

**STABILOMETRIC MEASUREMENTS IN THE  
CENTRAL NERVOUS SYSTEM DISEASES.  
DETECTING POSTURAL INSTABILITY**

**PhD Thesis**

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# 1. Introduction

## 1.1. Balance / postural stability

### 1.1.1. Definitions of balance / postural stability

**Balance** or **postural equilibrium** is the maintenance of **postural stability** of the body in sitting or standing upright position, **against gravity**. In the twentieth century the act of maintaining the position of the body against gravity was referred to as ‘balance’ in the literature. After 2000 the term ‘postural stability’ has been more generally widespread (Bronstein and Pavlou 2013, Pollock et al. 2000). The definition of human balance varies according to the specific context in which it is used, but generally it refers to the act of maintaining, achieving or restoring the state of balance in the case of any posture or activity (Pollock et al. 2000). Postural stability is necessary for maintaining and regaining balance (Nagymáté et al. 2018). According to a general conception given by the International Classification of Functioning, Disability and Health, balance is a functional ability contributing a person’s daily activity (Hugues et al. 2019). The human body has the ability of sensing a threatening to its stability and using muscular activity to counteract any force or gravity in order to prevent falling (Pollock et al. 2000). It is called **anticipatory postural adjustment** (Traub et al. 1980, Santos et al. 2010). **Gravitational perception** is the perception of **postural verticality**. **Postural control** and **spatial orientation** are also linked with each other. Spatial orientation and balance control are dependent on peripheral sensory inputs arising from the visual, proprioceptive, and vestibular systems (Manchester et al. 1989). The sensing of balance is centrally processed by peripheral (vestibular, visual and somatosensory) inputs, low-level reflexes, higher-order motor responses, and by the generation of conscious sensations (Sundstrup et al 2019).

Human stability is performed by maintaining, achieving or restoring a state of balance through the human sensory and motor systems (Pollock et al. 2000). Postural instability previously called balance is an integrated complex of peripheral input and central control. Postural stability is an important indicator of physical fitness and capability (Sundstrup et al. 2019).

### **1.1.2. The main structures and components involved in postural stability**

Sensory input for the maintenance of postural stability can derive from the vestibular system, the visual system, or the somatosensory system (Manchester et al. 1989, Alcock et al. 2018). The information coming from these systems is centrally processed.

### **1.1.3. Vestibular system**

The detection of equilibrium is the responsibility of the vestibular organ in the inner ear. Static equilibrium is the sensing of the orientation of the head in space. Dynamic equilibrium is the sensing of the rotational motion of the body (Fonyó 2011, Halmagyi et al. 2001).

The stabilization of the head has a vital importance. When the position of the head changes, the otolithic membrane of the inner ear adjusts its position and sends information to the brain. Small calcium carbonate crystals embedded in a gel matrix on the surface of the otolithic membrane are pulled down by gravity and bend the hair cells embedded in the membrane. The information is sent to the brain through the vestibular branch of the vestibulocochlear nerve. The stimulation of the semicircular canals is processed through the fasciculus longitudinalis medialis to the motor nucleus of the cranial nerves III, IV, and VI innervating the eye muscles (Fonyó 2011).

The stimuli are transferred from the receptor zones of the vestibular organ to the peripheral endings of the bipolar neurons located in the vestibular ganglion. The axons projecting towards the vestibular nerve end in one of the four vestibular nuclei (nucleus vestibularis lateralis, superior, inferior, and medialis) in the medulla oblongata (myelencephalon). The nucleus vestibularis, or Deiter's nucleus is a significant integration center, and it operates as a deep nucleus of the vestibulocerebellum. The lateral vestibulospinal tract is composed of the efferent axons leaving the Deiter's nucleus, and it has connections with the spine and the cerebellum as well. It uses the information coming from the vestibular organ, the cerebellum, and the proprioceptors, and it contributes to the generation of muscle tone and postural control as well (Fonyó 2011).

#### **1.1.4. Visual system**

The visual system's participation in the control of balance is anticipation, navigation, avoidance of obstacles, and providing feedback on body movements and postural sway (Bronstein and Pavlou 2013).

There is a centrally directed system to the indirect visual control of balance (Sozzi et al. 2019). Eye movements are coordinated and conjugated by the fasciculus longitudinalis medialis which is a very short tract, consequently its latency is very short (Fonyó 2011). Fixation has a primary importance in vision and it is supported by the vestibule-ocular reflex and the opto-kinetic response (Fonyó 2011). Although, the visual system has not a primary significance in the maintenance of postural stability, balance is reduced without vision.

However, the sensation of balance develops without visual sensory input as well. In an investigation it was demonstrated that the sighted and the visually impaired group of participants with congenital visual impairment behave in the same manner standing on an unstable surface with eyes closed (Alghadir et al. 2019).

#### **1.1.5. Somatosensory system**

There is a hierarchical principle in the organization of the somatosensory system. The lower levels are affected by the operation of the higher levels, but they are able to perform autonomous responses as well.

Proprioceptive information about the position of joints, deep pressure, and vibration are afferent stimuli for the somatosensory functions and they are processed by higher-order motor responses interacting with voluntary motor control generated by head orientation and movement. The proprioceptive information is sent to the spinal cord through dorsal roots, and it is transferred to the thalamus through an ascending pathway, the Goll and Burdach tract crossing in the medulla oblongata, and proceeds to the thalamus as medial lemniscus pathway.

Movements are generated through the procession of  $\alpha$ -motoneurons of the spine or the brainstem regulated by the central nervous system in the primary motor cortex. The cerebellum and the basal ganglion system are also connected in a parallel way to

the hierarchical system. The central nervous structure is continually informed about the tonic or static state of the muscles performing the body movements (Fonyó 2011). The somatosensory neurons and pathways in the tendons and the muscles respond to the changes of the position of the different body parts, playing a very important role in the maintenance of upright position (Fonyó 2011, Bronstein and Pavlou 2013). The injury of the proprioceptive function can be tested by graphesthesia test where different numbers or simple letters are written on the skin, or by the sensation of vibration on the bones (test of vibration), or by defining the placement of the different joints.

#### **1.1.6. Short summary of the peripheral inputs of postural stability**

The proprioception, the vestibular sensation and the vision form the peripheral inputs of the balance. Their significance in the development of postural stability is different from each other.

#### **1.1.7. Postural control strategies**

Postural control strategies can be **predictive** or **reactive**. The predictive strategy is called **anticipatory postural adjustment** where the muscle tense predicts the changing of balance, and the body prepares for it. The reactive strategy is called **compensatory postural adjustment** where the center of the body mass is moved by an environmental effect, and restored by the balance system (Pollock et al. 2000, Santos et al. 2010, Traub et al. 1980, Massion 1995, Chen et al. 2015, Aruin et al. 1998).

#### **1.1.8. Postural adjustment**

The perception of the human body's posture in space is a multimodal process generated through an integration of sensory information encoding the eye, head and body positions. The cervical, ankle, and plantar spinal afferents for multiple hierarchical central nervous system levels are particularly important in the control of balance. The relative position, and movement of the various body segments is controlled by proprioception and other elements of the somatosensory system (Lopez and Blanke 2010).

The role of the **muscles of the ankle**, especially that of the **gastrocnemius muscle** must be highlighted. In an investigation the effects of varying frequencies of vibration on the proprioceptive postural strategies were assessed by stabilometric measures. The varying dependence on the proprioceptive postural strategies of the muscles around the ankle was demonstrated (Ito et al. 2018).

#### **1.1.9. Additional factors affecting postural stability**

There are several **psychological factors** increasing the effects of neurological deficits and causing a balance disorder, such as **anxiety** (Brown et al. 2006, Martens et al. 2017), **depression** (Hassan et al. 2014), **fear of falling**, and **cognitive deficits** affecting **memory, attention, or executive functions**. According to several studies, altered responses regarding their standing, reactive and anticipatory postural control because of the **fear of falling** were demonstrated by the persons of older age or with movement disorders. It was pointed out in a study examining 68 healthy participants' **emotional response** to threat caused by standing on a high platform that a higher frequency of center of pressure oscillations and ankle muscle contraction in standing balance control can be observed (Zaback et. al. 2019).

The possibility of **orthostatic** (or postural) **hypotension**, a **peripheral vestibular disorder**, or a **cerebellar-brainstem disease** should also be taken into consideration (Bronstein and Pavlou 2013).

Balance impairment can also be a consequence of cerebral white matter integrity following a mild to moderate **traumatic brain injury**. In a Korean study a decreased axial diffusivity in the left inferior cerebellar peduncle was found to show positive correlation with the poor balance control in patients suffering from mild to moderate traumatic brain injury. According to the study this may be the indicative of the impaired balance control (Kim et al. 2019).

#### **1.1.10. Central organization of postural control**

Based on the International Classification of Functioning, Disability and Health, postural control is a body structure function reflecting orientation and stabilization of

the body (Hugues et al. 2019). Normal standing or sitting upright posture is maintained by a combination of phasic and tonic neuromuscular processes. Tonogenic structure participates in postural control. Several subcortical regions are involved in the maintenance of postural control. The mesopontine regions have connectivity to the spinal cord, the basal ganglia, cerebellum and also to certain cortical sensorimotor areas. The basal ganglia-brainstem-spinal pathways regulate postural tone and locomotion. Pathways from the substantia nigra pars reticulata to the pedunculopontine tegmental nucleus also participate in regulating postural tone. The mesencephalic locomotor region prepares the postural system to begin locomotion (Wright 2019).

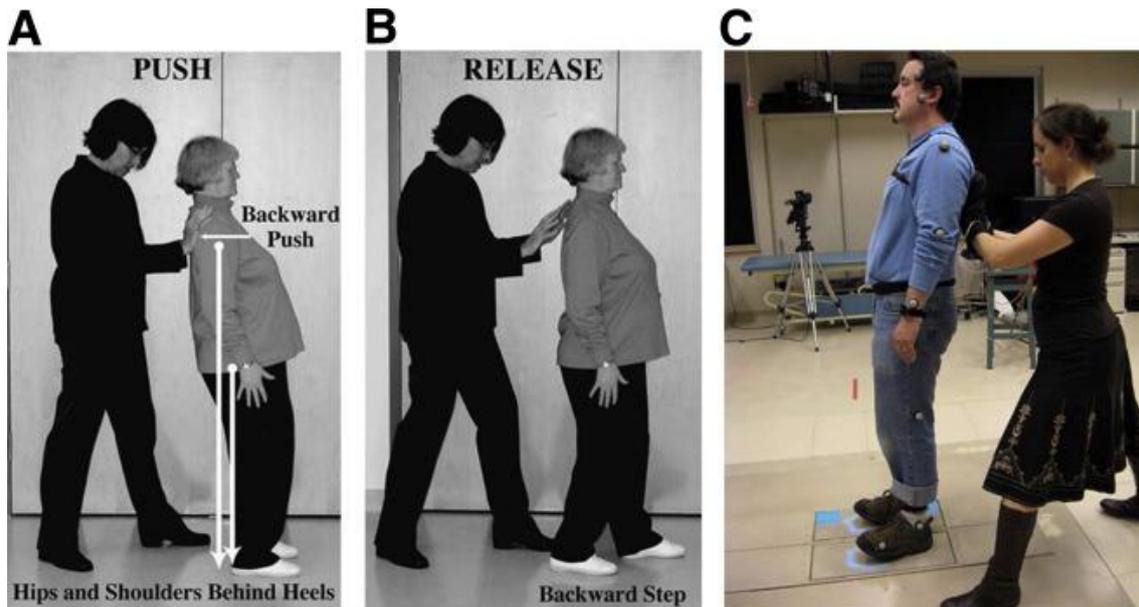
### 1.1.11. Cerebellum

Although the basal ganglia and the cortex are very significant, the cerebellum plays the most important role in balance control. Lesions of the cerebellum or its pathways lead to trunk ataxia and goal-oriented ataxia. The cerebellum also participates in **motor learning** and **control**. Recent studies have shown that the cerebellum has a significant role in **cognition** and **emotion** as well. The cerebellum and various cerebral regions, including the prefrontal and posterior parietal cortices are connected through the thalamus. Each cerebellar hemisphere is connected with the contralateral cerebral cortex (Palesi et al. 2016). The vestibulocerebellar tract, a projection to the vestibular nucleus, connects the vestibular nerve and the cerebellar cortex. The stimuli are transferred to the primary sensory cortex. The cerebellopontine angle also plays an important part in the vestibular system. The nuclei of the thalamus have multiple functions. It relays sensory signals, including motor signals to the cerebral cortex. On the adverse, the efferent pathways, the lateral and medial vestibulospinal pathway among them are placed in the spine and they are switched to the  $\alpha$ -motoneurons and participate in the generation and modification of muscle tone (Fonyó 2011, Bronstein and Pavlou 2013). A circuit of the spinal reflexes, the vestibular nuclei, the cerebellum, the basal ganglia, and primary motor cortex are together the great integrators of postural stability.

## 1.2. Assessment of postural stability in the literature

### 1.2.1. Assessment of postural stability with clinical tests

In the investigation of balance, the first step is to assess the degree of postural instability. The Push Test (Figure 1), the Berg Scale (Table 1) and tandem walking (Figure 2) are the most frequently used techniques of daily practice (Bronstein and Pavlou 2013, Kamieniarz et al. 2018).



**Figure 1. Representation of the Push test.**

1/A This figure shows that an individual is drawn backwards and she would not be able to keep her standing position if the examiner did not hold her.

1/B This figure shows that the person is able to make an adjustment when her shoulders are drawn backwards forcefully. She makes a step backwards.

1/C This figure shows that the person would spontaneously fall and the examiner prevents this by propping him up (El-Gohary et al. 2017).

Tandem walking or is also frequently applied for the detection of digression from a straight line to the right or left direction (Figure 2).

## Perform **Tandem Walking**

- ask the person to walk a straight line in a heel-to-toe fashion.
- This decreases the base of support and will accentuate any problem with coordination.



### Normal:

Person can walk straight & stay balanced

### Abnormal:

- Crooked line walk
  - Widens base to maintain balance
  - Staggering, reeling, loss of balance
  - An ataxia that did not appear now.
- *Inability to tandem walk is sensitive for an upper motor neuron lesion, such as multiple sclerosis.*

**Figure 2. Representation of tandem walking test.**

Figure 2 illustrates the method of the examination with tandem walking test (Habeeb 2017).

The assessment of a balance disorder is composed of identifying the patient's functional limitations, underlying impairments, and symptoms. Functional assessment comprises the examination of the patient's objective and perceived ability to perform various tasks requiring balance. There are several commonly used self-perception scales, the Push Test and the Berg Scale are the most frequently used among them.

The **Push-test** is the most frequently used method for the clinical assessment of balance impairment. It is performed by pulling or pushing the individual in a specific direction. The result of the test is negative when the patient is able to compensate the pushing instead of tilting or stepping. This is not a precise assessment as it is not quantifiable. Although it demands a complicated apparatus, it has been used in some investigations (Chen et al. 2015, Santos et al. 2010). A dynamic force-plate or cylinder

was used in other experiments in spite of the fact that it is a dangerous alternative for patients with severe symptoms (Bronte-Stewart et al. 2002, Ebersbach and Gunkel 2011). A spirited method of investigation was to induce postural perturbations by dropping loads hanging from balloons (Aruin and Latash 1995).

The **Activities-Specific Balance Confidence Scale** (Powell and Myers 1995) quantifies a person's confidence in their balance during various tasks. The **Falls Efficacy Scale** (Tinetti et al. 1990) is used for the quantification of the fear of falling. The **Vestibular Activities of Daily Living Scale** (Cohen and Kimball 2000) is used for the assessment of the perceived impairments in daily life due to dizziness. The **Dizziness Handicap Inventory** (Jacobson and Newman 1990) quantifies the perceived handicap due to dizziness or postural instability. The **Vertigo Symptom Scale** (Yardley et al. 1992) quantifies the frequency of vestibular and autonomic symptoms. The **Situational Characteristics Questionnaire** (Jacob et al. 1993) quantifies the severity of the visual vertigo symptoms. There are several balance or gait assessment scales. The **Timed "Up & Go"** (Podsiadlo and Richardson 1991) serves for functional gait and fall risk assessment. The **Performance-Oriented Mobility Assessment** (POMA) (Tinetti 1986), the **Dynamic Gait Index** (Shumway-Cook et al. 1997), and the **Functional Gait Assessment** (Wrisley et al. 2004) serve for the assessment of function gait, balance and fall risk.

