

2014

Effects of Parkinson's disease on optic flow perception for heading direction during navigation

C Lin, RC Wagenaar, D Young, EL Saltzman, X Ren, S Nearing, A Cronin-Golomb. 2014.

"Effects of Parkinson's disease on optic flow perception for heading direction during navigation."

Experimental brain research, Volume 232, Issue 4, pp. 1343 - 1355. <https://doi.org/10.1007/s00221-014-3853-9>

<https://hdl.handle.net/2144/34397>

"Downloaded from OpenBU. Boston University's institutional repository."



HHS Public Access

Author manuscript

Exp Brain Res. Author manuscript; available in PMC 2015 April 01.

Published in final edited form as:

Exp Brain Res. 2014 April ; 232(4): 1343–1355. doi:10.1007/s00221-014-3853-9.

Effects of Parkinson's disease on optic flow perception for heading direction during navigation

Cheng-Chieh Lin,

College of Health and Rehabilitation Sciences, Sargent College, Boston University, Boston, MA, USA. Department of Physical Therapy and Rehabilitation Science, University of Maryland School of Medicine, 100 Penn St. Room 106, Baltimore, MD 21201, USA

Robert C. Wagenaar,

College of Health and Rehabilitation Sciences, Sargent College, Boston University, Boston, MA, USA

Daniel Young,

College of Health and Rehabilitation Sciences, Sargent College, Boston University, Boston, MA, USA

Elliot L. Saltzman,

College of Health and Rehabilitation Sciences, Sargent College, Boston University, Boston, MA, USA

Xiaolin Ren,

College of Health and Rehabilitation Sciences, Sargent College, Boston University, Boston, MA, USA

Sandy Neargarder, and

Department of Psychology, Boston University, Boston, MA, USA. Department of Psychology, Bridgewater State University, Bridgewater, MA, USA

Alice Cronin-Golomb

Department of Psychology, Boston University, Boston, MA, USA

Cheng-Chieh Lin: clin@som.umaryland.edu

Abstract

Visuoperceptual disorders have been identified in individuals with Parkinson's disease (PD) and may affect the perception of optic flow for heading direction during navigation. Studies in healthy subjects have confirmed that heading direction can be determined by equalizing the optic flow speed (OS) between visual fields. The present study investigated the effects of PD on the use of optic flow for heading direction, walking parameters, and interlimb coordination during navigation, examining the contributions of OS and spatial frequency (dot density). Twelve individuals with PD without dementia, 18 age-matched normal control adults (NC), and 23 young control adults (YC) walked through a virtual hallway at about 0.8 m/s. The hallway was created by

random dots on side walls. Three levels of OS (0.8, 1.2, and 1.8 m/s) and dot density (1, 2, and 3 dots/m²) were presented on one wall while on the other wall, OS and dot density were fixed at 0.8 m/s and 3 dots/m², respectively. Three-dimensional kinematic data were collected, and lateral drift, walking speed, stride frequency and length, and frequency, and phase relations between arms and legs were calculated. A significant linear effect was observed on lateral drift to the wall with lower OS for YC and NC, but not for PD. Compared to YC and NC, PD veered more to the left under OS and dot density conditions. The results suggest that healthy adults perceive optic flow for heading direction. Heading direction in PD may be more affected by the asymmetry of dopamine levels between the hemispheres and by motor lateralization as indexed by handedness.

Keywords

Parkinson's disease; Visual perception; Optic flow; Navigation Locomotion

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disease that traditionally has been conceptualized as a motor disorder, with symptoms including tremor, rigidity, bradykinesia, and disturbances of posture, balance, and gait (Barbeau 1986; Hoehn and Yahr 2001; Martin et al. 1973). Though not as well known, visual and visuoperceptual deficits in individuals with PD have been reported in studies using neurophysiological and neuropsychological tests as well as self-administered questionnaires (Bodis-Wollner and Yahr 1978; Bodis-Wollner et al. 1982; Harris et al. 2003; Lee and Harris 1999; Lee et al. 2001a, b). Administering a line bisection test, researchers found that PD patients with predominantly left-sided motor symptoms (LPD) showed a shift to right when marking the midpoint of the line (Laudate et al. 2013; Lee et al. 2001a). LPD subjects also judged the size of rectangles presented in the left visual field to be smaller than same-sized rectangles in the right visual field (Harris et al. 2003). It was concluded that LPD subjects have a unilateral compression of the perceived left visual field. Davidsdottir et al. (2008) further reported after applying the line bisection test that LPD subjects have a shift in egocentric reference point, which coincided with veering to the right while walking through a virtual hallway.

Optic flow contains information relevant to heading direction during navigation and influences the coordination of gait (Chatziastros et al. 1999; Chou et al. 2009; Duchon and Warren 2002; Srinivasan et al. 1991; Young et al. 2010). The effectiveness of using vision to improve parkinsonian gait has been consistently reported, and motor freezing, one of the debilitating symptoms of PD, has been found to be strongly influenced by visual input (Davidsdottir et al. 2005; Ehgoetz Martens et al. 2013a, b; Lewis et al. 2000; Mestre et al. 1992; Morris et al. 1994, 1996). Hence, a thorough understanding of the impact of visuoperceptual disorders on optic flow perception during navigation may be critical for developing therapeutic interventions for PD. It is possible that the unilateral compression of one visual field results in the perception of an asymmetric optic flow speed (OS) and texture between the left and right visual fields, which could influence heading direction during navigation. For example, an asymmetry of OS between two visual field affects veering

direction in honeybees and humans (Chatziastros et al. 1999; Duchon and Warren 2002; Chou et al. 2009; Srinivasan et al. 1991; Young et al. 2010). In a study by Srinivasan et al. (1991), honeybees were trained to fly down the middle of a tunnel consisting of two walls with vertical, black-and-white gratings. During asymmetric manipulation of the OS of the two walls, the bees flew toward the wall with slower OS, but no significant veering occurred when optical spatial frequencies of the gratings were different between walls. Veering toward the side with slower OS has also been observed in humans during treadmill walking, over-ground walking, and simulated driving (Chatziastros et al. 1999; Chou et al. 2009; Duchon and Warren 2002; Young et al. 2010).

By contrast, by systematically manipulating optical spatial frequency of the gratings on both walls, Chatziastros et al. (1999) found that participants veered to the side with the higher spatial frequency while steering through a virtual tunnel. Duchon and Warren (2002) created a virtual corridor with the texture generated by a set of random seed points assigned with a random RGB (red, green, and blue) value with smaller patches representing a higher spatial frequency. Participants moved toward the wall with smaller patches while walking through a virtual corridor, a result that provided additional support for the effect of optical spatial frequency on heading direction. Chatziastros et al. (1999) also explored the effects of optical temporal frequency, which is the product of OS and optical spatial frequency, on veering during simulated driving. They found that with both walls having the same temporal frequency, participants veered to the side with slower OS rather than maintaining the midline of the tunnel, indicating a dominant effect of OS on heading direction. The manipulation of texture may also have an impact on the use of navigation strategies for heading direction. For example, Warren et al. (2001) found that subjects relied more on the egocentric reference point strategy in determining heading direction during walking with less texture available, but they relied more on the optic flow equalization strategy when more texture (and hence optic flow) was introduced to the virtual environment.

The generalizability of outcomes from studies to date may be limited for several reasons. The effects of OS, optical spatial frequency, and optical temporal frequency on veering in the study by Chatziastros et al. (1999) were assessed via a simulated driving task using joystick control. Walking is achieved by the coordination of head, trunk, and arm and leg movements (Donker et al. 2001; van Emmerik and Wagenaar 1996; Wagenaar and van Emmerik 2000), but most previous studies reported the effect of OS only on the change of walking speed, stride frequency, and length (Prokop et al. 1997; Schubert et al. 2005). In studies of PD itself, for example, Prokop et al. (1997) introduced an optic flow pattern with different speeds relative to walking speed while subjects walked on a self-driven treadmill and observed a decrease in walking speed with an increase in OS, which was achieved through adjusting stride length. Schubert et al. (2005) observed that the modulation effect of OS on walking speed was stronger and lasted longer in PD subjects compared to healthy control adults, suggesting a stronger visual dependence in PD subjects.

