

Balance and Gait Rehabilitation in Patients with Parkinson's Disease

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1. Introduction

Parkinson's disease (PD) is a neurodegenerative disorder characterized by cardinal features - resting tremor, rigidity, bradykinesia, and postural difficulties - which are thought to arise primarily from the loss of dopamine producing neurons and subsequent dysfunction of the basal ganglia-thalamo-cortical pathway (Konczak et al., 2009). Patients with PD have difficulties in performing various motor tasks, such as walking, writing and speaking. Furthermore, PD leads to abnormalities in two main components of postural control: orientation (maintaining a normal postural arrangement and alignment) and stabilization (maintaining equilibrium) (Vaugoyeau & Azulay, 2010). Postural instability (PI) is a disabling disorder, which is associated with sudden falls, progressive loss of independence, immobility and high costs for healthcare systems (Grimbergen et al., 2004). It usually occurs at the later stages of the disease and, unlike gait disorders, responds poorly to medication. Marked alteration of gait is common in advanced PD, although there is evidence suggesting that initial impairment in gait can be detected even early in the course of the disease (Stolze et al., 2005; Baltadjieva et al., 2006). Gait disorders, along with turning and balance disturbances, are the most important determinants of falls, which are recognized to be a major problem among people with PD. Falls occur despite maximal treatment with levodopa, confirming that axial disability in late stage PD is largely dopa-resistant (likely due to extranigral and non-dopaminergic brain lesions). Falls often have dramatic consequences, such as traumas and fractures. The high risk of fractures was demonstrated in a large case control study (Vestergaard et al., 2007), which showed that patients with parkinsonism (not just PD) had a more than two-fold increased risk of sustaining a fall-related fracture. It has been established that PD has a negative impact on the quality of life (QoL) of patients (Diamond & Jankovic, 2005). Interestingly, in PD, non-motor symptoms such as depression and cognitive impairment are major predictors of QoL (Martinez-Martin, 1998). Although investigators have examined the effect of specific PD symptoms such as tremor, rigidity and bradykinesia (Peto et al., 1995), medication-related complications (Chapuis et al., 2005), insomnia (Caap-Ahlgren & Dehlin, 2001), fatigue (Herlofson & Larsen, 2003) and sweating (Swinn et al., 2003), their relative contributions to the patient's QoL have

not been assessed. The negative impact of gait disorders on QoL is related to immobility (causing loss of independence) and increased risk of falling. 'Episodic' gait disorders, which are only intermittently present, are particularly incapacitating because patients cannot easily adjust their behaviour to these paroxysmal walking difficulties (Snijders et al., 2007). A textbook example is freezing of gait (FoG), in which patients with PD experience debilitating episodes during which they are unable to start walking, or while walking suddenly fail to continue moving forward. Because of its sudden and unpredictable nature, FoG is an important cause of falls and injuries. Perhaps not surprisingly, a recent study showed that FoG was independently associated with a decreased QoL (Moore et al., 2007). In the last 2 decades research studies focusing on the rehabilitation of patients with PD have progressively increased. Most of the rehabilitation studies have focused on the treatment of balance and gait disorders. It has been shown that exercise is beneficial to physical functioning, health related QoL, strength, balance and gait speed. Current models of rehabilitation often use compensatory strategies as the basis of therapeutic management. However, there is a growing body of evidence regarding the benefit of exercise in terms of neuroplasticity and the ability of the brain to self-repair. Animal models have found that exercise has protective benefits against the onset of symptoms in PD (Faherty et al., 2005). In PD, it has been found that exercise stimulates dopamine synthesis in the remaining dopaminergic cells, thus reducing symptoms. Fox et al. (Fox et al., 2006) suggest that there are five key principles of exercise that enhance neuroplasticity in PD: intensive activity maximizes synaptic plasticity; complex activities promote greater structural adaptation; activities that are rewarding increase dopamine levels and therefore promote learning/relearning; dopaminergic neurons are highly responsive to exercise and inactivity ("use it or lose it"); and if exercise is introduced at an early stage of the disease, progression can be slowed. In this chapter we aim to discuss several issues related to balance and gait rehabilitation in PD. First, we will describe the mechanism of balance and gait control in humans. Then, we will focus on the pathophysiology of balance and gait impairment in PD. In particular, we will discuss the role of defects in the processing of afferent inputs from the vestibular, proprioceptive and visual systems, in the pathogenesis of the postural orientation and stabilization disorders in PD. Furthermore, we will describe the relationship between the postural control deficit and the abnormal choice of postural strategies. A section will be dedicated to the dramatic problem of falls. As to gait disturbances, central nervous system (CNS) circuits involved in controlling automatic repetitive movement such as gait will be described. The role of the basal ganglia in enabling movement sequences and the role of sensory cues in compensating for the deficit of internal rhythm generation by the basal ganglia in PD will be discussed. Subsequently, a section will be dedicated to the usefulness and limitations of common clinical and instrumental assessments of balance and gait disturbances. Then, rehabilitation approaches to balance and gait impairment in PD will be reviewed. Advantages and limits of the rehabilitation approaches described will be discussed.

2. Human postural and gait control

2.1 Mechanisms of postural control

Postural control is a complex function, which is particularly evolved in humans. Postural control is important as it allows a person to maintain a stable position in different postural conditions (i.e. sitting, standing). Furthermore, it is essential to the stability of axial body

segments during the execution of voluntary movements (arms or whole body movements). The ability to stand upright, while standing still or moving, allows humans to have control over their environment. Maintaining this position is a challenging task because of the narrow base of support (feet) of bipeds. This task (maintaining the body upright) is even more difficult when a person has to move around the environment following straight or more complex trajectories. Nonetheless, by supporting themselves on one or both feet, humans perform various activities such as walking, going from sit to stand, turning etc. These activities may be further complicated by various environmental conditions such as in the case of uneven ground, climbing stairs, going downhill, carrying heavy or big objects etc. How can our postural and movement control systems accomplish all these challenging tasks, despite the perturbing effects of gravity and other external forces? Amblard et al. (Amblard et al., 1985) suggested the existence of a dual postural control system, part of which deals with body orientation with respect to gravity, and part of which deals with body stabilization. The first system allows a proper arrangement of body segments (i.e. erect axial segments aligned with gravitational coordinates and limbs positioned in such a way that the involvement of the muscles for joint stabilization is minimized). The second system, body stabilization, is aimed at maintaining the centre of the body mass within the limits imposed by the base of support (equilibrium). These two postural control systems do not operate independently, but most likely interact, providing a stable physical basis for perception and action (Vaugoyeau et al., 2007; Vaugoyeau & Azulay, 2010). When organizing a given movement, the CNS has to coordinate the control of body equilibrium and body orientation. In order to achieve this complicated organization, the CNS relies on three main distinct processes: 1) sensory organization, in which one or more of the orientational senses (somatosensory, visual and vestibular) are involved and integrated in the CNS; 2) a motor adjustment process involved with executing coordinated and properly scaled neuromuscular responses; 3) the background tone of the muscles, through which the changes in balance are affected (Horak et al., 1992).

2.2 Sensory organization

Erect human postural control (orientation and stabilization) is known to depend on vestibular, visual and somatosensory information, arising from sensory sources such as muscle, skin, and joints (Vaugoyeau et al., 2007). A recent work by Kuo (Kuo, 2005) describes how all these senses interact in human balance control. There are two types of vestibular organs. First, semicircular canals, which are fluid-filled canals in the inner ear, and detect the angular velocity of the head by sensing viscous motion of the fluid. Second, otoliths, which are crystal-like masses mounted on hair cells, and act as linear accelerometers. Thus, vestibular organs are able to detect motion and the position of the head with respect to gravitational coordinates. Vision is similarly sensitive to self-motion of the head. In order to maintain posture, the relevant signals are processed by motion detection circuitry, not only in the retina but also in the visual cortex, so that the vestibular nuclei receive signals proportional to rotational and translational motion of the visual field (Young, 1981). The somatosensors are also important receptors subserving postural control. They are responsible for proprioception—the sensing of joint motion and limb position. Proprioception is subserved by muscle spindles, joint and cutaneous receptors. These sensory signals are fed back to a series of hierarchical feedback loops to generate stabilizing motor commands.

2.3 Postural adjustments

In order to maintain balance, humans bring into play two types of postural responses, feedback and feedforward. The type of response activated depends on the postural task. Feedback postural responses have been well depicted in studies where subjects were submitted to unexpected disturbances of balance by means of controlled destabilizations. When the surface on which humans are standing unexpectedly moves, the body is destabilized in the direction opposite to that of the surface displacement (Leonard et al., 2009). To regain balance, humans produce medium-latency automatic postural responses in the supporting limbs that oppose the perturbation and drive the centre of mass (CoM) back toward its initial position relative to the support surface (Horak & Nashner, 1986). The latency from the initiation of the support surface movement to the onset of the evoked electromyographic (EMG) response is in the order of 80–120 ms in humans (Ting & Macpherson, 2004). These compensatory automatic postural responses are triggered by somatosensory feedback from the feet and legs (Bloem et al., 2000a, 2002), and unless prior warning of the upcoming perturbation is given (Jacobs & Horak, 2007) they are produced entirely using a feedback mode of neural control. Studies in animals and humans have examined feedback-based automatic postural responses to unexpected translations of the support surface in multiple directions with the aim of identifying strategies that the CNS may adopt to simplify the control of perturbed stance (Fung et al., 1995). These feedback responses may involve various levels of the CNS, depending on the complexity of the required response (Kuo, 2005). The route for all movement signals is the spinal cord, which also produces the lowest level of neural feedback. This feedback is in the form of local reflexes, in which stretch signals from a muscle are relayed to the spinal cord, passed across one or a few intermediate neural connections, and then fed directly back to the muscle, commanding a compensatory contraction. This short feedback loop has fast latency, in the range of 30–60 ms. However, the speed of such a loop comes with a disadvantage: local reflexes are the least integrative of postural responses, and are limited to relatively simple behaviours (Nashner, 1977). The second and most important level of feedback for balance control involves signals travelling up to the mid-brain. The brainstem serves as a relay and integration centre, receiving and sending great numbers of sensory and motor command signals. The mid-level feedback loop involves longer conduction paths and greater numbers of neural synapses, and consequently has a longer latency than spinal reflexes (often 90 ms and greater). However, the convergence of many signals and complexity of the connections allows the brain stem to generate much more complex movements, mostly of an automatic nature. The brainstem modulates the behaviour of lower level reflexes, and is itself modulated by the higher levels. The cerebral cortex and related structures generate highly complex movements, mostly of a voluntary nature, with longer latencies than the two lower feedback loops. The longer latencies suggest that the cerebral cortex has a modulatory, rather than a direct role in posture control. Unlike the condition of unexpected perturbation of balance, during daily life, most postural perturbations are caused by an individual's own movement (i.e. reaching forward). In this case, postural adjustments occur prior to movement onset, to prevent the CoM from shifting outside the base of support (Bouisset & Zattara, 1987; Commissaris et al., 2001). To ensure a controlled transition from one postural configuration to another, these adjustments of posture must be planned by the CNS in advance, and a feedforward mode of neural control sends commands to both focal and postural muscles to initiate and stabilize posture.