The commonly used **Berg Balance Scale** (Berg et al. 1992) is a multifactorial balance assessment measure. This scale is one of the most frequently used devices for the measurement of balance, but it is made up of a mixture of elements of static and dynamic posturography (Table 1). The Five times sit to stand (Csuka and McCarty 1985) is a functional assessment of balance and strength. The ability of using sensory information for standing balance can be assessed for example by the Clinical Test of Sensory Interaction and Balance (Shumway-Cook and Horak 1986).

**Table 1. Representation of the items of the Berg Balance Scale.**

Table 1 illustrates the items of the Berg Balance Scale (Kim et al. 2017).

<b>Item</b>	<b>Description</b>
B1	Sitting to standing
B2	Standing unsupported
B3	Sitting unsupported
B4	Standing to sitting
B5	Transfers
B6	Standing with eyes closed
B7	Standing with feet together
B8	Reaching forward with outstretched arm
B9	Retrieving object from floor
B10	Turning to look behind
B11	Turning 360°
B12	Placing alternate foot on stool
B13	Standing with one foot in front
B14	Standing on one foot

### **1.2.2. Short summary of the clinical tests of balance**

Although, there are a great number of clinical tests for the detection of postural instability, the disadvantage of these measurements is the lack of objectivity. The most widely used instruments are the Berg Balance Scale, the Push test and the tandem walking. The Berg Balance Scale includes elements of static and dynamic posturography.

### **1.2.3. Quantitative measurement for the study of postural stability**

We have already pointed out that balance is a dynamic, reversible, and quantifiable system. Provocation tests are necessary for the experimental study of balance. Theoretical mechanical models have been developed by the MTA BME Lendület Human Balance research group for the better understanding of the background of the process of balance. New methods have been initiated for example for the interpretation of instability affected by perturbation in standing position. One of their specific methods is balancing a rod on one's finger. The assay of the parameters of the model was a significant assignment. They were trying to define the process responsible for human balance in their study. In this regard, the interpretation of the delayed feedback was an important object (Insperger and Milton 2014, Insperger et al. 2013). Non-linear, analytical, and numeric bifurcation methods have been used and tested for the development of a mechanical model of the process of balance and to identify the possible control mechanism of human balancing.

A main question is whether balancing is based on a delayed feedback mechanism or on a predictor feedback (feedforward control based on an internal model) or a special combination of both. Considering the effect of sensory uncertainties, such as sensory dead zones, implies that pure predictor feedback is not a possible concept but delayed state feedback shall also be involved in some extent.

The elaboration of a physical model of balance has significantly contributed to the understanding of the process of balance. Although, these complex methods are appropriate for research work, the main goal of our study was the detection of the alterations of clinical stability, so the use of a simpler method was necessary.

### **1.2.4. Assessment of postural stability with static and dynamic posturography**

**Posturography** is the measurement of postural sway or postural instability in a quantifiable way (Bartlett et al. 2014, Leach et al. 2014, Di Fabio 1996, Nagymáté et al. 2018, Bronstein and Pavlou 2013). Its sensitivity and diagnostic accuracy can be intensified by different provoked tests (dynamic posturography). With a stabilometric assessment static and dynamic posturography can be more unequivocally differentiated.

The assessment of standing on one foot and standing in different positions on one foot were reviewed by Meszler (Meszler 2015). The precise assessment of balance can be performed by stabilometry where the alterations of plantar pressure are measured on a force plate connected with a computer software (Horváth 2007). When it is quantified it is called posturography (Bartlett et al. 2014, Leach et al. 2014, Di Fabio 1996, Nagymáté et al. 2018, Llorens et al. 2016). The path and the velocity, and the anterior-posterior and lateral sway of the person standing on a platform (a force plate) is measured. In static posturography the person is standing or sitting on a stable platform with the eyes open or closed. In dynamic posturography the person is standing or sitting on an unstable platform where the center of body mass is altered and it is necessary for the person to make compensatory movements to maintain postural equilibrium (Chen et al. 2015, Santos et al. 2010, Bronte-Stuart et al. 2002, Ebersbach et al. 2010). There was an ingenious assessment where the center of body mass was altered by various weights hanging on balloons held by the person (Aruin and Latasch 1995). The Sensory Organization Test (SOT) is a significant instrument in dynamic posturography for the assessment of the integration of visual, proprioceptive, and vestibular components of balance. A score of standing postural balance is provided by the test (Chaudry et al. 2004).

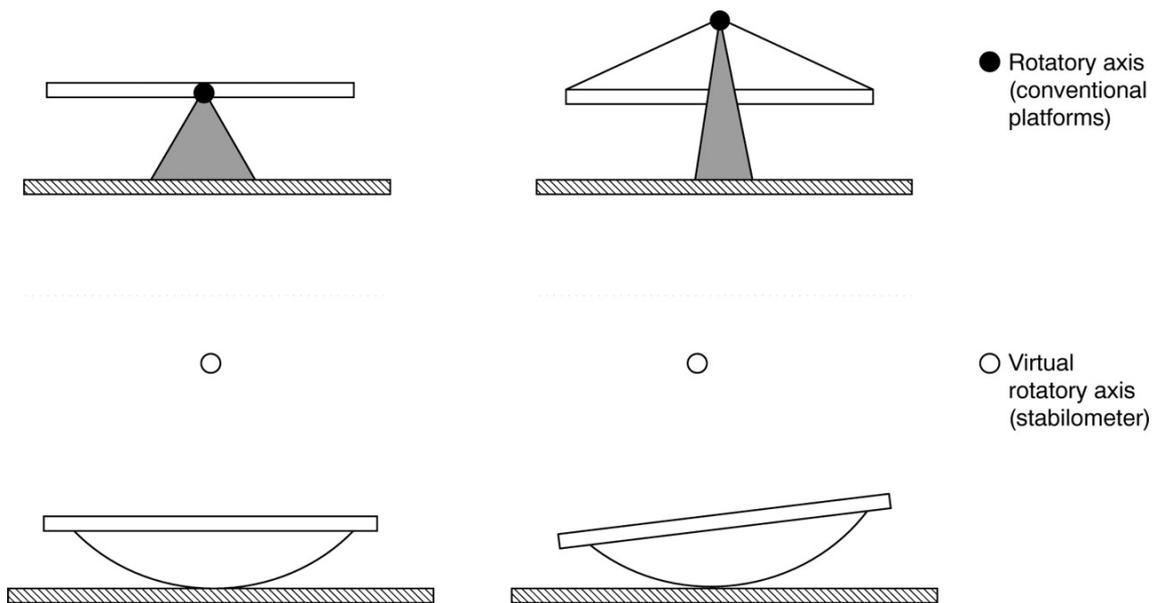
The postural stability control of healthy elderly people and patients with cognitive impairment were compared with the involvement of 36 participants. The control of stability in the sagittal plane was found to be similar between the two groups. Persons with cognitive impairment showed larger lateral oscillations (Cieřlik et al. 2019).

Static posturography is postural measurement with the eyes open or closed. It means the assessment of the ability to maintain balance on a fixed platform, with the eyes open and closed. The three main patterns that can be demonstrated by this method are the weight-bearing asymmetries, the increase of sway path reflecting unsteadiness, and the small limit of stability (Bronstein and Pavlou 2013).

Dynamic posturography means throwing someone's body mass off balance and assessing their compensatory movements on an unstable platform (Ahmed et al. 2017, Bronte-Stewart et al. 2002, Nardone and Schieppati 2006, Lee et al. 2012, Petró et al.

2017). The postural reactions to a translation/rotation of the support surface, visual surroundings, or both are quantified. The postural reflexes and the ability for postural adjustment can be analyzed by this method (Bronstein and Pavlou 2013). A simple device, a hemispheric ball is used for the improvement of balance in the everyday practice (Figure 3). The literature of dynamic posturography was reviewed by Petró et al. (2017).

The maintenance of balance becomes more difficult with divided attention or on an uneven surface, or it may be provoked by various everyday activities, including carrying a heavy suitcase or turning around in a narrow place. The loss of balance control in these specific cases can be predicted by dynamic posturography (Ahmed et al. 2017, Bronte-Stuart et al. 2012, Nardone and Schieppati 2006, Lee et al. 2012).



**Figure 3. Representation of postural instability on an unstable platform using cylindrical curved base.**

Figure 3 illustrates the measurement of postural instability on an unstable platform using cylindrical curved base. The subject needs to adapt posture continuously to keep balance (Müller et al. 1999).

#### **1.2.4.1. Assessment of postural stability with a force plate**

The assessment of balance or postural stability can be completed with a force plate. A force plate is a plain surface for the measurement of plantar pressure or center of foot pressure displacement during a given time period. The force plate can be connected to a computer through Bluetooth and the data of the subject's sway can be analyzed with a special software (Bronstein and Pavlou 2013, Bartlett et al. 2014, Leach et al. 2014, Di Fabio 1996, Llorens et al. 2016, Martinez et al. 2019, Ito et al. 2018, Kodama et al. 2019).

The quantification of balance performance in isolation, or with the use of a virtual reality scene and a force plate was proved to be very reliable in the case of 161 healthy participants (Chiarovano et al. 2015). The assessment of postural stability on the balance board can be combined with a haptic based vibrotactile biofeedback method. The person is warned to make a postural adjustment when the center of body mass is tilted in any direction (Kodama et al. 2019).

#### **1.2.4.2. Dual-tasking in the measurement of instability**

The dual-task concept is frequently applied in the assessment of postural stability in order to create a more challenging situation. In the dual-task condition two tasks need to be performed simultaneously. The primary task is usually a static or dynamic motor task, and there is an additional, a secondary cognitive task. Dual-task performance can have an influence on a balance exercise (e.g., tandem walking or standing on an unstable platform), while simultaneously performing a secondary task (e.g., counting backwards by 3, recounting daily activities). Postural instability is significantly deteriorated by the implementation of a second task (Bronstein and Pavlou 2013). There are a number of possible arrangements for this kind of investigation. As an example, the patients stand on a force plate exposed to balance perturbations and they are simultaneously asked to count backwards in a loud voice or read sentences on a screen in front of them. Any multitask condition can lead to a reduction in the performance of postural control, especially in older adults. Finding the most appropriate dual-task condition for older adults during static postural stability was aimed by a

research group, based on a systematic review and meta-analysis of the abundant literature in this topic (Petrigna et al. 2019).

#### **1.2.5. Short summary of posturography**

Posturography is an assessment-based quantification of balance. In our investigation static and dynamic posturography have been examined. Both of these methods are based on the measurement of plantar pressure standing on a balance board that can be made more difficult by different methods, e.g., standing on an unstable platform, and/or performing different cognitive tasks. Even the milder forms of balance disorder can be detected by these methods.

#### **1.2.6. General concepts of symptoms of balance disorders**

The concept of balance or postural stability refers to the maintenance of upright standing or sitting position against gravity. Balance is most frequently assessed in a standing position. There are various diseases affecting the central and peripheral nervous system that lead to balance impairments, and thereby to falls. Falls can have serious consequences for the individual and the society as well. One of the most frequent complications among individuals in post-stroke state is the risk of falls, and this can be a cause of the decrease in their daily life activities. 25-30% of post-stroke patients suffer from fractures (Cho et al. 2015). 73% of the bone fractures caused by balance impairment happens in the first year after the stroke (Verheyden et al. 2018) and this tendency is increased by age (Ugur et al. 2000, Weerdesteyn et al. 2008). The frequency of falls among post-stroke patients can be reduced with rehabilitation (Tsur and Segal 2010, Batchelor et al. 2010).

Postural instability can be a symptom of many central nervous system disease, or it may appear in healthy individuals due to dividing their attention. It can lead to falls and consequently the quality of life is deteriorated (Bronstein and Pavlou 2013, Kamieniarz et al. 2018). It can lead to falls and their quality of life can be deteriorated. Postural instability correlates with the risk of accidental falls within the population of

older adults, especially in patients with vestibular deficits (Soto-Varela et al. 2019, Siddiqi et al. 2019).

Balance can be disrupted by several illnesses and in these conditions the balance loss is accompanied by different nonspecific symptoms. When the patient's peripheral vestibular system and its connections are affected, subjective symptoms, such as rotational vertigo, dizziness, or light-headedness, and objective symptoms such as are unsteadiness, and gait disorder are reported. These symptoms can lead to a disruption in the performance of everyday activities. These symptoms can be very similar in general medical conditions (e.g., anemia, hypoglycemia, heart disease), neurological gait disorders (e.g., polyneuropathies, cerebellar disorders), and anxiety. Balance disorders can be the consequence of peripheral or common neurological disorders (Bronstein and Pavlou 2013).

#### **1.2.7. Short summary of the symptoms of balance disorders**

Balance disorders can be accompanied by falls, errors in walking, and the appearance of nonspecific symptoms, e.g., a vertigo. They can be peripherally or centrally originated.

### **1.3. Alterations of postural stability in Parkinson's disease, post-stroke state, and ataxia**

#### **1.3.1. Alterations of postural stability in Parkinson's disease**

Progression in Parkinson's disease is non-linear, and its primary symptoms are tremor, bradykinesia, rigor, and postural instability (Marsden 1994, Brown and Marsden 1998). Parkinson's disease is caused by genetic factors (Hariri and Weinberger 2003, Cheeran et al. 2008, Lipsky and Marini 2008, Paul et al. 2016, Davis et al. 2016), and environmental factors (Simon et al. 2015, Moccia et al. 2016). Genetic and environmental factors cannot be separated clearly (Simon et al. 2017). The progression of Parkinson's disease is non-linear and it cannot be effectively influenced by drugs. The age-dependency of the disease has been emphasized in a 9-year follow-up study (Hely et al. 1999). The progression of Parkinson's disease can primarily be affected by

factors, e.g., the gender, a tremor, or the cognitive status (Hely et al. 1999, Evans et al. 2011). All the studies share the opinion that the appearance of non-motor symptoms like postural instability or dementia consequently lead to the deterioration of the disease and the patient's life quality (Bonnet et al. 1987, Hely et al. 1999, Erro et al. 2016).

Postural instability cannot be detected at the onset of Parkinson's disease in Hoehn and Yahr stages 1 and 2. The presence of a clinically valuable balance impairment is a diagnostic criterion in these stages (Hoehn and Yahr 1967). It is Hoehn and Yahr stage 3 when the postural instability can be clinically detected. After the application of the Push test, the patient takes several steps in the direction of the pushing and is not able to compensate within one single step before regaining the normal standing position. In the daily life balance impairment appears in specific situations even when the push test is negative. However, a higher degree of instability detected on an unstable surface compared to age matched healthy controls may confirm the presence of balance disorder in the early stage of Parkinson's disease (Wright 2019).

The quality of life in patients with Parkinson's disease can be significantly worsened along with the appearance of non-motor symptoms (Hely et al. 1999). It is a hallmark of the disease when the postural instability can be detected with clinical examination, namely, when the pull test becomes positive and this is an indication of the Hoehn and Yahr stage 3. According to the present diagnostic criteria, postural instability is an enclosure symptom of the early phase of Parkinson's disease. If postural instability appears in the early stage of the disease, then another problem, multisystem atrophy (MSA) is assumed. A balance deficit in the early stage of the disease is a symptom of Multisystem Atrophy (MS). In later stages (Hoehn and Yahr stages 3 and 4) of Parkinson's disease a postural instability is present and it cannot be influenced by dopa (Minamisawa et al. 2012, Nardone and Schieppati 2006, Ahmed et al. 2017, Contin et al. 1996, Ebersbach and Gunkel 2011, Bronte-Stewart et al. 2002, Lee et al. 2012, Ickenstein et al. 2012, Nonnekes et al. 2013).

It is hypothesized that disequilibrium appears only in specific situations in the early phase of the disease. For example, the maintenance of balance becomes difficult with divided attention or on an uneven surface. Furthermore, postural instability may be provoked by various daily life activities, e.g., carrying a suitcase, turning around in a

small space that can lead to a fall. These incidents may be predicted by dynamic posturography (Ahmed et al. 2017, Bronte-Stewart et al. 2002, Nardone and Schieppati 2006, Lee et al. 2012). It is concurred in the publications that a clinically detectable balance impairment can be assessed proportionately by static and dynamic posturography as well (Minamisawa et al. 2012, Nardone and Schieppati 2006, Ahmed et al. 2017, Contin et al. 1996, Ebersbach et al. 2011, Bronte-Stewart et al. 2002, Lee et al. 2012, Ickenstein et al. 2012, Nonnekes et al. 2013). The results are reviewed by three excellent articles (Rinalduzzi et al. 2015, Kamieniarz et al. 2018, Petró et al. 2017), although their findings concerning Hoehn and Yahr stages 1 and 2 are controversial. Therefore, we focused on the early stage of Parkinson's disease, Hoehn and Yahr stages 1 and 2. The progression of the disease can be detected by the deterioration of balance (Lo et al. 2019).

