Parkinson’s disease patients compensate for balance control asymmetry

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Abstract

In Parkinson’s disease (PD) subtle balance abnormalities can already be detected in early stage patients. One feature of impaired balance control in PD is asymmetry: one leg produces more corrective joint torque than the other. We hypothesize that in mild to moderately affected PD patients, the least impaired leg compensates for the more impaired leg.

20 PD patients and eleven healthy matched controls participated. Clinical asymmetry was determined by the difference between the left and right body side scores on the Unified Parkinson’s Disease Rating Scale. Balance was perturbed using two independent continuous multisine perturbations in the forward-backward direction. Subsequently, we applied closed-loop system identification, that determined the spectral estimate of the stabilizing mechanisms, for each leg. Balance control behaviour was similar in PD patients and controls at the ankle, but at the hip stiffness was increased. Controls exhibited symmetrical balance control, but in PD patients the balance contribution of the leg of the clinically least affected body side was higher, whereas the leg of the clinically most affected body side contributed less. The ratio between both legs helped to preserve a normal motor output at the ankle.

Our results suggest that PD patients compensate for balance control asymmetries by increasing the relative contribution of the leg of their least affected body side. This compensation appears to be successful at the ankle, but is accompanied by an increased stiffness at the hip. We discuss the possible implications of these findings for postural stability and fall risk in PD patients.

Keywords: Parkinson’s disease; multi-segmental balance control; compensation; asymmetry; ankle and hip strategy;
Introduction

Patients with Parkinson’s disease (PD) have an increased risk of falling, especially in later disease stages (Pickering et al. 2007; Stolze et al. 2004). Subtle balance impairments, such as an increased body sway, have been detected in ‘de novo’ PD patients (Chastan et al. 2008; Mancini et al. 2011). In these earlier disease stages, actual falls are perhaps prevented because PD patients can compensate for such mild balance impairments. Indeed, functional imaging studies in PD patients during a hand task have suggested that preserved brain areas can take over the role of other brain areas that are affected by the disease process. Such compensatory mechanisms appeared to help in maintaining normal performance (van Nuenen et al. 2012; van Nuenen et al. 2009). Compensatory mechanisms can also help to maintain gait. For example, external visual or auditory cues can help to improve gait and alleviate freezing episodes (Keus et al. 2007; Nieuwboer et al. 2007). A recent paper showed that PD patients increased their cadence and decreased swing and cycle time to maintain walking velocity (Panyakaew and Bhidayasiri 2013). Whether compensatory mechanisms are also at play during a postural task has not yet been investigated.

PD is a neurodegenerative disorder that typically presents with asymmetrical motor symptoms (Djaldetti et al. 2006). Recent work suggests that balance control is no exception (Boonstra et al. 2014; Geurts et al. 2011; Rocchi et al. 2002; van der Kooij et al. 2007). Therefore, a possibility to assess postural compensation in PD patients is to investigate the balance responses of each leg separately. Patients might compensate for balance control asymmetries by augmenting the relative contribution of the least affected leg. This approach has been fruitfully applied in stroke patients, who compensate for the paretic leg by increasing muscle activation in the non-paretic leg (de Haart et al. 2004; Garland et al. 2003; Kirker et al. 2000).

It is unknown whether the least affected side in PD patients could compensate for the most affected side, and to what extent (partially or fully). Also, it is not clear whether postural compensation might differ between the ankle and the hip joints. Previous work showed that PD patients have increased postural stiffness (Grimbergen et al. 2004; Kim et al. 2009; Termoz et al. 2008), especially at the hip...
(Carpenter et al. 2004; Colnat-Coulbois et al. 2011; Maurer et al. 2003). Also, the hips are controlled by axial muscles (e.g., m. psoas major) and the axial musculature seems to be more affected in PD patients, compared to the appendicular (i.e., ankle) muscles (Carpenter et al. 2004; Kim et al. 2009). Furthermore, axial symptoms of PD (tested by rising from a chair, turning, pull test) respond less to dopaminergic treatment, suggesting that appendicular (i.e., limb control) and axial symptoms of PD are caused by dysfunction in different brain areas (Boonstra et al. 2008; Maurer et al. 2003). We hypothesized that this could affect the relative ability to develop a compensation strategy at the ankle versus the hip joint.

To investigate how and to what extent PD patients can compensate for their balance control asymmetries, and to investigate the hypothesized differences between the ankle and hip joints, we applied closed-loop system identification techniques that separate the balance control contribution of the left and right ankle and hip joint (Boonstra et al. 2013).

**Materials and methods**

The methods are described in detail elsewhere (Boonstra et al. 2013), but are described briefly below.

**Experimental approach**

We approached upright stance as a two Degree-of-Freedom (DoF) closed-loop multivariate system. The human body is modeled as a double-inverted pendulum, consisting of a leg, a Head-Arms-Trunk (HAT) segment and an ankle and hip joint (see Figure 1). This double inverted pendulum is inherently unstable and therefore, without proper corrective action the pendulum will fall over. In our approach, we assume that the stabilizing mechanisms (located in the Central Nervous System; CNS) generate stabilizing ankle and hip joint torques (i.e., the two outputs), based on the sensed ankle and hip joint angle (i.e., the two inputs). Hence, the system is a multiple-input-multiple-output (MIMO) closed-loop system. In such a closed-loop system, it is difficult to determine the dynamics of the
different components (i.e., the body and the stabilizing mechanisms) separately, as the dynamics of these components show up in both the input (joint angles) and output signals (joint torques). In other words, joint torques can compensate for body movement, but can also initiate body movement. Therefore, to “open” the loop and to separate the dynamics of the different components, the balance system needs to be perturbed (Fitzpatrick et al. 1996; van der Kooij et al. 2005).

In a pendulum with more than one segment, movements from one segment will influence the movements of the other segment and vice versa, due to mechanical coupling (Nott et al. 2010; Zajac 2002). This has consequences for the stabilizing mechanisms, as they have to correct for deviations from upright stance at both the ankle and the hip joint and compensate for the mechanical interaction. In our approach, this is expressed in the direct terms (\(C_{\theta_i \rightarrow \tau_i}\) and \(C_{\theta_{hi} \rightarrow \tau_{hi}}\)), correcting for joint angle deviations by generating corrective joint torques and the indirect terms (\(H_{\theta_{hi} \rightarrow \tau_{hi}}\) and \(H_{\theta_i \rightarrow \tau_i}\)), correcting for the mechanical effects of the coupled segments, resulting in a 2 by 2 matrix of the stabilizing mechanisms, see also Figure 2. Therefore, when estimating the dynamics in a MIMO system with two inputs, two (e.g., a translation and a force) perturbations need to be applied (Boonstra et al. 2013; Pintelon and Schoukens 2001). Using only one perturbation yields erroneous estimates of the stabilizing mechanisms (Boonstra et al. 2013).

