Chapter 5

Perception Bias for Acceleration in Observed Velocity Change is Less Strong in Parkinson’s Bradykinesia.

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_In Preparation_
5.1 Abstract

Estimating velocity implies the assessment of spatial displacement over time. In our previous fMRI experiment we obtained arguments that cerebral processing demarcates discrete intervals of minimal spatial change, associated with intrinsic cerebral processing time. The observed striatum contribution to such temporal measure was subsequently supported by the behavioral observation that patients with Parkinson’s Disease (PD) showed a selective deficit in velocity estimation.

To gain quantitative information on the postulated ‘minimal intervals’, 19 Healthy Volunteers (HV) and 17 PD patients repeatedly judged change in velocity of a moving ball. Initial trajectory was always passed in 1s (same velocity), while velocity either increased or decreased with variable magnitudes at the point of rebound from the upper side of a monitor screen. Trajectory lengths before and after rebound were the same. By pressing one of two buttons, subjects had to indicate whether they perceived the ball’s velocity to either change or not.

Based on the stimuli used in our paradigm the threshold for detecting velocity change was around 0.014 rad/s in both the PD and HV group. Next to this, both subject groups perceived velocity as equal when the ball actually decelerated, while unchanged velocity was perceived as an acceleration. This shift in perceived velocity change was 0.009 rad/s for healthy volunteers, and 0.007 rad/s for PD patients. Moreover, this reduced deviation of perceived velocity constancy in PD showed a positive correlation with the severity of bradykinesia. As trajectories before and after velocity change were the same, the detection of velocity change could also be expressed as detected change in the duration of stimulus displacement. In this way, the threshold for discriminating velocity change was around 75ms, while 100ms increase of stimulus duration was perceived as equal by HV. For PD, this value was on average 76ms.

The observed ‘acceleration bias’ might be explained by the ‘flash-lag’ effect in which the perception of successive locations of moving stimuli includes extrapolation over adjacent past and predicted locations. In this way the brain accomplishes ‘real time’ visuomotor control notwithstanding delays due to intrinsic cerebral processing time. In PD, visuomotor control might lack such small-scale feedforward processing, thus resulting in a slowing of movements: bradykinesia.
5.2. INTRODUCTION

Parkinson’s Disease (PD) is a neurodegenerative disorder that causes characteristic motor symptoms but also sensory, cognitive and affective symptoms. Converging evidence supports that these symptoms emerge from deterioration of an effective contribution of the basal ganglia to sensorimotor integration (Brown et al., 1997; de Jong et al., 1999a; Konczak et al., 2007). This inaccurate processing of sensory events affects the organization of behavior, not only due to sensory deficits but also because of an intrinsic disturbance of sensorimotor control.

One aspect of motor control is the temporal adjustment of movements to sensory events. With regard to perceptual timing, we recently obtained arguments that timing in dynamic visuospatial conditions makes use of discrete intervals of spatial change. Such interval an was proposed to be the consequence of intrinsic cerebral processing time. With fMRI, we found (1) striatal involvement in the estimations of these small intervals, inferred from velocity estimation, and (2) cerebellar involvement in the estimation of longer intervals (Beudel et al., 2009). This dissociation between striatal and cerebellar contributions to perceptual timing was further supported by a subsequent patient study on PD and cerebellar ataxia, that showed disease-specific disturbances in estimating velocity and predicting longer intervals, respectively (Beudel et al., 2008). These findings supported a role for the striatum in maintaining a ‘clock-like’ measure of time (Gibbon et al., 1984; Meck, 2005; Meck and Benson, 2002) and are consistent with previously described disturbances in temporal processing in PD patients (Koch et al., 2008; Smith et al., 2007).

In the present study we aimed to gain more insight in the magnitude of this minimal interval of spatial change. To that end subjects were asked to judge change in velocity of a moving ball relative to its initial velocity. Estimating the velocity of a moving object implies the assessment of its spatial displacement over time. The perception of a minimal change in velocity thus implies detection of a minimal difference in time to travel a given distance. Considering the postulate that the brain orders the perception of spatial change in distinct frames, the time difference associated with the threshold of perceived velocity difference provides an indicator for the time it takes the brain to constitute such a spatial frame, thus providing a time measure based on cerebral processing time. When this minimal interval would for example be 40ms, perceived equal velocity could be assumed to be in a range of -40ms and +40ms around actual equal velocity, when this minimal interval would be 2ms, per-
Received equal velocity be around -2 and +2 ms around equal velocity etc.