2.4 Background tone of the muscles

In the absence of external support, tonic activation of skeletal muscles is necessary to maintain the relative positions of body segments and to prevent the body from collapsing against gravity. Such ongoing subconscious muscular activity is referred to as “postural tone” (Cacciatore et al., 2010). Tonic muscular activity is assessed clinically as the resistance to passive joint rotation, typically in the limbs (Foster, 1892). However, because a clinician commonly supports the limb being examined, resistance to joint rotation does not explicitly reflect the state of postural tone, as skeletal muscles must be engaged in anti-gravity postural support for postural tone to manifest. While postural tone consists, in part, of low-level stable activity—typically a few percent of maximal voluntary contraction (Masani et al., 2009)—this baseline activity can be modulated dynamically to adapt to changes in joint position and load. Any time one part of the body moves, postural tone in both that and other parts of the body must be modulated to prevent resisting the movement and to maintain static equilibrium. Thus, modulation of postural tone can provide the body with both mechanical and operational flexibility for different types of movements.

2.5 Mechanisms of gait control

The coordination of limb rhythmic activities is one of the main features of locomotion (Dietz, 2002). Locomotor activity is driven by particular neural circuits located in the upper and lower spinal cord, called central pattern generators, which organize lower and upper limb movement respectively (Grillner, 1981). These circuits are coordinated by long propriospinal neurons, which couple the cervical and lumbar enlargements of the spinal cord (Dietz & Michel, 2009). It has been proposed that a flexible coupling of thoracolumbar and cervical centres allows humans to use the upper limbs for manipulative and skilled movements or, alternatively, for locomotor tasks. This implicates a functional, task-dependent gating of neuronal pathways between the neuronal circuits controlling lower and upper limb muscles during walking, which would stabilize the body during walking (Dietz & Michel, 2009). In fact, during gait the swing of the arms serves to regulate the rotation of the body. Therefore, swinging of the arms can be seen as an integral part of the dynamics of progression. Regulation of human locomotion requires a close coordination of muscle activation between the two legs. This pattern of interlimb coordination is in line with the presence of central pattern generators and the half-centre model proposed for generation of locomotor movements (Dietz, 2002). In this model, the neuronal circuits that coordinate the leg flexor activity of both sides during the swing phase of locomotion (i.e. the flexor half-centres) mutually inhibit one another. On the contrary, the extensor half-centres on each side have no mutual inhibitory connections, according with the coexistence of the stance phase on the two sides. There is also interlimb coordination of the arms, that appears to be organized in a similar way to that of the legs during rhythmic movements. This implicates similar control mechanisms of the upper and lower limbs (Zehr & Kido, 2001). There is some evidence that interlimb coordination is organized similarly in the lower and upper limbs during cyclic movements of humans. This indicates that the neuronal coordination is conserved within the human lumbar and cervical spinal cord (Dietz, 2002). A linkage between the cervical and lumbar enlargement of the spinal cord by propriospinal neuronal circuits with long axons has been inferred on the basis of H-reflex studies. For example, during rhythmic movements of one foot, a cyclic H-reflex modulation was observed in the upper limbs (Baldissera et al., 1998). According to previous studies using functional magnetic resonance imaging (Debaere

et al., 2001), the supplementary motor area might be involved in the supraspinal control of this coupling between upper and lower limbs movements. These observations indicate a flexible task-dependent neuronal coupling between upper and lower limbs (Dietz, 2002). The pathway that couples upper and lower-limb movements seems to become gated by the activity of the central pattern generators during walking. The stronger impact of leg flexors in interlimb coordination is in line with the increasing evidence that leg flexor and leg extensor muscles are differentially controlled in humans (Cazalets & Bertrand, 2000). It has been shown that arm and leg muscle activity is well coordinated during walking or swimming (Wannier et al., 2001). This indicates a coupling of the neuronal circuits controlling arm and leg movements, which is again under supraspinal control.

2.6 Differential control of upper-limb movements

The task-dependency of the neuronal coupling between upper and lower limbs might be based on a differential neuronal control of upper limbs during skilled hand movements and during locomotion. Direct cortico-motoneuronal connections to hand muscles are thought to determine the degree of dexterity in humans (Dietz, 2002). It has been suggested that these phylogenetically new components are integrated into pre-existing neuronal circuits (Maier et al., 1998). As a result of previous studies, there has been speculation that the greater influence of the direct cortico-motoneuronal system that parallels increased dexterity is accompanied by a decline in the indirect transmission of corticospinal excitation by propriospinal neurons in the upper cervical spinal cord (Nakajima et al., 2000). The strong direct cortico-motoneuronal input from the cortex enhances the possibility of selective activation of hand muscles during skilled voluntary hand movements. However, indirect evidence obtained by different experimental approaches indicates that propriospinal neuronal circuits persist, and most likely remain involved in the control of arm movement (Nicolas et al., 2001). It is possible that there is an indirect corticospinal pathway to upper limb motoneuron pools, in addition to the well-documented direct cortico-motoneuronal pathway (Dietz, 2002). Efficient corticospinal excitation of upper-limb motoneurons via propriospinal neurons might occur during automatically performed movements, such as locomotion. On the contrary, during skilled hand movements, strong cortico-motoneuronal input dominates and transmission through the propriospinal system becomes suppressed. This might explain why stimulating the pyramidal tract or the motor cortex fails to demonstrate the indirect corticospinal projection in humans (de Noordhout et al., 1999).

3. Pathophysiology of postural and gait abnormalities in Parkinson's disease

3.1 Postural control abnormalities

Patients with PD are typically impaired in both components of postural control: orientation and stabilization (Benatru, 2008; Vaugoyeau & Azulay, 2010). Clinical findings and experimental studies both in patients with PD and in animals provide evidence that the control of the axial orientation is markedly impaired in PD. Nevertheless, the postural orientation component has been poorly investigated. Indeed, most studies dealing with the postural disturbances of patients with PD have been devoted to research on pathophysiological mechanisms of the deficit of postural stabilization. The greater attention to the equilibrium component of posture is probably due to the fact that PI may frequently lead to falls, and thus worsening outcome of the later stages of PD.

3.2 Impairment of axial orientation

Clinical evidence shows that patients postural orientation abnormalities can be considered a hallmark of PD. Patients with PD may present several types of orientation difficulties, the most frequent being the presence of a stooped posture with a moderate flexion of the knees and trunk, with elbows bent and arms adducted. Other postural abnormalities include extreme neck flexion (antecoli), Pisa syndrome and Camptocormia. Camptocormia is characterized by an abnormal posture of the trunk in the antero-posterior plane with marked flexion of the thoracolumbar spine (Azher & Jankovick, 2005). Pisa syndrome (Gambarin et al., 2006) is characterized by a tilting of the trunk in the lateral plane, particularly when sitting or standing (see Benatru et al., 2008, for a review). Impairment of body orientation control has also been reported in animal experiments. Indeed, in rats and cats, unilateral lesions of the Substantia Nigra, performed by a local injection of 6 hydroxydopamine, provoke forced rotations, indicating a specific role of the basal ganglia in body rotation (Marshall & Ungerstedt, 1997). Lesions of a single caudate nucleus also influence the ability to orient the body towards the side opposite to the lesion. These results suggest a specific role of the basal ganglia in the control of axial posture. Although little attention has been geared towards body verticality control in PD (compared to balance control), a recent study by Vaugoyeau & Azulay (Vaugoyeau & Azulay, 2010) investigated the hypothesis that an impaired integration of proprioceptive signals may be a main cause of the deficit of postural orientation in PD. Authors used an original procedure, consisting in applying slow oscillations to the platform on which the subjects were standing. The perturbation was delivered at an amplitude and frequency kept below the semicircular canal perception threshold. The specific contribution of somesthetic cues (arising from sensory sources such as muscle, skin, and joints), possibly along with otolithic information, was tested in subjects who performed the task with their eyes closed. This paradigm was first tested on a group of young healthy subjects (Vaugoyeau et al., 2008). It was demonstrated that these subjects tend to align their bodies with the space vertical, despite the absence of vestibular and visual information. These data obtained with young healthy subjects confirm the predominance of proprioceptive information in the control of postural orientation in a quasi-static condition, and shows that the vestibular system requires large postural change to detect any change in body orientation. In a second experiment using the same experimental paradigm, authors compared the postural performances of patients with PD with those of control subjects. In this condition, the performances of patients with PD were much less efficient than those of the control group. They were unable to maintain the vertical trunk orientation without vision and they followed the oscillations of the supporting platform, whereas the control subjects kept their body upright when deprived of visual cues and vestibular information. These results demonstrated for the first time that patients with PD present a major deficit of postural orientation and that these deficits develop earlier than equilibrium impairment. Moreover, the patients were unable to properly control their postural orientation on the basis of the sensory information, probably due to a deficit of proprioceptive function. The comparison of the parkinsonian patients' postural performances with and without vision provides further evidence that visual inputs contribute to maintaining upright posture in patients with PD. The presence of an abnormal processing of sensory inputs in PD has

been emphasized in many previous studies (see Abbruzzese & Berardelli, 2003 for a review). Authors have suggested that not only is proprioceptive guidance during voluntary movements impaired in PD, but the sensory scaling of kinesthesia is also impaired. Kinesthetic deficit, and in particular deficit in axial kinesthesia, may thus be a major determinant of abnormal posturing in PD (Carpenter & Bloem, 2011). With regards to the pathogenesis of the stooped posture, some experiments suggest that an abnormality of the trunk alignment perception may have a causal role. For example, in situations where the support surface is shifted from a purely horizontal position, PD patients have difficulty in re-orienting themselves to a vertical position without the aid of visual cues (Vaugoyeau et al., 2007; Proctor et al., 1964). Because of their defective axial kinaesthesia, patients might also falsely perceive their subjective vertical to be shifted backward, forcing them to adopt a stooped posture (Kitamura et al., 1993). Some evidence supports this concept of incorrect trunk perception. In one experiment, patients were confronted with line drawings showing varying degrees of stoop and lateral deviation (Moore et al., 2000). When asked to identify the drawing that best resembled their self-perceived posture, patients were likely to underestimate the severity of their abnormalities. This suggests that patients have lost their normal sense of trunk position in space. This finding supplements clinical experience that many patients are surprised to observe their own posture in a mirror. The deficit of integration of somatosensory inputs may also be associated with body schema abnormalities, which may explain why patients with PD are often unaware of their stooped posture. It is worth noting that the possible role of body schema abnormalities in the pathogenesis of axial disturbances has been also emphasized in some studies dealing with other trunk deformities, such as adolescent idiopathic scoliosis (see Smania et al., 2008 for a review).