In healthy subjects, both feet exert even amounts of force to counteract the destabilizing effect of gravity or other perturbations, so it is justified to lump the corrective actions of both legs together in one stabilizing mechanisms. However, in neurological populations, such as stroke (Geurts et al. 2005; Roerdink et al. 2009) and Parkinson’s disease (Boonstra et al. 2014; Geurts et al. 2011; van der Kooij et al. 2007) balance control can be asymmetrical. Therefore, in this manuscript we define two parallel MIMO stabilizing mechanisms, one for each leg, comparable to (van Asseldonk et al. 2006).

Hence, we assumed that the left joint angles did not have a mechanical or neural effect on the right
joint torques. Both stabilizing mechanisms produce corrective torques, which sum up to the total required corrective torque to stabilize the body. With this approach, we can describe the behavior of the left and right stabilizing mechanisms in a quantitative way.

Figure 1 about here

Participants

20 PD patients and eleven healthy matched controls were included (Table 1). Patients were assessed in the morning, at least 12 hours after intake of their last dose of dopaminergic medication (practically defined OFF state). Disease severity was determined using the Hoehn and Yahr stages and the motor part of the Unified Parkinson’s Disease Rating Scale (Goetz et al. 2008). Clinical asymmetry was defined as a difference between the summed UPDRS scores of the left and right body side (items 3.3-3.8 and 3.15-3.17). The most affected body side was defined as the side with the highest UPDRS score. Participants were excluded with visual, vestibular, orthopaedic, psychiatric or other neurological diseases or with marked cognitive dysfunction (Mini Mental State Examination <24 or Frontal Assessment Battery <13 (Cohen et al. 2012; Crum et al. 1993; Royall 2001). All participants gave written informed consent prior to the experiment, which was approved by the local medical ethics committee and in accordance with the Declaration of Helsinki.

Apparatus and recording

Perturbations in the forward-backward direction were applied using a computer-controlled six DoF motion platform (Caren, Motek, Amsterdam, The Netherlands) and a custom-built actuated device (called the Pusher) attached to the platform. Specifically, the motion platform administered a translational perturbation, whereas the Pusher applied a force perturbation at the participant’s sacrum. Body kinematics and the platform movements were measured using motion capture (Vicon...
Oxford Metrics, Oxford, UK) at a sample frequency of 120 Hz. Reflective spherical markers were attached to the first metatarsal, calcaneus, medial malleolus, the sacrum, the manubrium and the last vertebrae of the cervical spine (C7). In addition, a cluster of three markers was attached to both anterior superior iliac spines on the pelvis. Also, markers were attached just below the lateral epicondyle and in front of the acromion and an additional marker was attached to each foot and lower leg. Three markers were attached to the platform. Reactive forces and torques from both feet were measured with a dual forceplate (AMTI, Watertown, USA), and were sampled at 600 Hz together with the perturbation of the pusher.

Procedure

Participants were instructed to maintain their balance without moving their feet, while independent multisine platform movements and multisine force perturbations were applied simultaneously in the forward-backward direction. They were not explicitly instructed to distribute their body weight evenly over both feet.

The perturbation signal was a sum-of-sines, i.e., multisine with a period of 34.13 s and contained power at 112 frequencies in the range of 0.06–4.25Hz (Boonstra et al. 2013; van Asseldonk et al. 2006; van der Kooij and de Vlugt 2007), see also Figure 3. A multisine has the advantage that it is unpredictable for participants, because the signal consists of many sinusoids (de Vlugt et al. 2003). In addition, compared to PRTS (Pasma et al. 2012; Peterka 2002) or white noise signals (Kiemel et al. 2011), multisines can be designed to have a desired power at specific frequencies, decreasing measurement time and increasing the reliability of the estimate of the stabilizing mechanisms.

For the platform, the power of the perturbation decreased with increasing frequency, whereas the signal for the pusher had a flat powerspectrum (Boonstra et al. 2013) and the signals were made independent of each other by crest optimization (Pintelon and Schoukens 2001). We aimed to use as large as possible perturbation amplitudes for each individual participant, to optimize the ratio
between external and internal destabilizing torques, thereby increasing the reliability of the
estimated stabilizing mechanisms (van der Kooij et al. 2005).

The average RMS of platform amplitude was 0.012m for the healthy controls and for the PD patients
(i.e., they were similar, t(60)=−0.12; p=0.90). The pusher’s RMS of the amplitude was 4.5Nm for the
healthy controls and 4.9Nm for the PD patients (t(60)=−1.20; p=0.20). Participants stood with eyes
open and arms folded in front of their chest on the dual forceplate, strapped to the pusher and wore
a safety harness to prevent falling. The harness did not constrain movements, provide support or
orientation information in any way. Four trials of 180s were recorded and if needed, the participants
were allowed rest in between trials.

Data Analysis

In order to determine the balance control contribution of each leg, we determined the corrective
joint torques of each leg separately. Subsequently, we related the joint angles to the joint torques, by
applying multiple-input-multiple-output closed-loop system identification techniques to determine
both the total contribution of the ankle and hip joint and their interactions, as well as the
contribution of the left and right joints separately. The method is described in detail below and
summarized in Figure 2.

Joint angles and joint torques

From the recorded movement trajectories of the markers, the position of the center-of-mass (CoM)
and the joint angles (i.e. left and right ankle and hip angle) were estimated by custom written
software (Koopman et al. 1995; Koopman 1989), similar to (van Asseldonk et al. 2007). Specifically,
from the 29 body markers and with regression equations, the mass, CoM position and the inertia
tensor moment of the predefined rigid coupled segments (i.e., two feet, two legs and HAT) and the
joint positions in 3D were determined (Brand et al. 1982; Chandler et al. 1975), using an optimization
algorithm. Movements from the knee were ascribed to the movements of the leg and movements
from the pelvis were incorporated in the movements of the HAT. The position of the HAT was first optimized, and the legs and feet subsequently branched off. The joints were modeled as ball-hinges with three independent degrees of freedom and the range of motion was constrained. The total body CoM was determined as the weighted sum of the separate segment CoM positions. From the static trial, the average distance in the sagittal plane from the ankle to the total body CoM (i.e., the length of the pendulum ($l_{\text{CoM}}$) was determined. Subsequently, the sway angle was calculated by taking the inverse sine of the ratio between the horizontal distance from the CoM to the mean position of the ankles and $l_{\text{CoM}}$. The applied platform perturbation was calculated based on the platform markers movement.