Previous human behavioural experiments have indicated that the discrete events of perception could be around 100ms (Vanrullen and Koch, 2003). In our preceding fMRI experiment with the paradigm that provided the base for the present study, we referred to the flash-lag illusion of around 100 ms when speculating on a time measure for processing the interval of minimal spatial change (Beudel et al., 2009). In that fMRI study, the flash-lag illusion was linked to the judgment of the location where the moving ball disappeared. In such a condition, the moving object’s position is known to project backward compared to a spatially concurrent stationary flash before the two disappear, which might indeed be better described as ‘flash-lead’ effect (Eagleman and Sejnowski, 2000; Roulston et al., 2006; Wojtach et al., 2008). In contrast, when the moving object does not disappear, but proceeds its trajectory, the moving object’s position is perceptually projected forward (Eagleman and Sejnowski, 2000). Given the magnitude of these intervals, we hypothesized that the temporal measure involved in postulated minimal interval of spatial change would be around this value of 100ms.

Next to this, our previous experiment on velocity assessment in PD showed that these patients had a selective deficit in judging whether stimuli moved either faster or slower than a reference velocity (Beudel et al., 2008). We therefore hypothesized that the processing time associated with this minimal interval of spatial change would be longer in PD patients than in healthy controls. Since the velocity of executed movements is reduced in PD, described as hypo- or bradykinesia, we also hypothesized that the length of minimal intervals would correlate with the severity of bradykinesia.

To address these questions, we designed an experiment in which a PD and a HV group repeatedly judged change in velocity of a moving ball. The initial trajectory was always passed in 1s (same velocity), while velocity either increased or decreased with variable magnitudes at the point of rebound from the upper side of a monitor screen. Trajectory lengths before and after rebound were the same. By pressing one of two buttons, subjects had to indicate whether they perceived the ball’s velocity to either change or not.
5.3. MATERIALS & METHODS

<table>
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<tr>
<th></th>
<th>Parkinson (n =17)</th>
<th>Healthy Volunteers (n=19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>61.58 (±10)</td>
<td>60.73 (±11)</td>
<td>0.81</td>
</tr>
<tr>
<td>Sex (m:f)</td>
<td>9:8</td>
<td>11:8</td>
<td>0.98</td>
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<tr>
<td>Education (years)</td>
<td>15.05 (±2.2)</td>
<td>16.42 (±2.2)</td>
<td>0.08</td>
</tr>
<tr>
<td>Vision (visual acuity)</td>
<td>0.98 (±0.19)</td>
<td>1.05 (±0.25)</td>
<td>0.34</td>
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<td>MMSE score (0-30)</td>
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<td>29.47 (±0.77)</td>
<td>0.80</td>
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<tr>
<td>FAB score (0-18)</td>
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<td>17.57 (±0.69)</td>
<td>0.01</td>
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<td>UPDRS III score (0-105)</td>
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<tr>
<td>UPDRS bradykinesia score (0 - 28)</td>
<td>7.94 (±4.3)</td>
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<tr>
<td>LEDD score (mg)</td>
<td>687 (±425)</td>
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<td>Disease Duration (years)</td>
<td>4.64 (±2.66)</td>
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Table 5.1: Characteristics of Parkinson’s Disease (PD) Patients and Healthy Volunteers (HV). The PD and HV group were matched for age, sex, visual acuity, and cognitive abilities that was reflected by their MMSE scores and the duration of their education. The two groups were compared on these items using two-sample t-tests from which the p-values are depicted in the right column. The PD and HV group only differed significantly from each other on the Frontal Assessment Battery (FAB).

5.3 Materials & Methods

Seventeen patients with idiopathic PD with a mean age (±SD) of 61 (±10) years (9 males) and 19 HV with a mean age of 61 (±11) years (11 males) participated in this study. The PD and HV groups were matched for age, cognition and sex (Tab. 5.1). None of the participants had neurological, ophthalmologic, or cognitive disorders, other than symptoms related to PD in the PD group. All participants were informed about the experimental procedures before consenting to be tested. The local medical ethical committee approved these procedures.