### **1.3.2. Short summary of postural instability in Parkinson's disease**

Postural instability cannot be detected by a clinical assessment at the onset of the disease in the stages of 1 and 2 of the Hoehn and Yahr Scale. The appearance of the balance disorder in stage 3 of the Hoehn and Yahr Scale is the sign of the serious deterioration of the disease. As it cannot be influenced by medication the quality of life is significantly worsened by it.

### **1.3.3. Alterations of postural stability in post-stroke state**

According to the data of the World Health Organization, approximately 25.7 million people suffered from stroke in 2013 (Hugues et al. 2019). Stroke is the primary cause of the decrease in the quality of life all over the world (Kubis 2016). Mental, locomotor, and coordination disorders can appear in the patients as a consequence of acute cerebrovascular accidents, and the risk of falls during standing or walking is significantly increased by these problems (Kubis 2016, Lee and Jung 2017). The decrease of the muscle strength and the coordination of the trunk frequently lead to balance impairments. An acute ischemic stroke can lead to a severe hemiparesis which is the cause of postural instability preventing the person even from maintaining a sitting upright posture (Andriuta et al. 2013). After a stroke event the enhancement of the

upright posture even in a sitting position is an indication of the improvement (Sorrentino et al. 2018). According to a study involving 203 post-stroke patients, the primary cause of functional deficits worsening the quality of life was the limitation of the mobility (Nordin et al. 2016). The examination of the ability of the trunk to maintain equilibrium was a good predictor of postural impairment (Duarte et al. 2002). On the basis of this hypothesis the Selective Trunk Exercise was applied in the case of 29 patients, and this program had a positive influence on their mobility and balance (An and Park 2017). The importance of the trunk stabilizing training has also been reinforced by a Hungarian and an international research team. Balance could be improved by trunk movements exercises completed for several weeks (Preszlerne and Nagy 2006, Hsu et al. 2018), and the postural instability of younger and older women was enhanced by computer games (Tihanyiiné et al. 2004).

Post-stroke patients have difficulties in standing upright position due to their uncoordinated leg movements, and the decreased use of their paretic leg. The shifts in their center of pressure were assessed by a three-dimensional motion capture system, and the deviation in the use of their lower limbs was assessed separately by two stabilometers (Wang et al. 2017). In another study 71 patients with ischemic stroke were examined. The patients were in subacute state, and less than three months following the stroke event. The asymmetry of weight distribution and the postural sway significantly increased in post-stroke state. Advanced age and impaired postural control significantly increased the risk of falls in post-stroke state (Lee and Jung 2017, Marigold et al. 2004). The oscillation was significantly higher according to the clinical severity of the patients. Although, the postural instability correlates with the velocity of the sway detected by posturography, the increased sway did not correlate with the weight bearing asymmetry in post-stroke state (Kamphuis et al. 2013). A strong correlation was detected between the dynamic vertical measurement and the static posturography with closed eyes in patients with post-stroke. A correlation of the amplitude, mean displacement, trajectory and speed measured with static and dynamic posturography has been found (Baggio et al. 2016).

Sensory training of the lower limb of post-stroke patients proved to be efficient. This result was reinforced by stabilometric assessments as well (Goliwas et al. 2015). In post-stroke the weight bearing asymmetry can be detected by two stabilometers. The

weight of the body mass can be separately distributed between the two stabilometers which may allow to detect the changes of improvement on the affected paretic limb during the training process (Genthon et al. 2008, Volovets et al. 2018). These measurements could be used for follow-up in rehabilitation. Evaluating the characteristics of post-stroke patients, the risk factors leading to falls, and the location of the lesion associated with the falls were investigated. The postural instability is influenced by different factors like gender, time of day, blood pressure, or metabolic state (Tsur and Segal 2010). Based on the evaluation of 293 post-stroke patients it was stressed that the postural instability was worsened by advanced age, and/or depression (Ugur et al. 2000). The danger of falls was maintained even after one month (Tsur and Segal 2010). The impairment of postural control was increased by cognitive deficits associated with stroke. The investigation of postural control and attention during standing and walking showed that the examination and development of these two factors are important not only among the individuals with postural instability but also among the old healthy persons (Wollacott and Shumway-Cook 2002).

The efficiency of the various treatments for the falls in post-stroke state was reviewed, based on the publications of this topic in a meta-analysis. The applied interventions in the reviewed studies included physical activity training, e.g., balance training, physical exercise, strength exercise; modifying the environment or enhancing knowledge; post-stroke care models, e.g., home care and standard rehabilitation; and medication, e.g., vitamin D supplementation for improving bone density (Batchelor et al. 2010). Consequently, rehabilitation plays a very important part in the maintenance of these persons' autonomy and quality of life. According to a meta-analysis of 145 studies and 5912 post-stroke participants, the functional task-training associated with musculoskeletal intervention, cardiopulmonary intervention, and sensory interventions were found to be effective in the improvement of balance and postural stability. Moreover, the superiority of treadmill training over the traditional rehabilitation was confirmed (Mustafaoğlu et al. 2018). The importance of biofeedback was stressed by Tsaih et al. (2018).

#### **1.3.4. Short summary of postural instability in post-stroke state**

There is a relatively small number of publications dealing with the appropriate measurement of postural instability, including posturography in post-stroke state. Postural instability is a complex symptom and it may arise from the weakness of the paretic leg, sensory impairments, or weight bearing asymmetry. However, when all of these have been improved, the postural instability may further be present. I demonstrated this problem in my PhD work.

#### **1.3.5. Alterations of postural stability in the various types of ataxias**

Ataxia can be caused by various diseases. Ataxia, or insecure gait can appear as a consequence of deep sensory impairment, or a central nervous system disease (Ashizawa and Xia 2016). The diseases of the peripheral nervous system can lead to sensory and motor polyneuropathy caused by several problems. Ataxia is one of the main symptoms that can appear (Jordan et al. 2012). The lesion of the spinal cord due to a metabolic cause such as the lack of B<sub>12</sub> can lead to spinal ataxia. In these cases, the lesion of the posterior fasciculus of Goll and Burdach tract can be seen. An atrophy of the spinal marrow generated by spinal stenosis causes a myelopathy where the symptom of spinal ataxia appears. In the central nervous system, the lesion or atrophy of the cerebellum is the most frequent underlying reason of ataxias.

There is a wide scale of cerebellar symptoms. Cerebellar lesions appearing for various underlying reasons can lead to ataxia which is characterized by uncoordinated movements associated with balance, posture, and eye movement deficits, and dysarthria (Schmahmann 2004). Ataxia is an impaired coordination of voluntary muscle movements. It can be a symptom of various disease processes, so the underlying etiology needs to be investigated together with the associated symptoms suggesting an underlying cause. Ataxia is most frequently caused by a cerebellar dysfunction or an impaired vestibular or proprioceptive afferent input to the cerebellum. Ataxia can have insidious, acute, or subacute onset. Its symptoms and signs can often be related to the location of the lesions in the cerebellum. Clinically it can be observed as the impairment of stance, gait ataxia, sensory ataxia, trunk ataxia, limb ataxia, dysdiadochokinesia/dysrhythmia kinesis, intention tremor, dysmetria,

dysarthria/scanning speech, nystagmus, saccades, or square-wave jerks/ocular flutter/opsoclonus. Usually the cerebellum and its afferent and efferent connections, and the proprioceptive sensory pathways are involved. Ataxias can be differentiated according to the age of onset (the specific types of ataxias appear at different ages), the tempo of onset (acute, subacute or chronic onset), and the clinical course (benign or sporadic, etc.). The associated symptoms can be clues to determine the underlying etiology. The symptoms of ataxias include impaired consciousness, visual impairments, trouble speaking and swallowing, focal sensory loss or weakness, vertigo, slow or abnormal movements, cognitive deficits, behavior changes, facial droop, diplopia, pupillary defects, tongue deviation, dysarthria, and dysphonia (Ashizawa and Xia 2016).

The symptoms of ataxia can hardly be improved by physiotherapy. Acute ischemic lesion of the cerebellum leading to ataxia was followed with stabilometer in twenty-three patients (Bultmann et al. 2014). Although in the case of the more serious infarcts the neurological symptoms could not be improved by treadmill training, there was a great improvement in the milder ataxias. The cerebellum and its connected pathways are usually affected in sclerosis multiplex. 381 patients were examined and compared with posturography. Those patients who only had a lesion of the pyramid path demonstrated greater improvement following physiotherapy than the patients with lesion of the cerebellum (Kalron et al. 2016). Children were also followed-up with posturography. The functional investigation was connected with MRI Diffusion Tensor Imaging methods of examination. The children participated in an antigravity treadmill training for 45 minutes 3 times a week for two months. The children's improvement of postural stability was objectively demonstrated by posturography (Sullivan et al. 2019, Schmahmann 2004, Bultmann et al. 2014).

The postural stability of twenty-one patients with spinal deformity and suffering a cervical laminectomy was assessed by posturography. Their balance impairment was indicated by a higher oscillation when standing on a force plate with the eyes closed (Tanishima et al. 2017).

In spinal ataxia the postural instability was more intense with the eyes closed, assessed by posturography on a stabilometer (Tanishima et al. 2017). Trunk ataxia is

caused by cerebellar lesion and it can be measured with an accelerometer placed over the chest. According to a study involving 20 ataxic and 20 healthy individuals, different components of postural control are affected depending on the different sensations of the trunk position (Kilinç et al. 2019). The trunk sway of 100 healthy adults was assessed with a chest-worn accelerometer in 12 quiet standing tasks and the results showed that this can be a useful alternative method for posturography using force platforms (Reynard et al. 2019).

#### **1.3.6. Short summary of postural instability in the ataxias**

Each of the different types of ataxias generates a serious postural instability causing an insecure gait. The functioning of the upper and lower limbs in the everyday life are significantly reduced because of the target ataxia and the intentional tremor. Ataxia can be caused by peripheral or central problems.

## 2. Goal of the PhD thesis

A significant deterioration of daily life is caused by the postural instability. From the onset of the balance disturbance the quality of life is harmed and the life expectation is shorter. It is very important to measure it with an objective method. This method is the posturography. Postural instability of patients with central nervous diseases were measured with static and dynamic posturography. These data were analyzed and discussed in my PhD.

The goals of this PhD thesis were the following:

1. We would like to introduce this simple, objective method into the daily routine in the field of neurology and rehabilitation. Each patients and control persons were measured by static and dynamic posturography.

Dynamic posturography is a sensitive method for the assessment of balance disorder. It requires a complicated and expensive apparatus. We introduced a simple method, which is handy to use for ambulatory measurements. It is cheap and comfortable. Our method is based on passing various weights around the body which moves the center of the body mass and the individual is forced to perform a permanent postural adjustment or correction. We analyzed if there is a correlation between the weight charge and the caused postural disturbances.

2. We intended to examine this phenomenon in an early stage of Parkinson's disease when postural instability cannot be detected in a clinical way (push test). We wondered to know if postural instability can be demonstrated by dynamic posturography. This could give information on the involvement of various pathway systems in the early stage of Parkinson's disease.

3. Parkinson's disease is a progressive degenerative disease where the appearance of postural instability is a hallmark of the non-motor symptoms of the disease. When it can be clinically detected, there is a significant deterioration in the quality of life. That is why we followed the involved individuals.

4. Dyskinesia is a side effect of levodopa therapy. The quality of life is deteriorated by dyskinesia at least as much as bradykinesia. We studied the dyskinesia among patients

with Parkinson's disease at its appearance and we examined whether its appearance can be predicted by the means of provocation.

5. It is well known that cerebellar and spinal ataxia leads to a balance disorder. In our research we wanted to find out which interventions lead to the increase of spinal and cerebellar ataxia. This examination can be a diagnostic aid for practicing neurologists.

6. The brain networks are influenced widely by stroke. The motor system and the cognitive system can be generally affected and this can lead to postural instability. In our work, we wanted to determine whether the balance disturbances persist for years in spite of the improvements of the muscle strength and the weight bearing asymmetry.

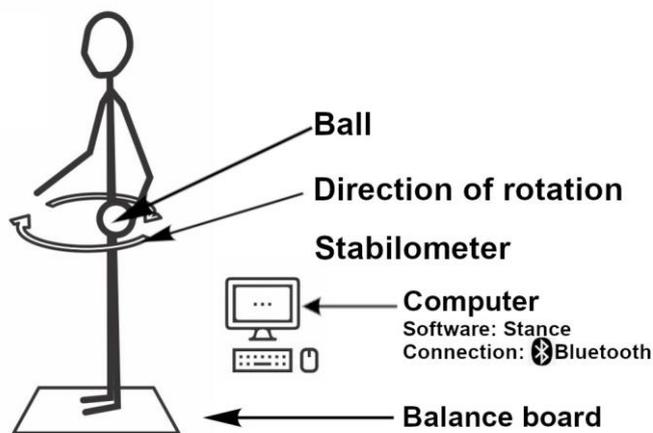
7. We compared our patients with age matched healthy controls to study the age dependency of postural instability. We wanted to differentiate between the features depending on age and disease.

8. Finally, we made theoretical and practical conclusions.

### 3. Method

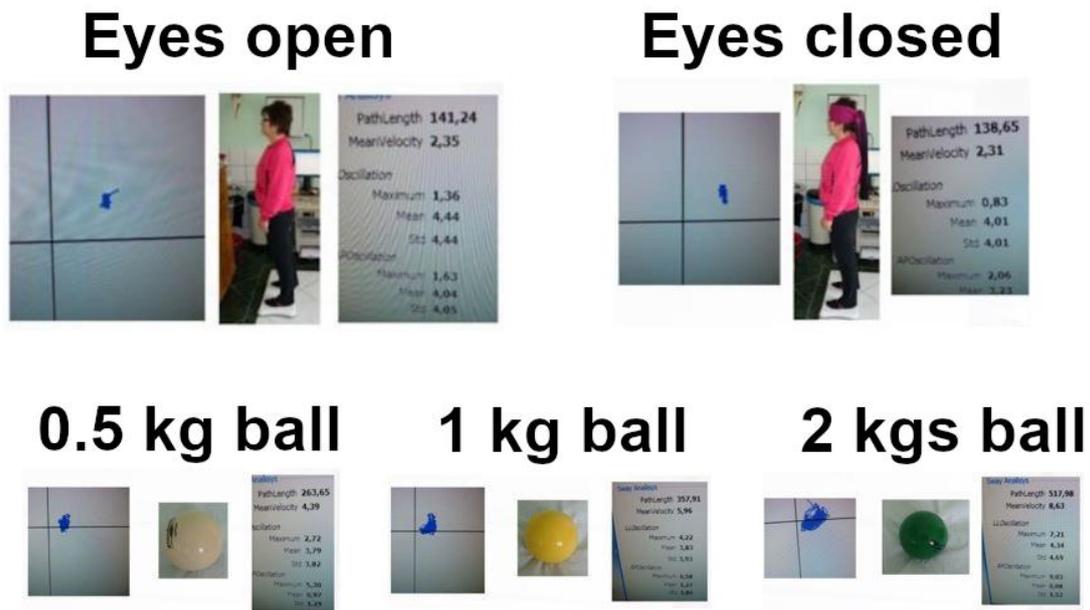
#### 3.1. Applied methods: static and dynamic posturography

In our study, patients were examined by pull test and posturography. Subjects were examined standing in an upright position with both legs on a force plate for one minute while their foot pressure was detected. The force plate was connected to a computer through Bluetooth. We used a Nintendo Wii balance board (Bartlett et al. 2014, Leach et al. 2014, Di Fabio 1996, Llorens et al. 2016). The sway of subjects was analyzed with the Stance program. The pathway, the velocity, the amplitude of latero-lateral and antero-posterior sway were measured and the data were processed. Subjects stood with the eyes open, and then with the eyes closed for one minute (static posturography). The patients were asked to turn balls with different weights (half kilogram, one kilogram, two kilograms) around their body. The center of the body mass was tilted by the balls and the patients had to adjust continuously (postural adjustment) (Figure 4, Figure 5).



**Figure 4. Our method of dynamic posturography.**

Figure 4 shows our method of dynamic posturography. The center of the body mass is continuously changing due to the weight of the balls turned around the body. The data of plantar pressure are registered by a computer program connected to a force plate via Bluetooth.



**Figure 5. Representation of our method of static and dynamic posturography.**

Figure 5 shows our method of static posturography and its results with the eyes open (left side above), our method of static posturography and its results with the eyes closed (right side above), and our method of dynamic posturography with the use of a ball of ½ kg (left side below), 1 kg (below in the middle), and 2 kgs (right side below).