The kinematic and kinetic data were filtered with a Butterworth filter (4th order low-pass; cut-off 8Hz) and subsequently resampled to 120Hz. The recorded forces and torques were corrected for the inertia and mass of the top cover of the forceplate (Preuss and Fung 2004).

On the basis of the corrected forces and torques and the recorded body kinematics, ankle and hip joint torques of the left and right leg were calculated with inverse dynamics (Koopman et al. 1995). The joint torques were calculated in a bottom-up approach; first the ankle torques were determined and then the hip torques. The forces and accelerations of one body side were not part of the calculations for the other body side. To check the accuracy of our calculations, we compared the center of mass-acceleration product with the sum of the forces (Newton’s 2nd law), where the center of mass position and acceleration were determined by the model and the forces were recorded with the forceplate. As there were no differences between RMS of the joint angles of the left and right body side, both in the control subjects (Ank: $t_{(22)}=0.22$, $p=0.82$; Hip: $t_{(22)}=0.13$, $p=0.89$) as in the PD patients (Ank: $t_{(78)}=0.36$, $p=0.71$; Hip: $t_{(78)}=0.036$, $p=0.97$), in the subsequent analysis ‘joint angle’ refers to the average joint angle of the left and right body side. The total joint torque is obtained by adding the joint torques of the left and right body side.
Furthermore, as we perturbed in the forward-backward direction, we only analyzed the responses in the sagittal plane. Inspection of the data showed that this was also the direction the largest response could be detected.

*Figure 2 about here*

**Frequency response functions**

To reliably identify the stabilizing mechanisms that generate ankle and hip torques based on sensory information of the joint angles (see Figure 1), we applied linear, time-invariant multiple-input-multiple-output (MIMO) system identification techniques, described in detail in (Boonstra et al. 2013; Koopman et al. 2010; Pintelon and Schoukens 2001) and calculated the frequency response functions (FRFs).

In short, the data of each of the four trials was segmented in response periods of the perturbation signal, yielding five periods of 34.13 s per trial, resulting in a total of 16 perturbation cycles for the estimation of the stabilizing mechanisms (the first cycle was discarded). Offsets and trends were removed from the data, hence possible differences in postural alignment did not influence our analysis. The data was Fourier transformed and averaged over the periods. Subsequently, the cross spectral densities (CSD) were calculated by multiplying the obtained Fourier coefficients of the perturbations (i.e., complex numbers) with the complex conjugate of the joint angles or joint torques. The CSDs were then smoothed by averaging over four adjacent frequency points (Jenkins and Watts 1969). The stabilizing mechanisms were estimated using the joint input-joint output approach (van der Kooij et al. 2005):

\[
\hat{C}_{\theta Tc}(f) = -\hat{G}_{pTc}(f)\hat{G}_{p\theta}^{-1}(f)
\]

(1)

With \(\hat{G}_{pTc}(f)\) and \(\hat{G}_{p\theta}^{-1}(f)\) the estimated CSD from the perturbations to the corrective torques of one body side and from the perturbations to the joint angles. Note that \(C\) is a two-by-two matrix (see also Figure 1), p is a vector with the two disturbances, \(\Theta_{ij}\) is a vector with ankle and hip joint angles, and \(T_c(f)\) is a vector with ankle and hip joint torques for each frequency \(f\), expressed as Fourier
coefficients. This resulted in eight FRFs, relating the ankle angle to the ankle torque \( C_{\theta_A \rightarrow T_A} \), the ankle angle to the hip torque \( C_{\theta_A \rightarrow T_H} \), the hip angle to the ankle torque \( C_{\theta_H \rightarrow T_A} \) and the hip angle to the hip torque \( C_{\theta_H \rightarrow T_H} \), for the left and right leg. The FRFs represent the multivariate stabilizing mechanisms of the participants.

The FRFs were normalized for the gravitational stiffness \( mgl \); \( m \): total body mass, \( l \): CoM height and \( g \): gravitational constant), because the exerted corrective torque depends on gravity. The average FRF over all participants was obtained by taking the mean over the individual normalized FRFs. Note that, as we used a dual forceplate, the obtained Fourier coefficients of the left and right FRFs were added to obtain the total FRFs.

**FRF characteristics**

The determined FRFs consist of two components: the gain that represents the normalized ratio between the joint angle and the joint torque relative to the pull of gravity, and the phase representing the relative timing between these two signals (see Figure 2). In our approach, the FRFs can be determined over the frequency range of the perturbations signal (0.06–4.25Hz). Up to 1 Hz, the gain of the FRF is dominated by the stiffness of the system (i.e., reaction to change in joint angle; length feedback), between 1 and 2.5 Hz the gain is dominated by the damping of the system (i.e., reaction to change in joint angle velocity; velocity feedback) and above 2.5 Hz, the inertia (i.e., the mass) determines the shape of the FRF (Schouten et al. 2008; Schouten et al. 2011).

**Balance contribution of the left and right body side**

The relative contribution of the left and right leg to the total amount of generated corrective torque to resist the perturbations was determined, by calculating the contribution of the gain and phase of each MIMO FRF to the gain and phase of the total MIMO FRF per frequency (Boonstra et al. 2013; van Asseldonk et al. 2006):
With FRF\(_r\), the left or right FRF and FRF\(_t\) the total FRF. The \(\bullet\) indicates the dot product of the FRFs.

The calculation is graphically depicted in Figure 2: the gain and phase of the FRF can be represented in the imaginary plane, where the gain of the FRF is represented by the length of the vector and the phase by the angle of the vector with the horizontal real axis. In the imaginary plane, the vectorial sum of the left and right stabilizing mechanism yields the total stabilizing mechanism (van Asseldonk et al. 2006). The contribution of the left and right leg to the total stabilizing mechanisms is then determined by projecting the vector of the stabilizing mechanisms of the left and right leg on the vector of the total stabilizing mechanism. By dividing the result by the total gain, the contribution of the left or right leg to the total balance control was expressed as a proportion. For example, a proportion of 0.8 for the left leg, means that the left leg contributed for 80% to the total body stabilization at that specific frequency of the perturbation signal. This was done for each separate MIMO FRF (see Eq 1).

