The multimodal integration disturbance of the proprioceptive system in the context of body schema and body image in Parkinson's Disease

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PhD thesis

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1 Introduction

The most common definition of kinesthesia could be described as the awareness of the body's and the limbs' position and movement in space. A disorder of kinesthesia is especially typical of Parkinson's. We use the term, kinesthesia, when defining the conscious cognition of the body's and the limbs' movement. Proprioception applies to the regulation of the reflexive and postural motor control. The importance of proprioception can be encountered with the motor functions, such as reaching and grasping, static balance and locomotion. With the decrease of proprioception, patients are still able to execute motor tasks, but goal-directed locomotive movement is greatly impaired. The accuracy of goal-directed movements as well as the postural and spinal reflexes change, which leads to problems with balance and walking. The basal ganglions play an important part in kinesthesia, movement cognition and purposeful movements. Those affected with Parkinson's disease (PD) possess lessened kinesthetic „feedback", which these patients compensate by directing increased focus at visual information.

Body schema and body image are fundamental elements of our own self-definition. According to Head and Holmes' (1911) classic definition, body schema is the system of proprioceptive and kinesthetic afferent impulses that also possesses sensomotoric organization responsible for localization of impulses generated by excitation of the body surface that is related to posture or body movement. Body schema is relatively independent of the visually controlled body image. Body schema relies on background information such as, posture, foot size and distance, balance, forward movement and turning. Body image relies on conscious information, and is directed visually and controlled, oriented and influenced by attitudes and beliefs.

An important subcase of body schema disorders is Parkinson's disease. The basal ganglions are involved in kinesthesia, movement cognition and in purposeful movements. With PD patients the processing of proprioceptive information is often impaired, which is evidenced by a deterioration of posture, walking, balance and sensomotor control. At the same time, dopaminergic resubstitution changes the stimuli's perceptive reliability. The impairments of the proprioceptive system, somesthesia, postural disfunctions and loss of balance are connected to the degeneration of cholinergic and dopaminergic systems in both patients with Parkinson's and the elderly.

During aging, the body image and the body schema changes. The body image carries individual characteristics based on life experiences and personal attitudes. In old age, in parallel with the decrease of sensory accuracy, as a form of compensatory mechanism, an increase of multisensory integration can be experienced. Depending on the examined leading modality, the integration of visual and somatosensory stimuli shows higher efficiency than in younger persons, while younger adults show an increase in the auditory-visual and auditory-somatosensory activation's condition. This means that the degree of compensation is specific to the modality. These processes aptly present that the operation of the body schema is directed by multimodal integration, and any damage to it will greatly alter the body's integrity.

Nowadays we connect our knowledge about the characteristics of Parkinson's disease (PD) to James Parkinson's 1817 study, even though earlier, in 1960, Pápai Pariz Ferenc has collected the disease's most characteristic symptoms. The motor symptoms appear on one side of the body, in the form of resting tremor, bradykinesia and rigidity, then later postural imbalance develops. As the disease progresses, the patient's quality of life, work capacity and cognitive functions are all decreased. 80-90% of patients afflicted with Parkinson's report neuropsychiatric symptoms, depression and anxiety.

The visual and spatial problems arise through the impairment of the basal ganglion circuits, which affects the posterior parietal cortex, whose main role lies in the performance of spatial abilities. The degradation of basal ganglions in PD patients can affect spatial cognition, and the decrease of dopamine the peripheral vision structures. Aside the classic cardinal musculoskeletal symptoms, walking and postural disorders can also be encountered with patients afflicted by Parkinson's, with the degradation of frontostriatal circuits as the culprit. As postural processes are greatly affected by sight, visual degradation in PD patients can be named as a great risk factor in relation to falling. The impairment of the proprioceptive system, disorders in body cognition, postural dysfunctions and loss of balance are all connected to the degeneration of cholinergic and dopaminergic systems in both healthy elders and Parkinson's patients as well.