3.3 Postural instability

Postural instability is a common feature of PD that usually occurs after the onset of non-motor symptoms and becomes a clinical concern in the middle-later stages of the illness (Jankovick, 2008). Postural instability consists of alterations in postural control strategies during standing tasks, when responding to an unexpected destabilizing perturbation, or when performing voluntary movements (Adkin et al., 2003). This is a highly disabling disturbance that is difficult to treat, and predisposes patients with PD to a loss of equilibrium and unexpected falls (Marchese et al., 2003). Postural instability has been widely studied at both the overall (Marchese et al., 2003; Pastor et al., 1993), and segmental levels (Bronstein et al. 1990), probably because falling has such serious effects on the daily life of patients with PD. The mechanisms of PI in PD are not well known, however it is speculated that they possibly involve dysfunction at the level of several neural subsystems. Studies on the pathophysiology of postural control in PD have found abnormalities in the processing of afferent inputs from vestibular, proprioceptive and visual systems. Deficiencies in postural control have also been found to be related to an abnormal choice of postural strategies under different surface conditions (Horak et al., 1992). Overall, PI in PD may involve changes in both anticipatory (feedforward) and compensatory (feedback) postural reactions (Lee et al., 1995; Schieppati et al., 1991). Based on the available evidence, it actually seems unlikely that axial kinaesthetic deficits contribute to the abnormalities in automatic postural reactions previously observed in PD. If balance impairment in patients with PD could be related to a

global loss in proprioception, then their postural responses would be expected to be attenuated, and potentially delayed if proximal deficits are involved. However, patients with PD have normal timing of postural reactions, and in fact show excessive muscle activity in their automatic balance reactions (Carpenter et al., 2004). Furthermore, unlike kinaesthetic abnormalities, which appear to be worsened by dopaminergic medication (Wright et al., 2007), postural reactions are typically not responsive to dopaminergic medications (Carpenter et al., 2011; Bloem et al., 1996). Similarly, deep brain stimulation can improve kinaesthesia in PD (Maschke et al., 2005), but provides a less convincing improvement in postural reactions of PD patients (Visser et al., 2008). Therefore, deficits in the timing and modulation of postural reactions in PD are unlikely to be caused by abnormalities in kinaesthesia. Another significant issue related to PI regards the tendency to retropulsion in patients with PD. Indeed, in spite of their forward inclination in upright posture, patients with PD tend to fall backwards very easily, with only a slight push, resulting in retropulsion (Grimbergen et al. 2004). Both axial rigidity and poor trunk coordination contribute to the poor stability of patients with PD in response to backward body sway. Horak et al. (Horak et al., 2005) studied patients with PD in their off-state and showed different stability margins for different directions of body sway. The smallest stability margin occurred for backward body sway in both narrow and wide stance, suggesting that patients with PD are more vulnerable to falls in the backward direction. The reduced stability margin in patients with PD was due to a slower rise and a smaller peak of their centre of pressure, when compared to control subjects. Therefore, widening the sustentation base is unlikely to help patients with PD to prevent backward falls. Previous studies suggested that a disturbance of the central integration of sensory inputs may partly account for the PI of patients with PD (Bronte-Stewart et al., 2002). Kitamura et al. (Kitamura et al., 1993) reported that in the absence of visual cues, the position of the CoP shifted significantly backward in patients with PD, whereas it shifted significantly forward in age-matched control subjects. This provides further evidence that visual inputs contribute to maintaining upright posture in PD patients. Similar results were obtained by Bronstein et al. (Bronstein et al., 1990), who studied the postural responses to slow displacements of the visual environment. In this situation, patients with PD produced exaggerated responses, probably due to hyperactivity of the visuo-postural loop. Concerning the proprioceptive contribution to postural control in PD, Smiley-Oyen et al. (Smiley-Oyen et al., 2002) showed that a similar adaptation to vibration occurred in both patients with PD and control subjects. The authors suggested that, in patients with PD, proprioceptive impairments might affect kinesthetic abilities more than their postural control. Vaugoyeau et al. (Vaugoyeau et al., 2007) assessed the proprioceptive contribution to postural control in PD by using particular perturbation of the supporting platform and showed that proprioceptive impairments contribute to disturb postural orientation control. They suggested that, in patients with PD, increased visual dependence might reflect the adaptive strategy to compensate their proprioceptive deficits. As the disease progresses and the proprioceptive deficits increase, the strategy consisting of re-weighting sensory inputs in favor of the visual sensory mode may no longer suffice. In regards to the neural subsystems involved in PI pathogenesis, studies of automatic leg responses to sudden platform movements have partially clarified that, unlike the situation in bradychinesia, PD postural abnormalities may not be related to a dysfunction of the dopamine systems (Beckley et al. 1993). This accounts for the fact that

some studies have shown that dopaminergic medications lead to a limited improvement of PI in PD (Bloem et al., 1994; Visser et al., 2008). In particular, the velocity of postural movements is not improved by drugs (Bronte-Stewart et al., 2002), and early automatic postural responses are only partially corrected, while later occurring postural corrections do not improve at all (et al., 1996).

3.4 Gait disturbances in Parkinson's disease

In PD dopamine depletion has been observed to be associated with increased synchronization of neuronal activity throughout the basal ganglia (Obeso et al., 2008). Thus, the balance of basal ganglia activity is shifted toward the indirect circuit that increases output from the globus pallidus pars interna and inhibits the thalamocortical projection with a consequent reduction of cortical activation associated with movement initiation. Moreover, the basal ganglia activity is shifted toward inhibiting cortically aided movements by an increased gain of the subthalamic nucleus-globus pallidus pars interna network and reduced excitability in the direct circuit (Obeso et al., 2008). Finally, the movements mediated by the brainstem are also functionally impaired by excessive basal ganglia inhibitory outputs. Other essential characteristic motor abnormalities in PD, such as difficulty in performing simultaneous and sequential movements and a progressive reduction in amplitude while performing a repetitive movement, do not find an adequate explanation in the current understanding of basal ganglia physiopathology (Obeso et al., 2008). Another known mechanism contributing to the locomotor disorder in patients with PD is the insufficient activation of leg extensor muscles and the poor adaptation to environmental influences as a consequence of a deficit in proprioceptive feedback. Also, an impaired quadrupedal neuronal coordination of lower and upper limbs has been described to contribute to the locomotor disorder (Dietz & Michel, 2008). Gait disturbances in PD can be divided into episodic and continuous disturbances. The episodic disturbances may occur randomly or intermittently and include start hesitation, festination and FoG. Festination is a feature of PD where patients take rapid small steps in an attempt to maintain their feet beneath their forward moving trunk. It is associated with involuntary shortening of steps and hastening of cadence part way through a task. In patients with gait festination, consecutive footsteps become progressively shorter with an accompanying reduction in walking speed. This has been hypothesized to be related with an insufficient motor cue production in the globus pallidus (Morris et al., 2008). In particular, in the presence of progressive delays in the timing of phasic firing from the globus pallidus pars interna to the cortex (supplementary motor area and pre-motor cortex), footsteps become shorter and the gait speed decreases. When the phasic firing is slow or absent, freezing occurs because the motor cortical regions are not able to generate force for the next step in the sequence. Gait festination is progressive, whereby each step in a long gait sequence becomes progressively shorter, eventually leading to blocking. Freezing of gait is defined as an inability to initiate walking sequences, a sudden cessation of stepping part-way through a locomotor task, or difficulty igniting subsequent steps in the sequence once motor block as occurred. On the contrary, the continuous alterations of gait are persistent and apparent all the time (Hausdorff, 2009). These disturbances include slowed ambulation (in part as a consequence of bradykinesia) with decreased or absent arm swing. The key element of these disturbances is the inability of patients with PD to generate adequate amplitude of movement and in particular a sufficient stride length (Morris et al., 1994). Thus, the shortened stride length

may explain other typical features of continuous gait disturbances in PD such as reduced walking speed, increased cadence and double support duration (i.e. more time with both feet spent on the ground during ambulation). In addition, increased left-right gait asymmetry and diminished bilateral coordination have to be included together with a loss of ability to produce a steady gait rhythm (Hausdorff, 2009). On the contrary, the base of support is typically normal in patients with PD (it is often widened in patients with atypical parkinsonism) (Snijders et al., 2007). As a whole, gait disturbances contribute to the increased risk of falls as the disease progresses (Hausdorff, 2009).

4. Falls in Parkinson's disease

It is well known that PI (Bronte-Stewart et al., 2002; Morris, 2000; Smania et al., 2010) predisposes patients with PD to unexpected falls (Marchese et al., 2003). Balance is certainly needed within the context of many functional tasks of everyday living to keep the body oriented appropriately while performing voluntary activities, during external perturbations and when the support surface or environment changes (Bronte-Stewart et al., 2002). Thus, impaired balance and PI occur mainly during walking, while maintaining upright stance and stability in, or when transferring from one position to another.