The weightbearing and balance control asymmetry values of the healthy controls were considered as normative in this study and were expected to fall within an interval of 0.43 -0.57 (Dickstein et al. 1984; Sackley and Lincoln 1997). Furthermore, we defined the most contributing leg as the leg with the highest balance control contribution and we calculated the average FRFs of the most and least contributing leg by taking the mean over the FRFs of each PD patient.

Statistics

Perturbation amplitudes and the amplitude of the concurrent responses (i.e., sway angle, joint angles and joint torques) between the PD patients and healthy controls were compared with independent t-tests. Specifically, the average response of each perturbation round for each participant was firstly
determined. Subsequently, the average root-mean-square (RMS) of the responses over both perturbation round of the PD patients and healthy controls were calculated and compared. The gain of each MIMO FRF was log transformed to make the data normally distributed. Subsequently, the gains were averaged within three frequency bands (<1Hz, 1-2.5Hz and 2.6-4.2Hz) and compared with either a paired t-test (within groups) for each frequency band or an independent t-test (between groups). To test for asymmetries, we first determined the normalized absolute balance control contribution in the following way:

\[ NABContr(f) = \left| \text{Contribution}(f) - 0.5 \right| \]  

(3)

This was done for each MIMO FRF. Subsequently, we grouped the normalized absolute balance control contribution of the MIMO FRFs in the low, mid and high frequency bands. Then, we compared the NABContr of the patients with the healthy controls with independent t-tests for each frequency band, both for the whole group as for individual PD patients. Hence, we classified PD patients as having asymmetrical balance control, when their balance contribution was significantly different from healthy controls. To compare the UPDRS scores of the different body sides, we used the Wilcoxon matched-pair signed-rank test. Alpha was set at 0.05 and to correct for multiple comparisons, the confidence level was adjusted with Bonferroni correction. For the comparison of the MIMO FRFs, we adjusted the confidence level per sub-FRF, i.e., the confidence level decreased to 0.05/3 (number of frequency bands) = 0.017.

For all statistical analysis we used IBM SPSS statistics, version 20.0.

**Results**

Both patients and controls were able to maintain their balance in the face of the applied perturbations. Furthermore, the response could be treated as linear and time-invariant, as indicated by low noise-to-signal ratio’s (data not reported, but see Boonstra et al. 2013), justifying the application of linear time-invariant closed-loop system identification techniques (Boonstra et al. 2013; van der Kooij and de Vlugt 2007).
Time series

Figure 3 shows the joint angles and torques of a representative healthy control and PD patient in response to the perturbations. PD patients tended to have had smaller hip joint angle excursions, compared to healthy controls ($p<0.05$, for RMS values see Table 2) and this was accompanied by a smaller exerted total ankle and hip joint torque. On the group level, the RMS amplitudes of the joint angles of the left and right body side did not differ significantly, both for healthy controls (Ank: $t(22)=0.22, p=0.82$; Hip: $t(22)=0.13, p=0.89$), as well as for PD patients (Ank: $t(78)=0.36, p=0.71$; Hip: $t(78)=0.036, p=0.97$). Comparing the joint angles of the left and right body side on an individual basis yielded similar results. Hence, in the PD patients asymmetry in joint torques was accompanied by symmetry of joint angles.

Sway amplitude did not differ significantly between PD patients and healthy controls. In addition, compared to healthy controls, PD patients, on average, had smaller joint torques at the left body side compared to the right side, while healthy controls exerted the same amount of torque at each body side (see Table 2).

Multiple input multiple output frequency response functions

Figure 4 shows the MIMO FRFs of stabilizing mechanisms of the healthy controls and PD patients, averaged over the populations. In general, the gain of the stabilizing mechanism of the ankle increased with frequency until 2Hz; above 2Hz the gain decreased. The gain of the hip stabilizing mechanism was flat until 0.7Hz, decreased until 2Hz, and subsequently increased. The stabilizing mechanism from hip to ankle remained roughly constant over the frequency range, whereas the stabilizing mechanism from ankle to hip increased above 2Hz. At the lower frequencies (<1 Hz), the gain was always at least one, indicating that the participants produced enough corrective torque to
resist the perturbations. The phase of all the stabilizing mechanisms decreased with frequency (i.e. a phase lag), indicating the presence of a neural time delay.

There were no significant differences in FRF gain between healthy controls and PD patients at the ankle joint, nor at the cross-coupling from hip joint angle to ankle torque. However, in the cross-coupling from ankle angle to hip torque, there was a trend ($F_{(26)}=3.85; p=0.08$; uncorrected $p$-value) toward a higher gain at the lower frequencies for the PD patients. Furthermore, the FRF gain of the hip below 1Hz was significantly higher in PD patients compared to healthy controls ($t_{(30)}=-0.53; p=0.01$; uncorrected $p$-value). Note that the significance level decreased to 0.02 due to the Bonferroni correction. Hence, PD patients produced relatively more corrective hip torque in response to body movement. As the gain of the FRF at lower frequencies is dominated by stiffness (Schouten et al. 2011), this result indicates a higher hip stiffness in PD patients.

**Balance control contribution of the legs**

PD patients exerted different amounts of torque with the left and right leg, i.e., there were asymmetries in balance, see Table 2. Figure 5 indicates the balance control contribution of the right leg of the PD patients, calculated on the basis of the MIMO FRFs (see Figure 2). The healthy controls had an average absolute (a)symmetry of 0.06, 0.07 and 0.09 for the low, mid and high frequencies, whereas the PD patients had absolute asymmetries of 0.14, 0.16 and 0.17, respectively. Comparing the absolute balance control asymmetry values of the PD patients against the normative values of the healthy controls, showed that about 15 patients controlled their balance asymmetrically (see Table 3), hence, one leg was contributing more (i.e., the most contributing leg) to upright stabilization than the other leg. As can be seen from Figure 5, in our sample, most patients used their right leg the most to control their balance. The asymmetries were evident at both the ankle and the hip joint and in the joint interaction terms. Furthermore, the asymmetries were most evident in the
low (< 1Hz) and middle (1-2.5Hz) frequency bands, but were smaller (or absent) at the higher frequencies (> 2.5Hz), see Table 3.

Balance control behavior of the most and least contributing leg

Figure 6 depicts the average FRFs of the most and least contributing leg of the group of PD patients together with the right leg of the healthy controls. The average gains of the least and most contributing leg of the PD patients differed significantly for all FRFs and all frequency bands ($p < 0.01$). This indicates that both stiffness and damping of one leg were increased. The left and right leg of the healthy controls contributed equally to upright stabilization.