There is evidence that different walking patterns emerge as a result of systematically increasing walking speed (Donker et al. 2001; van Emmerik and Wagenaar 1996; Wagenaar and van Emmerik 2000). A transition from an in-phase to out-of-phase relation between pelvic and thoracic rotation in the transverse plane and left and right arm movements in the

sagittal plane at about 0.8 m/s was supported by increased phase and frequency relation between the movements of body segments. Few studies to date have explored the relation between visual information and the coordination pattern during walking. Young et al. (2010) found that individuals with PD veered toward the side with the slower OS, a result that could not be explained by the asymmetry in the gait pattern between the left and right body side. Most findings regarding the effects of OS on stride parameters and heading direction have been investigated using treadmill instead of overground locomotion (Duchon and Warren 2002; Prokop et al. 1997; Schubert et al. 2005). Furthermore, Chatziastros et al. (1999) imposed OS values of 10 and 20 m/s, which are much faster than a comfortable walking speed (about 1.2 m/s). Hence, it remains open to further investigation whether similar effects of optic flow on heading direction during navigation would be obtained during overground walking while using optic flow speeds similar to comfortable walking speed.

The aim of the present study was to systematically explore the effects of OS and dot density on heading direction during overground walking. The implementation of virtual reality technology during overground walking allowed us to overcome some of the limitations mentioned above (Giphart et al. 2007). We used a systematic manipulation of dot density on the walls instead of applying mathematically defined vertical gratings, in order to avoid rhythmic cueing effects in the PD subjects (Azulay et al. 1999; Morris et al. 1994). On the basis of previous research, it was expected that introducing asymmetric OS across the left and right visual fields while keeping dot density the same on both walls would lead to healthy subjects veering away from the faster moving wall, with more veering related to increasing differences in OS between the walls. We also expected that introducing asymmetric dot density while keeping OS the same on both walls would lead to healthy adults veering away from the wall with higher dot density, with more veering related to increasing differences in dot density between the walls. In both cases, it was expected that the heading direction in PD subjects would be predominantly influenced by their egocentric reference point, as was implicated in our previous studies of PD (Davidsdottir et al. 2008; Young et al. 2010). Finally, we predicted that walking speed, stride frequency, stride length, phase, and frequency relations between body segments would decrease with an asymmetric increase in OS or dot density on one wall of the virtual hallway.

Methods

Participants

Twelve mild-to-moderate (Hoehn and Yahr stages I–III) non-demented individuals with idiopathic PD (7 men and 5 women; all right handed; mean age 64.4 ± 8.1 years, age range 47–75 years), 18 healthy age-matched normal control (NC) adults (7 men and 11 women; 16 right handed and 2 left handed; mean age 66.1 ± 9.3 years, age range 49–81 years), and 23 healthy younger control (YC) adults (13 men and 10 women; 22 right handed and 1 left handed; mean age 19.2 ± 2.1 years, age range 18–27 years) from the Boston area were recruited for the present study. Handedness was assessed with the Edinburgh Handedness Questionnaire (Oldfield 1971). All participants were native English speakers. There was no significant difference in body height between groups, $F(2,48) = 1.02$, $p = 0.37$ (174.6 \pm 8.7 cm for YC group, 171.0 \pm 14.7 cm for NC group, and 168.8 \pm 9.5 cm for PD group).

For the PD group, mean disease duration was 6.1 years (SD 3.1; range 2–13) and the median Hoehn and Yahr (H&Y) stage of motor disability was 1.5 (range 1–3) (Hoehn and Yahr 2001). Body side of initial motor symptom onset was obtained through self-report and confirmed through neurologist report. Six patients had motor symptoms that presented initially on the right side of the body (RPD), five had motor symptoms that presented initially on the left side of the body (LPD), and one showed motor symptoms that initially presented bilaterally. Information on medication use was not available for two PD participants. The majority of PD participants used levodopa (6 patients, 60 %) and/or dopamine agonists (9 patients, 90 %). One participant used catechol-O-methyltransferase inhibitors and one participant used a monoamine oxidase inhibitor. One participant used amantadine, and one used anticholinergic medication. The mean levodopa equivalent dose was 445.4 ± 334.5 mg (range 100–975 mg).

Exclusion criteria for all participants were as follows: physical disabilities that prevented them from moving freely (such as past knee or hip surgeries or lower back pain); co-existing serious chronic medical diseases (including psychiatric or neurological) besides PD; use of psycho-active medications, with the exception of antidepressants and anxiolytics in the PD group only; history of intracranial surgery, traumatic brain injury, alcoholism, or other drug abuse; and eye diseases or visual abnormalities as noted on neuro-ophthalmological examination. Individuals with PD were classified as not demented if they received scores of 26 or higher on the Mini-Mental State Examination and 135 or higher on the Mattis Dementia Rating Scale (Folstein et al. 1975; Mattis 1976, 1988). None of the NC and PD subjects demonstrated binocular acuity worse than 20/40 at a distance of 10 feet (304.8 cm). The study protocol was approved by the Institutional Review Board of Boston University, and informed consent was obtained according to the Declaration of Helsinki prior to subject participation.

Apparatus

Virtual reality system—A virtual hallway was created using an Onyx2 Infinite Reality workstation (SGI, Mountain View, CA) at a frame rate of 60 Hz via WorldToolKit software (Sense8, Inc., San Rafael, CA). The two side walls of the virtual hallway were textured with randomly placed white dots, 9.4 cm in diameter, on a black background. The front wall, ceiling, and floor of the hallway were black with no texture (Fig. 1a, b). To emulate depth perception, the size of dots was inversely proportionally to the distance to the observers, with smaller dots on the far end of the hallway. The width, height, and depth of the hallway were 2.0, 2.55, and 15.0 m, respectively. The visual scene was displayed via a ProView 60 head-mounted display (Kaiser Electro-Optics Inc, Mountain View, CA) with a weight of 1.4 kg. The head-mounted display consisted of two, full color, active, LCD panels with a 60° (horizontal) × 40° (vertical) binocular field of view and a resolution of 640 × 480 pixels per panel. The participant's head position and orientation were tracked and updated using an IS-900 hybrid inertial/ultrasonic tracker (InterSense, Burlington, MA) at a sampling rate of 60 Hz with an accuracy of 4-mm RMS error for position and 0.1° RMS error for orientation data. To facilitate the full immersion into the virtual environment, all remaining ambient light from the laboratory room was eliminated with an additional mask that weighed 0.2 kg.

Three-dimensional kinematics—Three-dimensional (3D) kinematic data were collected by means of an Optotrak 3020 system (Northern Digital Inc., Waterloo, ON, Canada). Two Optotrak position sensors consisting of a bank of three cameras were placed on each side of the walkway, and a third one was placed at the front end of the walkway in order to capture full three-dimensional movements. The mean calibration error was 0.7 mm or less. Twelve active infrared light-emitting diodes (IREDs) were attached bilaterally to participants' major bony landmarks: ankle (midpoint between medial and lateral malleolus), knee (patella), wrist (radiocarpal joint), shoulder (humeral head), cheek (2 cm below zygomatic arch), and hip (anterior superior iliac spine). Four IREDs were attached to the ends of two T bars, which were mounted on harnesses and fixated around the hip and the thorax, allowing for the recording of pelvic and thoracic rotations in transverse plane. Two additional IREDs were attached to the chin and the head-mounted display, respectively. The instantaneous position of each IRED was sampled at a rate of 100 Hz and stored on a hard drive for further off-line processing.

Walking speed gates—Two photoelectric gates (Safe House, Fort Worth, TX) placed 6 meters apart were used to provide real-time feedback regarding participants' walking speed during training.

Procedure

The experiment consisted of the manipulation of optic flow speed (OS) and dot density (DD). Before the trials of optic flow manipulation, participants were trained to keep their speed constant at approximately 0.8 (± 0.05) m/s. Throughout the experiment, participants were instructed to walk in the middle of the hallway. They walked a total of 10 m per trial; data from only the middle six meters were analyzed. Previous studies of the coordination dynamics of walking have demonstrated that inter-limb and trunk coordination patterns are relatively unstable at these walking speeds (Donker et al. 2001; van Emmerik and Wagenaar 1996; Wagenaar and van Emmerik 2000). At walking speeds below 0.7 m/s, the arms and legs move at a 2:1 frequency ratio (two swings per stride) with a nearly in-phase relation between transverse thoracic and pelvic rotation. At walking speeds above 0.9 m/s, the arms and legs move at a 1:1 frequency ratio (1 swing per stride) with a nearly out-of-phase relation between transverse thoracic and pelvic rotation. Hence, we expected that the effect of OS and DD manipulations on interlimb coordination during walking could be more easily demonstrated when participants walked at approximately 0.8 m/s.

The experiment was conducted during peak medication period for the PD patients ("on" phase). Dyskinesias did not affect this sample of individuals.