4.1 Epidemiology of falls

Patients with PD experience falls and suffer fall-related injuries, including fractures and head traumas, more often than age-matched people (Melton et al., 2006; Pickering et al., 2007). In particular, a study by Bloem et al. showed that patients with PD had a 9-fold increased risk of sustaining recurrent falls when compared to age-matched people without PD (Bloem et al., 2001). It has been emphasized that the incidence of falls in PD is high. In the past few years, six prospective studies have examined fall rates and consequently falls among community-dwelling patients with PD living in Canada, Netherlands, Australia and United Kingdom (Ashburn et al., 2001; Bloem et al., 2001; Bloem & Bathia, 2004; Hely et al., 1999; Temlett & Thompson, 2006; Morris, 2000). All these studies included patients suffering from Idiopathic PD who were able to walk and had no other causes for falls. The duration of follow-up ranged from 3 to 12 months and falls were ascertained by means of a falls diary or by phone calls made weekly/monthly. Results showed that 70% of patients reported at least one fall (Wood et al., 2002) in the previous months. A recent meta-analysis by Pickering and colleagues addressed an important point on the incidence of falls in PD (Pickering et al., 2007). For the first time, the potential predictors of falling for patients who had never fallen before was studied. The authors provide a large sample size (473 patients) by pooling the six prospective studies previously mentioned. Each of these studies involved sufficiently similar methods, allowing the data to be pooled. The prospective follow-up data were therefore recalculated for a comparable 3-month period in order to determine the actual number of falls over the first 3 months. Results underscore the high frequency of falling in PD during a relatively brief follow-up of only 3 months, as the fall rate was 46% (95% confidence interval: 38-54%) and 21% (95% confidence interval: 12-35%) among patients with or without prior falls, respectively. Another study determined the frequency of falls in a group of 350 ambulatory people with PD. They reported that 46% of people with PD fell at least one time per week and 33% fell at least 2 or more times per week (Balash et al., 2005). High fall rate was also observed in the Sydney multicentre study (Hely et al., 2008), in which 136 newly diagnosed patients with PD were

followed for 20 years. Of the 36 survivors, 87% had experienced falls and 35% had sustained multiple fractures. Hip fractures are associated with considerable morbidity and even an increased mortality in patients with PD, and are a leading reason for nursing home admission (Idjadi et al., 2005; Coughlin & Templeton, 1980).

4.2 Falls phenomenology

A fall is "an event that results in a person coming to rest unintentionally on the ground or other lower level, not as a result of a major intrinsic event or overwhelming hazard" (Clarke et al., 1993). Another phenomena that has been taken into account in outcome studies in PD is near-falls. A near-fall is defined as the feeling that an individual feels/thinks that they were going to fall but do not actually do so (Steinberg et al., 2000).

4.3 Pathogenesis of falls in Parkinson's disease

The pathogenesis of falls in PD has more than one determinant. Obviously, PI is perhaps the main cause of the loss of balance leading to a fall in PD. However, several other manifestations of PD have shown to have a potential role in falls pathogenesis. One of these manifestations is difficulty in turning. This difficulty is clinically evident at the early stages of the disease, when individuals with PD have trouble turning in bed. In addition, they have difficulties turning in the seated position, and in particular in the standing position, even when straight walking is unaffected (Crenna et al., 2007). Turning whilst walking is a challenging component of locomotor ability, due to the need of complex integration between functionally different control mechanisms. These include neural commands for redirecting the cyclical motion of the lower limbs by asymmetric tuning step lengths and ground reaction forces (Hase & Stein, 1999; Orendurff et al., 2006), controlled rotation and bending of the axial segments aimed at coping with a curved path and preserving dynamic stability (Patla et al., 1991; Imai et al., 2001), and anticipatory orientation of gaze toward the intended direction of travel (Grasso et al., 1998; Hollands et al., 2002). These turning movements while standing are performed slowly (Visser et al., 2007), with small and abnormally timed steps (Huxham et al., 2008; Stack et al., 2004) and 'en bloc' (i.e. without the normal multi-segmented axial flexibility) (Crenna et al., 2007; Vaugoyeau et al., 2006). Turning problems may result from inability to adequately maintain an interlimb coordination (Baltadjieva et al., 2006; Hausdorff et al., 2003; Plotnik et al., 2007). This is especially difficult during turning when -by necessity- the two legs have to move more "in phase" rather than "out of phase," as is usual during over ground straight walking. Another important factor is axial "stiffness" and loss of intersegmental flexibility (Boonstra et al., 2008). One study (Wright et al., 2007) measured trunk resistance to passive axial rotations and found an increased axial rigidity in PD. Most importantly, patients who took levodopa showed no improvement, again suggesting that axial disability is largely dopa-resistant, unlike the appendicular movements, which appear to be controlled by separate dopaminergic neural systems (Boonstra et al., 2008). The great relevance of these findings lies within the relation to falls and injuries. Turning around the body's axis is the most important cause for FoG in PD (Schaafsma et al., 2003; Snijders et al., 2008). During turning, FoG is an important risk factor for falls in PD (Latt et al., 2009; Kerr et al., 2010). Falls occurring while turning cause the subject to fall sideways, and this is commonly associated with hip fractures (Greenspan et al., 1998). It would be helpful to have simple tools to detect turning difficulties, to estimate the risk of falling, and to record the outcome of therapeutic

interventions. Several recent studies (Boonstra et al., 2008) have shown that simply timing a patient's performance and counting the number of steps during a 180 degree axial turn may suffice, as patients with PD require more steps and turns lower than controls. Another relevant disturbance that may have an influence on falls is FoG (Brichetto et al., 2006). The freezing phenomenon indicates sudden and short-lasting breaks in voluntary motor activity that interrupts the execution of a complex movement or switching from one movement to another (Giladi et al., 1992). Freezing of gait is frequent in patients with advanced PD and is characterized by a large variability of manifestations. Patients may freeze when starting to walk (start-hesitation), during turning, or when approaching a narrow space such as doorways (Giladi et al., 1992; Schaafsma et al., 2003). Freezing of gait seems mainly related to disease progression and is influenced by cognitive and emotional factors (attention, anxiety and stress), but its definite pathophysiology is still uncertain (Brichetto et al., 2006). In recent years, some studies have recognized that walking and postural stability are not purely automatic tasks regulated by subcortical control mechanisms, but also require some conscious attention (Boonstra et al., 2008). Under particular circumstances gait and maintenance of equilibrium may also involve higher-order attentional processes. For example, when challenged with multiple simultaneous tasks, patients with PD may decrease their postural control, predisposing themselves to the risk of falling (Bloem et al., 2006). Stepping responses are effective strategies aimed at correcting balance and preventing falls in case of a great displacement of the centre of body mass. Forward stepping responses have reduced magnitudes in patients with PD. Recent studies (Jacobs & Horak, 2006; King & Horak, 2008) have shown that patients with PD have difficulties initiating a compensatory step. It is worth noting that patients showed significant more PI and falls when stepping was required for postural correction in response to lateral disequilibrium. This bradykinetic characteristic of the stepping responses helps to explain the greater rate of falls in subjects with PD.

4.4 Fear of falling

Patients with PD often develop a fear of falling while performing daily activities, resulting in a progressive loss of mobility (Adkin et al., 2003; Bloem et al., 2001; Morris, 2000; Pickering et al., 2007). This reduced mobility is associated with a host of negative consequences, including muscle weakness, promotion of osteoporosis and an overall deterioration of fitness, leading to cardiovascular disease and reduced survival (Pickering et al., 2007).

5. Evaluation of motor functions in Parkinson's disease

In the last decades some clinical scales have been developed in order to evaluate motor function in PD (i.e. gait, freezing, turning), while others have been designed to evaluate the impact of disease in activities of daily living. Recently, some instrumental devices that carry out quantitative and qualitative testing of specific motor functions (i.e. gait) have been introduced into clinical practice. All these testing procedures may be used to evaluate the effectiveness of rehabilitation treatment in patients with PD.

5.1 Clinical methods

A wide range of clinical tests have been used to assess balance and gait in elderly people and in people with neurological disorders. Smithson et al. (Smithson et al., 1998) have

identified five main groups of tests: (1) tests that measure the ability to maintain steady standing in different foot positions; (2) tests that measure the ability to maintain stability in standing while coping with perturbations to balance by self-initiated movements such as arm raises, lifting a foot up and down onto a step, or reaching forward; (3) tests of postural responses to expected and unexpected external perturbation; (4) functional tests of balance during activities such as walking, standing up, and turning; (5) tests to evaluate the ability to integrate visual, somatosensory, proprioceptive, and vestibular input in order to maintain stability in standing (sensory organization). Many of these tests correlate with frequency of falls in elderly people (Smithson et al., 1998).

5.1.1 Balance in steady standing

The assessment of balance in steady standing can be tested by determining an individual's ability to maintain various stance positions, with eyes open and with no hand support. There are various stance positions. For example, feet 10 cm apart, feet together, and stride stance, with the subject's feet placed 10 cm apart and with the heel of the front foot in line with the toes of the rear foot (Goldie et al., 1990). Another stance position is tandem stance, in which the subject stands with one foot directly in front of the other foot and with the toes of the rear foot contacting the heel of the front foot. Finally, there is the single-limb stance, in which the individual stands on one foot with the opposite knee held at 45 degrees of flexion and both hips in the anatomical position. During this stance both feet should be tested. During feet apart, stride stance, and tandem stance conditions, the individual should be requested to stand on footprint templates, and stride stance and tandem stance should be tested with each of the feet in the front position. The tests are completed if the individual changes their stance position, if the examiner provides assistance to the individual with external support, or if the individual maintains the position for the maximum testing period of 30 seconds. In order to control for the effect of fatigue and other variables, the best of 3 scores should be recorded if all scores are less than 10 seconds. If the score exceeds 10 seconds in any trial, that time must be recorded without further trials (Goldie et al., 1990).

5.2 Perturbation of standing balance by self-initiated movements

5.2.1 Arm raise test

This test requires an individual to stand with their feet placed 10 cm apart and is instructed to lift their arm up and down to shoulder height as many times they can in 15 seconds. The individual begins when the examiner says go. Prior to the start of the test, the examiner demonstrates the required action by passively moving the individual's arm up to 90 degrees of flexion and down again twice. Performance for one trial of the right and left arms should be recorded (Goldie et al., 1990).

5.2.2 Step test

This test involves an individual standing with their feet 10 cm apart, with a 15-cm-high step positioned 5 cm in front of their toes. The examiner delivers the following instructions: "When I say go, step your foot onto then off the step as many times as you can until I say stop. Make sure that all of your foot contacts the step each time". The number of times the individual can successfully place the foot onto the step in 15 seconds is recorded. This procedure must be completed for both feet (Hill et al., 1996).

5.2.3 Functional reach test

The test measures the maximal distance that an individual is able to reach while maintaining a fixed base of support in standing. The individual is asked to stand with their right side close to, but not touching a wall, and with their feet set 10 cm apart. The first position requires the individual to raise their right arm to 90 degrees with the hand outstretched and the position of the third digit is recorded on the wall with removable adhesive tape. The second position requires the individual to reach as far forward as they can without moving their feet, and the position of the third digit is again recorded. The difference between the first and second position is recorded using a tape measure. To reduce fatigue and the duration of testing, only one trial of this test should be performed (Duncan et al., 1990).