The body side of the most contributing leg had a lower total UPDRS score (total: 7.25) compared to the least contributing leg (11.05; $p$ = 0.02), indicating that the larger balance control contribution (i.e., a higher gain) coincided with the clinically least affected body side. Hence, the leg of the less symptomatic body side was stiffer than the most symptomatic leg, but also had an increased damping, as determined with our MIMO method. Furthermore, the most contributing leg also had a lower UPDRS leg score (1.85), compared to the least contributing leg (2.55), but this difference was not significant ($p = 0.12$). Also, we did not find a difference between the leg rigidity (as tested with item 3.3 of the motor part of the UPDRS) of the most (0.95) and least (0.85) contributing leg ($p = 0.63$).

Bear in mind that the results in Figure 4 depicted that the total gains of the ankle FRFs over the whole frequency were similar for PD patients and healthy controls for the all MIMO FRFs, except the FRF that related the hip angle to the hip torque. Hence, at the ankle the decreased balance control contribution (most pronounced at the lowest frequencies) of one leg was cancelled out by the increased balance control contribution of the other leg. This pattern was also observed at the hip,
but here there was an imbalance between balance contribution of the least and most contributing leg, resulting in a total increased hip stiffness.

Discussion

In this study, we determined the balance control responses of PD patients and controls for each leg separately, by applying mechanical perturbations in the sagittal plane. Our results demonstrate that PD patients had marked asymmetries in their balance control; the leg of the clinically least affected body side contributed more to upright stabilization, compared to the leg of the clinically most affected body side. The ratio between the most and least affected leg helped to preserve a normal motor output at the ankle; the total contribution (summed for the left and right ankle) equaled the total balance response of controls. However, at the hip, the same strategy was associated with a total increased joint stiffness.

The leg of the clinically least affected body side contributes the most to upright stabilization in PD patients

PD is an asymmetrical disease; one side of the body is affected first, and this asymmetry is preserved throughout the disease (Djaldetti et al. 2006). In addition, the motor asymmetry corresponds to the asymmetric loss in dopamine producing cells in the substantia nigra (Djaldetti et al. 2006). Recent work suggested that balance control (which intuitively appears to be a very symmetrical task) can also be affected asymmetrically in mild to moderately affected PD patients (Geurts et al. 2011; van der Kooij et al. 2007). The present results confirm these findings, showing that PD patients controlled their balance asymmetrically. Specifically, we demonstrated that the leg of the clinically least body affected side (as determined with the UPDRS) contributed most to balance control. This greater balance contribution of the leg of the clinically least affected body side was reflected by a higher stiffness (resistance to movement) and higher damping (resistance to speed) compared to the leg of
the clinically most affected body side. The increased stiffness could not be attributed to an increase in rigidity, as we did not find differences in rigidity scores between the most and least contributing leg. We therefore think it is more likely, that PD patients increased their dynamical response. In addition, whether rigidity (as determined clinically with the UPDRS) is related to our measure of stiffness has not been investigated, that is, it is not clear whether rigidity and stiffness can be ascribed to the same pathophysiological mechanism.

PD patients compensate for balance control asymmetries

For PD patients, the balance control contribution of both legs added together equalled that of healthy controls, except for at the hip joint. Hence, these results show that the balance control contribution of the leg of the clinically least affected body side cancelled out the decreased balance control contribution of the leg of the clinically most affected body side, resulting in a generation of a sufficient amount of corrective torque. That is, the PD patients did not fall or step more often compared to the healthy controls in this study. In the PD patients, this can only be achieved (assuming that before disease onset the PD patients behaved the same as the controls), if the leg of the clinically least affected body side increased its balance control contribution. We therefore hypothesize that the clinically least affected body side compensated for the most affected body side, possibly by increasing the common neural input. The ability to compensate for an impaired body side has been shown previously in stroke survivors; (Garland et al. 2003; Kirker et al. 2000); these patients increased their muscle activity at the non-paretic side to counteract postural perturbations.

In this paper, we investigated one specific form of (postural) compensation, namely whether one leg can compensate for impaired balance control of the other leg, by determining the balance control actions of each leg separately. This approach has not yet been applied yet in human PD patients, however, an animal study showed similar results (Woodlee et al. 2008). That is, inducing hemi-parkinsonism in rats (by unilateral infusion of 6-hydroxydopamine) resulted in postural instability in their impaired forelimb. Interestingly, the unimpaired limb showed enhanced functioning over the
course of time, suggesting that the unimpaired body side compensated for the impaired body side. The enhanced functioning of the non-impaired body side was associated with cerebral reorganisation and probably involved non-dopaminergic pathways. Neuro-imaging studies in stroke patients showed similar results; the unlesioned hemisphere became more active after a stroke (Grefkes and Ward 2013). Furthermore, connectivity between the affected and non-affected hemisphere decreased and this was positively correlated with functional recovery.

While stroke patients generally have only one hemisphere that is damaged, in PD patients the substantia nigra of both hemispheres become affected, although the initial body side typically remains the most affected (Djaldetti et al. 2006; Hughes et al. 1992). Therefore, whether the compensatory mechanisms found in stroke patients can be generalized to PD is not clear. However, recent studies show that the latency between cell loss and symptom onset (PD manifests itself clinically after loss of 60-80% of dopaminergic neurons (Lloyd 1977)) can be explained by compensatory mechanisms in the brain (Bezard et al. 2003; van Nuenen et al. 2009). These remain active when the disease symptoms are manifested (Helmich et al. 2007). Furthermore, a study by Schieppati and colleagues (Nardone et al. 2012), showed that, although sway was normal in de novo PD patients (compared to controls and without any apparent asymmetries), asymmetrical medium-latency responses were present. Future studies should therefore investigate whether between-hemisphere compensation is also possible in human PD subjects.

Increasing the corrective forces at one body side effectively aggravates balance asymmetries, therefore, the observed asymmetries are most likely due to the balance impairment (asymmetry) caused by the disease itself, plus the compensation strategy. This compensation strategy could possibly explain why we did not find any differences in previous self-reported falls between patients with and without asymmetrical balance control (unpublished results), as it leads to a sufficient amount of corrective torque to resist the pull of gravity. From this perspective, asymmetric balance control might paradoxically be a good phenomenon in certain stages of the disease, possibly preventing falls. Results of a recent animal study actually point in this direction: in a primate injected
with MPTP to induce Parkinson and an additional unilateral lesion in the nigrostriatal projection (effectively introducing an asymmetry between the brain hemispheres) improved clinical signs (Blesa et al. 2011).