Manipulation of optic flow speed (OS) and dot density (DD)—The asymmetric OS manipulation was established by having the dot pattern moving opposite to the participant's walking direction, with the speed on one wall fixed at 0.8 m/s, and the dot speed on the other wall varying across 0.8, 1.2, and 1.8 m/s. During all OS trials, DD on both walls was fixed at 3 dots/m² (Fig. 1a). To examine the effects of DD manipulation, the DD value on one wall was fixed at 3 dots/m² while the DD value on the other wall was varied across 1, 2, and 3 dots/m². The OS on both walls was fixed at 0.8 m/s during DD manipulation trials (Fig. 1b).

Five trials were conducted for each condition for both the right and left wall manipulations, for a total of 90 trials performed by each subject. Subjects were allowed to take short breaks during the experiment. The order of OS and DD conditions was determined via computerized randomization across participants. To enhance the effect of the optic flow manipulation, the depth of the virtual hallway was fixed at 15 m so that the hallway appeared endless to prevent a looming effect of the front wall which may have induced braking behavior and affect walking speed. A spotter walked behind the participant to insure safety throughout the experiment.

Dependent variables

Lateral drift—The midpoint between left and right hip markers was calculated, and the difference of the midpoint in the mediolateral direction between the last and first stride was used to represent the lateral drift. A positive value indicated rightward drift, and a negative value indicated leftward drift.

Stride parameters—Average walking speed was determined by dividing the displacement of the chin marker by the total time elapsed between the left heel strike of the first and last stride. The displacement of chin marker was calculated based on Pythagorean theorem ($c^2 = a^2 + b^2$), with a and b representing the position change in anteroposterior and mediolateral direction of the chin marker. Stride frequency for both legs was estimated by dividing the number of strides by the elapsed time. Stride length for both legs was obtained by dividing the total displacement of the left and right ankle markers in the anteroposterior direction by the number of strides taken.

Relative Power Index—The frequency relations between ipsilateral arm and leg movements were analyzed using the angular displacements of arm and leg movements. The arm's angular displacement was defined by the angle formed by the shoulder and wrist markers relative to the vertical in the sagittal plane, while the hip and ankle markers were used to define the leg angle relative to the vertical in the sagittal plane. The frequency content of arm and leg angular displacement was analyzed using the power spectral density method (Fast Fourier Transform algorithm using the Welch method for power estimation and a Hanning window for smoothing) (Wagenaar and van Emmerik 2000). The power spectral density was normalized by dividing each frequency power by the mean power calculated over the 0.2–2.5 Hz frequency range for each trial. The frequency with the largest power was defined as the stride frequency in the power spectral density of leg movement with the step frequency occurring at twice the stride frequency. Power at the stride and step frequencies for arm movements was identified using the stride and step frequencies obtained from the power spectral density of the leg movements. To quantify the frequency ratio of arm and leg movements, a Relative Power Index was calculated as:

$$\text{Relative Power Index} = \frac{P1 - P2}{P1 + P2}$$

with P1 and P2 representing the power of the arm movements at stride and step frequency, respectively. Relative Power Index values range from –1 to 1. A value of Relative Power

Index equal to 1 indicates that arm movements lock onto stride frequency, representing a 1:1 frequency relation between arm and leg movements, and a Relative Power Index value equal to -1 indicates that arm movements lock onto step frequency, representing a 2:1 frequency relation between arm and leg movements.

Point estimate of relative phase—A point estimate of relative phase for limb pair was calculated by using the moment (t_{limbx} and t_{limby}) at which the positive maxima were reached for the angle of each body segment with the following equation:

$$\theta(i) = \frac{t_{limby}(i) - t_{limbx}(i)}{t_{limbx}(i+1) - t_{limbx}(i)}$$

with $limby$ and $limbx$ representing ipsilateral leg and arm (Donker et al. 2001; Wagenaar and van Emmerik 2000). In the case of 1:1 frequency ratio between leg and arm movements, the maximum of the arm movements relative to its preceding maximum of the leg movements was used for calculating the point estimate of relative phase. In the case of 2:1 frequency ratio between arm and leg movements, for each stride, the moment of maximum amplitude of the limb with the shorter and longer movement period was identified as t_{limbx} and t_{limby} , respectively (Fig. 2). The mean and SD of the point estimate of relative phase for each trial were calculated by means of circular statistics (Batschelet 1981).

Data analysis

Data across five trials were averaged for each condition. All statistical analyses were carried out with version 15.0 of the SPSS statistical software package (SPSS, Inc. Chicago, IL). A series of six mixed design ANOVAS was performed to examine the effects of group (YC, NC, and PD), side of fixed wall (left and right), and either levels of OS (0.8, 1.2, and 1.8 m/s) or DD (1, 2, and 3 dots/m²) on lateral drift, walking speed, stride frequency, stride length, Relative Power Index, and relative phase between the ipsilateral arm and leg. One ANOVA was performed for each dependent variable. Given the potentially large number of significant main effects and interactions, only those explaining differences in group performance were reported (i.e., the most complex interactions where group was included as a variable, and in the absence of significant interactions, all significant main effects). Follow-up analyses of significant interactions of interest consisted of a series of *a priori* *t* tests aimed at examining differences between YC and NC subjects and between NC and PD subjects across conditions. Tukey's post hoc analyses or dependent groups *t* tests were used to examine significant main effects. Finally, post hoc linear contrasts were performed to examine predicted linear patterns in performance whenever there was a significant main effect of OS or DD. For all statistical analyses regarding stride length, stride frequency, Relative Power Index, and relative phase, a within-group factor (Body Side) was defined, with levels defined as non-dominant or dominant in YC and NC groups, and initially affected or secondarily affected in the PD group. Comparisons were made between YC/NC and PD groups for only the dominant vs. secondarily affected sides (the "better" sides of each group) and the non-dominant vs. secondarily affected sides (the "worse" sides of each group). These comparisons were motivated, in part, by the finding that grip strength is stronger on the dominant side than non-dominant side in healthy right handers (Armstrong

and Oldham 1999) and that motor function may degrade to a larger extent in the initially affected side than the secondarily affected side in PD subjects (Djaldetti et al. 2006).

Results

Optic flow speed (OS) manipulation

For lateral drift, a significant interaction between OS, side of fixed wall, and group was found, $F(4,88) = 3.6, p < 0.01$. *A priori t* tests showed that compared to the YC group, the NC group veered more to the left when OS was at 1.8 m/s, $t(59) = 2.2, p < 0.03$. The PD group veered more to the left than the NC group for each of the OS conditions (0.8 m/s: $t[58] = 3.4, p < 0.01$; 1.2 m/s: $t[40] = 2.3, p < 0.03$; and 1.8 m/s: $t[37] = 2.3, p < 0.03$). Tests of contrasts showed significant linear effects of OS on lateral drift for both the YC group, $F(1,22) = 24.6, p < 0.01$, and the NC group, $F(1,17) = 7.7, p < 0.01$, but not for the PD group, $F(1,11) = 0.04, p = 0.85$. Both the YC and NC groups veered toward the slower moving wall, and the lateral drift increased with increasing differences in OS between the left and right walls (Fig. 3a). The linear effect of OS on lateral drift was observed when OS was fixed on the right wall; when OS was fixed on the left wall, the effect was seen between 1.8 m/s and the other speeds, whereas the drift was relatively unchanged between the 0.8 and 1.2 m/s conditions. For walking speed, a significant interaction between OS and side of fixed wall was noted, $F(2,100) = 3.6, p < 0.03$. *A priori t* tests showed that walking speed was faster when OS was fixed at 0.8 m/s on the left wall compared to when it was fixed at 0.8 m/s on the right wall, $t[52] = 4.3, p < 0.03$. There were no significant differences in walking speed between the left wall and right wall for the 1.2 ($p = 0.06$) or 1.8 ($p = 0.48$) m/s OS conditions. There was no significant linear effect of OS on walking speed, $F(1,50) = 0.7, p = 0.42$.

For stride frequency, there were significant main effects of OS, $F(2,99) = 5.0, p < 0.01$, and group, $F(2,50) = 14.9, p < 0.01$, but no significant interactions. For the main effect of OS, dependent groups *t* tests showed that stride frequency was significantly less at 1.2 m/s compared to 0.8 m/s, $t[211] = 4.1, p < 0.01$, and 1.8 m/s, $t[211] = -2.2, p < 0.03$. For the main effect of group, Tukey's post hoc analyses showed that stride frequency was significantly higher in the PD group than the NC group, $p < 0.02$, and higher in the NC group than the YC group, $p < 0.02$. With groups combined, there was no linear effect of OS on stride frequency, $F(1,50) = 0.8, p = 0.37$.