### **Other methods**

A number of questionnaires were administered to the participants, but their results are not discussed in my PhD thesis. The Unified Disability Rating Scale (UPDRS, Fahn and Elton 1987); cognitive tests, including the Trail Making Test (Reitan 1992); several dual tasks; the Mini Mental Rating Scale (Folstein et al. 1975) were administered to the patients with Parkinson’s disease. The National Institute of Health Scale (NIHSS), and the Functional Independence Measure (FIM) were administered to the patients with stroke. Ataxias were not measured with clinical questionnaires.

## 3.2. Participants

### 3.2.1. Participants with Parkinson's disease

The Regional Ethical Research Committee of Petz Aladár County Hospital in Győr has provided permission for the present trial. According to the Helsinki Declaration, a written informed consent was given by all of the participants involved in the study. Patients and normal controls were recruited from 2016 to 2019 in the Neuro Rehabilitation in Sopron, who visited the Institute due to rehabilitation. The inclusion criteria were the following: Parkinson's disease responded well to levodopa. Persons with slight hypertonia under drug treatment were involved. Exclusion criteria were dementia, and any other chronic disease. Forty-five patients with Parkinson's disease were involved in the present study. They were divided into two groups according to their age, below and above 65 years. Demographic data are presented in Table 2. Patients with Parkinson's disease in their Hoehn and Yahr stages 1 and 2 (Hoehn and Yahr 1967) whose pull test was negative were enrolled in the study. They did not have clinically measured postural instability. Posturography was assessed under the influence of drugs. Patients took levodopa and entacapone, and they did not take dopa agonists. We had a separate group with dyskinesia (N=18). Table 3 shows the demographic data of patients with dyskinesia. Patients with dyskinesia took a higher dose of levodopa than patients without it (Parkinson's disease  $\leq$  65 years:  $298.14 \pm 182.12$  mg/d Parkinson's disease with dyskinesia:  $481.81 \pm 194.00$  p < 0.01, Parkinson's disease > 65 years:  $280.55 \pm 191.84$  mg/d, Parkinson's disease with dyskinesia:  $521.42 \pm 152.36$  mg/d p < 0.01).

**Table 2. Demographic data of the patients with Parkinson's disease.**

Table 2 shows the demographic data of the 45 patients with Parkinson's disease participating in our examination divided into two groups according to their age (under and above 65 years). There was no significant difference between the two groups in the duration of the disease, the level of Hoehn and Yahr stage, and the dose of Levodopa.

<b>Demographic data of patients with Parkinson's disease</b>		
	<b>≤ 65 years</b>	<b>&gt; 65 years</b>
<b>Number</b>	27	18
<b>Age in years</b>	57.18 ± 6.96	73.6 ± 5.3
<b>Female/Male</b>	14/13	11/7
<b>Tremor/Akinesia</b>	10/17	11/7
<b>Duration of the disease</b>	6.07 ± 3.14	5.5 ± 4.0
<b>Hoehn and Yahr stage</b>	1.57 ± 0.53	1.88 ± 0.58
<b>Dopa dose mg/d</b>	298.15 ± 182.12	297.37 ± 200.33

**Table 3. Demographic data of the patients with Parkinson's disease with dyskinesia.**

Table 3 shows the demographic data of the 18 patients with Parkinson's disease with dyskinesia divided into two groups (under and above 65 years). There was no significant difference between the two groups in the duration of the disease, the level of Hoehn and Yahr stage, and the dose of Levodopa.

<b>Demographic data of Parkinson's disease patients with dyskinesia</b>		
	<b>≤ 65 years</b>	<b>&gt; 65 years</b>
<b>Number</b>	11	7
<b>Age in years</b>	58 ± 8	70 ± 4
<b>Female/Male</b>	6/5	5/2
<b>Tremor/Akinesia</b>	4/7	2/5
<b>Duration of the disease</b>	8.3 ± 2.9	11.3 ± 4.9
<b>Hoehn and Yahr stage</b>	2.1 ± 0.73	2.1 ± 0.4

<b>Dopa dose mg/d</b>	470 ± 200	475 ± 98
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### 3.2.2. Participants with post-stroke

Stroke has become an endemic by now and its prevalence has been increasing every year, therefore significant conclusions can be drawn from the results of the experiments conducted with the participation of an appropriately selected group of patients, and these conclusions can be applied in the case of a large number of patients.

It has been observed that the patients have been afraid to leave their home because of the balance disorder even if they have only a very few symptoms of the paresis, therefore we concluded that the investigation of post-stroke state was very important. The demographic data of this group of patients is demonstrated in Table 4.

**Table 4. Demographic data of the participants in post-stroke state.**

Table 4 shows the demographic data of the 29 participants of our examination in post-stroke state (with one stroke event) divided into age groups (under and above 65 years). The occurrence of hemorrhage in the age group under 65 years was twice the age group above 65 years. The number of infarcts had the highest value in both groups. There was no significant difference in the duration of the disease between the two groups.

<b>Demographic data</b>		
	<b>≤ 65 years</b>	<b>&gt; 65 years</b>
Number	15	14
Age in years	54 ± 11	71 ± 3.5
M/F	10;5	9;5
Infarct	9	11
Hemorrhage	6	3
Duration after stroke	3 ± 2.4	4.7 ± 3.3

### **3.2.3. Participants with ataxia**

Although, posturography was introduced into the measurement of ataxias, the possibilities of static and dynamic posturography are not discovered fully. I involved patients with different types of ataxia into my PhD. Their trunk ataxia was measured by static and dynamic posturography.

The occurrence of spinal and cerebellar ataxias is less frequent than in the other central nervous system diseases (Parkinson's disease and post-stroke) discussed in our PhD thesis, therefore we described them by indicating the distinct diagnoses. The distinction of the individual cases was necessary due to the heterogeneity of the different diseases. Spinal ataxia is dominated by the lesion of the cervical spinal cord where the lack of vitamin B12 is the cause of the spinal ataxia. A brain injury caused by inflammation, hemorrhage, or traffic accident were among the causes leading to cerebellar symptoms (Table 5).

**Table 5. Demographic data of patients with spinal and cerebellar ataxia.**

Table 5 shows the demographic data of the patients with ataxia. This table includes the data of 5 patients with spinal ataxia, and 6 patients with cerebellar ataxia. The diagnosis leading to the ataxia in the case of each patients is provided. The duration of the disease was 2-18 years. Most of the patients belonged to the younger age group.

<b>Demographic data</b>				
<b>Spinal ataxia</b>				
<b>Name</b>	<b>Gender</b>	<b>Age (years)</b>	<b>Diagnosis</b>	<b>Duration (years)</b>
T.A.	Female	42	Avitaminosis of vitamin B12	7
Z.É.	Female	64	Stenosis canalis spinalis cervicalis	4
H.I.	Female	56	Syringomyelia	23
S.B.	Male	62	Discuss hernia C5	6
H.B.	Male	79	Discuss hernia C3, C6	10
<b>Cerebellar ataxia</b>				
M.G.	Male	26	Haemorrhagia subarachnoidalis, traffic accident	2
K.A.	Male	54	Cerebellar infarct	18
J.B.	Female	30	Haemorrhagia subarachnoidalis, traffic accident	4
L.K.	Male	35	Meningoencephalitis recovered in 2013	2
C.E.	Female	63	Paraneoplastic syndrome	2
H.I.	Female	42	SM	13

### 3.2.4. Age-matched healthy control persons

Thirty-five age-matched healthy controls were involved in the present study. They were divided into two groups according to their age, below and above 65 years. Demographic data are presented in Table 6.

**Table 6. Demographic data of age-matched healthy control persons under and above 65 years.**

Table 6 shows the demographic data of the age-matched healthy controls under and above 65 years.

<b>Demographic data of controls</b>		
	$\leq 65$ years	$> 65$ years
Number	22	16
Age in years	$56.8 \pm 6.9$	$69.0 \pm 3.8$
Female/Male	11 / 11	6 / 10

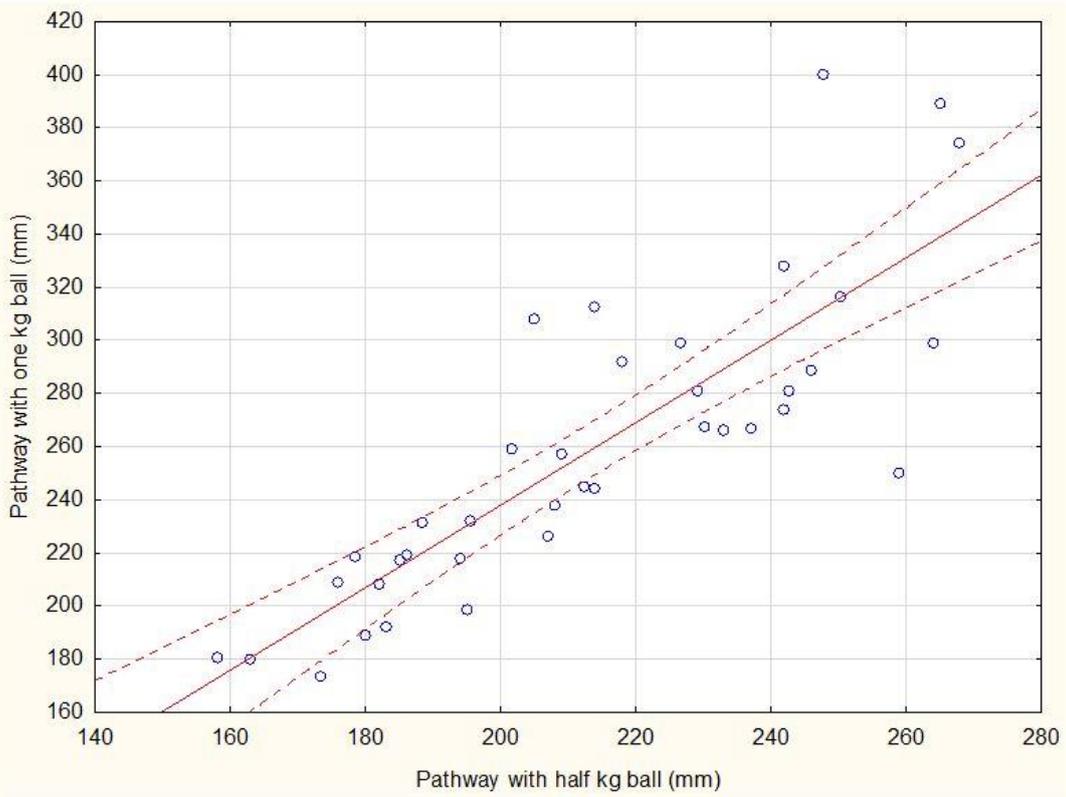
### 3.3. Statistical analysis

Results are expressed as the mean  $\pm$  standard deviation of mean (S.D.) and sample size (N) for each treatment group. The normality of data was checked by applying the Shapiro-Wilk's test. When non-normal data could not be rejected, homogeneity of variances was assessed through the Levene's test. Groups means were compared by parametric one-way ANOVA test. The linear correlation (Pearson r-values) analysis was made to show the effect of the ball characteristics with the scatter plot diagram. The Fisher r-to-z transformation was applied to assess the significance of the difference between the two correlation coefficients. The analysis was two-sided or one-sided, with a level of significance of  $\alpha = 0.05$ . All statistical analyses were done using the SAS 9.4 (SAS Institute Inc., Cary, NC, USA.) software package.

## **4. Results**

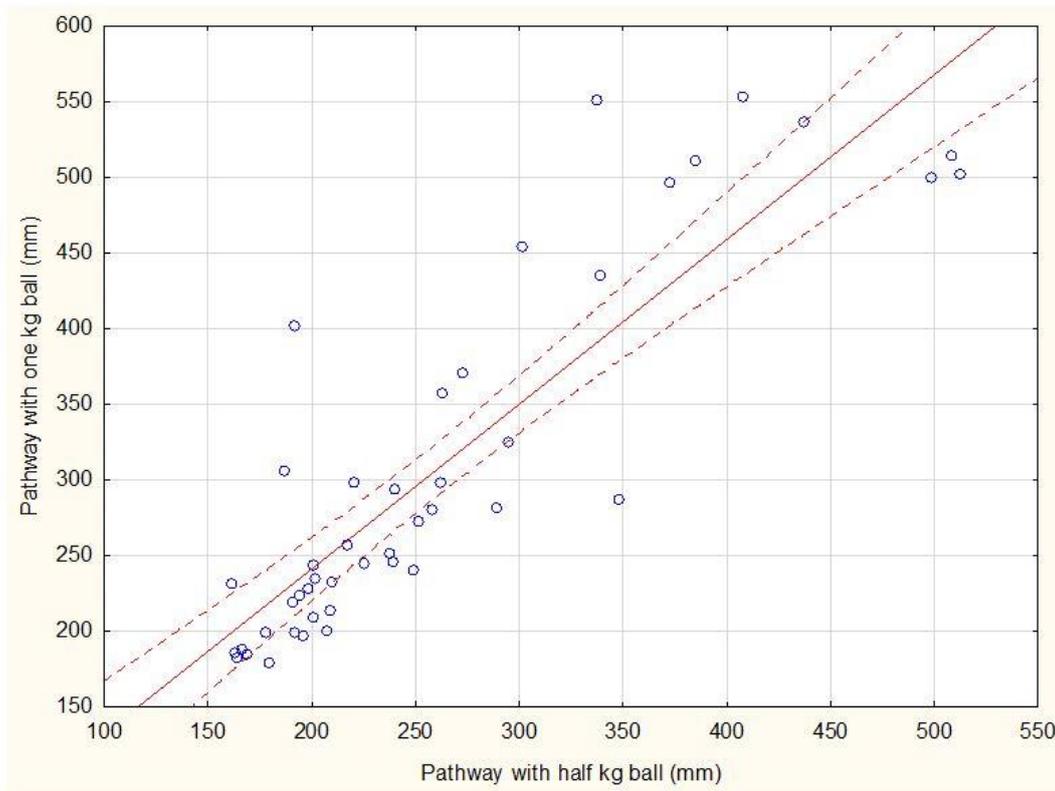
### **4.1. Correlation of balls and pathway assessed by dynamic posturography**

A new method of dynamic posturography was applied in our present study. It is necessary to analyze whether the weight loading proportionally changes the postural instability. There was a high correlation between the weights of the balls and the provoked imbalance. The correlation coefficient was high between half kg and 1 kg ( $r=0.837$   $p < 0.001$ ) (Figure 6) in the control group, and between 1 kg and 2 kgs ( $r=0.826$ ,  $p < 0.001$ ) (Figure 7) in the group of patients with Parkinson's disease. The imbalance was demonstrated in the change of the pathway. It means that the loading with weights passed around the body is an appropriate provoked test for postural instability since the provoked imbalance and the weights were highly correlated.



**Figure 6. Dynamic posturography assessed by a half kg and one kg ball turning around the body, in the group of the control persons.**

Figure 6 shows that the dynamic posturography assessed by a half kg and one kg ball turning around the body. The pathway of tilting was detected by a stabilometer for one minute. The correlation was high ( $r = 0.837$   $p < 0.001$ ) between the two different weights in control persons ( $N = 38$ ). It means that the increased loading proportionally increased the postural instability.



**Figure 7. Dynamic posturography assessed by different weights of balls, in the group of patients with Parkinson’s disease.**

Figure 7 illustrates the pathway of tilting for one minute assessed by a stabilometer. There was a high correlation between the weight loading and the postural instability ( $r = 0.826$   $p < 0.001$ ) in patients with Parkinson’s disease ( $N = 45$ ) in Hoehn and Yahr stages 1 and 2. According to the comparison of correlation coefficients, the patients with Parkinson’s disease showed a higher sensitivity to elevating and turning the weights. The elevation was higher than in the control group.

## **4.2. Limit of the method**

The use of dynamic posturography is restricted in post-stroke state. If the patient with stroke cannot stand in upright position or cannot catch a ball, he or she is unable to take part in this process.

In severe cases of dyskinesia or trunk ataxia the difficulty is that the persons cannot maintain their upright position.

## **4.3. Short summary of our new method**

Our method of passing balls induces changes in the subjects' normal posture, requiring active postural adjustments. The plantar pressure was altered by the balls, and postural adjustment was needed to regain the upright position. The method was adopted from that introduced by Halmi et al. (2019). The weights of the balls highly correlated ( $r = 0.83$ ) with the pathway and velocity measurements being directly proportional to the ball weights. The obtained values were repeatable and reproducible. The simplicity of this method makes it applicable for the daily use.