So far, the most effective medication to Parkinson's is the one that also causes the most long-term side effects: levodopa. Levodopa is a precursor to dopamine. With its use the symptoms can be lessened, especially the ones related to movement. The use of dopamine agonist substances is immensely important in perspective of the delay of the appearance of later levodopa side effects and symptom control. At the onset of Parkinson's, they can be used in monotherapy, and in the advanced stages together with levodopa. Some of the dopamine agonist medicines have anti-depressive effects similar to classic antidepressants. Out of the medicinal treatment alternatives the use of products that block the breakdown of dopamine (MAO-B and COMT enzyme blockers) is suggested along with amantadine. Although the repetitive transcranial magnetic stimulation cannot be viewed as medicinal treatment, it is nevertheless useful in decreasing depression during the early and later stages of Parkinson's. The advanced stage of Parkinson's disease is the stage where per os medication can no longer be used to treat the motor complications. When the symptoms of an advanced Parkinson's can no longer be truly enhanced with the optimization of per os medication, then the use of apomorphine pump, levodopa-carbidopa intestinal gel (LCIG) and deep brain stimulation are the next step.

Parkinson's affects both the patient and its environment. Decreased physical and mental capacities are consequences of the ailment. Those affected have difficulty accepting this new situation and the disease itself. All of this can mean intense psychological strain for their environment (spouse/partner/caregiver). Helping the communication between parties can play a very important role. Due to its mechanism of action, there are numerous strong empirical evidence supporting the results of cognitive behaviour therapy (CBT) in treating mood and fear disorders. Several additional rehabilitational procedures are known in the treatment of PD patients, such as music therapy to treat depression, the use of robotics in the application to proprioceptive trainings, or the use of consoles, smartphones whose home use facilitates the patient's participation in the rehabilitation program.

2 Aims

The goal of our aforementioned series of studies is to examine the changes affecting the multimodal integration that creates the body schema and body image as the age advances, as well as to find out the ways in which this proprioceptive organization can be affected by a global injury with a fundamentally biological origin. As further goals of this study, I hope that the expected results can be used directly in enhancing the patients' rehabilitation. Because aside the motor and cognitive symptoms, rehabilitation depends to a great degree on affective factors as well, furthermore what are the ways a patient's participation can be won for the active and committed adherence-based treatment and how can the patient utilize their personal resources despite anxiety and depression. I aim to reach the above elaborated goals on one hand through a more detailed understanding of the correlation between the visual, tactile and proprioceptive stimuli that take part in the multimodal integration of the body schema and body image, on the other, through the investigation of the correlations between gait-pattern observable during goal-oriented locomotion and the affective state. The study builds upon two studies that may be connected to each other.

Specific aims:

1) **I. Examination:**
   The present study explores between-group differences in gait pattern and investigates the association between depression and the components of goal directed locomotion. The authors hypothesized that each examined gait component, velocity, cadence, and stride length, would significantly differ between patients with PD and age-matched healthy controls. In addition, the rate of gait disorder would demonstrate a strong association with depression in patients.

2) **II. Examination:**

   The present study proposes that the rubber hand illusion is an appropriate method for assessing multimodal integration capability differences between junior and senior adult participants when the stimuli are presented in the synchronous or asynchronous setting. Two main components of the body representation are to be examined: the ownership and disownership experiences and the proprioceptive reorganization of the spatial location of the corporeal body indicated by proprioceptive drift. Considering the age-related acuity decline in perception of ones' own body and the response differences between the junior and middle-aged adults to RHI we propose the decrease in sensitivity to RHI will be progressed in aging. In particular, the visuo-tactile-related ownership and the real hand disownership will be a decline in the senior group when synchronous multisensory stimulation is induced. In contrast, we suppose that visuo-proprioceptive integration in senior adults will show lifespan stability. Although the trimodal proprioceptive processing declines with increasing age, the body model system is continuously recalibrated to keep the movement activity both in healthy young and healthy elderly persons consequently, the magnitude of proprioceptive drift remains unchanged.

3) I. Examination: Association of Gait Characteristics and Depression in Patients with Parkinson's Disease Assessed in Goal-Directed Locomotion Task

3.1. Participants, Procedure and Analysis

Participants

Following Mini Mental State Examination (MMSE), 40 patients with PD and 49 controls were recruited for experimental analysis. Considering the required free walk locomotion test condition, patients were only asked for participation who were classified as patients with PD in Hoehn and Yahr stages 3-4 and freezing was not detected. All patients were prescribed levodopa (L-dopa). All participants provided written informed consent prior to experimentation. Handedness LateralityQuotients were 70% or higher for the right hand in all subjects. This study was performed in accordance with the Helsinki Declaration and approved by the Regional Research EthicsCommittee of the Medical Center in the State University.