For stride length, there was a significant main effect of OS, $F(2,97) = 3.4, p < 0.04$, and a significant interaction between body side and group, $F(2,50) = 3.7, p < 0.03$. For the main effect of OS, Tukey's post hoc analyses showed that stride length was significantly smaller at 0.8 m/s compared to 1.8 m/s, $t[211] = -2.1, p < 0.04$ (Table 1). For the interaction between body side and group, *a priori t* tests showed no significant difference in stride length between the YC group and the NC group, $t[244] = -0.2, p = 0.82$, for non-dominant body side (mean stride length = 1.129 ± 0.114 m for the YC group and 1.132 ± 0.112 m for the NC group), and $t[244] = -0.4, p = 0.72$ for dominant body side (mean stride length = 1.127 ± 0.114 m for the YC group and 1.132 ± 0.113 m for the NC group). However, stride length was significantly larger in the NC group than the PD group, $t[114] = 4.9, p < 0.01$, for non-dominant body side in the NC group and initially affected body side in the PD group

(mean stride length = 1.132 ± 0.112 m for the NC group and 1.024 ± 0.165 m for the PD group), and $t[114] = 4.8$, $p < 0.01$ for dominant body side in the NC group and secondarily affected body side in the PD group (mean stride length = 1.132 ± 0.113 m for the NC group and 1.024 ± 0.166 m for the PD group). There was no significant linear effect of OS on stride length, $F(1,50) = 3.0$, $p = 0.09$.

Results for walking speed, stride frequency, and length are shown in Table 1. Stride length and frequency were calculated for both body sides for each participant. For the sake of brevity, in the table, we present only the values from the non-dominant body side in the YC group and the NC group and from the initially affected body side in the PD group.

For Relative Power Index, there were no observed significant interactions or main effects, though there was a trend toward an interaction between body side and group, $F(2,50) = 3.0$, $p = 0.06$. Results are shown in Table 2. For relative phase between ipsilateral arm and leg movements, no significant main effects or interactions were found (Table 3).

Dot density (DD) manipulation

For lateral drift, a significant main effect of group was obtained, $F(2,50) = 8.1$, $p < 0.01$. Tukey's post hoc analyses showed that, during DD manipulation, there was no significant difference in lateral drift between the YC group and NC group, $p = 0.39$ and that the PD group veered significantly more to the left than NC, $p < 0.02$. There was a trend toward a main effect of DD, $F(2,100) = 2.95$, $p = 0.07$. No other main effects or interactions were significant. There was also a trend toward a linear effect of DD on lateral drift with groups combined, $F(1,22) = 24.6$, $p = 0.09$. Participants veered toward the wall with lower DD, and lateral drift increased with increasing difference in DD between the left and right walls (Fig. 3b).

For walking speed, significant main effects of DD, $F(2,90) = 5.5$, $p < 0.01$, and group, $F(2,50) = 4.5$, $p < 0.02$, were found. No other main effects or interactions were significant. Tukey's post hoc analyses showed that the YC group walked at a significantly slower speed than the NC group, $p < 0.02$. No significant difference was found between NC group and PD group, $p = 1.00$. Note that the participants were asked to walk at a specific speed and not at their preferred walking speed. There was a significant linear effect of DD on walking speed, $F(1,50) = 4.4$, $p < 0.04$, indicating that walking speed decreased with the decrease in DD on one wall.

For stride frequency, there were significant main effects of DD, $F(2,92) = 5.3$, $p < 0.01$, and group, $F(2,50) = 15.3$, $p < 0.01$, and no significant interactions. There was a trend toward a main effect of body side, $F(1,50) = 3.9$, $p = 0.05$. Tukey's post hoc analyses showed that the YC group walked at a significantly lower stride frequency than the NC group, $p < 0.02$, and the NC group also walked at a significantly lower stride frequency than the PD group, $p < 0.02$. There was a significant linear effect of DD on stride frequency, $F(1,50) = 8.0$, $p < 0.01$, indicating that stride frequency decreased with the decrease in DD on one wall.

For stride length, a significant interaction between body side and group was obtained, $F(2,50) = 3.1$, $p < 0.05$. *A priori t* tests showed that there was no significant difference in

stride length between the YC group and the NC group, $t[244] = -0.1, p = 0.92$, for non-dominant body side (mean stride length = 1.128 ± 0.115 m for YC and 1.127 ± 0.117 m for NC), and $t[244] = -0.1, p = 0.96$ for dominant body side (mean stride length = 1.126 ± 0.114 m for YC and 1.127 ± 0.118 m for NC). *A priori t* tests also showed that stride length was significantly larger in the NC group than the PD group, $t[118] = 4.6, p < 0.01$ for non-dominant body side in the NC group and initially affected body side in the PD group (mean stride length = 1.127 ± 0.117 m for the NC group and 1.024 ± 0.165 m for the PD group), and $t[118] = 4.6, p < 0.01$ for dominant body side in the NC group and secondarily affected body side in the PD group (mean stride length = 1.127 ± 0.118 m for the NC group and 1.023 ± 0.166 m for the PD group).

Results for walking speed, stride frequency, and length are shown in Table 1.

For Relative Power Index, a significant interaction between body side and group was obtained, $F(2,50) = 3.2, p < 0.05$. *A priori t* tests showed that Relative Power Index values were significantly smaller in the YC group than the NC group, $t[244] = -4.40, p < 0.01$ for the non-dominant body side, and $t(234) = -6.40, p < 0.01$ for the dominant body side. Relative Power Index values were also significantly higher in the secondarily affected body side in the PD group than the dominant body side in the NC group, $t(130) = -4.20, p < 0.01$. The coordination pattern was more stable in the NC group than the YC group and the asymmetry of Relative Power Index between body sides in the PD group resulted in the significantly larger Relative Power Index in the secondarily affected body side in the PD group than the dominant body side in the NC group (Table 2).

For relative phase between ipsilateral arm and leg movements, there was an interaction between DD, side of fixed wall, and group, $F(3,81) = 3.57, p < 0.02$. *A priori t* tests showed that the values of relative phase between ipsilateral arm and leg movements were larger in the NC group than the YC group across all DD conditions, $t(121) = -3.6, p < 0.01$ for 1 dot/m^2 , $t(119) = -3.7, p < 0.01$ for 2 dot/m^2 , $t(128) = -3.8, p < 0.01$ for 3 dot/m^2 (Table 3), and there was no significant difference for the values of relative phase between ipsilateral arm and leg movements between the NC group and the PD group, $t(62) = 0.4, p = 0.70$ for 1 dot/m^2 , $t(118) = -0.5, p = 0.59$ for 2 dot/m^2 , and $t(64) = 0.5, p = 0.65$ for 3 dot/m^2 . There was no significant linear effect of DD on the relative phase between ipsilateral arm and leg movements for any group, $F(1,22) = 0.01, p = 0.91$ for the YC group, $F(1,17) = 0.10, p = 0.77$ for the NC group, and $F(1,11) = 0.01, p = 0.94$ for the PD group.

Discussion

This study investigated the effects of optic flow speed (OS) and dot density (DD) on heading direction and coordination of walking in individuals with PD compared to age-matched normal and younger control adults. Both NC and YC subjects veered to the visual field with lower OS, and the veering increased with increasing difference of OS between left and right visual fields. There was a trend for all groups to veer toward the wall with lower DD. At the same time, the PD patients veered significantly more to the left than did NC and YC subjects despite the manipulations of OS or DD on one side of wall of the virtual hallway.

The observed effects of OS on lateral drift in YC and NC subjects are consistent with previous studies that found that honeybees (Srinivasan et al. 1991) and humans (Chatziastros et al. 1999; Chou et al. 2009; Duchon and Warren 2002; Young et al. 2010) steer down a hallway by equating the speed of optic flow between the left and right visual field. By contrast, in regard to DD, whereas Chatziastros et al. (1999) reported veering toward the side with higher optical spatial frequency in order to equalize the number of stripes at a given optical angle during a simulated driving task, in the present study, we found a trend of veering toward the side with lower DD. The outcomes of the present study are supported by reports that subjectively perceived speed of random-dot cinematograms is affected by DD. For example, Watamaniuk et al. (1993) found that the perceived speed of dots increased when the DD of a cinematogram was increased. Hence, we propose that participants in the present study perceived a higher OS on the side with higher DD and, as a result, veered toward the wall with the lower DD.

This relation between texture and perceived speed may explain PD-related changes in the subjective experience of movement of vehicles and people on the street (Lee and Harris 1999). The compressed visual field may result in an increase in texture density and with it, the perception of an increase in speed of movement of vehicles and pedestrians. In addition, PD patients have abnormalities in basic vision, including in contrast sensitivity, which has been associated with increased propensity to motor freezing (Davidsdottir et al. 2005, decreased contrast sensitivity at low spatial frequencies in PD; Mestre et al. 1992, increased contrast sensitivity in one individual without PD with spontaneous episodes of freezing). The relation between motor freezing, basic vision, and higher-order visual perception and cognition requires further investigation.