## **4.4. Results of Parkinson's disease patients compared with age matched healthy controls**

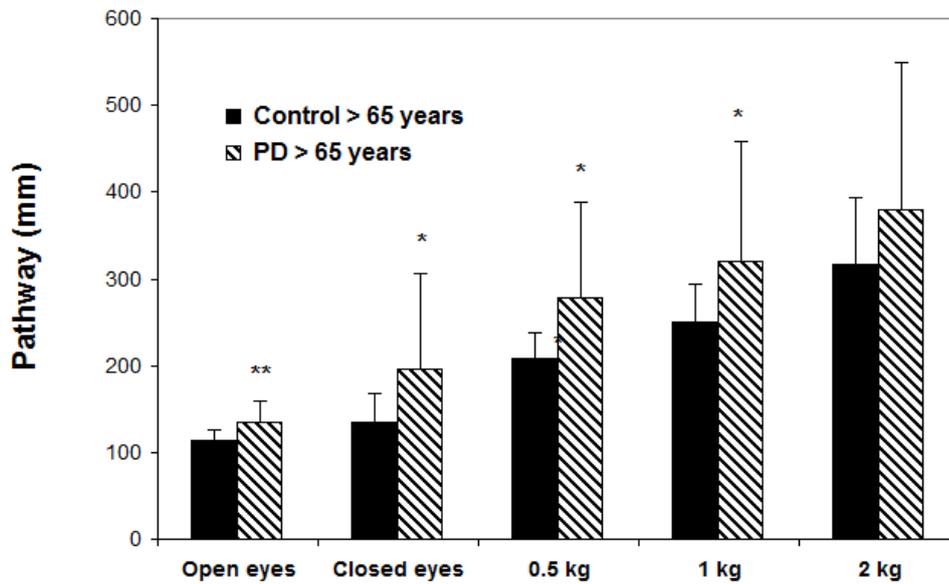
Our comparative study was based on the evaluation of the pathway, the velocity of tilting and the amplitudes of sway in the antero-posterior and latero-lateral directions in stance upright position on a force plate. The velocity and the pathway of the patients (N=27) under 65 years were congruent with the age-matched healthy controls (N=22). However, a significant difference was observed in the amplitude of the oscillations during dynamic posturography (Table 7).

**Table 7. Oscillation of patients with Parkinson’s disease compared with controls during dynamic posturography.**

Table 7 shows that the oscillation in the antero-posterior direction in Parkinson’s disease was significantly higher than in the age matched healthy controls, but the oscillation of latero-lateralis did not change, except in the cases loaded with half kg (\* =  $p < 0.05$ ).

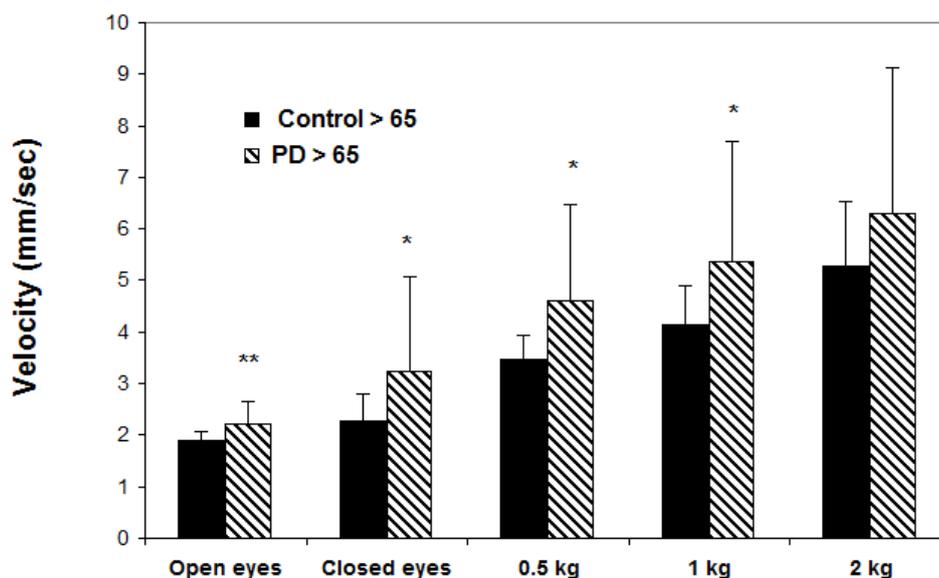
<b>≤ 65 years</b>				
	<b>Control</b>		<b>Parkinson’s disease</b>	
Number	22		27	
	Antero-posterior (mm)	Latero-lateralis (mm)	Antero-posterior (mm)	Latero-lateralis (mm)
½ kg	-0.14 ± 1.7	4.92 ± 0.97	0.97 ± 1.45*	3.98 ± 1.39*
1 kg	-0.12 ± 1.64	4.97 ± 1.09	0.89 ± 1.37*	4.13 ± 1.4
2 kgs	-0.18 ± 1.54	4.91 ± 1.24	0.80 ± 1.54*	4.14 ± 1.37

Values of the pathway (Figure 8) and the velocity (Figure 9) of the patients over 65 years were significantly higher in static and dynamic posturography than those of the age-matched healthy controls. They showed a greater sensitivity to the dynamic posturography compared to the younger group. The values of the pathway and the velocity of the patients with Parkinson’s disease followed for two years demonstrated no change.



**Figure 8. Static and dynamic posturography in patients with Parkinson’s disease >65 years compared with age-matched healthy controls.**

Figure 8 shows the static and dynamic posturography in patients with Parkinson’s disease > 65 years (Hoehn and Yahr stages 1 and 2) (N = 18) compared with age-matched healthy controls (N = 16). Postural instability of patients over 65 years assessed by static and dynamic posturography was significantly higher than that of the control persons. Columns represent the mean  $\pm$  SD, \* =  $p < 0.05$ , \*\* =  $p < 0.01$ .

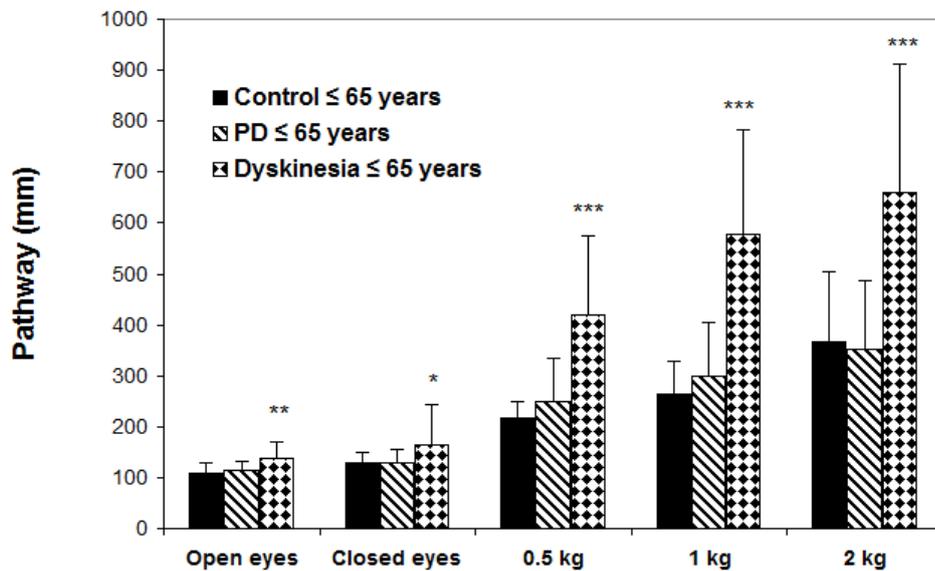


**Figure 9. The velocity of static and dynamic posturography was assessed in patients > 65 years with Parkinson’s disease in Hoehn and Yahr stages 1 and 2.**

Figure 9 represents the velocity of static and dynamic posturography that was assessed in patients > 65 years with Parkinson’s disease Hoehn and Yahr stages 1 and 2. Both kinds of posturography showed a significantly higher velocity in patients compared to age-matched healthy controls. The columns represent mean  $\pm$  SD, \* =  $p < 0.05$ , \*\* =  $p < 0.01$ .

Although, the patients under 65 years did not show any difference from the controls in the respect of static posturography, namely, with the eyes open and closed, the patients above 65 years showed a significant elevation in the pathway and velocity in static posturography ( $p < 0.05$ ,  $p < 0.001$ ). Further examined our patients with dynamic posturography the elevation was significant in the pathway and the velocity with a weight of half kg and one kg in the age group of the persons above 65 years ( $p < 0.05$ ) (Figure 8 and Figure 9). However, we found no significant differences in the age group above 65 years with a weight of 2 kgs. Albeit, the SD was very high in the group of patients with Parkinson’s disease. These results indicate the existence of a significant age-dependent difference in the age groups of the patients with Parkinson’s disease under 65 years and above 65 years, assessed by posturography.

Those patients with dyskinesia had a high standard deviation reflecting the fluctuating state of their dyskinesia. This group of patients showed significantly higher postural instability with static and dynamic posturography than patients without it. Patients with dyskinesia in both groups represented a much higher increment in postural instability during the dynamic posturography than patients without dyskinesia (Figure 10).



**Figure 10. Pathway of patients with Parkinson’s disease ≤ 65 years with and without dyskinesia.**

Figure 10 shows the pathway of patients with Parkinson’s disease ≤ 65 years with (N = 11) and without dyskinesia (N = 27). The pathway was assessed by static and dynamic posturography in patients ≤ 65 years. They were compared with age-matched healthy controls (N = 22). The dynamic posturography highly significantly increased the postural instability in patients with dyskinesia. Columns show the mean ± SD, \* =  $p < 0.05$ , \*\* =  $p < 0.01$ , \*\*\* =  $p < 0.001$ .

During the assessment of static posturography a postural instability was present in the case of patients with dyskinesia even in the age group under 65 years, while the

patients with Parkinson's disease in the age group under 65 years showed no significant difference with the eyes open or closed, compared to the control persons. The pathway of the assessment with posturography in the group of patients with dyskinesia under the age of 65 years showed a difference of a significance of  $p < 0.001$  in the case of the eyes open and  $p < 0.05$  in the case of the eyes closed. The increase of the pathway during one minute was the most highly visible during the dynamic posturography where the level of significance was  $p < 0.001$ . Despite the high level of variance due to the extensive individual differences the pathway was growing dramatically in the different ball tests (half kg, one kg, 2 kgs), although the distinction among the different weights was maintained. The state of dyskinesia developed by the administration of levodopa deteriorates the quality of life to a higher extent than Parkinson's disease because the evolving serious balance disorder can lead to falls (Figure 10) (Halmi et al. 2019).

#### **4.4.1. Short summary of the results of Parkinson's disease**

Patients ( $\leq 65$  years) with Parkinson's disease in their early phase of the disease (Hoehn and Yahr stages 1 and 2) did not show any difference from the age matched healthy controls assessed by static posturography. However, a highly significant difference was detected by dynamic posturography between the two groups. There was a strong age-dependency in the changes. Patients above 65 years presented a highly significant elevation in the pathway and velocity assessed by both static and dynamic posturography. The patients with dyskinesia had extremely elevated pathway and velocity with dynamic posturography.

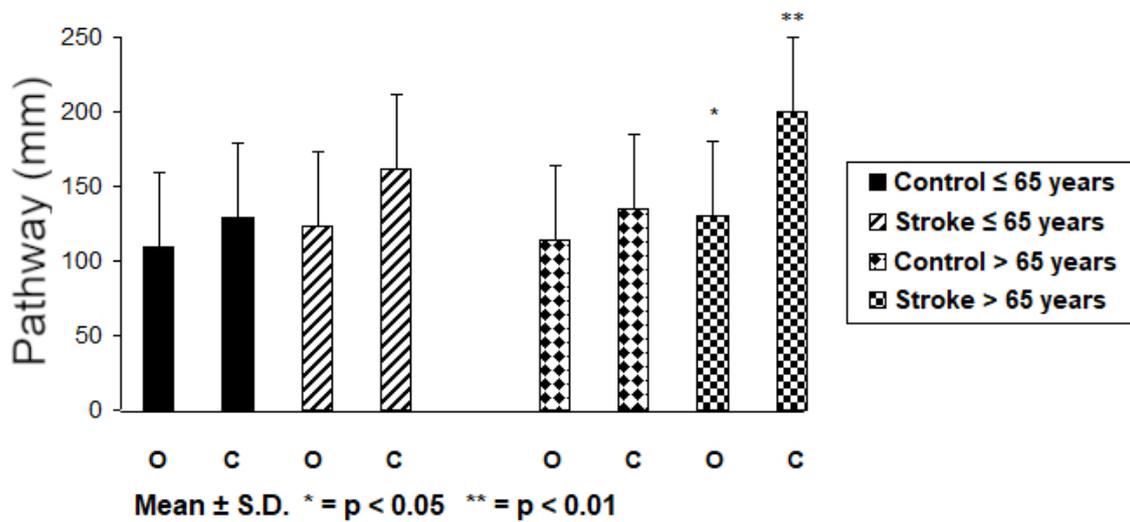
#### **4.5. Results of post-stroke patients compared with aged-matched healthy controls**

Patients were recruited from 2016 to 2019 in the Neuro Rehabilitation Institute of Sopron. They visited the Institute for rehabilitation. Our inclusion criteria were the occurrence of only one stroke event, the maintenance of a stable state with no change of symptoms for one year before the study, the ability to stand alone without help, and the ability of catching a ball and passing it around the body. Exclusion criteria were

dementia, fluent aphasia, requiring help in standing, and the inability to catch and release an object. The pathway and velocity were assessed by static and dynamic posturography (Halmi et al 2020).

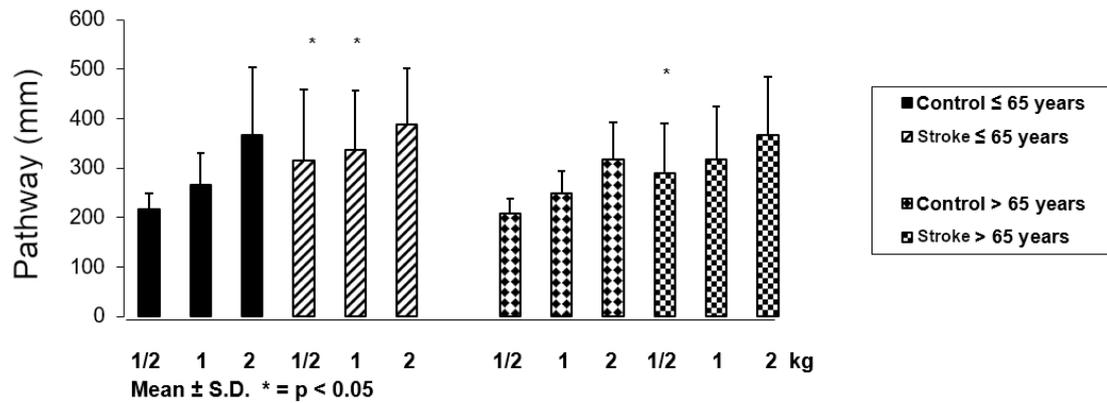
Our main finding was that four years after the stroke the pathway and the velocity of the body motion assessed by static and dynamic posturography were increased. The results of the static posturography are presented in Figure 11. None of the control groups ( $\leq 65$  years  $<$ ) showed any difference in the stance on the balance board with open or closed eyes. No higher values in the pathway and velocity were observed in the younger group of patients with stroke. Patients above 65 years had significantly attenuated higher pathways with open eyes ( $p < 0.05$ ) and with closed eyes ( $p < 0.01$ ) compared with the controls.

There were no significant differences between the younger and older groups of controls according to the dynamic posturography (Figure 12). However, patients under 65 years assessed by dynamic posturography showed significantly higher pathway and velocity of the body motion after passing 0.5 and 1 kg balls around the body ( $p < 0.05$ ). The poststroke patients above 65 years had significantly higher pathway after passing the 0.5 kg ball around their body ( $p < 0.05$ ) (Figure 12). Although, the dynamic posturography with 1 kg and 2 kgs showed higher values than in the controls, these results were not significant. Velocity results are not presented in the figures, for clarity, but the tendency was the same as those with the pathways of body motion. The latero-lateral and antero-posterior oscillation of patients with stroke were not significantly different from the control groups 3-4 years after the onset of stroke.



**Figure 11. Postural instability assessed by static posturography in post-stroke state.**

Figure 11 shows the pathway of body motion for one minute (ordinate axis). The first four columns illustrate data for patients under 65 years of age, while the second four columns are for patients over 65. Data are shown for eyes closed (C) and eyes open (O) conditions. No significant differences were seen for the groups under 65. For patients over 65 years of age, the movement pathways were significantly elevated in the post-stroke group (\*p<0.05; \*\*p<0.01).