The balance control contribution of the leg of the clinically least affected body side leads to an increased hip stiffness in PD patients. At the hip, a similar pattern as at the ankle was observed: the balance control contribution of the leg of the most affected body side was lower compared to the contribution of the leg of the clinically least affected body side. This resulted in a significant increased total hip stiffness. We speculate that the compensation strategy (i.e., increasing the balance control contribution of the leg of the least affected body side) had a different effect at the ankle compared to the hip, due to increased axial stiffness of the PD patients (Boonstra et al. 2008; Carpenter et al. 2004; Maurer et al. 2003; Wright et al. 2007). Apparently, the PD patients were not able to separate the effect of the compensation strategy for the separate joint stiffness of the ankle and the hip. This hypothesis is confirmed by other studies that showed that PD patients are unable to uncouple the control actions of the ankle and hip joints (Horak et al. 1992; Maurer et al. 2003), perhaps because of decreased structural connectivity between locomotor pathways (Fling et al. 2013).

However, it has also been suggested that increasing axial stiffness could be a compensation strategy, as it locks an extra degree of freedom and thereby simplifies the problem of maintaining an upright posture (Grimbergen et al. 2004). This stiffening strategy has also been detected in healthy controls, when standing on an elevated platform that induced a fear of falling (Carpenter et al. 2001). In sum, we speculate that the observed higher hip stiffness in PD patients is the result of the primary disease processes (i.e., increased axial stiffness) and the compensation strategy (increased balance control contribution of the leg least affected body side, including increased joint stiffness). Our results point in this direction, but cannot directly prove this theory.
Future studies should therefore focus on whether increased axial stiffness is a direct effect of the disease, a compensatory strategy, or a combination of both, by e.g. prospectively following newly diagnosed PD patients. Another possibility could be to artificially in- or decrease axial stiffness in healthy controls (Gruneberg et al. 2004) and PD patients (also for the left and right leg separately) and assess the effects on balance control.

**Balance control is disturbed in PD patients due to increased hip stiffness**

Our results indicated that the total gain at the lower frequencies for the hip angle to hip torque was significantly higher in PD patients, compared to healthy controls. In this paper we applied system identification techniques and performed the analysis in the frequency domain, which has the advantage that it can assess the dynamics over a broad frequency range where the low frequencies (<1Hz) are dominated by stiffness. Hence, it can be concluded that the PD patients in our study had an increased total hip stiffness.

Increased hip stiffness in PD patients has been reported before in mild to moderately affected patients (Carpenter et al. 2004; Kim et al. 2009; Termoz et al. 2008). Our results confirm these findings and this shows that this finding is robust across applied methodologies. For example, (Carpenter et al. 2004) used platform rotations, whereas (Kim et al. 2009) used platform translations.

An increased ankle stiffness in PD has also been proposed (Carpenter et al. 2004; Lauk et al. 1999), but there also have been reports of a decreased ankle stiffness (Colnat-Coulbois et al. 2011; Kim et al. 2009). Our results indicate that the total ankle stiffness in PD patients was similar to healthy controls.

**Intersegmental balance control in PD patients**

We found a trend toward an increased intersegmental coordination in PD patients. An increased intersegmental coupling has also been proposed by Maurer and colleagues (Maurer et al. 2003), but they studied a much smaller group of only eight patients that differed markedly from the patients in...
our sample: their patients were more severely affected and had been treated with STN-DBS. Another study by Horak and colleagues also report higher intersegmental feedback gains (Kim et al. 2009) and together with our results, this suggests that PD patients have a higher intersegmental stiffness. Other studies have shown that increased hip and intersegmental stiffness is probably due to excessive co-contraction and a larger background muscle activity (Burleigh et al. 1995; Carpenter et al. 2004; Horak et al. 1996). Previous mentioned studies used either no external balance perturbations (Termoz et al. 2008), or only one perturbation (Carpenter et al. 2004; Colnat-Coulbois et al. 2011; Kim et al. 2009; Maurer et al. 2003), whereas we used two perturbations. This methodological approach, instead of differences in patient characteristics, could also explain why results differed from previous work. That is, it has been shown that healthy subjects react differently (i.e., other feedback gains) to a platform translation, compared to a force perturbation (Kim et al. 2012).

Methodological limitations

We determined the average healthy control FRFs on the postural responses of only eleven healthy controls, which is a relatively small group. However, the FRFs of this control group had a small variation, as reflected by the tight standard deviations. Furthermore, the control group also controlled their balance very symmetrically and the symmetry values found in this study are comparable with reported values of a large study (n=403), also for the age group investigated here (Sackley and Lincoln 1991). It must be noted though, that these studies only investigated weight distribution, whereas we investigated joint torques. However, in healthy controls balance control and weight distribution are tightly interrelated (van Asseldonk et al. 2006) and therefore, we assume that the symmetry values here are representative for healthy controls.

As pointed out in the ‘Experimental Approach’ section, movements from one segment influence the movements of another segment and a neural controller should take this coupling into account. We, however, assumed a simplified controller, as left body side movements were not used to partly
calculate right body side torques and vice versa. This could potentially have influenced our results, by
masking or aggravating balance control asymmetries. We think that the influence of this
simplification is small though, as left and right body side angles were similar, signaling virtually non-
existing movements in the transverse plane. Moreover, if one want to identify the left-right
coupling, another two perturbations are necessary, which would complicate the experimental
design.

It must also be noted, that we only investigated balance control with a static, re-active balance
task. PD patients do have difficulties with maintaining balance during static situations, but are
especially impaired when they have to change their behavior (De Nunzio et al. 2007; Visser and
Bloem 2005; Winogrodzka et al. 2005) or prepare or initiate a movement (Kim et al. 2013).
Therefore, how our findings relate to anticipatory balance control, walking or fall risk in PD patients
warrants further investigation.

Finally, in order to investigate multisegmental balance control with our applied method, the patient
must be able to withstand postural perturbations. This could be a potential problem in patients who
have marked balance control instability, making the method less suitable for more severely impaired
patients.

**Future perspectives**

Our results indicate that multisegmental balance control is altered in PD patients, due to an
increased hip stiffness, and suggest that PD patients can partly compensate for their balance control
asymmetries with the leg of the least affected body side, by increasing the exerted force. Future
studies should follow PD patients over the course of their disease to monitor the progression of
asymmetrical balance control. Does the least affected leg compensate for the most affected leg
already from symptom onset? When is the least affected leg no longer able to compensate, and does
this correlate with a worsening of clinical signs (greater postural instability) and onset of falls? What
is the effect of levodopa on the overall balance control and on balance control asymmetries? Can we
positively influence postural compensation? What is the origin of balance control asymmetry, could it be a proprioceptive problem (Carpenter and Bloem 2011)? In healthy controls postural compensation could be tested by manipulating the balance control ability of one leg, with e.g. a cuff or tendon vibration. With this knowledge, interventions to stimulate postural compensation can be designed and evaluated.