Procedure

Global motor function was assessed using the UPDRS by a movement disorder specialist (N.K), when medication was controlled during regular visits to the outpatient clinic. Patients' L-dopa equivalent dosage (LED) was calculated as described by Tomlinson et al.. All patients took theirmedication in the morning approximately 2 h prior to examination. Participants were invited into a laboratory room and asked to perform two subsequent tasks that were originated fromthe clinical practice and modelled the everyday locomotion. To assess the gait characteristics, the patients and healthy controls were directed to approach a target in an examination room, where the main gait components of PD were evaluated using operationalized methods. At the beginning of the trial, participants were instructed to stand in front of a visible gray cross target (25 × 25 cm) placed 4m away on a white wall. They were directed to lift their right arm and to point to a target with their right index finger. Next,

while maintaining this arm and finger position, participants were instructed to approach the target and touch it. The goal-directed locomotion test contained two types ofmultiple task conditions: a simple visual control (VC) and complex nonvisual control (VnC). The first trial was conducted with VCand served as an introductorymotor exercise to assess the gait characteristics of participants and to determine stability in circumstances with VC. Following the introductory VC task, three test trials were performed in the VnC condition. During this task, at the start line, after a visual fixation of the target, the participant's eyes were covered by nontransparent swimming glasses and asked to approach and touched the estimated place of the target. The participants were followed up by an assistant. The procedure was safe or falling or other complications did not happen. Under VC and VnC conditions, the participants' gait characteristics, including cadence, stride length, and velocity, were recorded and assessed on a large carpet using a visible scaled ruler. The measurement of gait components was initiated when patients took their first step toward the target andmaintained throughout their route

towards the goal. Offline video recordings of the route of locomotion were analyzed by two independent raters. Three main gait parameters were assessed, including velocity (m/s),

cadence (number of steps from start to target), and stride length (distance in cmbetween successive heel contact points of the same foot).

Statistical Analysis.

SPSS version 22.0 was used for statistical analysis (Chicago, IL, US). For group comparisons, patients with PD and healthy participants were compared. A two-tailed *t*-test for parametric and a Mann–Whitney *U* test for nonparametric data were used to assess between-group differences in age, sex, education level, MADRS, cadence, stride length, and velocity. Kolmogorov-Smirnov tests were

used to assess the normality of variables. Logarithmic transformation was applied for cadence data in parametric comparisons. Moreover, Pearson's correlation analyses were used in the control group to assess within-group associations between movement parameters and MADRS data. In addition, in the patients' group, Pearson's correlation analyses were performed to evaluate the relationship between L-dopa dosage andMADRS, disease duration, cadence, stride length, and velocity variables. Gait data differences between groups were analyzed using multivariate test initially (MANCOVA, adjusted for age and gender), with follow-up univariate tests (ANOVA). For multiple comparisons between gait data and depression (following Feldmann et al.'s [4] method MADRS, cutoff = 13 was used) a $2 \times 2 \times 2$ Analysis of Variance (ANOVA) was used with regard to the factors of velocity, cadence, stride length, and MADRS for all dependent variables (two conditions: locomotion with VC and locomotion with VnC) in healthy controls and patients with PD. Post hoc Scheffˇe-tests were applied to evaluate significant pairwise differences between variables. Reasonable results were listed in post hoc tables only. Levene's test was used to detect differences in the homogeneity of variance. Analyses were two-tailed and significance was set at 0.05.

A Parkinson-kórra utaló vizsgálati változókra (lépéshossz: beteg és egészséges csoportok között, PK betegeknél motoros vizsgálat) gyakorolt prediktor változók hatását általánosított lineáris modellel (GLM) vizsgáltuk. A felállított modellkompozíciókból az Akaike Information Criterion (AIC), a ΔAIC (az általánosan elfogadott 2 alatti értékekkel rendelkező modellek) és a modellsúly alapján szelektáltuk. A GLM vizsgálatokat R 3.4.3 környezetben (R CORE-TEAM) 'AICmodavg', 'lme4' és 'effects' csomagok felhasználásával végeztük.

3.2 Results

The Coherence of Gait Pattern and the Related Affective Associations in Visually Controlled and Visually Noncontrolled Conditions.