5.2.4 Bend-reach test

This test measures the maximal distance that each subject can bend and reach to pick up an object from the ground. The individual is asked to stand on footprint templates and the target object is placed at 5-cm intervals in a straight line from the templates. The maximum distance that the individual can successfully reach to retrieve an object without touching down on the ground with their hands, requiring external support from the examiner, or changing foot position must be recorded for one trial. This test has not been validated, however it has been used in research as patients with PD have demonstrated difficulty retrieving objects from the ground (Smithson et al., 1998).

5.3 Balance in response to an externally generated perturbation

This test consists in giving the individual an external perturbation (shoulder tug) and recording his response. The individual is positioned in a steady stance with their feet 10 cm apart. The examiner stands directly behind the individual and delivers the following instruction: "I am going to tap you off balance, and I won't let you fall". Without giving any information regarding the direction and timing of the perturbation, the examiner delivers a brief and quick tug to the individual's shoulders in a posterior direction with sufficient force to destabilize the individual. The amount of the destabilizing force is determined by the examiner, based on the individual's weight. Postural reactions in response to the shoulder tug is recorded by the examiner using the 5-point clinical rating scale described by Pastor et al. (Pastor et al., 1993): (1) the individual stays upright without taking a step, (2) the individual takes one step backward but remains steady, (3) the individual takes more than one step backward but remains steady, (4) the individual takes one or more steps backward, followed by the need to be caught and (5) the individual falls backward without attempting to step. Bloem et al. (Bloem et al., 2000) have a similar balance evaluation, however the individuals are not informed of the shoulder pull. Thus, the individual's reaction to an unexpected shoulder pull is scored on a 4-point scale, including the speed of restoring balance.

5.4 Functional tests of balance

5.4.1 Berg Balance Scale

The Berg Balance Scale is a 14-item (0-4 points per task; high=best performance) validated scale that evaluates balance abilities during sitting, standing and positional changes. Total scores are indicative of overall balance abilities, with a score of 0 to 20 indicating wheelchair bound; a score of 21 to 40 indicating walking with assistance, and 41 to 56 indicating independent. A score of 43.5 or below suggests risk of falls. It is simple to administer in

approximately 15 to 20 minutes and uses a quantitative scale format that has strong internal consistency and good inter and intra-rater reliability with patients with PD (Qutubuddin et al., 2005).

5.4.2 Time 'Up & Go'

The "Get-up and Go" test measures mobility in elderly people and is considered a useful tool for quantifying locomotor performance in individuals with PD. This test requires an individual to stand up from a chair, walk 3 m, turn around, walk back to the chair, and sit down again. The individual is videotaped, and then mobility is rated on a 5-point scale, ranging from "normal" to "severely abnormal" (Morris et al., 2001).

5.4.3 Tinetti mobility scale

The Tinetti Performance-Oriented Mobility Assessment, also referred to as the Tinetti Mobility Test (TMT), is a reliable and valid clinical test used to measure balance and gait in elderly people and patients with neurological disease. The TMT is easily administered in less than 5 minutes and provides information regarding an individual's ability to ambulate and transfer safely. The TMT assesses tasks that reportedly most often lead to falls and predict balance confidence in individuals with PD, such as turning, initiating gait, and slowing to sit down (Kegelmeyer et al., 2007).

5.4.4 Six-minute walk test

This test assesses walking capacity during a 6 minute period. Individuals are instructed to walk back and forth along a 20-m corridor and to cover the maximum distance possible in 6 minutes, taking rests as needed. The maximum distance covered is recorded. Examiners provide standardized encouragement every 30 seconds, by telling individuals "you're doing well, keep up the good work." Two trials should be performed at baseline, approximately 30 minutes apart. During the rest interval, participants can sit down. If an assistive device is used, the type of device is recorded (Falvo & Earhart, 2009).

5.4.5 Ten-meter walk test

This test assesses gait speed performance by requesting an individual to walk 10 m. A distance of 10 m must be marked on the floor with coloured tape, with subsequent marks placed 2 m from the starting point and 2 m from the ending point, thus creating a 6-m timed middle section for the test. The individual may be instructed to walk at a comfortable speed and is provided the following instructions "Walk all the way to the last piece of tape at your comfortable walking speed; you can start when I say 'go'". Alternatively, the individual may be requested to walk fast and is provided with the following instructions: "Walk all the way to the last piece of tape as fast as you can safely walk; you can start when I say 'go'". Timing begins when the individual crosses the initial 2-m mark and ends when the subject crosses the final 2-m mark. Time is measured in seconds and converted to meters per second. Four trials are performed, 2 at a comfortable walking speed and 2 at a fast walking speed (Brusse et al., 2005).

5.4.6 Fall efficacy scale

This test was designed to operationalize fear of falling based on Bandura's theory of self-efficacy. According to this theory, self-efficacy refers to a person's perception of his or her

own capabilities within a particular domain of activities. The Fall Efficacy Scale assesses the degree of perceived confidence at avoiding a fall in various situations and has been shown to be useful in assessing fear of falling in elderly communities, as well as subgroups of patients with PD (Thomas et al., 2010).

5.4.7 Freezing of gait questionnaire

This questionnaire constructed by Giladi et al. (Giladi et al., 2000) evaluates the FoG in patients with PD. This detailed gait and falls questionnaire consists of 16 items that assess gait in daily living, frequency and severity of FoG, frequency of festinating gait and its relation to falls, and finally frequency and severity of falls. Responses to each item are on 5-point scales where a score of 0 indicates absence of the symptom, while 4 indicates the most severe stage (Giladi et al., 2000).

5.5 Tests to evaluate the ability to integrate visual, somatosensory, proprioceptive, and vestibular input

5.5.1 Sensory organization balance test (SOT)

The SOT is a validated timed balance test that evaluates somatosensory, visual and vestibular function for maintenance of upright posture. This test requires that patients maintain standing balance during a combination of three visual and two support surface conditions. Tasks are performed with the eyes open and with the eyes closed; a visual conflict dome is used to produce inaccurate visual and vestibular inputs. The support surface conditions include a hard, flat floor and an 8 cm section of 20.4 kg firm density foam rubber that reduces the quality of the surface orientation input. During the test, subjects stand barefoot in the upright position with their arms alongside the body and their feet on the pre-designated site. If the subject activates any postural reaction, the test is stopped immediately and the number of seconds standing prior to the violation constitutes the trial score. The test is performed under six conditions: (1) eyes open – stable surface; (2) eyes open – compliant surface; (3) eyes closed – stable surface; (4) eyes closed – compliant surface; (5) visual and vestibular conflict (wearing visual dome) – stable surface; (6) visual and vestibular conflict (wearing visual dome) – compliant surface. Five trials are carried out for each test condition. Each trial lasts 30 seconds. Total scores for each condition are the sums of the scores of each trial (maximum score for each test condition: $30 \times 5 = 150$) (Cohen et al., 1996; Di Fabio & Badke, 1990).

5.6 Instrumental methods

5.6.1 GAITRite™ system (CIR Systems, Inc, Clifton, NJ)

The GAITRite System was developed to measure and record temporal and spatial parameters of gait by using a walkway approximately 3 or more meters long with grids of embedded, pressure-sensitive sensors connected to a personal computer (Nelson et al., 2002). While the individual walks across an instrumented mat, electronic recordings of each footfall are made and stored as a computer file. The computer records components of locomotion, including cadence, step time, step length, mean normalized velocity, step length ratio, heel to heel base of support, single support and double percentage and stance percentage. Temporal and spatial parameters of gait are automatically calculated and displayed and can be printed after the individual completes a trial (Nelson et al., 2002).

5.6.2 Gait analysis

Gait analysis is an instrumental method for gait measurement in the clinical setting. Markers (either reflective or light emitting) are placed on the patient's skin and aligned with bony landmarks and/or particular axes of joint rotation. The primary technology that underpins gait analysis includes optica-electronic video camera-based systems that measure the displacement of the markers. Multiple cameras are configured around a calibrated measurement volume. Three-dimensional (3-D) marker trajectory paths are then stereometrically reconstructed from the two-dimensional (2-D) camera image data. Gait analysis is becoming a main system in research on movement disorders in humans (Davis, 1997).

5.6.3 Posturography

Static posturography is an instrumental method to measure postural sway. Individuals stand on a dual force plate platform, with one foot on each force plate. They are instructed to maintain an upright standing position, with arms at their sides, eyes open with their gaze straight ahead at an art poster, and feet shoulder width apart. The centre of the foot pressure (CoP) of each foot (CoPleft and CoPright) and the total body CoP are computed from the vertical forces. The CoP is the point location of the ground reaction force vector and reflects the sway of the body (biological noise) and the forces used to maintain the centre of gravity within the support base. Computerized dynamic posturography is another quantitative method for assessing upright balance function under a variety of conditions that simulate conditions encountered in daily life. Subjects stand on a moveable platform in a loosely fitting harness. Their feet are aligned over defined axes on force plates measuring vertical forces. These measures along with the height and the weight of the patient are used to calculate the centre of gravity (CoG) position and the CoG sway (Nardone & Schieppati, 2010).

5.6.4 Equitest system (NeuroCom International, Inc, Clackamas, OR, USA)

This device determines the COP displacement as well as the sway of COM in different conditions. It can be used to determine the equilibrium score (ES) and postural stability index (PSI). A key assessment of the Equitest device is that it provides information about the integration of the visual, proprioceptive and vestibular components of balance which leads to an outcome measure called the ES, reflecting the overall coordination of these systems to maintain standing posture (Chaudhry et al., 2011). The Equitest System consists of a support surface (platform), a visual surround, and a harness to prevent falls during testing. The device performs a SOT with six conditions: conditions 1, 2 and 3 with the platform fixed and conditions 4, 5 and 6 with the platform moving. When the platform moves, it is referenced to the subject's sway such that as the individual leans forward, the platform tilts forward to minimize the degree of changed proprioceptive input from the self-generated sway. This platform adjustment is called "sway-referenced motion". Similarly, in conditions where the visual surround moves, the surround is referenced to the person's sway so as to minimize the ability to obtain visually relevant information about how far the individual is from the vertical. In other conditions, visual input is removed instead by asking the subject to close his or her eyes. Participants are asked to stand quietly and steadily for 3 trials in each of the following 6 conditions: (1) eyes open, surround and platform stable, (2) eyes closed, surround and platform stable, (3) eyes open, sway-referenced surround, (4) eyes open,

sway-referenced platform, (5) eyes closed, sway-referenced platform and (6) eyes open, sway-referenced surround and platform (Chaudhry et al., 2011).