**Figure 12. Pathway of postural instability assessed by dynamic posturography in post-stroke state.**

Figure 12 shows the pathway of postural instability assessed by dynamic posturography. The pathway of body motion was measured for one minute (ordinate axis). The first six columns illustrate the data of the patients under 65 years of age, and the second six columns indicate patients over 65. The columns indicate the different ball weights used for the tests (1/2, 1, 2 kg). Movement for stabilization was increased in the younger post-stroke patients using the 1/2 or 1 kg balls, but only for the 1/2 kg ball in patients over 65 years of age (\*p<0.05).

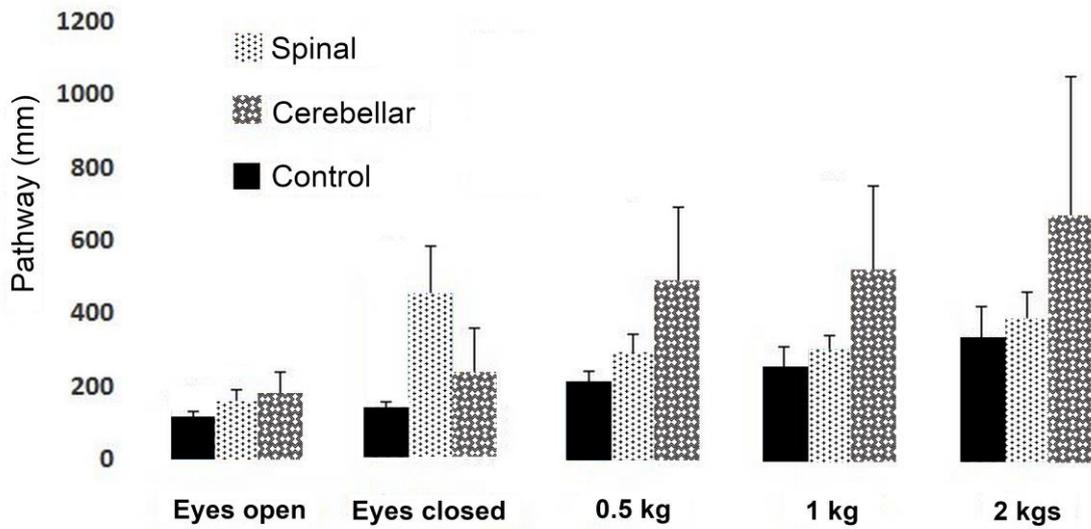
#### 4.5.1. Short summary of the results of post-stroke state

It is very important that there was a significant difference in the static posturography between the younger and the older groups of patients with stroke. While the older group of patients experienced instability in stance, the younger group did not. However, both groups of patients had increased velocities and pathways measured by dynamic posturography, which might explain the difficulties in balance when walking on an uneven ground. With the application of a sensitive and reproducible method to assess static and dynamic adjustments for the maintenance of balance we concluded that postural instability is significantly greater in the post-stroke patients than in the control subjects.

#### **4.6. Results of patients with different types of ataxia compared with age-matched healthy controls**

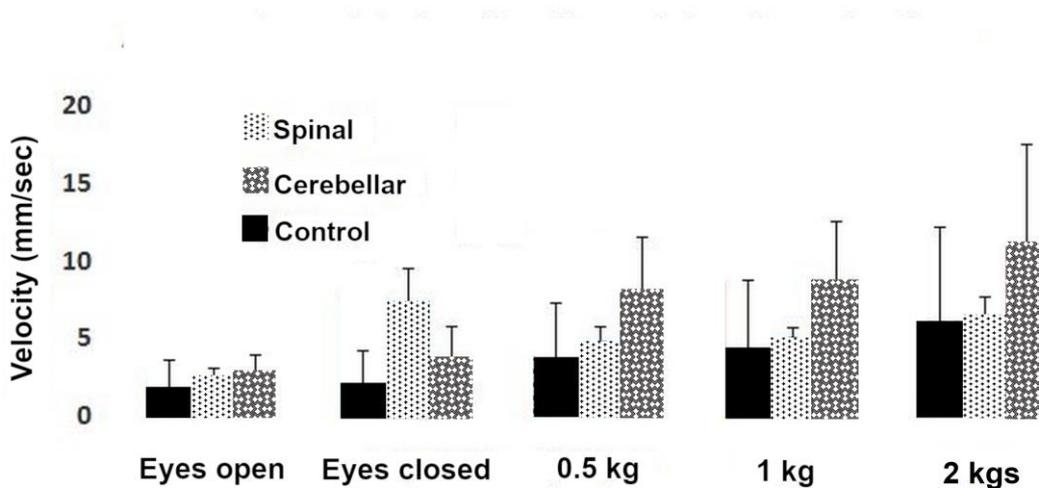
Patients with different types of ataxia were involved in the study. Basically, we made a differentiation between spinal ataxias and cerebellar ataxias. The causes of ataxias were presented in the section of Participants (Table 5).

Although, our case number was quite low, in the case of spinal ataxia the increase in the velocity with the eyes closed was four times higher compared to the control persons. This is a pregnant difference and it has a biological significance. However, in the case of cerebellar ataxia the velocity is double the velocity of the control group, assessed by a weight of half kg. A parallel, and even more heightened alteration could be observed in the case of the weights of 1 and 2 kgs. Spinal and cerebellar ataxia could be definitely separated with this method, namely, the static and dynamic methods of posturography (Figure 13 and 14).



**Figure 13. Alterations of postural stability in the ataxias, assessed by a stabilometer.**

Figure 13 shows the alterations of the pathway of postural stability assessed by a stabilometer in spinal ataxia (N = 5), cerebellar ataxia (N = 6), and aged-matched healthy control persons (N = 13) assessed by a stabilometer. Postural instability caused by different types of ataxia was compared with aged matched healthy controls. During the static posturography the measurement with the eyes closed showed a big increment in the pathway for one minute in patients with spinal ataxia. Contrary to this observation the cases with cerebellar ataxias represented a higher elevation during dynamic posturography. Significance cannot be indicated because of the low number of cases.

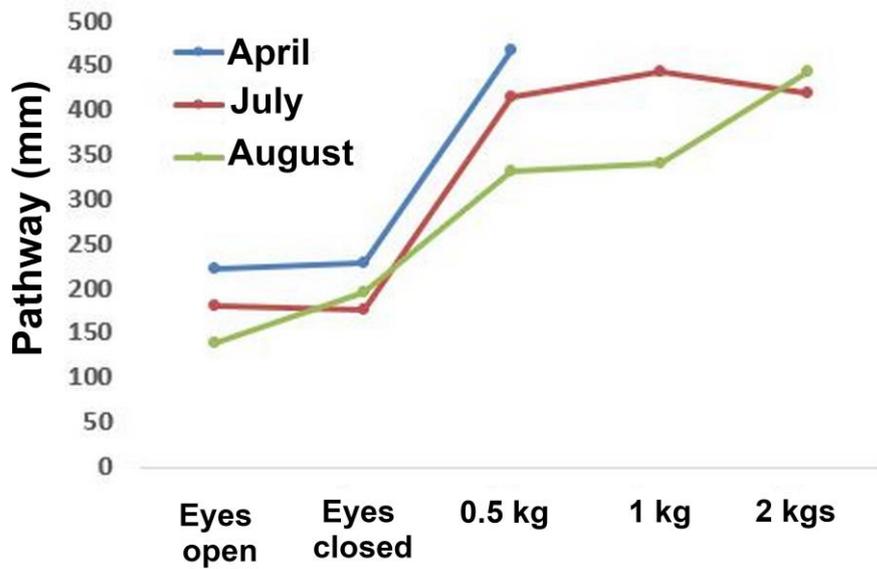


**Figure 14. Alterations of postural stability in the ataxias, assessed by a stabilometer.**

Figure 14 shows the alterations of the velocity of postural stability in spinal ataxia (N = 5), cerebellar ataxia (N = 6), and aged-matched healthy control persons (N = 13) assessed by a stabilometer. This figure shows the changes in velocity after having been detected for one minute. The tendency of velocity was the same as the pathway. While the closed eyes condition modified the spinal ataxia, the velocity was increased by dynamic posturography.

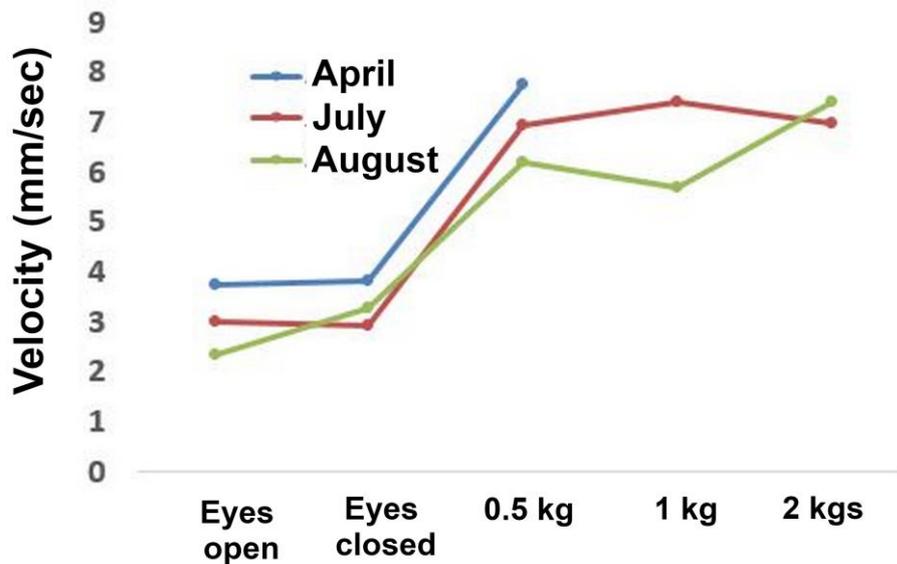
The following two figures (Figure 15 and Figure 16) show a case report with cerebellar ataxia. The patient was followed for three months. The figure representing the pathway and the velocity well illustrate the alteration, namely, the amelioration in the state of patient, that in the legends of the figures is given a particularly detailed explanation.

The following two figures (Figure 15 and Figure 16) show a case report with cerebellar ataxia. The patient was followed for three months. The figure representing the pathway and the velocity well illustrate the alteration, namely, the amelioration in the state of patient, that in the legends of the figures is given a particularly detailed explanation.



**Figure 15. G.M.'s alterations of the pathway of postural stability in a case of ataxia.**

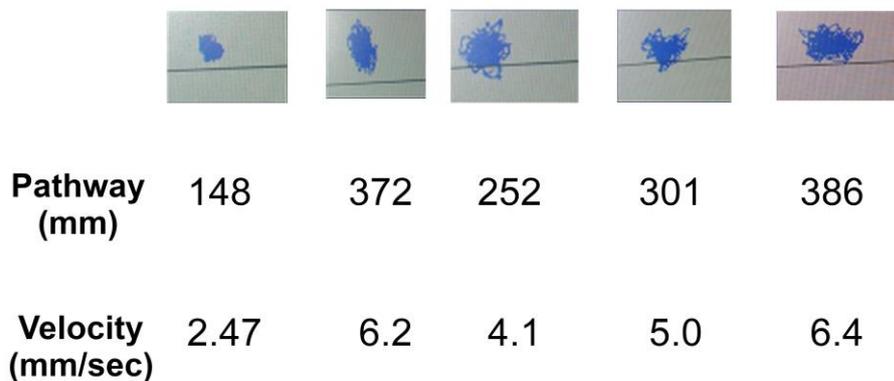
Figure 15 represents a case report at three different times. This figure shows the alterations in the pathway for one minute after static and dynamic posturography. While we did not observe changes in static posturography, the pathway was highly increased by dynamic posturography. In April the dynamic posturography could not be performed appropriately because of the severity of trunk ataxia. The ataxia showed improvement during the next two months, because the values were smaller in the next months of follow-up. The lines well demonstrate the changes between the static and dynamic posturography and the improvement in the specific months.



**Figure 16. G.M.’s alterations of the velocity of postural stability in a case of ataxia.**

Figure 16 represents a case report at three different times. This figure shows the alterations of velocity for one minute after static and dynamic posturography. While we did not observe changes in static posturography, the velocity was highly increased by dynamic posturography. In April the dynamic posturography could not be applied completely because of the severity of trunk ataxia. The ataxia showed improvement during the next two months.

A computer program provided for the possibility of illustrating postural instability by tractography. The postural instability is demonstrated spectacularly by the small “balls” that represent the changes of the pathway and the velocity. On the figure below (Figure 17) a case of combined ataxia is demonstrated where the values were heightened with static and dynamic posturography as well.



**Figure 17. Diagnostic recommendation based on an assessment with a stabilometer in a case of ataxia.**

Figure 17 demonstrates a case with spinocerebellar ataxia. S.A. (31 years old) suffers from cerebrotendinosus xantomatosis (mutation of CYP27A1 gene caused by the elevation of cholesterol in different tissues). This figure represents the results assessed by tractography, and the pathway for one minute, and the velocity for one minute. The first column represents the static posturography with open eyes, the second column represents the static posturography with closed eyes, the third column shows the dynamic posturography with a ½ kg ball, the fourth column shows the dynamic posturography with a 1 kg ball, and the fifth column shows the dynamic posturography with a 2 kgs ball. The increased tangles with closed eyes are characteristic in spinal ataxia, and the enhancement of the tangles after dynamic posturography are characteristic in cerebellar ataxia. The patient has xanthomas in her spinal cord, cerebellum, and several tendons.

#### **4.6.1. Short summary of the results of ataxias**

I examined different types of ataxias. Although, the number of cases was low, the big and characteristic increment in spinal ataxia with closed eyes and the high

elevation in cerebellar ataxia with dynamic posturography let us draw the conclusion that these ataxias with posturography can be safely differentiated.

## **5. Discussion**

### **5.1. Discussion of posturography**

#### **5.1.1. Discussion of the importance of posturography**

In my PhD thesis I examined the changes of postural instability in different diseases of the central nervous system compared with age matched healthy controls. In the first part of the PhD I analyzed our method developed previously for the dynamic posturography in the Neuro Rehabilitation in Sopron. In the therapeutic parts of my thesis I dealt with the postural instability of patients with Parkinson's disease and post-stroke state. In the short part of the therapeutic paragraph, I suggested a possible way of distinction between spinal and cerebellar ataxia with posturography.

I applied a method with Nintendo Wii balance board connected with a computer program. The applicability of this method for the quantification of postural instability has been published in several studies (Bartlett et al. 2014, Leach et al. 2014, Di Fabio 1996, Llorens et al. 2016).

My work confirmed the results of the previous studies, namely, that the Nintendo Wii balance board with a computer program is a proper, objective method for the detection of postural instability. The revealed values reflect the changes of balance more properly than the clinical examinations with different score systems. In the daily life we have to strive for the parametric measurement of postural instability to compel the different therapies. Our examination of patients with different diseases and healthy controls confirmed the usefulness of this cheap method in the neurological examinations. The measurement with static posturography examining the person in standing position with the eyes open and closed showed a difference in the age group above 65 years.

#### **5.1.2. Confirmation of the validity of dynamic posturography with balls**

The efficiency of posturography can be increased by various provocation methods, e.g., by a moving plate (Nagymáté et al. 2018, Petró et al. 2017, Petró et al. 2018). This very expensive method could hardly be adapted to the daily routine of neurology, so a simple ball test for dynamic posturography has been created in the

Neuro Rehabilitation Institute, Sopron. The persons' center of body mass in a standing position was moved permanently with different weights of balls. The changes in the pathway and velocity of balance well correlated with the weight of the balls. In the section of Results the correlation between the alterations caused by the weights of balls is represented in Figure 6 and 7. We concluded that in this respect it is an appropriate method for dynamic posturography and it is suitable for the scientific analysis of balance.

## **5.2. Discussion of our results in the reflection of other published studies of balance disorder in Parkinson's disease**

### **5.2.1 Discussion of our results with patients in the early stages of Parkinson's disease**

In our first analysis we compared patients with Parkinson's disease, and age-matched healthy controls. Our main goal was to reveal the postural instability in the early stages of Parkinson's disease when the balance disorder could not be detected by any other clinical tests, e.g., the Push Test. Forty-five patients in the Hoehn and Yahr stages 1 and 2 of Parkinson's disease were involved in our study. The examinations with static and dynamic posturography were conducted under the effect of medication. The results of their clinical tests were negative, so these patients were claimed not to have postural instability in the Hoehn and Yahr stages 1 and 2 of Parkinson's disease (Contin et al. 1996, Ahmed et al. 2017, Ferrazzoli et al. 2015). Despite the general opinion, we assessed a higher oscillation in the antero-posterior direction in the younger group of parkinsonian patients ( $\leq 65$  years) by dynamic posturography (Halimi et al. 2019). However, the static and dynamic posturography did not show any significant difference in the pathway and velocity in the younger group of patients with Parkinson's disease compared with the age matched healthy controls. The patients over 65 years had significant increment in the pathway and velocity measured for 1 minute during the static and the dynamic posturography. According to our study a strong age-dependency was observed in the balance disorder in the early phase of Parkinson's disease (Halimi et al. 2019).