Acknowledgements

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Schouten AC, Mugge W, and van der Helm FC. NMClab, a model to assess the contributions of muscle visco-elasticity and afferent feedback to joint dynamics. *J Biomech* 41: 1659-1667, 2008.


Figure Captions

Figure 1: Experimental approach. The stabilizing mechanisms represent the dynamics of the combination of active and passive feedback pathways and generate joint torques to correct for the deviation of upright stance. The direct terms ($C_{A \rightarrow T_{AC}}$ and $C_{H \rightarrow T_{HC}}$) represent the corrective torques of the ankle ($T_A$) and the hip ($T_H$), based on the ankle ($A$) and hip joint ($H$) angle. Note that movements from the lower segments will influence the movements of the upper segments due to the mechanical coupling, therefore the stabilizing mechanisms have to compensate for the mechanical coupling, which is expressed in coupling terms between ankles and hips (i.e., $C_{T_A \rightarrow T_H}$ and $C_{T_H \rightarrow T_A}$). The system is perturbed with two independent mechanical perturbations, administered by a movement platform ($S_x$) and an actuated backboard ($F_{ex}$), called the pusher.

Figure 2: Explanation of closed-loop system identification techniques to determine the relative balance control contribution of each leg.

Figure 3: A: Time series of the platform and pusher perturbations. B: Joint angles, sway angle and joint torques in response to the applied perturbations of a representative healthy control (left) and PD patient (right). The average over the eight perturbation cycles is indicated with the black line; the grey area depicts the SD. Perturbation amplitudes and phase of the perturbation cycle were the same for the healthy control and the PD patient.

Figure 4: Multi segmental frequency response functions of the total stabilizing mechanisms (i.e., both legs added together). The healthy controls are depicted with the solid line, the PD patients with the dashed line. The dotted vertical lines indicate the borders of the frequency bands (i.e., low, mid, high) used in the statistical analysis. The * indicates a significant difference. There were no
differences between the healthy controls and the PD patients for the $C_{\theta_s \rightarrow T_s}$, $C_{\theta_s \rightarrow T_2}$, and $C_{\theta_s \rightarrow T_H}$ FRFs. For the $C_{\theta_s \rightarrow T_s}$ FRF there was a significant difference of the gain in the lower frequency band, indicating a higher hip stiffness in PD patients.

Figure 5: Balance control contribution of the right leg of the healthy controls (average depicted by the solid black line with in grey the 95% confidence interval) and of the individual PD patients (indicated by the dashed grey lines). Healthy controls controlled their balance symmetrically, whereas in PD patients one leg contributed more to upright stabilization than the other leg.

Figure 6: Gains of the Multiple Input Multiple Output Frequency Response Functions of the right leg of the healthy controls (average indicated by the solid black line, with 95% confidence interval in grey) and of the most (..) and least (-.) contributing leg of the PD patients. The dashed vertical lines represent the frequency bins used for the statistical comparison; the * indicates a statistical significant difference.

For all FRFs the most contributing leg of the PD patients had a higher gain than the least contributing leg ($p<0.001$). In healthy controls there were no differences between the left and the right leg for all FRFs. For the $C_{\theta_s \rightarrow T_s}$ and the $C_{\theta_s \rightarrow T_2}$ FRFs the least contributed had a smaller gain than the right leg of the healthy controls, whereas at the hip ($C_{\theta_s \rightarrow T_H}$ and $C_{\theta_s \rightarrow T_H}$) the least contributing leg had a similar gain compared to the healthy controls. Note that the scale of the vertical axis of the upper panels is different that the lower panels.
Table 1: Participant characteristics. Patients were tested OFF medication.

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=20)</th>
<th>Controls (n=11)</th>
<th>Group differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>63.3 (8.35)</td>
<td>64.2 (7.95)</td>
<td>NS</td>
</tr>
<tr>
<td>Women (%)</td>
<td>30</td>
<td>37</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>84.13 (12.20)</td>
<td>78.12 (8.77)</td>
<td>NS</td>
</tr>
<tr>
<td>Length (m)</td>
<td>1.74 (0.04)</td>
<td>1.75 (0.04)</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration (yrs)</td>
<td>5.21 (3.11)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MMSE</td>
<td>28.25 (1.86)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FAB</td>
<td>15.55 (2.46)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>H&amp;Y (1</td>
<td>2</td>
<td>3)</td>
<td>3</td>
</tr>
<tr>
<td>Total UPDRS III</td>
<td>27.55 (10.44)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Left UPDRS III</td>
<td>10.95 (6.53)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Right UPDRS III</td>
<td>8.45 (3.84)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Data reflect means (standard deviation between brackets). N; number of subjects, NS; not significant, MMSE; Mini Mental State Examination; FAB; Frontal Assessment Battery, UPDRS; Unified Parkinson ’s Disease Rating Scale, H&Y; Hoehn & Yahr, 1: Unilateral signs, 2: Bilateral signs without balance impairments, 3: Mild to moderate involvement, physically independent, but needs assistance to recover from pull test.
Table 2: Average root mean square (RMS) values of joint angles and joint torque responses of healthy controls and Parkinson’s disease patients.

<table>
<thead>
<tr>
<th></th>
<th>Healthy controls</th>
<th>PD patients</th>
<th>Group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>std</td>
<td>mean</td>
</tr>
<tr>
<td>Ankle angle (deg)</td>
<td>0.61</td>
<td>0.18</td>
<td>0.61</td>
</tr>
<tr>
<td>Hip angle (deg)</td>
<td>0.59</td>
<td>0.20</td>
<td>0.51</td>
</tr>
<tr>
<td>Sway angle (deg)</td>
<td>0.57</td>
<td>0.05</td>
<td>0.59</td>
</tr>
<tr>
<td>Ankle torque (total; Nm)</td>
<td>9.81</td>
<td>2.85</td>
<td>8.80</td>
</tr>
<tr>
<td>Ankle torque (left; Nm)</td>
<td>4.90</td>
<td>1.42</td>
<td>4.40</td>
</tr>
<tr>
<td>Ankle torque (right; Nm)</td>
<td>5.02</td>
<td>1.50</td>
<td>6.35</td>
</tr>
<tr>
<td>Hip torque (total; Nm)</td>
<td>9.02</td>
<td>2.66</td>
<td>8.09</td>
</tr>
<tr>
<td>Hip torque (left; Nm)</td>
<td>4.51</td>
<td>1.33</td>
<td>4.05</td>
</tr>
<tr>
<td>Hip torque (right; Nm)</td>
<td>4.72</td>
<td>1.29</td>
<td>6.17</td>
</tr>
</tbody>
</table>

Uncorrected p-values; the significance level decreased to 0.006 due to Bonferroni correction. Significant differences are indicated with an asterix (*)
Table 3: Comparison of the absolute asymmetry index of the PD patients with normative values of the healthy controls. The comparison was made in the low, mid and high frequency bands for each individual PD patient, averaged for all FRFs.

