and Psychiatry*, 57: 567–571, 1994.

Scatton B, Javoy-Agid F, Rouquier L, Dubois B, and Agid Y. Reduction of cortical dopamine, noradrenaline, serotonin and their metabolites in Parkinson's disease. *Brain Research*, 275: 321–328, 1983.

Schell GR and Strick PL. The origin of thalamic inputs to the arcuate premotor and supplementary motor areas. *Journal of Neuroscience*, 4: 539–560, 1984.

Schubotz RI and von Cramon DY. Interval and ordinal properties of sequences are associated with distinct premotor areas. *Cerebral Cortex*, 11: 210–222, 2001.

Shin JC and Ivry RB. Spatial and temporal sequence learning in patients with Parkinson's disease or cerebellar lesions. *Journal of Cognitive Neuroscience*, 15: 1232–1243, 2003.

Stanislaw H and Todorov N. Calculation of signal detection theory measures. *Behavior Research Methods, Instruments, and Computers*, 31: 137–149, 1999.

Tokuno H, Kimura M, and Tanji J. Pallidal inputs to thalamocortical neurons projecting to the supplementary motor area: an anterograde and retrograde double labeling study in the macaque monkey. *Experimental Brain Research*, 90: 635–638, 1992.

Yu H, Sternad D, Corcos DM, and Vaillancourt De. Role of hyperactive cerebellum and motor cortex in Parkinson's disease. *Neuroimage*, 35: 222–233, 2007.

Zatorre RJ, Chen JL, and Penhune VB. When the brain plays music: auditory–motor interactions in music perception and production. *Nature Reviews Neuroscience*, 8: 547–558, 2007.