### 5.2.2. Discussion of balance disorder in Parkinson's disease

It is well-known that the late phase of Parkinson's disease is characterized by a severe postural instability, and their balance impairment leads to a serious deterioration in their quality of life.

In the published studies there is an agreement that in the presence of a clinically detectable balance instability the changes of balance are proportionally demonstrated by static and dynamic posturography (Minamisawa et al. 2012, Nardone and Schieppati 2006, Ahmed et al. 2017, Contin et al. 1996, Ebersbach and Gunkel 2011, Bronte-Stewart et al. 2002, Lee et al. 2012, Ickenstein et al. 2012, Nonnekes et al. 2013, Doná et al. 2016, Johnson et al. 2013). It was reviewed by Rinalduzzi et al. (2015), Kamieniarz et al. (2018), and Petró et al. (2017). Although, the clinical and posturographic measurements in the severe cases of Parkinson's disease showed a high correlation, the results in the early phase of Parkinson's disease are contentious (Nardone and Schieppati 2006, Ferrazzoli et al. 2015, Ebersbach and Gunkel 2011, Ganesan et al. 2010, Bonnet et al. 2014, Stylianou et al. 2011). Our main goal was to detect the postural instability in the Hoehn and Yahr stages 1 and 2 of Parkinson's disease (Halmi et al. 2019).

Our present study focused on postural instability in the early stage of Parkinson's disease, when no instability can be denoted by the push test. The relationship between age and postural instability was also scrutinized. The subjects involved in our study were divided into two groups, under 65 years and above 65 years. One of our main findings was that the oscillation significantly increased  $\leq 65$  years. Another important finding was that in spite of the fact that the oscillation significantly increased  $\leq 65$  years, the balance impairment could not be detected with clinical tests. Both the static ( $p < 0.05$ ) and the dynamic posturography confirmed the appearance of postural instability in Parkinson's disease over 65 years ( $p < 0.05$ ), while the age-matched healthy controls did not show any detectable balance problems. At the appearance of the symptoms of Parkinson's disease in an older age the balance impairment provoked by closing the eyes or an everyday thrust must be taken into consideration. In this respect our observations partly confirm Bronte-Stewart's study where significantly higher scores were found in Parkinson's disease assessed by Postural Instability and Gait Disorder and Sensory Organization Test of dynamic

posturography, but no postural instability in static measurements was found. Furthermore, the authors did not identify any age dependency of balance instability (Bronte-Stewart et al. 2002).

In contrast to their observations, we detected an increased postural instability in the older age group with mild parkinsonian symptoms, with static and dynamic posturography as well. Nevertheless, our results are consistent with Ickenstein et al. (2012). They studied the static posturography of elderly patients with Parkinson's disease, where the results of static posturography with the eyes closed significantly differed from the age-matched healthy controls, as it was perceived in our study, too. They concluded that the age alone showed significant differences in the balance assessed by posturography (Ickenstein et al. 2012, Manchester et al. 1989). However, this statement was not confirmed by our negative results of age matched healthy controls. The increased sway was associated with a major risk of falls (Doná et al. 2016), so the dynamic posturography together with the clinical tests can predict the probability of falls among patients with Parkinson's disease (Rossi-Izquierdo et al. 2014, Johnson et al. 2013, Nonnekes et al. 2013). Although, there was a higher level of sway among the patients with Parkinson's disease, other authors were not able to make a differentiation with posturography between those who fell and those who did not (Nardone and Schieppati 2006). In the group of > 65 years not only a higher pathway, but also a higher velocity was detected. The results of our observation confirmed a former study where a high mean velocity was detected in Parkinson's disease > 65 years (Minamisawa et al. 2012). The division of the groups of patients with Parkinson's disease and age-matched healthy controls made it possible to detect patients  $\leq$  65 years in Hoehn and Yahr stages 1 and 2. There were no significant differences in the pathway and the velocity while standing on a force plate for one minute, but increased amplitudes of the oscillations in the antero-posterior direction were measured. This may reflect an increased instability assessed by dynamic posturography. The published studies of dynamic posturography are controversial in the respect of the body sway standing on a force plate (Ebersbach and Gunkel 2011, Termoz et al. 2008, Stylianou et al. 2011). Ebersbach and Gunkel (2011) observed a lower level of sway in the patients with Parkinson's disease than in the control subjects, but the tilting was increased in the patients with more severe clinical symptoms of postural instability (Ebersbach and

Gunkel 2011). A lower level of sway can be observed in the patients with stiff ankles which is a common symptom of Parkinson's disease. This may decrease the sway in the antero-posterior direction (Nardone and Schieppati 2006, Carpenter et al. 2004, Horak and Diener 1994). Other studies presented a higher level of sway in the Hoehn and Yahr stages 1 and 2 of Parkinson's disease than in the controls, and our results were also supported by these findings (Contin et al. 1996, Ahmed et al. 2017, Ferrazzoli et al. 2015). The comparison of the different studies is quite difficult because not all of them separated the subjects according to their age. The comprehensive studies of age-dependency indicate that the onset of the disease in older age is associated with a faster progression of Parkinson's disease (Reinoso et al. 2015, Post et al. 2007, Spica et al. 2013, Mályy et al. 2018). An additional difficulty, that the subjects with Parkinson's disease are not separated according to their Hoehn and Yahr stages 2 and 3 in the former studies (Johnson et al. 2013, Blaszczyk et al. 2007, Minamisawa 2012). The postural instability and the quality of life of these stages are very different from each other.

### **5.2.3. Discussion of the etiology of balance disorder in Parkinson's disease**

#### **5.2.3.1. Discussion of the stiff ankle**

The postural instability in Parkinson's disease cannot be explained by only one reason. According to Horak et al. (1992) the sensory inputs (somatosensory, visual, and vestibular) are integrated in the central nervous system. Coordinated and scaled neuromuscular responses are given while maintaining an upright position during perturbations (Horak et al. 1992, Manchester et al. 1989). The tone of the muscles participating in balance is necessary for the upright position. Upright stance and the maintenance of balance are due to the anticipatory and compensatory postural adjustment (Santos et al. 2010). Somatosensory input enters the central nervous system and coordinated muscle responses that torque the ankle to compensate the various perturbations (Chen et al. 2015, Park et al. 2004, Horak et al. 1996). The contraction of the gastrocnemius muscle and the tibialis anterior muscle assessed by electromyography (EMG) has an effect on the stabilization of the ankle in the opposite direction in patients with Parkinson's disease (Dietz et al. 1988). When the gastrocnemius muscle was stretched, the EMG sign decreased until the EMG sign of the tibialis anterior muscle

inverted and increased. There was an uncoordinated contraction after the retraction of body. The angular rotation in the ankle joint responding to the displacement was slower in the patients with Parkinson's disease (Dietz et al. 1988). The exaggerated and uncoordinated contraction in the antagonistic muscles around the ankle may initiate a disturbed sensory activation in Parkinson's disease (Dietz et al. 1988). The middle latency and late latency spinal cord reflexes in the muscles of the ankle showed an alteration assessed by EMG. This fact may be a primary cause of instability in Parkinson's disease (Beckley et al. 1991). The middle latency reflex in the gastrocnemius muscle was significantly enhanced and the long latency reflex in the tibialis anterior muscle was inverted and reduced (Beckley et al. 1991, Bloem et al. 1992). The long latency reflex was shown to be related to stability (Rothwell et al. 1983). The uncoordinated reaction of the muscles around the ankle, and the malfunctioning motor program together may be the primary causes of postural instability. However, an influence from the environment followed by a weakened automatic postural response that can lead to a fall should also be taken into consideration (Horak et al. 1996). Postural instability is not, or only partly affected by our gold standard levodopa (Horak et al. 1992, Horak et al. 1996, Bronte-Stewart et al. 2002). The maintenance of the upright stance on a force plate requires an effective ankle torque strategy, and it is better with levodopa (Baston et al. 2016). Notwithstanding, it was published that levodopa significantly increased the postural sway for one, and two hours post-dose (Contin et al. 1996). As a matter of fact, the gait and the bradykinesia are improved, and the musculoskeletal rigidity is decreased by levodopa, but it has no therapeutic effect on postural instability.

### **5.2.3.2. Discussion of the cerebellum**

Evidence shows that beside the lesion of dopaminergic pathways, there are destroyed non-dopaminergic connections. The deterioration of postural instability is one of them. The upright stance is a combination of anticipatory postural adjustment and the maintenance of balance during perturbation (Santos et al. 2010). The earlier studies concluded that anticipatory postural adjustment is directed by central circuits, and primarily the cerebellum should be taken into consideration (Horak and Diener 1994, Khadrawy et al. 2017). These experiments were also confirmed by a clinical study. The

training of balance tasks for six weeks increased the volume of some parts of the brain, including the cerebellum assessed by morphometric MRI examination (Sehm et al. 2014). Postural instability assessed by dynamic posturography may support the idea of the involvement of the cerebellum in the early phase of Parkinson's disease. There is a direct connection between the striatum, the subthalamic nucleus and the cerebellum (Bostan et al. 2010). Even in the early stages of Parkinson's disease, the cerebellum may have a role as important as the striatum in the formation of the symptoms. The role of the cerebellum in Parkinson's disease is summarized in two excellent reviews (Wu and Hallett 2013, Lewis et al. 2013). The early involvement of the cerebellum was reinforced by fMRI in Hoehn and Yahr stages 1 and 2 in Parkinson's disease. An elevated activity of the cerebello-thalamo-cortical (CTC) motor circuit was detected, and it was increased with the development of the disease (Sen et al. 2010).

Our patients' severity of the disease corresponded with those in the previous study. We observed a slight postural instability assessed by dynamic posturography, and their study with fMRI detected an increased activity in the CTC circuit. They explained their observation as a compensatory activity for the decreased functional activity of the basal ganglia. The same assumption was taken by Yu et al. (2007). In their studies, an over-activity in the ipsilateral cerebellum was assessed by fMRI which did not correlate with the severity of rigidity in Parkinson's disease patients. In their opinion it was a compensatory mechanism instead of the decreased activity of the basal ganglia. In our present study we suppose that it may be an early appearance of the enhanced postural instability caused by the deterioration of the non-dopaminergic connection involving the cerebellar pathways (Halmi et al. 2019). All of the experimental and clinical studies confirm the important role of the cerebellum in the early stages of Parkinson's disease. A limitation of our present study is that dynamic posturography cannot be used but with those subjects who are able to stand in an upright position, and who are able to hold and pass a weight around their body. Our conclusion for the etiology of postural instability in Hoehn and Yahr stages 1 and 2 was drawn theoretically, and it was not based upon an actual assessment.

#### **5.2.4. Discussion of the dyskinesia caused by levodopa**

Dyskinesia (involuntary movement) is a characteristic side effect of long-term dopa substitution. Dyskinesia is a common problem in Parkinson's disease after ten years of treatment with levodopa (Heumann et al. 2014, Picazio et al. 2018). The levodopa dose was significantly higher in patients with dyskinesia than without it. The main difficulty is whether or not to increase the dose of levodopa. The quality of life is deteriorated with dyskinesia but the exaggerated bradykinesia also has a negative effect on the patients' daily lives (Marsden 1994, Brown and Marsden 1998). According to our study, patients with dyskinesia have a vulnerable postural instability, which leads to falls. A highly significant increase in the pathway (Figure 10) and velocity of balance after dynamic posturography is demonstrated in the section of Results in my thesis. These results confirm the previous data, where the Abnormal Involuntary Movement Scale was compared with the exaggerated sway caused by levodopa-induced dyskinesia (Chung et al. 2010). The increment in the pathway and the velocity according to the measurements repeated every half year on the force plate predicted the appearance of dyskinesia (Mály, personal remarks). These results can be a warning to the neurologists not to elevate the levodopa dose because dyskinesia and bradykinesia can deteriorate the quality of life nearly to the same extent (Marsden, 1994, Brown and Marsden 1998).

### **5.3. Discussion of our results in the reflection of the literature in patients in post-stroke state**

#### **5.3.1. Discussion of the importance of balance in post-stroke state**

Another important question of my thesis is the instability in post-stroke state. Stroke has become the primary cause that leads to the deterioration of the quality of life (Barcley-Goddard et al. 2004).

Although, life-expectancy is not shortened by post-stroke state, the quality of life is strongly deteriorated by it. The independence of post-stroke patients is reduced, since they are restricted to their own house or forced to live in a care-take home generating further diseases, mainly depression. In this respect our primary objective was to find out whether the improvement of the paresis leads to a progress of balance. Therefore,

patients in post-stroke state 4 years after the onset of the stroke were involved in our study.

It is well-known that postural instability is increased after stroke. The balance impairment in poststroke state is complex. It includes weight-bearing asymmetry (WBA) (Bohannon and Larkin 1985, Sackley 1991, Roerdink et al. 2009, Peurala et al. 2007, De Haart et al. 2004, Marigold and Eng 2006, Kamphuis et al. 2013), muscle weakness (Marigold et al. 2004), disturbed perception (Bonan et al. 2004), destroyed ankle proprioception (Niam et al. 1999), cognitive failure (Mignardot et al. 2014, Whitney et al. 2019) and consequently an increased visual dependency (Bonan et al. 2004, Mansfield et al. 2013). All of these factors lead to a postural instability, and finally to falls. Earlier, weight-bearing asymmetry was considered to be the main cause of postural instability in post-stroke state, and to be increased by age (Lee and Jung 2017). However, while the balance disorder is improved by the restoration of weight-bearing asymmetry when the stance symmetry between the paretic and nonparetic leg is reconditioned (Aruin et al. 2009, Chaudhuri et al. 2000), the postural stability cannot entirely be re-established (Chaudhuri et al. 2000, Pal et al. 1994). Furthermore, while the paretic leg is loaded more, it does not contribute to the balance control to a greater extent than the less loaded limb (Mansfield et al. 2013, Geurts et al. 2005).

Postural instability in post-stroke state can be objectively assessed by posturography (Bartlett et al. 2014, Leach et al. 2014, Di Fabio, 1996, Nagymáté et al. 2018, Petró et al. 2018, Lee and Jung 2017). An increased postural sway was demonstrated with static and dynamic posturography after stroke. This correlated with the extended asymmetry of weight bearing (Marigold and Eng 2006, Barclay-Goddard et al. 2004, Peurala et al. 2007). According to the previous studies, neither the improvement in muscle strength nor the increased charge of the paretic leg led to the improvement of the equilibrium of the patients with hemiparesis (De Haart et al. 2004, Pal et al. 1994, Barclay-Goddard et al. 2004, Winstein et al. 1999). The nonparetic leg seems to play the main role in the maintenance of balance in standing and walking in an upright position (Van Asseldonk et al. 2006, Mansfield et al. 2013, Roerdink et al. 2009). Postural instability in post-stroke state cannot be effectively influenced by physiotherapy (Gandolfi et al. 2019, Winstein et al. 1999, Barclay-Goddard et al. 2004, Kalron et al. 2015).

### 5.3.2. Discussion of my results in post-stroke state

Our results confirmed that postural instability might persist even after a restored state of the patients with stroke. In Figure 11 and 12 we demonstrated that patients with post-stroke state under 65 years showed a higher pathway and velocity compared to the age-matched healthy controls according to the assessments with dynamic posturography. The equilibrium of the patients over 65 years deteriorated significantly during the static and the dynamic posturography compared to the age-matched healthy controls. However, the healthy persons of younger and older age did not show any difference in the respect of their age (Halmi et al. 2020). As for the stroke, the disease affected differently the persons of different ages. Although, the patients in post-stroke state has the ability of walking and being self-independent in their house, they are strongly restricted in and afraid of walking outside, especially on an uneven road. Their quality of life is destroyed mainly because of the maintenance of balance disorder years after the stroke.