5.3.1 Patient characteristics

PD patients with a mild to moderate disease progression were selected from an outpatient population based on a Unified Parkinson Disease Rating Scale motor score (UPDRS-III) between 5 and 30 (range 0-108), (Fahn and Elton, 1987). Furthermore, subjects were excluded in case of cognitive impairments, reflected by a Mini Mental State Examination score (MMSE) of less than 26 (range 0-30), (Folstein et al., 1975) or executive dysfunction, reflected by a Frontal Assessment Battery (FAB) score of less than 15 (range 0-18) (Dubois et al., 2000). To assess the motor velocity of the PD patients, the items on the UPDRS III assessing the velocity of leg and hand movements (items 23-26) and overall brady- and hypokinesia (item 31) were used as a sub-scale named
‘bradykinetic items’ (range 0-36). Such sub-scales were also made for rigidity (item 22, range 0-20) and (resting) tremor (item 20, range 0 -20). One PD patient was not able to complete the heel-tapping task with her left leg due to a temporary injury. For this reason, her average bradykinetic item score (1.3) was assigned to this item. To optimally achieve an equal effect of dopaminergic medication within the PD group, the patients conducted the experiment just before taking their next dose of medication. Levodopa Equivalent Daily Dosage (LEDD) scores were obtained for all PD patients. The mean time between the last dose and the experiment was 3.8 (±1.8) hours. The characteristics of the PD and HV group are depicted in table 1 including the p-values of their mutual comparisons.

5.3.2 Experimental procedure

Subjects watched a visual display of a moving ball on a grey monitor screen. The ball successively appeared, moved in diagonal direction upward to the middle of the upper edge, bounced from the upper edge and moved downwards until it disappeared from the screen (Fig. 5.1). The ball started either on the left or the right side of the screen and travelled over the same distance before and after rebound. The duration of upward movement was fixed at 1000ms (velocity 0.10 rad s⁻¹) provided the ‘reference velocity’ (Fig. 5.1). The downward movement lasted between 500 and 2000ms (velocity 0.05-0.20 rad s⁻¹) and was referred to as ‘new velocity’. Within this range 33 stimuli were designed with 13 different new velocities that were faster than the reference velocity (range 500-1000ms) and 19 stimuli of which the new velocity was slower (range 1000-2000ms). One stimulus had a downward new velocity equal to the reference velocity (1000ms). The change in velocity varied between 50 and 200 % of the reference velocity. These magnitudes of change were based on a preceding pilot study in healthy controls that provided an indication in which range velocity changes were perceived. After the ball had disappeared, a blank screen was presented between 1000 and 2500ms, which implied that every trial lasted 4000ms (Fig. 5.1). Subjects were asked to press either a right- or a left mouse button to indicate whether the ball had respectively changed velocity after rebound from the upper edge or not. They did not receive feedback on their judgment. PD patients gave responses with their least affected hand, healthy volunteers with their dominant hand. They were not asked to respond as fast as possible. Stimuli were presented with the ‘Presentation’ program (NeuroBehavioral Systems, Inc. CA, USA) in which responses and reaction-times were logged.
Figure 5.1: Stimulus Presentation. The solid line indicates the trajectory of the moving ball. The two balls point at the successive locations of respectively uncued appearance and stop and disappearance. In the first part of its trajectory (1), the ball moved with equal velocity in every stimulus (total duration 1s). In the second part of its trajectory (2) the velocity of the ball varied in a way that the duration of this part could last between 500 and 2000ms. After the ball had disappeared a blank screen was presented (3) until the total trial presentation lasted 4s (varying from 1000 to 2500ms). Subjects had to compare the velocity of the second part of the trajectory with the first part by indicating whether the velocities were perceived as equal or not.
The experiment was preceded by a 1-minute practice run, repeated until subjects could correctly conduct the task. The actual experiment consisted of three runs that lasted 6 minutes each. Every run, except for the practice run, contained 80 stimuli, which were presented in 8 blocks of 10. A grey screen with the word ‘rest’ was presented in between blocks (5s). In each run each of the stimulus trials with a new velocity was presented twice ($2 \times 32$), while the trial with the non-changing velocity was presented 16 times. In this way, for each subject a total of 6 judgments concerning each of the changing velocity trials were obtained and 48 on the equal velocity trial. All stimuli were presented in a pseudo-randomized order. To overcome fatigue, subjects rested 5 minutes in between runs.