<table>
<thead>
<tr>
<th>Frequency band</th>
<th>Low</th>
<th>Mid</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD patient uncorrected p-values</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.13</td>
</tr>
<tr>
<td>2</td>
<td>0.05</td>
<td>0.32</td>
<td>0.47</td>
</tr>
<tr>
<td>3</td>
<td>0.001*</td>
<td>0.14</td>
<td>0.66</td>
</tr>
<tr>
<td>4</td>
<td>0.42</td>
<td>0.41</td>
<td>0.59</td>
</tr>
<tr>
<td>5</td>
<td>0.91</td>
<td>0.06</td>
<td>0.12</td>
</tr>
<tr>
<td>6</td>
<td>0.006*</td>
<td>0.01*</td>
<td>0.50</td>
</tr>
<tr>
<td>7</td>
<td>&lt;0.001</td>
<td>&lt;0.001*</td>
<td>0.006*</td>
</tr>
<tr>
<td>8</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.003*</td>
</tr>
<tr>
<td>9</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.02</td>
</tr>
<tr>
<td>10</td>
<td>&lt;0.001*</td>
<td>0.37</td>
<td>0.93</td>
</tr>
<tr>
<td>11</td>
<td>&lt;0.001*</td>
<td>0.005*</td>
<td>0.05</td>
</tr>
<tr>
<td>12</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.02</td>
</tr>
<tr>
<td>13</td>
<td>0.19</td>
<td>0.16</td>
<td>0.82</td>
</tr>
<tr>
<td>14</td>
<td>0.006*</td>
<td>0.05</td>
<td>0.66</td>
</tr>
<tr>
<td>15</td>
<td>&lt;0.001*</td>
<td>0.001*</td>
<td>0.003*</td>
</tr>
<tr>
<td>16</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.66</td>
</tr>
<tr>
<td>17</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.24</td>
</tr>
<tr>
<td>18</td>
<td>0.001*</td>
<td>0.002*</td>
<td>0.16</td>
</tr>
<tr>
<td>19</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.002*</td>
</tr>
<tr>
<td>20</td>
<td>0.04</td>
<td>0.21</td>
<td>0.17</td>
</tr>
<tr>
<td>Group</td>
<td>&lt;0.001*</td>
<td>0.007*</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

*Statistical significant difference

Note that the p-value decreased to 0.017 due to Bonferroni correction.
Stabilizing mechanisms

<table>
<thead>
<tr>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>$C_{\theta_A \rightarrow T_A}$</td>
<td>$C_{\theta_A \rightarrow T_A}$</td>
</tr>
<tr>
<td>$C_{\theta_H \rightarrow T_A}$</td>
<td>$C_{\theta_H \rightarrow T_A}$</td>
</tr>
<tr>
<td>$C_{\theta_A \rightarrow T_H}$</td>
<td>$C_{\theta_A \rightarrow T_H}$</td>
</tr>
<tr>
<td>$C_{\theta_H \rightarrow T_H}$</td>
<td>$C_{\theta_H \rightarrow T_H}$</td>
</tr>
</tbody>
</table>

Mechanical perturbations

Body

Joint angles

$T_A$

$T_H$

$\theta_A$

$\theta_H$

$F_{\text{ex}}$
1. Apply perturbations
To determine the contribution of the ankle and hip joint, two perturbations have to be applied. A periodic sum-of-sines perturbation signal was used and applied multiple times, via a platform translation (dPlatform) and a force at the sacrum (dPusher).

2. Determine the participant’s response
The ankle joint ($\theta_{\text{Ank}}$) and hip joint angle ($\theta_{\text{Hip}}$) were determined, together with the left and right ankle and hip joint torque ($T_{\text{Ank}}$ and $T_{\text{Hip}}$).

3. Transform data to the frequency domain
The response cycles are transformed to the frequency domain with Fourier transformation. Subsequently, the cycles are averaged to obtain the mean response.

4. Determine frequency response functions
With the joint-input-output method, the relationship between the generated joint angles and the joint torques are determined, for both the left and right leg, characterized by the frequency response function (FRF). The gain of the FRF represents the ratio between the amplitude of the joint angle and joint torque. The phase represents the shift in time between the two signals. This resulted in eight FRFs, characterizing the relationship between a) the ankle angle and ankle torque, b) ankle angle and hip torque, c) hip angle and ankle torque, and d) hip angle and hip torque; see Figure 1, i.e., four for each leg.

5. Calculate proportion of left and right joint torque to the generated total torque in response to body sway
FRFs are complex numbers and each complex number can be depicted as a vector in the imaginary plane, spanned by the imaginary (Im) and real (Re) axis. The contribution of the left and right leg stabilizing mechanisms to the total stabilizing mechanism was determined by projecting the vector of each leg to the total vector. Division of the result by the total gain led to the contribution of each of the stabilizing mechanisms to the total, expressed as a proportion.
A

Perturbations

Platform

Pusher

time (s)

B

Responses

Healthy control

PD patient

θ_{Ank} (deg)

θ_{Hip} (deg)

θ_{Swayy} (deg)

T_{Ank} (Nm)

T_{Hip} (Nm)

time (s)
\[ C_{\theta_A \rightarrow T_A} \]

- Healthy Controls
- PD patients

\[ C_{\theta_H \rightarrow T_A} \]

\[ C_{\theta_A \rightarrow T_H} \]

\[ C_{\theta_H \rightarrow T_H} \]

Frequency (Hz)

Gain

Phase (deg)

-180
180
-1
10

Gain

1

Phase (deg)

-180
180
-1
10

Frequency (Hz)
95% CI
Healthy controls
Right leg PD patients

Contribution

Frequency (Hz)