Correlation analyses in the control group revealed a coherent pattern for velocity, stride length, and cadence. Under both VC and VnC conditions, the association of the three main gait components demonstrated the same coherent configuration (Table 2). During goal-directed locomotion, fast walkers typically exhibit a small cadence and long stride length while small cadence associated with long stride length. In the present task, the depression did not show a significant association with gait pattern under a simple VC conditions; however, in the multitask VnC condition, high depression scores correlated with low velocity, high cadence, and short stride length. The correlation analysis of patients with PD demonstrated a coherent gait pattern (low velocity, high cadence, and long stride length) similar to that of healthy controls in both the VC and VnC conditions. However, contrary to healthy controls, the depression was linked to low velocity, high cadence, and short stride length in the VC condition. A similar association was not found in the multitask VnC condition between depression and gait parameters. This indicates that the depression associated gait pattern was reverted in the VC and VnC conditions for the control and PD groups. PD-specific UPDRS scores correlated with depression and all gait parameters excluding stride length in the VnC condition. LED values correlated with velocity and stride length only in the VC condition, and disease duration was found to associate with L-dopa dose (Table 2).

Multivariate Analyses and Multiple Comparisons.

Comparison of the gait variables in the two groups (PD and healthy controls) showed the presence of significant differences concerning the mean gait scores [MANCOVA Wilks $\lambda = .569$; (6, 88) = 10.083; $p < 0.001$], after controlling for age and gender. Analysis of covariance found significantly lower stride

length and higher cadence in patients with PD compared with healthy controls in VC and VnC conditions. The velocity was significantly different in the two groups in the VnC condition only.

Pairwise Results by Scheff˝e-Test in Cadence.

Comparisons of cadence between healthy controls and patients with PD indicated significant differences, wherein patients with PD demonstrated a significant increase in cadence (Table 4). Similar significant results were identified in comparisons of condition (VC × VnC) and with regard to affective disturbance (depression × nondepression). Higher cadence was identified in patients with PD, in the VnC condition, and in participants with a higher depression score. Healthy controls × the VnC condition demonstrated lower cadence compared to patients in the VnC condition. In addition, comparison of healthy controls with depression versus PD patients with depression revealed an increased cadence in PD patients who suffered from depression.Therefore, higher levels of depression and visuospatially deprived examination conditions (VnC) augmented the contrast in cadence between healthy controls and patients with PD, wherein cadence is increased in PD. Further analysis indicated that cadence was increased in the VC condition in patients with PD and depression, compared to the VnC condition. Therefore, patients with PD and higher depression scores demonstrated increased cadence in visuospatially deprived conditions.

Pairwise Results by Scheff˝e's Test in Stride Length.

Differences in stride length between the VC and VnC conditions were significant, wherein stride length was reduced in the visually deprived condition. Patients demonstrated a significantly shorter stride length than healthy controls. Participants with elevated depression scores exhibited shorter stride length than participants without indications of depression. In addition, significant differences were identified between nondepressed healthy subjects and nondepressed patientswith regard to stride length,wherein the stride length of patients with PD was reduced. Next, stride length was found to decrease in the VnC condition in patients with PD, compared to the VC condition. Therefore, it is possible to suggest that, in patients with PD and depression, the VnC condition significantly decreases stride length.

Pairwise Results by Scheff˝e's-Test in Velocity.
Higher velocity was detected in healthy controls compared to patients with PD. Moreover, lower velocity was identified in PD patients in the VnC condition compared to healthy participants).

Table 1: Pearson's correlation of gait characteristics and affective scales in the healthy control group in two conditions (VC = visually controlled condition; VnC = visually noncontrolled condition), MADRS (Montgomery- ˚Asberg Depression Rating Scale); Parkinson's Disease Quiestionnaire-39 (PDQ-39).

index	1.	2.	3.	4.	5.	6.	7.	8.
1.VelocityVC	-	-0,84***	0,87***	0,80***	-0,61***	0,71***	-0,21	0,27
2.CadenceVC		-	-0,94***	-0,64***	0,79***	-0,66***	0,27	-0,28
3.Stride lengthVC			-	0,72***	-0,78***	0,75***	-0,21	0,24
4.VelocityVNC				-	-0,73***	0,78***	-0,32*	0,34*
5.CadenceVNC					-	-0,86***	0,39**	-0,35*
6.Stride lengthVNC						-	-0,31**	0,32*
7.MADRS							-	-0,53**
8.PDQ-39								-

*: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$

Table 3: Persons' correlation of gait characteristics and depression scale in Parkinson's disease group in two conditions (VC = visually controlled condition; VnC = visually noncontrolled condition): MADRS (Montgomery- ° Asberg Depression Rating Scale); Parkinson's Disease Quiestionnaire-39 (PDQ-39); UPDRS (Unified Parkinson's Disease Rating Scale); LED values; duration of disease.