5.3.3 Data analysis

The obtained data were first treated at subject level. A mean subject score was attributed to each of the 33 stimulus types. This score thus concerned the whole range of velocity changes in the presented stimulus trials, and represented for each magnitude of velocity change the fraction of all responses relative to the judgment that no velocity change was perceived (‘fraction-of-equal’ score). In order to assess the threshold at which subjects perceived a change in velocity, we identified for each subject the serried scores of 1.0 (i.e., all responses for a distinct stimulus trial were perceived as being equal to the reference velocity). If only one deviation was found within such a series of 1.0 scores, i.e., a score of 0.83 (when 5 out of 6 responses were judged as equal instead of 6 out of 6) this score was considered to be part of the series (Fig 5.2). In this way, the limits of this series provided the thresholds for the perception of change in velocity. For each subject, these limits were used to quantify the range that included the actual changes in stimulus duration corresponding with the scores that represented 100% perception of equal velocity. For both groups, these range values were averaged and mutually compared using a two-sample t-test.

The stimulus trial with changing velocity that was most often perceived as equal was obtained. This was done by smoothing the scores for the fraction of perceived equal velocity that were obtained for all 33 stimulus trials by averaging each score with the neighboring values of faster and slower stimuli. This resulted for each subject in an smoothed ‘fraction-of-equal’ score for each stimulus types. From these smoothed data we took the highest score given to the stimulus trial that was most often judged as having equal velocity. In case multiple maxima existed, the stimulus durations corresponding
Figure 5.2: Rules for interval assessment. For each velocity difference the stimulus was presented 6 times. Each had to respond with either ‘equal to reference velocity’ or ‘unequal to reference velocity’. The score on these 6 responses varied between 0/6 (never equal) and 6/6 (always equal). (A) interval of 4 successive stimuli in which 6 out of 6 stimuli were judged to have an equal velocity as the reference velocity. The corresponding range is 120ms. (B) interval of 4 stimuli in which 6 out of 6 stimuli were judged to have an equal velocity as the reference velocity interrupted by one stimulus with a 5/6 score. The corresponding range is 120ms (C) non-interval since more than one stimulus in between the maxima had a score of 5/6.
with these maxima were averaged. For both groups, mean scores were calculated from the subject scores, while the highest mean score was analyzed with a one-sample t-test to test for differences with the score attributed to actual equal velocity. The difference between the two groups with regard to the maximal ‘fraction-of-equal’ scores were analyzed using a two-sample t-test.

To analyze the effect of bradykinesia on the response profile of PD patients, the PD group was divided into a group consisting of the 8 PD patients with the lowest and a group of 8 PD patients with the highest scores on the bradykinesia items of the UPDRS III score. The response curves of these two sub-groups were plotted. For further quantitative analysis, correlation analyses using Spearman’s rank correlation coefficient were conducted to assess a relation between bradykinesia and (1) the threshold for perceived velocity change and 100% perceived equal velocity as well as (2) the actual velocity difference in the stimulus trial to which the maximum ‘fraction-of-equal’ score was given. Similar analyses were conducted for rigidity and tremor. All subjects included were able to perform the task. However, from the 20 PD patients that were tested, 3 patients had a response profile that had no relation with the task instructions. After their exclusion, data of 17 patients were used for further analysis. One subject of the HV group was excluded for the same reason, leaving 19 subjects for the further analyses.