6. Rehabilitation of postural and gait disturbances in Parkinson's disease

6.1 Rehabilitation of postural instability and strategies to prevent falling

Despite gains made in the field of pharmacotherapy and deep brain stimulation in PD, dopaminergic medications may produce a limited improvement in PI (Bloem et al., 1994; Visser et al., 2008). Thus, physiotherapy is the most commonly used procedure as an adjunct to drug therapy to treat PD movement disorders (Deane, 2001a, 2001b). At the moment, there is no uniformity of approaches for physiotherapy in PD. Rehabilitation for PD covers a number of different treatment techniques, largely centered on active exercises and re-education of mobility (Morris, 2000), mainly aimed at maximizing functional ability and minimizing secondary complications within a context of education and support for the person. Two Cochrane reviews on the general physical management of patients with PD (Deane, 2001a, 2001b) underlined that there is insufficient evidence to support or refute the efficacy of physiotherapy or one form of physiotherapy over another. Most of the trials included in these systematic reviews recruited small sample size (less than 20 patients) and were performed with poor research design and methodology. In light of this, the authors highlighted the need for more randomized control trials involving a large sample size to support or refute the efficacy of physiotherapy in patients with PD. In regards to rehabilitation of PI, only recently have a number of studies assessed the effect of specific training (Smania et al., 2010; Ashburn et al., 2007; Ebersbach et al., 2008; Hirsch et al., 2003; Protas et al., 2005; Qutubuddin et al., 2007; Toole et al., 2000; Jöbges et al., 2004; Cakit et al., 2007). It is interesting to note that as the pathophysiology of PI is multifaceted, the different rehabilitative approaches proposed are also very different. Moreover, the dosage of rehabilitation therapy was an inconsistent parameter among the various studies. Different approaches can be identified: exercises aimed at improving sensorimotor integration; balance training; a combination of strengthening and balance exercises; balance training with stepping; treadmill training; training for reducing falls. Studies have reported promising results regarding these different approaches, as well as demonstrated that specific rehabilitation programs can improve PI in patients with PD.

6.2 Sensorimotor integration training

As previously mentioned, increasing evidence suggests that patients with PD have abnormalities in both the peripheral afferent input and in the brain response to this sensory input, leading to a defect in the sensorimotor integration process. Among the different potential causes, it has been suggested that patients with PD usually have disturbances of proprioceptive regulation, possibly related to the abnormal muscle stretch reflexes in the upper and lower limbs (Abbruzzese & Berardelli, 2003). Because of this deficit in proprioceptive perception and processing, muscle vibration has been proposed to excite primary muscle spindles, as well as activate proprioceptors during voluntary movements in patients with PD. Previous neurophysiological findings have shown that the experimental stimulation of proprioceptors using muscle vibration can improve the trajectory of the voluntary movements of the ankle joint in patients with PD (Khudados et al., 1999). This finding suggests that PD may produce a general impairment of proprioceptive guidance

and that muscle vibration could be a tool for improving sensorimotor processing. Whole body vibration (WBV) has been demonstrated to be a possible tool to improve balance by enhancing sensorimotor processing in both elderly subjects (Bruyere et al., 2005) and patients with neurological impairment (cerebral palsy, Multiple Sclerosis and stroke) (Ahlborg et al., 2006; Schuhfried et al., 2005; Van Nes et al., 2006). Bruyere et al. investigated the effectiveness of WBV intervention in improving gait and balance in a group of forty-two elderly volunteers by means of the Tinetti test, Time Up&Go and the health related QoL (SF-36) (Bruyere et al., 2005). Patients were randomized in two groups. Both groups received physiotherapy as maintenance therapy, consisting of a standard exercise program (gait and balance exercises, training in transfer skill, strengthening exercises with resistive mobilization of the lower limbs) administered for 10 minutes, 3 times weekly over 6 weeks. In addition to the standard physiotherapy, the experimental group underwent WBV intervention. During the WBV intervention the patient was required to stand on a vertical vibrating platform for 4 series of 1 minute of vibration alternated with 90 seconds of rest. After treatment, patients who underwent WBV plus physiotherapy showed a significant improvement on all outcome measures. As to PD, it has been suggested that the WBV intervention could have beneficial effects on motor symptoms assessed by the UPDRS. In particular, in the study performed by Haas et al., promising effects have been reported, showing that this approach can improve UPDRS score as follows: gait and PI items showed 15% improvement on average, bradykinesia scores were reduced by 12% on average, and tremor and rigidity scores improved 25% and 24% respectively (Haas et al., 2006). Since the UPDRS was the only outcome measure used to evaluate the WBV post-treatment effects, a detailed discussion on the influence of this intervention on balance is not possible. Furthermore, no follow-up evaluation was performed, and hence long lasting effects were not documented. All these drawbacks were partially overcome in the study by Ebersbach et al. (2008). The study was undertaken in order to identify the influence of WBV on balance and gait in 27 inpatients with PD and clinical evidence for PI. Patients were randomized to receive 30 sessions of either WBV on an oscillating platform or conventional balance training. The former consisted of two 15 minute sessions a day, 5 days a week, with intervention on a vibrating platform that thrusts the right and left leg upward alternately with a frequency of 25Hz and an amplitude of 7 to 14mm. The conventional balance training consisted of standard therapy comprising three 40-minute sessions a day (5 days a week), which mainly included relaxation techniques (i.e. muscle stretching, relaxation, body perception) and occupational therapy. During intervention, the daily schedule for all patients enrolled in the study included 150 minutes of exercise, with 30 minutes being exclusively dedicated to balance. Patients were assessed before and after treatment by means of a broad multiple testing procedure for evaluating balance (Tinetti Balance Scale, stand-walk-sit test, pull test, dynamic posturography) and gait (10-meter walking test). A final follow-up assessment was repeated 4 weeks post treatment. In contrast to the previous studies, WBV was found to have no significant effects on equilibrium and gait when compared to conventional balance exercises. Both treatments were associated with improvements on all clinical assessments of mobility and postural strategy. In regards to dynamic posturography, a non significant effect in lower sway was reported at the end of the treatment and at follow-up, even though it was the only parameter that was differentially influenced by type of treatment. Another type of training aimed at stressing

sensory motor integration function was proposed by Qutubuddin et al. (2007). Patients were trained to maintain balance under different sensory conditions by using the Computerized Dynamic Posturography (CDP). In this pilot study, fifteen patients with mild-moderate PD were randomized to receive CDP therapy or standard physical therapy treatment. The main aim of the study was to evaluate the feasibility of this new approach in the treatment of balance disorders in PD. Data demonstrated that treatment was tolerated by a high percentage of patients (68%). In regard to the results recorded on the selected outcome measures, results failed to reveal any differences between the two groups.

6.3 Balance exercises

It is well known that pharmacological treatment is insufficient to improve non-dopaminergic symptoms such as lack of balance control and resulting falls. Therefore, rehabilitation programs are warranted for improving PI in patients with PD. Smania et al. (Smania et al., 2010) performed a randomized controlled trial in order to evaluate the effectiveness of a specific training aimed at improving balance control in patients with PD, Hoehn and Yahr (H&Y) stage III-IV. The training consisted of three different predetermined categories of exercises aimed at improving both feedforward and feedback postural reactions: 1) Exercises of self-destabilization of the center-of-body mass involving mainly feedforward control. For instance, patients were required to perform voluntary actions in both static and dynamic conditions such as transferring her/his body weight onto the tips of the toes and onto the heels or bouncing a ball during gait with their 2 hands alternating to the right and to the left side. 2) Exercises of externally induced destabilization of the CoM involving mainly feedback control. During these tasks the patient was required to maintain balance while standing on foam support bases of different consistency, on moveable platforms with different degrees of stability, or while the therapist was applying sternal or dorsal pulling. 3) Exercises emphasizing coordination between leg and arm movement during walking as well as locomotor dexterity over an obstacle course. These types of exercises required continuous feedback and feedforward postural adjustment. Each exercise was individualized to the patient's balance ability documented before training. During the course of the training the complexity of the tasks was progressively increased as the patient improved. The effects of the experimental training were compared with the effects of a training given to a control group, which consisted of exercises not specifically aimed at improving postural reactions (i.e. active joint mobilization, muscle stretching and motor coordination exercises carried out in supine, prone and sitting positions). Both trainings were performed as individual treatment in an outpatient setting with the same duration and frequency as follows: 21 treatment sessions of 50 minutes each, 3 days a week, for 7 consecutive weeks. Outcome measures, consisting of clinical and instrumental assessments, were delivered by a blinded rater before, after, as well as 1 month post-treatment. Results showed that specific balance training could improve postural stability and the level of confidence perceived while performing daily activities that required balance, as evaluated by the Activities Balance Confidence Scale. Furthermore, patients who underwent the balance training, which was not specifically designed to teach strategies to prevent falls, reduced the frequency of falls. Improvements were maintained at the 1-month follow-up. In contrast, patients undergoing the non-specific rehabilitation training (control group) showed no significant changes in any of outcome measures. The authors discussed that the balance training allowed the patient to improve postural control and the ability to plan an

appropriate postural strategy, as demonstrated by the center of foot pressure (CFP) self-destabilization and control test (Smania et al., 2010). The CFP self-destabilization and control test is a tool for assessment of balance control ability in PD, proposed for the first time in this study (Smania et al., 2010). In particular, this test could be suitable to evaluate both "corrective" and "protective" postural responses, which are normally impaired in PD (Jöbges et al., 2004; Horak et al., 1992, 1996). After the balance training, patients showed a significant improvement on the CFP self-destabilization and control test. In contrast, no significant changes were seen in the control group. A few recent reports have assessed the effect of specific rehabilitation programs aimed at improving balance, but most of them included a wide variety of treatment approaches and have differences in methodology, and thus a comparison of the different studies cannot be performed. However, it is worth noting that the training proposed by Smania et al. (Smania et al., 2010) showed that the effects on balance abilities acquired after treatment can potentially extend to untrained activities, such as strategies to prevent falls. These results were strengthened by the fact that the study was a randomized controlled trial conducted on a considerable sample of patients (N=64). Moreover, the methods used to assess balance included multiple tests that provided a comprehensive picture of the different aspects of PI (Hirsch et al., 2003; Jacobs & Horak, 2006).