Individuals with PD veered more to the left than both YC and NC subjects across the OS and DD manipulation conditions. The findings from studies on turning behavior in healthy adults and individuals with PD suggest that the leftward drift may relate to handedness and hemispheric dopamine asymmetry (Bracha et al. 1987; Mohr et al. 2003). Mohr et al. (2003) tested the tendency of turning direction in 93 healthy adults with a lightweight sensor worn for 20 h for three consecutive days and found that right handers preferred turning to the left and non-right handers preferred turning to the right. De la Fuente-Fernandez et al. reported a significant positive association between bimanual performance of the Purdue Pegboard Test and dopamine levels in the right hemisphere (de la Fuente-Fernandez et al. 2000). On the basis of those findings, Mohr et al. (2003) proposed that the inherent demand for interhemispheric connectivity to accomplish bimanual actions may be similar to axial movements (e.g., turning), and hence, left-sided turning behavior in right handers may be related to higher dopamine levels in right hemisphere. In support of this possibility, a bias to the left on a line bisection task in 20 right-handed healthy subjects was also found to be associated with a larger volume of their nigrostriatal dopamine system (superior longitudinal fasciculus) in the right than the left hemisphere using diffusion imaging tractography (Thiebaut de Schotten et al. 2011).

A relation between turning preference and inferred asymmetry of dopamine level has also been reported in PD (Bracha et al. 1987). In this study, five PD patients with predominant symptoms on the right body side showed a tendency to turn to the left, corresponding to the

left hemisphere with lower dopamine levels. In our previous study of veering in PD subjects (Davidsdottir et al. 2008; also Young et al. 2010 with an overlapping sample), we tested 38 right-handed individuals during walking under natural and virtual reality conditions and found that a group of 8 right-side motor onset patients (RPD) and 16 NC veered leftward, whereas a group of 14 patients with left-side onset (LPD) veered rightward, in accordance with predictions based on inferred dopamine asymmetry. We also tested two left handers (1 LPD and 1 NC) who both veered rightward, in line with Mohr et al.'s finding with non-right handers. In the present study, only three out of fifty-three participants were left handers, and hence, the leftward veering across groups is consistent with the leftward turning behavior in right handers reported in Mohr et al.'s study. We did not formally analyze the data by RPD (six participants) and LPD (5 participants) because of the relatively small sample sizes, but visual inspection indicated that the RPD group veered further leftward than the LPD group. When considering potential differences in results across studies, one would expect variability in the direction and extent of veering based on the proportion of RPD and LPD, and the proportion of right- and left handers, in the study samples. We have also reported differences in direction of veering for men vs. women with PD, another factor to consider in study samples (Davidsdottir et al. 2008).

The results of the analysis of Relative Power Index showed an asymmetric coordination pattern between body sides in PD subjects. A significantly smaller standard deviation of relative phase between arm and leg movements on the secondarily affected body side than the initially affected body side ($t = 3.3, p < 0.01$ for the DD manipulation) suggests a more stable coordination pattern on the secondarily affected body side. This finding confirms that interlimb coordination can be affected by the unilateral onset of PD, which is also consistent with the findings of an asymmetric gait pattern in PD subjects reported in previous studies (Lewek et al. 2010; Plotnik et al. 2005; Young et al. 2010). Moreover, de la Fuente-Fernandez et al. found a significant correlation between the degree of right-hand preference (as indexed by performance on the Purdue Pegboard Test) and dopamine levels in the left putamen; that is, motor lateralization is related to asymmetry in the nigrostriatal dopamine system (de la Fuente-Fernandez et al. 2000). The unilateral motor symptoms (arising from predominant hemispheric pathology) combined with hand dominance may potentially result in a larger asymmetry of motor function between body sides (e.g., larger motor asymmetry between body sides may be seen in LPD subjects with right-hand dominance than LPD subjects with left-hand dominance). In the present study, as in most PD studies, the patients were tested while on dopaminergic medication ("on" phase). PD patients off medications may demonstrate a yet larger asymmetry in stride frequency, stride length, and coordination of walking, as well as the consequent impact of the gait asymmetry on heading direction.

The finding of differences between body sides in stride length in the healthy young adults is consistent with previous findings of asymmetry between left and right leg in velocity profile, step, and stride length, which could be a result of relative contributions of control and propulsion between left and right leg during locomotion (Sadeghi et al. 2000, 2001). PD patients showed an increased asymmetry in coordination of gait compared to a control group; further, patients who experienced freezing episodes showed more asymmetry in coordination of gait than patients who did not experience freezing (Plotnik et al. 2005;

Yogev et al. 2007). Taken together the results indicated that the coordination of gait is a sensitive measure to investigate the impact of PD on locomotion and may then be associated with further gait abnormalities.

The findings on the significant effect of DD on walking speed and stride frequency suggest that these gait parameters are sensitive to texture in the visual environment during navigation. Several studies exploring the mechanism underlying the perception of OS by the visual system have indicated that the perceived OS may be affected by changes in optical spatial frequency as well as dot density. For example, studies using vertical gratings reported that the perceived speed of the gratings increased with the increase in the optical spatial frequency without changing its actual moving speed (Chen et al. 1998; Diener et al. 1976; McKee et al. 1986). As noted earlier, Watamaniuk et al. (1993) found that the perceived speed of dots increased when the DD of the cinematogram was increased. Hence, it may be expected that individuals would increase their walking speed with the perception of slower optic flow speed caused by the decrease in dot density, which is opposite to our findings. The change of walking speed during dot density manipulation in the present study may reflect the participants' adoption of a cautious gait pattern while walking through the hallway with decreased dot density, as has been shown in eyes-closed walking (Cromwell et al. 2002; Halleman et al. 2010).

We did not find any significant effects of the asymmetric manipulation of OS on walking speed, stride length, stride frequency, or coordination patterns between ipsilateral arm and leg. The effect of systematic OS manipulation on walking parameters reported in previous studies could reflect the effects of a symmetric optic flow pattern, whereas we used asymmetric flow, and a wider range of OS than we used. For example, in studies of healthy young adults conducted by Prokop et al. (1997, 2005), the OS ranged from -1 to 3 times the actual walking speed. In previous studies in our laboratory (Chou et al. 2009; Young et al. 2010), the OS ranged from 0 (no flow) to 1.6 m/s, whereas in the present study, the OS ranged from 0.8 to 1.8 m/s. Preferred walking speed has been found to be higher in younger than older adults (Cromwell et al. 2002) as well as in NC subjects relative to PD subjects (Azulay et al. 1999), and hence, the walking speed at which the transition of coordination happens may be lower in individuals with PD than in healthy younger and age-matched participants. As a result, individuals with PD may already walk with a stable coordination pattern at a walking speed of 0.8 m/s, which would reduce the modulation effect of optic flow on the coordination pattern observed in previous studies. The investigation of the effect of optic flow manipulation on heading direction and coordination of walking at preferred (rather than predetermined) walking speed is currently underway in our lab.

From the outcomes of the present study, it can be concluded that OS may be perceived to control heading direction by equalizing the OS between the left and right visual fields during locomotion. The trend of the effect of DD on lateral drift suggests that dot density may also be perceived for heading direction during navigation. Because of a strong effect of spatial frequency manipulation on veering found with the simulated driving task reported by Chatziastros et al. (1999), it is important to investigate the differences between the effects of DD and those of vertical gratings with different spatial frequencies during locomotion. In the case of the individual with increased contrast sensitivity to low-to-intermediate

spatiotemporal frequencies who had episodes of freezing (Mestre et al. 1992), it was suggested that the inability to abolish freezing by use of transverse floor stripes may have been due to the wide distance between stripes (low spatial frequency). Likewise, Davidsdottir et al. (2008) reported a link between contrast sensitivity (this time reduced) and freezing (this time in PD). These findings together indicate that a virtual environment consisting of gratings of spatial frequencies appropriate to individuals with PD may be more likely to reduce freezing episodes and improve parkinsonian gait.

The finding of a leftward veering bias suggests an association of handedness with the direction of veering. The significantly more leftward veering in the PD than the control groups across OS and DD conditions indicates that the effect of handedness and the effect of differences in dopamine levels between the hemispheres on veering direction may be more salient than optic flow in individuals with PD, perhaps especially under conditions with less visual information from the environment (reduced light) or from PD-associated visual impairments (e.g., reduced contrast sensitivity). The ability to perceive optic flow for heading direction is compromised in individuals with PD. Handedness as well as the difference in dopamine levels between hemispheres (natural asymmetries and those related to side of onset of PD) may play important roles in the direction of turning and locomotor veering. Consideration of all of these factors should be incorporated into future studies of navigation in healthy younger and older adults as well as in individuals with PD.