5.4 Results

5.4.1 Threshold for perceiving velocity change

The upward movement of all stimuli lasted 1000ms while the subsequent downward movement, over an equal distance, took between 500ms and 2000ms. In the HV group, the range of actual velocity changes within which velocity was perceived as equal was associated with a range of changes in stimulus duration of 142 ms (SD ± 126ms) (Fig. 5.3A). For the PD group this range was 161ms (SD ±162ms). These intervals did not significantly differ between the two groups (19ms, p=0.73) and were not significantly different from the hypothesized 100ms interval either (HV p= 0.23, PD p = 0.19). In the HV group, one subject had a range of perceived equal velocity that was more than 3 SD’s from the average range. This was a reason to exclude him from this analysis. In the PD group, the severity of bradykinesia did not correlate with the range within which 100% of the stimulus velocity were judged as equal (σ 0.00, p = 0.88).
Figure 5.3: Threshold for Perception of Equal Velocity. A. Average interval of the HV and PD group in which 100 % of the variable velocities were perceived as equal and its standard deviation. B. Variable velocity that was most often judged as non-changing and its standard deviation for the HV and PD group. Statistical values obtained from comparison with the reference velocity are depicted under the bars. *** = p<0.001, ** = p<0.01, ns = non-significant.
5.4.2 Perception of equal velocity

Next to the detection of a threshold for perceiving change in velocity, a remarkable observation was that when velocity of the presented stimulus did not change, subjects tended to perceive an acceleration of the observed ball. In line with this finding, both groups most often indicated that they did not perceive velocity change when the ball actually slowed down compared to its initial velocity (Fig. 4A). For HV the velocity decrease associated with a 100ms longer stimulus duration (mean, SD ± 97ms) was preferentially judged as unchanged (Fig. 5.3B). The ‘fraction-of-equal’ score assigned to this 100ms change significantly differed from the score attributed to the stimulus trial in which no actual velocity change occurred (p <0.001). For the PD group this velocity decrease, which was perceived as unchanged, was associated with a stimulus duration that was 76ms longer (mean, SD ± 101ms). The ‘fraction-of-equal’ scores for this value also differed significantly from the score assigned to the stimulus without actual change (p=0.007). The presented velocity change which was maximally perceived as remaining equal did not significantly differ between the PD and HV group (24ms, p=0.47).

In PD, the severity of bradykinesia positively correlated with the ball’s new velocity in the stimulus trial of which the actual velocity change was maximally perceived as remaining equal (Fig. 5.5A, σ 0.23, p = 0.05). For other items on the UPDRS III score, rigidity or tremor, no such relation was present (Fig. 5.5B/C, rigidity σ 0.00, p = 0.99, tremor: σ 0.03, p = 0.46). This was also the case for the total UPDRS III score (that included the bradykinesia items) and the UPDRS III without the bradykinesia items (UPDRS III total: σ 0.19, p = 0.07, UPDRS III without bradykinesia: σ 0.10 p = 0.20). In this, the bradykinesia items had a very strong correlation with the UPDRS III score (σ 0.77, p <0.001) but not with tremor (σ 0.01, p = 0.59) or rigidity (σ 0.03, p = 0.50). Next to this, none of the other co-variants, age, MMSE, FAB & LEDD score or disease duration, had a noteworthy correlation with the presented velocity change that was perceived as equal velocity. Plotting the two response profiles of 8 PD patients with the mildest bradykinesia and 8 patients with the most severe bradykinesia, particularly illustrates the bradykinesia-related shift towards perception of equal velocity in stimulus trials with smaller velocity decreases (Fig. 5.4B).
5.4. RESULTS

Figure 5.4: Relation between Perception of Equal Velocity and Velocity Changes. A. The two curves indicate the fraction of equally perceived velocities (y-axis) in respectively the Healthy Volunteer (HV, white) and the Parkinson’s Disease (PD, black) group. On the x-axis, the duration of the variable velocities are depicted both absolute (rad/s) and relative to the reference velocities (ms). The individual values are an average of the value itself and the two most adjacent longer and shorter stimulus durations. B. Conventions as in A. The two curves indicate the fraction of equal perceived velocities in respectively the 8 PD patients with the mildest bradykinesia (white) and the 8 PD patients with the most severe bradykinesia (black).
Figure 5.5: Effects of UPDRS III Items on Perception of Equal Velocity. A. Correlation of the score of bradykinesia items (0-36) on the UPDRS III (x-axis) and the maximal equally perceived velocity (y-axis) of the 17 PD patients. The dots represent values of individual subjects. The solid line represents the regression line. CC = 0.23 p = 0.05. B. Conventions as in A. Correlation of the score of rigidity items (0-20) on the UPDRS III. CC = 0.00 p = 0.99. C. Conventions as in A. Correlation of the score of tremor items (0-20) on the UPDRS III. CC = 0.03 p = 0.46.
5.5 Discussion