6.4 Combined training: Strengthening and balance exercises

It has been well documented that patients with PD have a reduced level of physical activity compared to healthy individuals, and that they have a lower level of strength and functional ability. However, it has been shown that muscle weakness is not simply a secondary consequence of ageing and inactivity, but is also an elementary symptom of PD (Goodwin et al., 2008). Some studies have reported significantly lower muscles torque values in patients with early stage Parkinsonism, compared to age-matched healthy controls in both upper and lower limbs (Koller, W. & Kase, 1986; Toole et al., 2000; Goodwin et al., 2008). Furthermore, a number of studies on older adults free of pathology have found that PI and an increased tendency to sway result from decreased ankle, quadriceps and hamstring strength. It has been shown that a specific approach, which combines strength and balance exercises, may be useful in improving PI in older adults (Orr, 2010; Keus et al., 2007). A recent review by Orr et al. examined the relationship between muscle strength, power and balance performance in healthy older adults (Orr, 2010). Findings from this review indicate that there is substantial evidence for the contribution of muscle strength and muscle power to balance performance in older adults (more than 60 years). An overall examination of the literature showed that 54% of studies reported significantly improved strength and balance measures and 73% showed improved power and balance following resistance/power training intervention. However, 84% and 86% of cross sectional studies observed significant associations between balance and strength/power outcomes respectively (Orr, 2010). Although the studies reviewed varied in regards to muscle groups trained and tested, including not only those muscle groups specific to balance (ankle plantiflexor and dorsiflexor, hip abductor and adductor, knee extensor and flexor) but also those that have little bearing on postural control (i.e. hand grip strength), most showed that strengthening the quadriceps and hip muscles is essential for improving static balance in older subjects (Orr, 2010). In contrast, increasing ankle plantarflexion strength in balance impaired older adults demonstrated greater protection against backward slips by enhancing ankle postural control strategies (Hess et al., 2006). The use of strength training in

patients with PD has been recently explored (Toole et al., 2000; Hirsch et al., 2003). Toole et al. (Toole et al., 2000) evaluated whether a combined strength and balance training program could improve both lower limb strength and PI in patients with PD (H&Y Stage 1-3) (Toole et al., 2000). Patients were randomized in an experimental or control group. The experimental group underwent 10 weeks of lower limb strength training and balance exercises, three times per week, for 1 hour each session. Patients trained the knee flexor and extensor muscle groups bilaterally, using leg extension and side lying leg flexion machines at 60% of a four-repetition maximum force test. The strength assessment included peak torque during ankle inversion, knee extension and knee flexion evaluated by Biodex. The peak torque was defined as the maximal rotational tendency of a joint and it was chosen because of its ecological validity. The peak torque, in fact, relates to when the body starts to fall and the maximal peak torque is produced by lower limb muscles to centre the body back over the base of support, thus preventing loss of balance. The authors measured the ankle inversion instead of dorsiflexion because it has been demonstrated that it is highly correlated with balance. The training load for each muscle was adjusted weekly to keep the stimulus on 60% of the patients' maximum force. Patients were required to perform three sets of 10 repetitions for each exercise. Balance training consisted of exercises performed under a variety of destabilizing environments (i.e. posterior, anterior and retropulsion exercises) in both eyes-open and eyes-closed condition. These exercises were designed to challenge the vertical position of the body and increase the limits of stability in order to improve equilibrium when the body was destabilized. After training the patients who received strength and balance training demonstrated significant improvements in both balance and strength evaluated by the EquiTest, whereas the control group showed no improvement in any outcome measure. These results are consistent with those reported by Hirsch et al. (Hirsch et al., 2003). They investigated whether balance training combined with lower limb strength training is more effective than balance exercises alone in improving balance in patients with PD. For this purpose, fifteen patients were randomized in two groups. Both groups underwent 10-week balance training under altered visual and somatosensory conditions (3 times a week). Additionally, one group performed a high intensity lower limb resistance training combined with the balance training. The authors showed that both groups improved in balance performance evaluated by means of the Sensory Orientation Test (SOT), but the rate of improvement was higher for the patients who underwent the combined strengthening and balance training. Furthermore, muscle strength increased marginally in the balance group while it increased substantially in the combined training group. Data suggest that muscle strengthening is a safe procedure in patients with PD. Moreover, it has the potential to improve PI in spite of the degenerative nature of the illness. In regards to the potential mechanisms that could have benefited from the strengthening training, and thus improved PI, several factors can be identified. First, strengthening intervention could facilitate the use of proprioceptive, visual and vestibular cues in order to stabilize the body, increase equilibrium and consequently prevent falls. Additionally, muscle strengthening may have improved the musculoskeletal system, allowing individuals to have more force to counteract sway during moments of threatened stability. In particular, the subjects used increased muscular strength in the hamstring group and in the quadriceps group to benefit equilibrium. Consistent with this finding, Dietz et al. (Dietz et al., 1993) showed that patients with PD regulated their stance mainly by modulation of leg flexor activation.

6.5 Stepping training

Many researches have focused on the study of postural responses in patients with PD, demonstrating that patients often fall because they respond to a sudden loss of balance with abnormally short (hypometric) steps that are inadequate to help them recover equilibrium (Jacobs & Horak, 2006). Recently, King et al. (King et al., 2010) showed that patients with PD have significantly more PI and falls than age-matched controls, when stepping is required for postural correction in response to lateral disequilibrium. Although they normally choose the same type of postural stepping strategies as the age-matched control subjects, consisting of lateral stepping instead of the cross-over strategy, they have longer latencies of postural responses to external perturbation (King et al., 2010) than age-matched controls. This longer latency turns into a delay in the postural response execution, which may not allow the patient to execute a prompt postural reaction, thus resulting in a fall. It is likely that patients with PD were not able to quickly shift their weight adequately, thus preventing them from taking a fast large step. Furthermore, this deficit did not significantly improve with levodopa antiparkinsonian medication, probably due to the involvement of nondopaminergic pathways (King et al., 2010). These findings support the need to develop specific rehabilitation programs aimed at improving the planning and the execution of postural stepping strategies. It is worth noting here that studies have shown that a specific training for stepping practice could improve lateral postural reactions in both younger and older healthy subjects (Hanke & Tiberio, 2006; Rogers et al., 2001). Jöbges et al. (Jöbges et al., 2004) addressed this issue in patients with PD. The authors enrolled fourteen patients with PD and PI (H&Y stage: 2,5-4) in a case-control study design where each patient's baseline data were compared to his/her post-treatment data. Before training, after training, and 2 weeks and 2 months later, patients were evaluated by means of multiple specific tests containing both clinical and instrumental procedure to evaluate the different effects of PI. Clinical procedures also included the assessment of the quality of life questionnaire (PDQ-39). Instrumental procedures consisted of the analysis of the compensatory steps performed by the patient after the destabilization occurred. Length and initiation of the compensatory steps were recorded by using an ultrasound device (CMS 50; Zebris, Isny, Germany). Gait analyses were performed in order to measure step length, cadence and double support (Win Gait 2.14; Zebris), while posturographical testing was performed using a balance platform to record vertical and horizontal shear forces and to allow calculations of the centre of gravity over time. The training was directed at maintaining stability after the pushes, using large compensatory steps. Thus, the training consisted of repetitive pulls to the patient's back and pushes to her/his right and left side applied by the physiotherapist. The strength of the pulls and pushes was adapted to the degree of the patient's individual PI and in the case of satisfactory compensatory steps, a positive feedback was given, and the intensity of the pulls and pushes was continuously increased. Otherwise, the intensity of pulls and pushes was reduced. Patients were trained for 20 minutes twice daily for two weeks in an outpatient setting. Within these 20 minute training sessions, approximately 180 to 230 pulls and pushes were applied. After training, the length of compensatory steps increased and the step initiation shortened. Gait analysis showed that the cadence and the step length increased, gait velocity improved, and the period of double support shortened. The "mobility" subscore of a quality of life questionnaire (PDQ-39) also improved. All these changes were significant and they were maintained for two months without additional training. In light of this study, a repetitive training of compensatory steps could be

beneficial for improving PI also in patients with PD. These effects occurred not only during static tasks but also during gait. Therefore, these findings could have important effects in the rehabilitation of PI in patients with PD. As the authors stated, further studies with larger populations are needed to infer from these findings to the general population with PD and PI prior to this training being included as a standard treatment.

6.6 Treadmill training

Gait abnormalities are one of the most common disabling conditions in PD, consisting of several deficits such as difficulties in gait initiation, turning and balance difficulties. Protas et al. (Protas et al., 2005) showed that in eighteen patients (stage H&Y 2-3) with PD, gait training consisting of walking on the treadmill with body weight support could not only improve gait and dynamic balance, but also reduce the frequency of falls. Cakit et al. (Cakit et al., 2007) replicated these effects in a sample of fifty-four patients randomized to receive experimental training or usual care. Patients who underwent experimental training participated in an eight-week exercise programme using incremental speed-dependent treadmill training. All patients were evaluated before and after the training program by means of a comprehensive battery of tests including balance, gait and fear of falling evaluation. After treatment, the patients in the experimental group showed improvements not only in the outcome measures dealing with gait, but also in the Berg Balance Scale and in the Fall Efficacy Scale. No significant improvements were measured in the control group. Although no follow-up evaluation session was performed in order to evaluate if these important effects may be maintained over time, this treatment method can be applied to patients. Not only is the goal to increase walking speed, and hence give individuals a greater behavioural repertoire in everyday life, but also to reduce the risk of falling and resultant morbidity in the elderly general population and in patients with PD.

6.7 Programs aimed at reducing falls

Exercises programs individually prescribed at home have been shown to be effective in reducing fall frequency among the elderly population. Ashburn et al. (Ashburn et al., 2007) evaluated the effectiveness of a personalized home programme of exercises and strategies for repeat fallers with PD. Participants (n=142) were randomized in the experimental or control group. The experimental group underwent a personalized 6-week home-based exercise and strategy program comprising muscle strengthening, range of movement, balance training and walking. Balance training consisted of static, dynamic and functional exercises, which were chosen at the appropriate level for each individual and if possible progressed by increasing practice repetition. Participants were requested to complete the exercises daily and were given instructions with illustrations for each exercise. The control group underwent usual care, that, for the vast majority, was comprised of contact with a local PD nurse. Findings from the trial showed a consistent trend of reduced rates of falls and injurious falls among participants in the exercise program, even though these differences were not significant. Similar findings were reported in the randomized control trial performed by Allen et al. (Allen et al., 2010). Patients allocated to the exercise group attended a monthly exercise class run by one or two therapists and performed the remaining exercise sessions at home (three times a week) over a 6-month period. Exercises included both strengthening and balance exercises. After treatment, the exercise group showed a greater, but not significant, improvement than the control group in the fall risk score. In

contrast, there were statistically significant improvements in the exercise group compared with the control group in FoG Questionnaire, and time sit-to stand. However, no significant trends were found in the exercise group for measures of walking, strength, fear of falling and standing balance. Larger scale studies are warranted to explore this issue (Ashburn et al., 2007; Allen et al., 2010; Canning et al., 2009) because to date no adequately powered studies have investigated exercises interventions aimed at reducing falls in patients with PD. Furthermore, the real cost effectiveness of exercise programs, from the health provider's perspective, has not been established. Hence, recently a study protocol focusing on these important issues has been proposed (Canning et al., 2009). Programs aimed at reducing falls has also been proposed by Brichetto et al. (Brichetto et al., 2006), who performed a pilot study aimed at investigating the effectiveness of a rehabilitation protocol in patients with PD and FoG. Twelve outpatients (H&Y stage 2-3) were selected because of their subjective compliant and occurrence at clinical examination of FoG during the "on" phase of medication. Patients underwent treatment which included different exercises to improve balance, postural control and walking over a period of 6 weeks (three sessions every week). Before, after and 4 weeks after the end of the rehabilitation treatment, patients were examined by means of the UPDRs (motor section), FoG Questionnaire, Parkinson Disease QoL Questionnaire and gait analysis. After treatment, results showed a significant reduction in score on both the FoG Questionnaire and the Parkinson Disease QoL Questionnaire, while no significant changes were found at follow-up. Although this study was based on a small sample, it suggests that the potential short-term efficacy of a rehabilitative approach aimed at FoG in PD may be due to the effects of exercises mainly focused at improving stability and gait (Brichetto et al., 2006).