Acknowledgments

This work was supported by the National Institute of Neurological Disorders and Stroke 1R01NS067128 to ACG. The study was presented in part at the ACRM-ASNR Annual Conference, 2011. Our recruitment efforts were supported, with our gratitude, by Marie Saint-Hilaire, MD and Cathi Thomas, RN, MSN, of Boston Medical Center Neurology Associates, and by Boston area Parkinson disease support groups. We thank Chelsea Toner and Laura Pistorino, who assisted in participant recruitment and data management, and Boston University's Scientific Computing and Visualization staff members Erik Brisson and Robert Putnam, who provided expert technical support. We are deeply grateful to all of the individuals who participated in this study. We dedicate this paper to the memory of our colleague and friend, Robert Wagenaar.

References

- Armstrong CA, Oldham JA. A comparison of dominant and non-dominant hand strengths. *J Hand Surg Br.* 1999; 24:421–425. [PubMed: 10473148]
- Azulay JP, Mesure S, Amblard B, Blin O, Sangla I, Pouget J. Visual control of locomotion in Parkinson's disease. *Brain.* 1999; 122(Pt 1):111–120. [PubMed: 10050899]
- Barbeau, A. Parkinson's disease: clinical features and etiopathology. In: Vinken, P.; Bruyn, G.; Klawans, H., editors. *Handbook of clinical neurology.* Vol. 49. Elsevier; Amsterdam: 1986. p. 87-152.
- Batschelet, E. *Circular statistics in biology.* Academic Press; London: 1981.
- Bodis-Wollner I, Yahr MD. Measurements of visual evoked potentials in Parkinson's disease. *Brain.* 1978; 101:661–671. [PubMed: 737524]
- Bodis-Wollner I, Yahr MD, Mylin L, Thornton J. Dopaminergic deficiency and delayed visual evoked potentials in humans. *Ann Neurol.* 1982; 11:478–483. [PubMed: 6125124]
- Bracha HS, Shults C, Glick SD, Kleinman JE. Spontaneous asymmetric circling behavior in hemiparkinsonism; a human equivalent of the lesioned-circling rodent behavior. *Life Sci.* 1987; 40:1127–1130. [PubMed: 3821375]

- Chatziastros, A.; Wallis, GM.; Bühlhoff, HH. The use of splay angle and optical flow in steering a central path (Technical Report 72). Max Planck Institute for Biological Cybernetics; Tubingen: 1999.
- Chen Y, Bedell HE, Frishman LJ. The precision of velocity discrimination across spatial frequency. *Percept Psychophys.* 1998; 60:1329–1336. [PubMed: 9865074]
- Chou YH, Wagenaar RC, Saltzman E, Giphart JE, Young D, Davids-dottir R, Cronin-Golomb A. Effects of optic flow speed and lateral flow asymmetry on locomotion in younger and older adults: a virtual reality study. *J Gerontol B Psychol Sci Soc Sci.* 2009; 64:222–231. [PubMed: 19276239]
- Cromwell RL, Newton RA, Forrest G. Influence of vision on head stabilization strategies in older adults during walking. *J Gerontol A Biol Sci Med Sci.* 2002; 57:M442–M448. [PubMed: 12096730]
- Davidsdottir S, Cronin-Golomb A, Lee A. Visual and spatial symptoms in Parkinson's disease. *Vision Res.* 2005; 45:1285–1296. [PubMed: 15733961]
- Davidsdottir S, Wagenaar R, Young D, Cronin-Golomb A. Impact of optic flow perception and egocentric coordinates on veering in Parkinson's disease. *Brain.* 2008; 131:2882–2893. [PubMed: 18957454]
- de la Fuente-Fernandez R, Kishore A, Calne DB, Ruth TJ, Stoessl AJ. Nigrostriatal dopamine system and motor lateralization. *Behav Brain Res.* 2000; 112:63–68. [PubMed: 10862936]
- Diener HC, Wist ER, Dichgans J, Brandt T. The spatial frequency effect on perceived velocity. *Vision Res.* 1976; 16:169–176. [PubMed: 1266057]
- Djaldetti R, Ziv I, Melamed E. The mystery of motor asymmetry in Parkinson's disease. *Lancet Neurol.* 2006; 5:796–802. [PubMed: 16914408]
- Donker SF, Beek PJ, Wagenaar RC, Mulder T. Coordination between arm and leg movements during locomotion. *J Mot Behav.* 2001; 33:86–102. [PubMed: 11303522]
- Duchon AP, Warren WH. A visual equalization strategy for locomotor control: of honeybees, robots, and humans. *Psychol Sci.* 2002; 13:272–278. [PubMed: 12009050]
- Ehgoetz Martens KA, Pieruccini-Faria F, Almeida QJ. Could sensory mechanisms be a core factor that underlies freezing of gait in Parkinson's disease. *PLoS ONE.* 2013a; 8:e62602.10.1371/journal.pone.0062602 [PubMed: 23667499]
- Ehgoetz Martens KA, Pieruccini-Faria F, Silveira CRA, Almeida QJ. The contribution of optic flow to freezing of gait in left- and right-PD: different mechanisms for a common phenomenon? *Parkinsonism Relat Disord.* 2013b; 19:1046–1048. [PubMed: 23891343]
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975; 12:189–198. [PubMed: 1202204]
- Giphart JE, Chou YH, Kim DH, Bortnyk CT, Wagenaar RC. Effects of virtual reality immersion and walking speed on coordination of arm and leg movements. *Presence.* 2007; 16:399–413.
- Hallems A, Ortibus E, Meire F, Aerts P. Low vision affects dynamic stability of gait. *Gait Posture.* 2010; 32:547–551. [PubMed: 20801658]
- Harris JP, Atkinson EA, Lee AC, Nithi K, Fowler MS. Hemi-space differences in the visual perception of size in left hemi-Parkinson's disease. *Neuropsychologia.* 2003; 41:795–807. [PubMed: 12631530]
- Hoehn MM, Yahr MD. Parkinsonism: onset, progression, and mortality. 1967. *Neurology.* 2001; 57:S11–S26. [PubMed: 11775596]
- Laudate TM, Nearing S, Cronin-Golomb A. Line bisection in Parkinson's disease: investigation of contribution of visual field, retinal vision, and scanning patterns to visuospatial function. *Behav Neurosci.* 2013; 127:151–163. [PubMed: 23356329]
- Lee A, Harris J. Problems with perception of space in Parkinson's disease: a questionnaire study. *Neuro-Ophthalmology.* 1999; 22:1–15.
- Lee AC, Harris JP, Atkinson EA, Fowler MS. Evidence from a line bisection task for visuospatial neglect in left hemiparkinson's disease. *Vision Res.* 2001a; 41:2677–2686. [PubMed: 11520513]
- Lee AC, Harris JP, Atkinson EA, Fowler MS. Disruption of estimation of body-scaled aperture width in Hemiparkinson's disease. *Neuropsychologia.* 2001b; 39:1097–1104. [PubMed: 11440762]