In the present study we obtained quantitative data concerning the time it takes the brain to construct the representation of a moving object’s spatial location. The theoretical concept behind the initial question was that the succession of observed displacements of say a moving ball is not registered as a continuous line but ordered as spatial frames defined by discrete intervals of spatial change (Beudel et al., 2009). By asking subjects whether they either did or did not perceive change in the observed velocity of a moving ball, the established threshold for perceived change provided a temporal measure for a minimal interval of spatial change. In case of equal displacements, such a minimal interval is associated with the smallest time difference between two consecutive durations of a moving stimulus that are perceived as equal durations. With the stimulus durations used in the present paradigm this minimal interval was around 150ms. It was not different between PD patients and healthy volunteers and did not correlate with the severity of bradykinesia in PD.

Next to this, the perception of equal velocity did not correspond with the actual similarity of consecutive stimulus durations. We found that 100ms longer stimulus duration relative to the preceding reference duration (i.e. deceleration) was maximally perceived as equal velocity by healthy volunteers. Indeed, when no change in the actual velocity occurred, subjects perceived an acceleration of the stimulus, which we referred to as an acceleration bias. For the entire PD group this bias was 76 ms, while in severe bradykinesia it was further reduced.

**Velocity threshold and a minimal interval**

The range of various stimulus trials to which subjects responded with 100% perception of equal stimulus duration revealed that within approximately 150ms a difference between stimulus displacements was not perceived in our experiment. As indicated in the introduction, such range consists of two parts that represent the deviation in two directions, i.e. acceleration or deceleration. In this respect, the minimal interval is around 75ms. The demarcation of such a well-defined interval is consistent with the concept that perception is established by means of discrete perceptual frames and that it is not continuous (Vanrullen and Koch, 2003). This interval might reflect the time required to construct a single ‘spatial frame’. The value of 75ms was obtained in a paradigm with stimuli that had the same initial velocity over the same distance (in 1000ms). In order to assess to what extent this minimal interval is
associated with a general constancy, future analysis of variation in the initial stimulus velocity may provide further insight in the magnitude of this temporal measure.

The absence of a significant difference between PD patients and healthy volunteers with regard to the threshold for perceiving change in velocity suggests that cerebral processing implicated in demarcating discrete intervals of minimal spatial change is unaffected in PD. The absence of a correlation between the threshold for perceived velocity change and bradykinesia indeed supported the similarity concerning this aspect of perceptual time processing between the two groups, and implies that another neuronal process must be responsible for the perceptual timing deficits that have been described in PD.

Acceleration bias and the perception of equal velocity
In our task, the ball’s reference velocity was inferred from the ascending part of its trajectory. For a (virtual) moment the ball stopped at the upper border of the screen and changed direction after which the estimation of velocity change was made in the descending part of the stimulus trajectory, before the stimulus disappeared. The observed bias for acceleration after turning might be explained by the ‘flash-lag’ effect. In the latter, a moving object’s position is perceptually projected forward compared to a spatially concurrent stationary flash, provided that the ball proceeds its trajectory (see introduction) (Eagleman and Sejnowski, 2000; Roulston et al., 2006). If one assumes that the ‘image’ of the turning point resembles the stationary flash for comparing the perceived locations of the moving and stationary stimuli, the ball’s location on the trajectory of movement is perceived forward compared to the ‘stationary’ moment of rebound. This holds in case the actual velocity has not changed. The forward projection is counteracted when the ball decelerates at turning, resulting in the perception of equal velocity, while actual acceleration enhances the perception of change.