6.8 Gait rehabilitation in Parkinson's disease

Walking impairments, a hallmark of PD, are characterized by a slow, short stepped, shuffling, forward-stooped gait with asymmetrical arm swing (Morris, 2000, 2006; Morris & Iansek, 1996). To date, many physiotherapy approaches in PD consist mainly of mixed exercises, aimed at the overall remediation of many disturbances that may be associated to PD, including gait. In recent years, many studies have shown that using several sensory cueing strategies may be a valuable approach in order to improve gait performance in patients with PD. Cueing is defined as using external temporal or spatial stimuli to facilitate movement (gait) initiation and continuation. Recent reviews on cueing suggest that it can have an immediate and powerful effect on gait performance in people with PD, indicating improvements in walking speed, step length and step frequency. The influence of cueing has mainly been studied in single-session experiments in laboratory settings (Lim et al., 2005). Results have shown a short-term correction of gait and gait initiation, and suggest that carry-over to uncued performance and its generalisation to activities of daily living (ADL) is limited. Using cues in a therapeutic setting is more complex, as the "modality" of cue delivery (visual, auditory or somatosensory) and the cue "parameter" selected for movement correction (frequency or size of step) have to be adapted to the needs of the patient. Furthermore, improved mobility with cues may have an adverse effect by distracting attention and increasing the risk of falling (Lim et al., 2005). Gait facilitation in patients with PD by means of cueing has been reported since 1942 (Von Wilzenben, 1942). The first detailed analysis of external cueing effect on gait was performed by Martin in 1967 (Martin et al., 1967). To define the word cue is quite problematic. According to Cools et al.

(1993), cues are "contextual or spatial stimuli which are associated with behaviour to be executed, through past experience". Conversely, Horstink distinguishes between cues and stimuli, stating that "cues give information on how an action should be carried out and are hence more specific than simple stimuli" (Horstink et al., 1993). Based on these observations and given that Parkinsonian symptoms particularly affect complex and sequential movements, we decided to define external rhythmical cueing as "applying rhythmical temporal or spatial stimuli associated with the initiation and ongoing facilitation of motor activity".

6.8.1 Putative mechanisms of action

The basal ganglia are the focal point of impairment in PD. They have been shown to be involved in the execution of automatic and repetitive movement (Cunnington et al., 1995; Georgiou et al., 1993). To enhance basal ganglia function, some studies provided external rhythmic auditory cues in order to supplement the deficient internal rhythm. Other studies used visual cues to set the proper stride length, thus providing external information to help augment the defective motor set. To reroute the movement through a non-automatic pathway, attentional cues have been used to focus attention on walking, thus shifting away from the automatic basal ganglia pathway. Alternatively, visual cues may be employed to activate the visual motor pathway instead of the automatic motor pathway.

6.8.2 Auditory cueing

Rhythmic auditory cueing has been gaining popularity over the last years. There is strong evidence that rhythmical auditory cueing enhances gait speed in patients with PD (Lim et al., 2005). Moreover, limited evidence was available for improving stride length and cadence with the use of auditory stimulation (Lim et al., 2005). These improvements have been described to remain evident in the immediate short term even after the cues were removed (Lim et al., 2005). In terms of actual gait training, patients who trained daily while listening to music with an overlaid rhythmic auditory stimulation beat showed more significant and more lasting improvements in gait than patients who did the same exercise program without rhythmic auditory cueing (McIntosh et al., 1997). It has been suggested that perhaps rhythmic auditory stimulation provides an external rhythm that is able to compensate for the defective internal rhythm of the basal ganglia. The finding that the improvements remained even when the cues were removed suggests that rhythmic auditory stimulation may also provide a sort of rhythmic training mechanism. Picelli et al. (Picelli et al., 2010) recently performed a preliminary investigation about the three-dimensional motion analysis of the effects of auditory cueing on gait pattern in patients with PD who underwent auditory cueing respectively at 90, 100 and 110% of their mean cadence at preferred pace. The authors reported that in the presence of auditory cues, walking speed and stride length showed an increase that became more significant matching the higher cueing frequencies. Moreover, the analysis of kinetic gait parameters showed a significant variation of maximal values within the pull-off phase of the hip joint power when subjects were asked to match the rhythm of their stepping to the higher cueing frequency, suggesting that subjects improved their gait by adopting a motor strategy based on a more effective activation of hip flexors and not increasing the more destabilizing ankle extensors function.

6.8.3 Visual cueing

Placement of visual cue floor markers is an approach that can be very effective in regulating stride length. Floor markers were reported to be effective in improving the gait of patients with PD as early as 1967 (Azulay et al., 1999). In some cases, the patient is instructed to walk over each marker to achieve the desirable stride length for each step. In alternative, the patient may be given no specific instructions regarding the floor markers. Interestingly, only certain visual stimuli are apparently effective in improving gait in patients with PD. Transverse lines are effective, whereas zigzag or parallel lines are not. In addition, the lines must be separated by an appropriate width and have a colour that contrasts with the floor in order to achieve the best results. Limited evidence was found for improving speed and stride length when patients with PD were provided with floor markers to externally cue their stepping patterns (Lim et al., 2005). However, a retained positive carryover effect even after the cues were removed has been reported (Rubinstein et al., 2002). Visual cues have also been suggested to be helpful in alleviating freezing episodes (Rubinstein et al., 2002). For example, carrying an inverted walking stick, so that the handle acts as a horizontal cue at foot level, was able to decrease the number of freezing episodes in certain patients. It is not clear exactly how visual cues improve gait in PD. One possibility is that visual cues help to fill in for the motor set deficiency by providing visual data on appropriate stride length (Morris et al., 1996). When patients are told to step over each marker, they are forced to take properly sized steps, normalizing their stride length. Another theory is that visual cues help because they focus attention on gait (Morris et al., 1996). Once the patient is concentrating on walking, it is no longer an automatic task that is being processed through the defective basal ganglia.

6.8.4 Attentional cueing

To evaluate attentional cueing strategies, the effects of different verbal instructional sets on gait have been studied in PD (Rubinstein et al., 2002). Interestingly, while different instructions were able to improve gait speed, the effects were not equivalent. The greatest increase in speed was seen when patients were told to walk fast. However, the resulting gait was abnormal, with an elevated cadence and small stride length. In contrast, walking while focusing on arm swinging or large steps improved the overall velocity to a lesser degree, but resulted in an almost normal gait pattern.

6.8.5 Combined sensory cueing training

In 2007, Nieuwboer et al. (Nieuwboer et al., 2007) performed a single blind, randomized clinical trial with a crossover design (the RESCUE trial) on 153 patients with PD who underwent a 3-week cueing training program (consisting of their preferred modality among auditory, visual and somatosensory) carried out at home by one therapist and a 3-week no training period. The authors observed improvements after intervention on postural stability and gait performance also reporting a reduction in FoG (Nieuwboer et al., 2007). The findings of the RESCUE trial were extended by Rochester et al. (Rochester et al., 2010), who observed that gait training with external rhythmical cues increased single and dual-task cued walking speed and step length.

6.8.6 Physiotherapy combined with sensory cueing

A number of studies have evaluated the effects of physiotherapy combined with sensory cues. In particular, programs that utilized visual and auditory cues as triggers to facilitate

initiation and speed of movement or rhythmic and auditory cues to assist in continuous movement have been compared with a control group that did not receive any exercise training. Authors found that the experimental group showed significant improvement in gait immediately after the program, whereas the control group did not (Rubinstein et al., 2002). Other studies compared the effects of a conventional physiotherapy protocol to those of the same physiotherapy protocol enhanced by sensory cueing, reporting that patients who underwent walking training with rhythmic auditory stimulation had significant improvements in gait parameters, whereas the other patients who performed conventional training did not (Rubinstein et al., 2002). Moreover, sensory-enhanced physiotherapy programs have been found not only to improve patients' skills immediately after training, but also at follow-up assessment.

7. References

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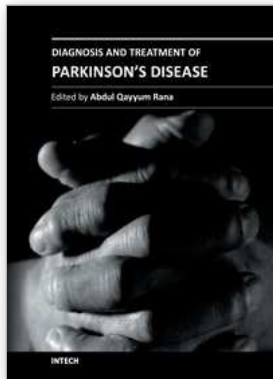
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Diagnosis and Treatment of Parkinson's Disease

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Parkinson's disease is diagnosed by history and physical examination and there are no laboratory investigations available to aid the diagnosis of Parkinson's disease. Confirmation of diagnosis of Parkinson's disease thus remains a difficulty. This book brings forth an update of most recent developments made in terms of biomarkers and various imaging techniques with potential use for diagnosing Parkinson's disease. A detailed discussion about the differential diagnosis of Parkinson's disease also follows as Parkinson's disease may be difficult to differentiate from other mimicking conditions at times. As Parkinson's disease affects many systems of human body, a multimodality treatment of this condition is necessary to improve the quality of life of patients. This book provides detailed information on the currently available variety of treatments for Parkinson's disease including pharmacotherapy, physical therapy and surgical treatments of Parkinson's disease. Postoperative care of patients of Parkinson's disease has also been discussed in an organized manner in this text. Clinicians dealing with day to day problems caused by Parkinson's disease as well as other healthcare workers can use beneficial treatment outlines provided in this book.

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