- Lewek MD, Poole R, Johnson J, Halawa O, Huang X. Arm swing magnitude and asymmetry during gait in the early stages of Parkinson's disease. *Gait Posture*. 2010; 31:256–260. [PubMed: 19945285]
- Lewis GN, Byblow WD, Walt SE. Stride length regulation in Parkinson's disease: the use of extrinsic, visual cues. *Brain*. 2000; 123:2077–2090. [PubMed: 11004125]
- Martin WE, Loewenson RB, Resch JA, Baker AB. Parkinson's disease. Clinical analysis of 100 patients. *Neurology*. 1973; 23:783–790. [PubMed: 4578348]
- Mattis, S. Mental status examination for organic mental syndromes in the elderly patient. In: Bellak, LK.; Toksoz, BE., editors. *Geriatric psychiatry*. Grune & Stratton; New York: 1976. p. 77-121.
- Mattis, S. *Dementia rating scale: professional manual*. Psychological Assessment Resources Inc; Odessa, FL: 1988.
- McKee SP, Silverman GH, Nakayama K. Precise velocity discrimination despite random variations in temporal frequency and contrast. *Vision Res*. 1986; 26:609–619. [PubMed: 3739236]
- Mestre D, Blin O, Serratrice G. Contrast sensitivity is increased in a case of nonparkinsonian *freezing* gait. *Neurology*. 1992; 42:189–194. [PubMed: 1734301]
- Mohr C, Landis T, Bracha HS, Brugger P. Opposite turning behavior in right-handers and non-right-handers suggests a link between handedness and cerebral dopamine asymmetries. *Behav Neurosci*. 2003; 117:1448–1452. [PubMed: 14674863]
- Morris ME, Ianssek R, Matyas TA, Summers JJ. The pathogenesis of gait hypokinesia in Parkinson's disease. *Brain*. 1994; 117(Pt 5):1169–1181. [PubMed: 7953597]
- Morris ME, Ianssek R, Matyas TA, Summers JJ. Stride length regulation in Parkinson's disease. Normalization strategies and underlying mechanisms. *Brain*. 1996; 119:551–568. [PubMed: 8800948]
- Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia*. 1971; 9:97–113. [PubMed: 5146491]
- Plotnik M, Giladi N, Balash Y, Peretz C, Hausdorff JM. Is freezing of gait in Parkinson's disease related to asymmetric motor function? *Ann Neurol*. 2005; 57:656–663. [PubMed: 15852404]
- Prokop T, Schubert M, Berger W. Visual influence on human locomotion. Modulation to changes in optic flow. *Exp Brain Res*. 1997; 114:63–70. [PubMed: 9125452]
- Sadeghi H, Allard P, Prince F, Labelle H. Symmetry and limb dominance in able-bodied gait: a review. *Gait Posture*. 2000; 12:34–45. [PubMed: 10996295]
- Sadeghi H, Sadeghi S, Allard P, Labelle H, Duhaime M. Lower limb muscle power relationships in bilateral able-bodied gait. *Am J Phys Med Rehabil*. 2001; 80:821–830. [PubMed: 11805454]
- Schubert M, Prokop T, Brocke F, Berger W. Visual kinesthesia and locomotion in Parkinson's disease. *Mov Disord*. 2005; 20:141–150. [PubMed: 15390031]
- Srinivasan MV, Lehrer M, Kirchner WH, Zhang SW. Range perception through apparent image speed in freely flying honeybees. *Vis Neurosci*. 1991; 6:519–535. [PubMed: 2069903]
- Thiebaut de Schotten M, Dell'Acqua F, Forkel SJ, Simmons A, Vergani F, Murphy DG, Catani M. A lateralized brain network for visuospatial attention. *Nat Neurosci*. 2011; 14:1245–1246. [PubMed: 21926985]
- van Emmerik RE, Wagenaar RC. Effects of walking velocity on relative phase dynamics in the trunk in human walking. *J Biomech*. 1996; 29:1175–1184. [PubMed: 8872274]
- Wagenaar RC, van Emmerik RE. Resonant frequencies of arms and legs identify different walking patterns. *J Biomech*. 2000; 33:853–861. [PubMed: 10831760]
- Warren WH Jr, Kay BA, Zosh WD, Duchon AP, Sahuc S. Optic flow is used to control human walking. *Nat Neurosci*. 2001; 4:213–216. [PubMed: 11175884]
- Watamaniuk SN, Grzywacz NM, Yuille AL. Dependence of speed and direction perception on cinematogram dot density. *Vision Res*. 1993; 33:849–859. [PubMed: 8351856]
- Yogev G, Plotnik M, Peretz C, Giladi N, Hausdorff JM. Gait asymmetry in patients with Parkinson's disease and elderly fallers: when does the bilateral coordination of gait require attention? *Exp Brain Res*. 2007; 177:336–346. [PubMed: 16972073]

Young DE, Wagenaar RC, Lin CC, Chou YH, Davidsdottir S, Saltzman E, Cronin-Golomb A.
Visuospatial perception and navigation in Parkinson's disease. *Vision Res.* 2010; 50:2495–2504.
[PubMed: 20837045]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

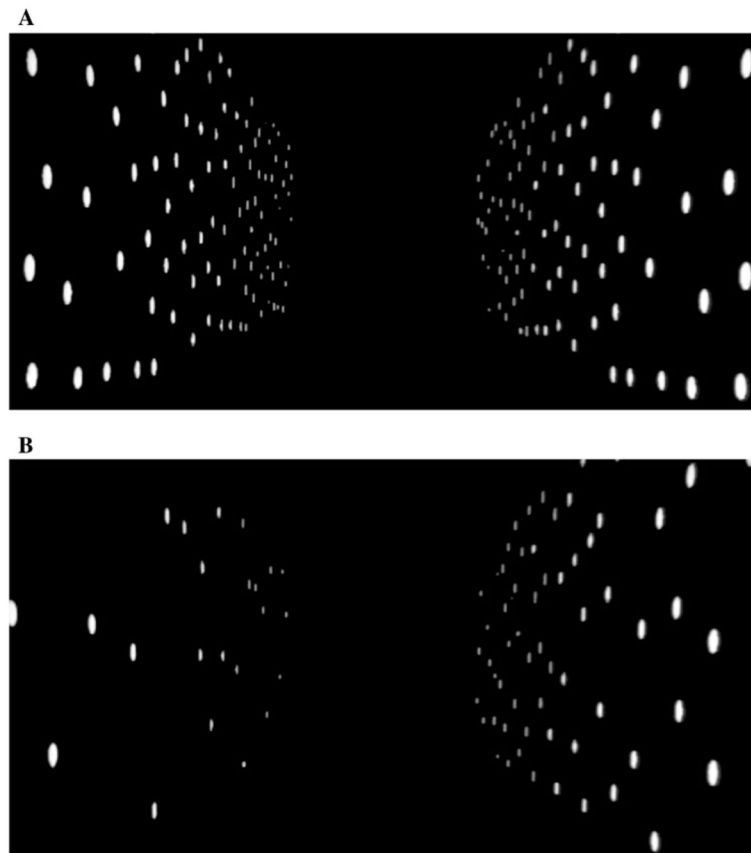


Fig. 1. The virtual hallway under condition of **a** optic flow speed manipulation with 3 dots/m² for both left and right walls; **b** dot density manipulation with 1 dot/m² on left wall and 3 dots/m² on right wall