Although no significant difference was seen between the acceleration bias in PD patients and that in healthy volunteers, this bias was less pronounced and even absent in patients with increasingly severe bradykinesia. The fact that this bias reduction was not a common characteristic of the entire patient group might be due to the fact that only patients with mild or moderate PD participated in our study. Moreover, bradykinetic symptoms were in general mild. Next to this, an effect of dopaminergic medication cannot be excluded although subjects were tested just before taking their next dopaminergic medication. On the other hand, even though patients were not completely withdrawn from
medication, the obtained UPDRS III score did reflect their motor status at the moment that the experiment was conducted. This made it legitimate to use the bradykinesia score as a regressor. As subjects were not urged to make a response as fast as possible, a bias in the results due to velocity of motor execution was circumvented (Wearden et al., 2008).

Parkinson’s bradykinesia

The reduction of the acceleration bias in more bradykinetic PD patients would thus indicate a reduced flash-lag effect (Eagleman and Sejnowski, 2000). Impairment of such small-scale feedforward processing might be due to an absence of visuomotor integration by the basal ganglia. Perceptual processing of the dynamic stimulus trajectory and the relative stationary moment of rebound would logically fit segregation between respectively dorsal- and more ventral visual processing streams (Milner and Goodale, 2008). Such segregation is accompanied with temporal dispersion in the representations of simultaneous stimulus events. We recently proposed that the striatum plays a crucial role in ordering the effects of such dispersion leading to sequential regularity (Beudel et al., 2009). In the absence of such internally defined sequence order, overt motor behavior may be stronger influenced by sensory stimuli via direct cortical interactions (de Jong et al., 1999a; Praamstra et al., 1998; Praamstra and Plat, 2001). This would imply that cerebral processing time needed for assessing spatial change is not affected in PD, but that striatum dysfunction is expressed in a failure of small-scale feed-forward processing of spatial changes, which indeed requires continuous ordering of recent and anticipated spatial information.

The proposed impairment of small-scale feed-forward estimations means that the perception of visual motion lacks behind in PD patients, compared to healthy subjects. As a consequence, the internal initiative to undertake goal directed action implies that motor preparation is based on a delayed representation of the ongoing stream of external change, resulting in movement pattern that slows down. A relation between perceptual and motor timing skills (Keele et al., 1985; Treisman et al., 1992) has been reported earlier. E.g., the fact that the administration of dopaminergic antagonists both worsens such perceptual and motor timing skills (Rammsayer and Vogel, 1992) indicates a role for the dopaminergic system in a common time keeping mechanism. At millisecond level, this automatic mechanism acts beyond cognitive control (Rammsayer, 1993) and is strongly related to motor circuitry (Lewis and Miall, 2003). Common involvement of cortical- and subcortical structures, including the striatum, underscores functional overlap between perceptual and
motor timing (Bueti et al., 2008; Schubotz et al., 2000), and illustrates that motor circuits are also implicated in sequencing and timing of observed movements, independent of motor implementation (Schubotz et al., 2000). If observed movements are mapped onto the motor system in a sequential order, one might argue that when the striatum is affected, in case of PD, such sequential transformations are slower resulting in slowing of movements: bradykinesia.

Alternatively, one might consider that the reduced acceleration bias in bradykinetic PD patients might be due to a reduced velocity of ocular pursuit movements (Lekwuwa et al., 1999; Rascol et al., 1989). This would imply that disturbed efferent controlled motion perception, i.e. motion perceived by following objects (Dichgans et al., 1975), results in a relatively faster judgment of the initial part of the stimulus. As a consequence, the second part of the stimulus needs to go proportionally faster to be judged as having an equal velocity. In this case, the altered perceptions of faster movements could be due to bradykinetic movements themselves. At present, we cannot definitely solve this issue because we did not register eye movements.

5.6 Conclusions

The threshold for perceiving change in velocity indicates that processing an interval of minimal spatial change takes around 75ms, both in PD patients and healthy volunteers. Next to this, velocities that are slightly slower than a reference velocity are perceived as having an equal velocity, while equal velocity is perceived as an acceleration. This acceleration bias might be explained by the ‘flash-lag’ effect at the point of rebound. This implies that the perception of successive locations of moving stimuli includes near-future extrapolation of minimal spatial intervals, thus enabling ‘real-time’ visuomotor control. This mechanism appeared impaired in bradykinetic PD. In this way, a model is proposed by which reduced perceptual anticipation is consistent with slowing of planned movements: bradykinesia.