Postural instability after stroke occurs for many functional reasons and prevents the independence of the patients. Our results indicate that the younger group of patients with stroke has a good stable stance in an upright position, while the older group has a postural instability assessed by static posturography with the eyes open and closed, compared to the aged matched healthy controls (Halmi et al. 2020). Uncertain equilibrium assessed by dynamic posturography appears when walking on uneven ground. The different aspects of the age-dependent disturbances of postural instability may arise because different brain networks are involved in the degeneration of pathways. As Winstein (1999) concluded, balance during standing is not the same as that used in locomotion (Winstein et al. 1999). Our data confirm the previous results that the enhanced sway assessed by posturography after stroke occurs in parallel with the poststroke state (Geurts et al. 2005, Kamphuis et al. 2013). It is not surprising that during the first three months after the onset of stroke the muscle weakness determines the balance, which cannot be measured in severe cases. Three and 12 months later, when the paretic leg is strong enough to be able to stand in an upright position, the reduction of weight bearing asymmetry parallel with the sway of the body motion and reduced visual dependency characterize the post-stroke state (Geurts et al. 2005, Lee

and Jung 2017, Wolpert et al. 1998, De Haart et al. 2004, Marigold et al. 2004). However, the postural instability – in spite of the improved parameters of the paretic leg – lacks normalization (De Haart et al. 2004, Marigold et al. 2004, Geurts et al. 2005). These findings were confirmed by a previous study, which required well-recovered patients in a poststroke state to load their paretic and nonparetic leg separately on one side (Pal et al. 1994). The successful disposition of the body weight on the side of the paretic leg was 20 percent, while that of the side of the nonparetic leg was 47 percent, further confirming the persistence of balance instability after stroke mainly in provoked circumstances (Pal et al. 1994). Our results may confirm that even 4 years after stroke the values from dynamic posturography represented postural instability, which was demonstrated using different weights of balls in our study.

According to a published review about the balance disturbances in the poststroke state, the severity of weight-bearing asymmetry correlated with the postural sway, but it did not correlate with the clinical balance tests and falls (Kamphuis et al. 2013), consequently the weight-bearing asymmetry does not correlate with balance disturbances. However, the velocity of posturography is well correlated with the Berg Balance Test on an unstable surface (Cho et al. 2014) and with falls (Lee and Jung 2017). The correlation of the velocity of static and dynamic posturography is very strong with the postural instability assessed by clinical tests (Niam et al. 1999, Geurts et al. 2005). In this respect, our results reflect well the postural instability assessed by posturography after stroke, in the younger and older groups of patients 3 or 4 years after the onset of stroke as well.

The previous studies confirmed that the paretic leg did not substantially contribute to the postural stability even if the extent of the weight-bearing asymmetry was decreased (Gandolfi et al. 2019, Mansfield et al. 2013, De Haart et al. 2004). Although, when the amount of weight-bearing asymmetry was reduced with a 10 mm insert in the shoe of the nonparetic leg, the balance of the stance was improved but the postural instability could not be significantly changed (Aruin et al. 2009, Chaudhuri et al. 2000). The general consequence of the balance studies in the poststroke state was that the postural instability was dependent of the nonparetic leg even if it was loaded with the majority of weight (Kamphuis et al. 2013, Mansfield et al. 2013, Van Asseldonk et al. 2006).

According to the daily practice and comparing studies of the equilibrium of patients in the poststroke state, balance cannot be effectively influenced by physiotherapy (Winstein et al. 1999, Barclay-Goddard et al. 2004, Gandolfi et al. 2019). It may mean that the quality of life after stroke is threatened by the persistence of the postural instability after the restoration of the paresis. In this respect, our observation concerning the maintenance of balance instability for years after the stroke is important. Although, rehabilitation is concentrated on the improvement of the paretic side, the instability in standing and walking positions cannot be compensated by the restoration of the paresis. The important role of the central nervous system in the maintenance of postural instability after stroke can be considered. In this respect, the function of the cerebellum seems very important. It is a part of the motor network and it may be affected by any motor pathway lesion. As for the organizational function of the cerebellum, and its importance in the control of movement and stability, our results may imply that long-lasting disturbances of those functions persist, and contribute to the damage in the motor network (Wolpert et al. 1998).

It was an interesting aspect of our thesis that older patients with Parkinson's disease or stroke were affected in the stance upright position and walking on an uneven surface which was quantified by static and dynamic posturography. In the younger age group, the deterioration of balance was only indicated by a significant elevation of the pathway and velocity of the dynamic posturography walking on an uneven surface. It may suggest that a wider range of brain areas are involved in the postural instability in the older age group of patients with Parkinson's disease and post-stroke.

#### **5.4. Discussion of our results in patients with different types of ataxias**

There are many types of ataxias, and in order to find the appropriate treatment it is essential to establish a proper diagnosis. In the general neurological practice the heterogeneous ataxias are generally diagnosed via brain imaging, blood tests or genetic testing (De Silva et al. 2019, Schmitz-Hübsch et al. 2006). These methods are complicated and expensive, require a great apparatus and expertise, and cannot be evaluated quickly. Therefore, we wanted to find a way for a simpler assessment to distinguish spinal and cerebellar ataxias. The distinction of spinal and cerebellar ataxias

is a very important diagnostic question for the treatment of these diseases. The fact that there can be hardly found any findings in the literature concerning this problem highlights the importance of our work.

Nevertheless, we had a small number of patients with ataxias, we still could draw a strong conclusion for the differentiation of spinal and cerebellar ataxia. While spinal ataxia was increased by static posturography with the eyes closed, cerebellar ataxia was elevated by dynamic posturography. A simple and objective way is provided by this method for the differentiation of these two types of ataxia in just a few minutes.

## 6. Conclusion

1. Static and dynamic posturography is not only a simple and cheap, but also a quantified, sensitive, and reproducible method for the assessment and comparison of equilibrium in various diseases.
2. Our main conclusion is that there is a detectable postural instability assessed by dynamic posturography in the early stages of Parkinson's disease, and the supposed involvement of non-dopaminergic pathways in the deterioration in the early phase of Parkinson's disease is strongly supported by this fact.
3. Strong age-dependency was observed with static and dynamic posturography in the stages 1 and 2 of Parkinson's disease.
4. The most expressive increment in the pathway and velocity with dynamic posturography was shown by Parkinson's disease patients with dyskinesia, therefore they have a higher risk to fall.
5. Our results in post-stroke state confirmed that postural instability persisted for years following the stroke. In spite of the improvement of the paresis, a weight bearing asymmetry can be seen.
6. There was a strong age-dependency in the static posturography, namely, the patients under 65 years did not show any deterioration, while the older aged patients had difficulty in upright position. The age-matched healthy controls did not show any difference in their balance.
7. My theoretic conclusion was that the involvement of the cerebellum in the postural instability may be independent of age.
8. According to my study of balance in the central nervous system diseases, wider brain areas are involved in the postural instability in older age than in younger age.
9. Postural instability cannot be influenced by medication. The importance of physiotherapy in the early, and any stage of the disease is crucial.

## 7. Summary of the new results of my thesis

- I proved that the new ball test is a suitable method for the assessment of dynamic posturography.
- I observed postural instability in the early stages of Parkinson's disease when it could not be detected by any other clinical measurements.
- The postural instability can be detected late after the onset of stroke in spite of the improvement of the paresis.
- I discovered that the characteristics of postural instability are age dependent.
- The brain reacts differently to the diseases in younger age than in older age.
- I pointed out the etiopathological importance of the cerebellum in both of my papers.
- I stress the usefulness of physiotherapy in every stage of the central nervous system diseases.

## 8. Short summary in English and in Hungarian

### 8.1. Short summary

Postural instability is one of the primary symptoms of the central nervous system diseases, independently of its etiology. Although balance impairment is very well described in the late phase of Parkinson's disease (PD), its presence is debated in the early stages of the disease. Stroke is accompanied by balance impairment, but its persistency in course of the disease is unknown. The distinction of spinal and cerebellar ataxias is very difficult, therefore with the presentation of various cases I highlighted some major characteristics of ataxias.

**My thesis** is aimed at the unrevealing of the instability and its characteristics in the early stages of Parkinson's disease with static posturography (SP), and dynamic posturography (DP). In the second part of my work I discussed the postural instability maintained several years post-stroke. I was striving to find some etiological and practical conclusions.

**Method:** we used a stabilometer, a Nintendo Wii that was based on plantar pressure. We made assessments for one minute with the eyes open, and with the eyes closed. For the dynamic posturography we used the ball test elaborated in the Neuro Rehabilitation Institution in Sopron.

**Patients:** 45 patients with Parkinson's disease (Hoehn and Yahr stages 1 and 2), 29 post-stroke patients ( $4.7 \pm 3.3$  years after the stroke), 11 patients with ataxia, and 38 healthy control persons were involved in the study.

**Our results:** no differences were found in the results of posturography of the control persons' two age groups. The results of the static posturography differed from the control group neither in the patients with Parkinson's disease nor in the post-stroke patients under 65 years, while the dynamic posturography was significantly increased ( $p < 0.05$ ). In the age group above 65 years the static posturography ( $p < 0.05$  and  $p < 0.01$ ) and the dynamic posturography ( $p < 0.05$ ) was significantly higher than in the control group. Spinal ataxia increased with the eyes closed, and cerebellar ataxia increased as a result of dynamic posturography.

**Conclusions:** Balance impairment can be detected with dynamic posturography in the early phase of Parkinson's disease, even under 65 years. In Parkinson's disease, and in post-stroke state an age-dependent alteration of the postural instability could be seen. Namely, postural instability was significantly higher assessed with static posturography and dynamic posturography in the age group above 65 years. Although, the paresis significantly improved in post-stroke state, the balance instability was maintained, and therefore the quality of life was decreased. More neuronal pathway systems are affected in these patients (Parkinson's disease and stroke) >65 years than in the younger age group. Since the balance impairment cannot be influenced by levodopa, the involvement of non-dopaminergic pathways, primarily the cerebellum can be supposed to be involved even in the early stages of Parkinson's disease. The importance of physiotherapy from the onset of these diseases is confirmed by the results of my PhD.

## 8.2. Short summary in Hungarian / Összefoglalás magyar nyelven

A központi idegrendszeri betegségek egyik fő tünete etiológiától függetlenül a tartási instabilitás. Noha a késői Parkinson-kórban (PD) jól ismert az egyensúlyzavar, a korai Parkinson-kórban vitatott. A stroke együtt jár egyensúlyzavarral, de nem ismert perzisztenciája a betegség folyamán. Nem könnyű a spinalis és cerebellaris ataxia elkülönítése, ezért néhány esettel az ataxiák jellegzetességére hívtam fel a figyelmet.

**Munkám célja** volt, hogy a korai Parkinson-kórban feltárjam statikus (SP) és dinamikus poszturográfiával (DP) az instabilitást és annak jellegzetességeit. Munkám második felében a stroke után évekkel fennálló poszturális instabilitással foglalkoztam. Kerestem, hogy milyen etiológiai és gyakorlati következtetések vonhatók le.

**Módszer:** a talpnyomásméréseken alapuló stabilométer, a Nintendo Wii volt. A méréseket nyitott és csukott szemmel, 1 percen át végeztük. A dinamikus poszturográfiára a soproni Neuro Rehabilitáción kidolgozott labda tesztet használtam.

**Beteganyag:** a vizsgálatokba 45 parkinsonos (Hoehn-Yahr I-II. stádium), 29 stroke-on átesett ( $4,7 \pm 3,3$  év stroke után), 11 ataxiás és 38 egészséges kontroll személyt vontunk be.

**Eredményeink:** a kontroll személyeknél nem volt életkori különbség a poszturografiákban. A 65 év alatti Parkinson-kóros és post-stroke csoportban a statikus poszturográfia nem tért el a kontroll csoporttól, míg a dinamikus poszturográfia szignifikánsan különbözött ( $p < 0,05$ ). A 65 év feletti csoportokban mind a statikus poszturográfia ( $p < 0,05$  és  $p < 0,01$ ) mind a dinamikus poszturográfia ( $p < 0,05$ ) szignifikánsan különbözött a kontroll csoporttól. A spinalis ataxia behunytt szemre, míg a cerebellaris ataxia dinamikus poszturográfiára fokozódott.

**Következtetések:** A korai Parkinson-kórban dinamikus poszturográfiával már 65 év alatt kimutatható az egyensúlyzavar. Parkinson-kórban és stroke-ban korfüggő változást észleltünk a poszturális instabilitásban. Nevezetesen, a 65 év feletiekben mind statikus poszturográfiával, mind dinamikus poszturográfiával szignifikánsan fokozódott az instabilitás. Bár post-stroke állapotban a bénulás jelentősen javult, az egyensúlyzavar továbbra is fennállt, ez pedig rontotta az életminőséget. A betegség (Parkinson-kór és stroke) >65 év több pályarendszert érint, mint a fiatalabb korcsoportban. Mivel az

egyensúlyzavar nem reagál levodopára, ezért a non-dopaminerg pályák, elsősorban a cerebellum érintettsége már Parkinson-kór korai stádiumaiban felvethető. Munkám felhívja a figyelmet arra, hogy a központi idegrendszeri betegségekben fontos az egyensúlygyakorlatok folyamatos végzése.

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## **10. List of publications**

1. Halmi Z, Stone T, Dinya E, Málly J. (2020) Postural Instability Years after Stroke. *J Stroke Cerebrovasc Dis*, 29: 1-6.
2. Halmi Z, Dinya E, Málly J. (2019) Destroyed non-dopaminergic pathways in the early stage of Parkinson's disease assessed by posturography. *Brain Res Bull*, 152: 45-51.

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## 12. Appendix - Explanation of the terms used in this thesis

**Anticipatory postural adjustment (APA):** predictive muscle tense with which the organization prepares for the alteration and compensation of balance (Aruin 2016, Santos et al. 2010).

**Balance / postural stability:** the maintenance of standing or sitting position against gravity; the ability of maintaining one's balance (Alghadir et al. 2019).

**Base of support (BOS):** the area beneath a person that includes every point of contact that the person makes with the supporting surface (Pollock et al. 2000).

**Center of gravity (COG):** a point from which the weight of a body can be considered to act. In uniform gravity it is the same as the center of mass (Adolphe et al. 2017, Pollock et al. 2000).

**Center of body mass (COM):** it is a unique point around which the body mass is equally distributed in all directions. In a uniform gravitational field, the center of mass and the center of gravity coincide (Adolphe et al. 2017, Pollock et al. 2000).

**Center of pressure (COP):** the point of application of the ground reaction force vector. The person is in the state of balance when the pressure of body mass and the center of body mass concur (Benda et al. 1994).

**Compensatory postural adjustment (CPA):** the operation of balance system to restore postural stability after the center of the body mass has been moved by an environmental influence (Aruin 2016).

**Dynamic posturography:** assessment with posturography on an unstable platform where the individual's center of body mass is shifted and needs to be adjusted (Petró et al. 2017).

**Hoehn and Yahr stages:** Parkinson scale divided into 1-5 stages according to the severity of the disease (Hoehn and Yahr 1967).

**Post-stroke state:** Stroke occurs most commonly after age 65 and it is the leading cause of severe long-term disability. Falls occur as the result of the inability to recover from a

loss of balance, and the loss of postural stability plays a major role (Marigold et al. 2004).

**Postural adjustment = alignment:** compensation of the sway of the body (Aruin 2016).

**Postural reflexes:** spinal reflexes: short latency, middle latency and long latency reflexes help to maintain the postural stability of the body (Rothwell et al. 1983, Bronstein and Pavlou, 2013).

**Postural stability / Balance:** the maintenance of standing or sitting position against gravity; the ability of maintaining one's balance (Alghadir et al. 2019).

**Posturography:** quantification of postural instability (Petró et al. 2017, Rossi-Izquierdo et al. 2014, Soto-Varela et al. 2019, Ebersbach et al. 2011, Di Fabio 1996, Ferrazzoli et al. 2015, Genthon et al. 2008, Ickenstein et al. 2012, Llorens et al. 2012, Nonnekes et al. 2013).

**Stability:** the body is stable when its center of gravity falls within the base of support. Stability increases with a larger base of support, a lower center of gravity, or a more central center of gravity within the base of support (Pollock et al. 2000).

**Stabilometer:** a device used for the assessment of plantar pressure (Nagymáté et al. 2018, Petró et al. 2017).

**Static posturography:** assessment in standing or sitting position with the eyes open or closed (Ickenstein et al. 2012).

**Unified Parkinson Disability Rating Scale (UPDRS):** Parkinson scale for the rating of the symptoms (Fahn and Elton 1987).

**Weight bearing asymmetry (WBA):** The weight of the body is charged in an unequal proportion to each side of the body in a way that the majority of body mass is charged on the non-affected side. Weight bearing asymmetry often appears after stroke (Kamphuis et al. 2013).