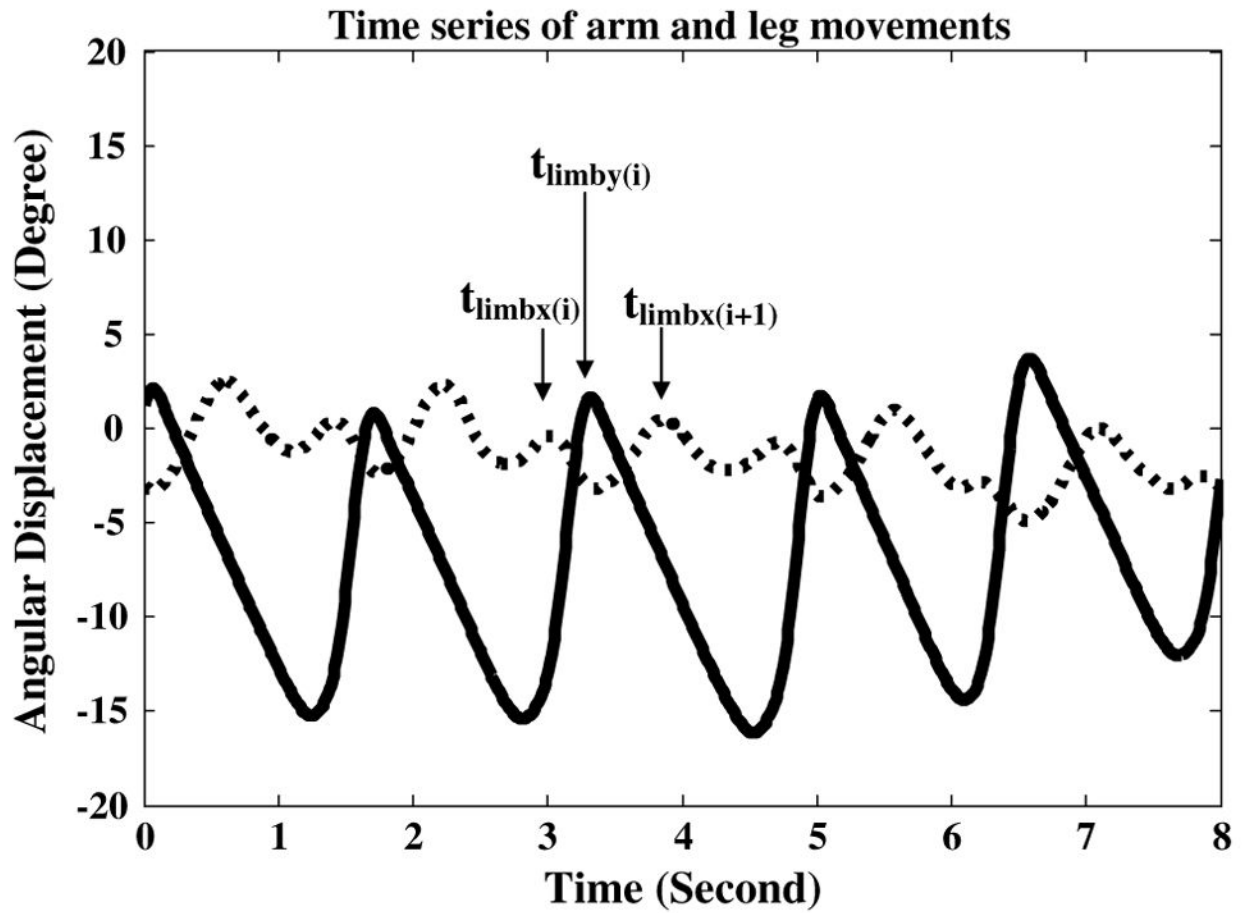


Fig. 2. Example of peak selection in the arm and leg time series for the calculation of point estimate of relative phase (in degrees) between arm and leg moving at a 2:1 frequency ratio (two arm swings per one stride). The *solid line* represents the leg movements, and the *dotted line* represents the arm movements

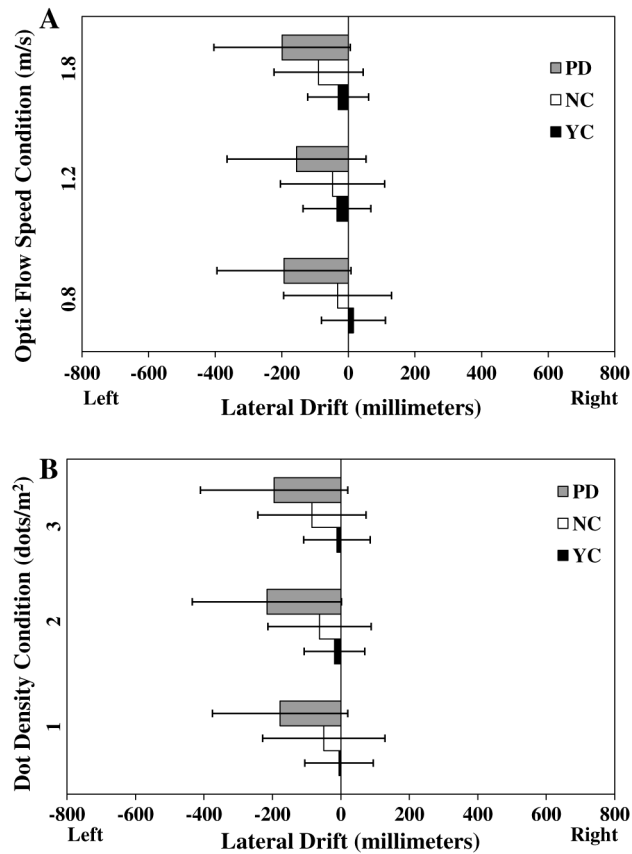


Fig. 3. Lateral drift value in millimeters (mm) for young control (YC), normal control matched to the PD group (NC), and individuals with Parkinson's disease (PD) under different optic flow speed and dot density conditions. **a** Average value of lateral drift during the optic flow speed manipulation on the both left and right walls. **b** Average value of lateral drift during the dot density manipulation on the both *left* and *right* walls. *Negative values* represent veering toward the left whereas positive values represent veering toward the right

Walking speed, stride frequency, and stride length in young control (YC), normal control matched to the PD group (NC), and individuals with Parkinson's disease (PD) during optic flow speed (OS) and dot density (DD) manipulation. The values of stride frequency and length are calculated from non-dominant body side in YC and NC, and initially affected body side from PD

Table 1

Manipulation	Walking speed (m/s)			Stride frequency (Hz)			Stride length (m)		
	YC	NC	PD	YC	NC	PD	YC	NC	PD
OS									
0.8	0.82 ± 0.08	0.91 ± 0.11	0.90 ± 0.15	0.73 ± 0.04	0.80 ± 0.08	0.89 ± 0.14	1.13 ± 0.10	1.14 ± 0.10	1.03 ± 0.18
1.2	0.81 ± 0.08	0.91 ± 0.10	0.88 ± 0.12	0.72 ± 0.05	0.81 ± 0.06	0.88 ± 0.14	1.12 ± 0.10	1.14 ± 0.12	1.02 ± 0.17
1.8	0.81 ± 0.10	0.90 ± 0.10	0.89 ± 0.15	0.72 ± 0.05	0.79 ± 0.08	0.89 ± 0.14	1.13 ± 0.11	1.14 ± 0.13	1.02 ± 0.15
DD									
1	0.81 ± 0.09	0.89 ± 0.10	0.89 ± 0.14	0.72 ± 0.05	0.79 ± 0.07	0.88 ± 0.14	1.13 ± 0.11	1.13 ± 0.12	1.02 ± 0.17
2	0.82 ± 0.08	0.92 ± 0.11	0.89 ± 0.13	0.73 ± 0.05	0.81 ± 0.07	0.88 ± 0.13	1.13 ± 0.09	1.14 ± 0.12	1.03 ± 0.15
3	0.82 ± 0.08	0.91 ± 0.11	0.90 ± 0.15	0.73 ± 0.04	0.80 ± 0.08	0.89 ± 0.14	1.13 ± 0.10	1.14 ± 0.12	1.03 ± 0.18

Table 2

Relative Power Index in young control (YC), normal control matched to the PD group (NC), and individuals with Parkinson's disease (PD) under conditions of the manipulation of optic flow speed (OS) at 0.8, 1.2, and 1.8 m/s and manipulation of dot density (DD) at 1, 2, and 3 dots/m²

Manipulation	YC		NC		PD	
	ND	D	ND	D	IA	SA
OS						
0.8	0.69 ± 0.32	0.66 ± 0.30	0.84 ± 0.27	0.86 ± 0.21	0.83 ± 0.27	0.95 ± 0.06
1.2	0.67 ± 0.30	0.61 ± 0.34	0.86 ± 0.20	0.85 ± 0.22	0.81 ± 0.28	0.94 ± 0.06
1.8	0.62 ± 0.35	0.57 ± 0.42	0.86 ± 0.19	0.87 ± 0.21	0.82 ± 0.33	0.95 ± 0.06
DD						
1	0.65 ± 0.36	0.61 ± 0.36	0.82 ± 0.24	0.84 ± 0.25	0.82 ± 0.26	0.94 ± 0.06
2	0.69 ± 0.27	0.59 ± 0.38	0.85 ± 0.24	0.86 ± 0.19	0.84 ± 0.26	0.95 ± 0.05
3	0.69 ± 0.32	0.66 ± 0.30	0.84 ± 0.27	0.86 ± 0.21	0.83 ± 0.27	0.95 ± 0.06

ND non-dominant body side, D dominant body side, IA initially affected body side, SA secondarily affected body side

Table 3

Relative phase between ipsilateral arm and leg movement in young control (YC), normal control matched to the PD group (NC), and individuals with Parkinson's disease (PD) under conditions with the manipulation of optic flow speed (OS) at 0.8, 1.2, and 1.8 m/s and manipulation of dot density (DD) at 1, 2, and 3 dots/m²

Manipulation	YC		NC		PD	
	ND	D	ND	D	IA	SA
OS						
0.8	165.7 ± 13.1	164.1 ± 15.1	177.4 ± 18.5	176.9 ± 18.0	175.5 ± 43.3	167.7 ± 31.9
1.2	165.4 ± 11.4	163.9 ± 14.9	178.1 ± 20.3	179.0 ± 17.5	179.9 ± 49.5	170.3 ± 23.4
1.8	166.0 ± 14.6	163.4 ± 17.5	176.3 ± 18.8	173.9 ± 23.9	181.9 ± 48.0	178.8 ± 15.5
DD						
1	168.4 ± 12.1	165.7 ± 14.7	176.6 ± 20.0	173.4 ± 22.2	162.6 ± 43.0	161.7 ± 42.9
2	167.0 ± 14.2	163.7 ± 16.4	176.2 ± 20.0	176.3 ± 19.7	174.7 ± 39.1	174.4 ± 19.4
3	165.7 ± 13.1	164.1 ± 15.1	177.4 ± 18.5	176.9 ± 18.0	175.5 ± 43.3	167.7 ± 31.9

ND non-dominant body side, D dominant body side, IA initially affected body side, SA secondarily affected body side