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1.Velocity VC	-	-0,86***	0,92***	0,75***	-0,74**	0,21	-0,34*	0,32*	-0,44**	0,34**	0,21
2.Cadence VC		-	-0,91***	-0,73**	0,82***	-0,20	0,33*	-0,23	0,37**	-0,27	-0,24
3.Stride length VC			-	-0,75***	-0,79***	0,16	-0,31*	0,21	-0,36*	0,34*	0,22
4.Velocity VNC				-	-0,85***	0,42**	-0,25	0,32*	-0,34*	0,18	0,16
5.Cadence VNC					-	-0,34*	0,25	-0,26	0,38**	-0,14	-0,16
6.Stride length VNC						-	-0,13	0,18	-0,15	0,04	0,08
7.MADRS							-	-0,66**	0,47**	-0,28	-0,21
8.PDQ-39								-	-0,50**	0,01	-0,10
9.UPDRS									-	-0,03	0,09
10.LED values										-	0,63***
11. Duration											-

*: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$

Multiple comparisons: A comparison using Scheffé-test in relation to cadence

During a comparison of Healthy controls vs PD patients, cadence is increased significantly with PD patients (3. Table).

Gait parameteres	Mean (SD)						ANOVA intercept	Group comparison	Scheffé Post hoc p <
	He	PK	VC	VNC	NoD	DE			
Cadence	8,9 (2,5)	12,5 (6,0)	8,86 (3,0)	12,7 (5,6)	9,07 (2,8)	11,08 (5,7)	F = 904,14 df = 1; p <0,001	He vs. PK	0,001
								VC vs. VnC	0,001
								NoD vs. DE	0,001
								He x VnC vs. PK x VnC	0,001
								He x DE vs. PK x DE	0,004
								PK x VC x DE vs. PK x VnC x DE	0,006
Stride length (cm)	43,5 (10,8)	33,4 (11,6)	42,8 (11,2)	35,2 (12,1)	42,7 (11,3)	35,6 (12,1)	F = 1813 df = 1; p <0,001	HE vs. PK	0,001
								VC vs. VnC	0,001
								NoD vs. DE	0,001
								He x NoD vs. PK x NoD	0,005
								PK x VC x DE vs. PK x VnC x DE	0,047
Velocity (m/s)	0,58 (1,44)	0,38 (0,39)	0,50 (0,45)	0,44 (0,74)	0,59 (1,61)	0,40 (0,42)	F = 185,48 df = 1; p <0,001	He vs. PK	0,001
								He x VnC vs. PK x VnC	0,048

Table 3. Multiple group comparisons between patients and control persons, visually controlled and visually not controlled conditions and depressed and not depressed groups, complemented with walking components. Abbreviations: He= Healthy control group, PD= group with Parkinson's disease, VC = Visually controlled condition, VNC = visually not controlled condition, NoD = no depression group, DE = depression group.

Results of generalized linear models

An earlier study notes that as the disease advances, stride length and cadence decreases, these might be good indicators to establish the disease's stage when creating a rehabilitation program, because due to changes in motor function the cadence that describes patient's gait, is comprised of smaller and less secure steps. This gives patient's a "shuffling" gait. We established based on the correlative coefficients that the parameters describing different gaits correlate strongly with each other. In order to model them, we examined the changes of this gait parameter in relation to other predictor effects that change as the symptoms do. Based on the model selection, we examined 3 in more detail, because their delta AIC values were in the below 1 territory. The three main models we emphasized were the depression (MADRS), life quality (PDQ-39) and the cognition subscale of the life quality survey (PDQ-39; Cognition). As the disease progresses, patient's life quality, work capacity and cognitive functions decrease, that is why we thought it important to map the cognitive values which are crucial to life quality, in relation to stride length. We chose an additional subscale of the PDQ-39 (discomfort), but we only examined the models with a big enough model weight. Thus, no additional models were further examined, because they had no significant effect. We only used the visually not controlled data of the stride length affecting GLM examination, because earlier we described the purported effect of visual control on the measured gait parameters. Using all three models, we established that the healthy subjects have a larger stride length (and he patients have smaller stride lengths). The model highlighted the healthy group, because their values were probably rated as stronger effects. In the first model, the depression signaling MADRS-value showed a negative effect, which conformed significantly to the regressive line. Based on this, it is evident that depression shows a smaller value for healthy people than for patients.

3.3 Discussion
The depression links to gait characteristics as a comorbid affective factor in PD. The findings reported above serve as a laboratory-based demonstration of gait specificity in PD and revealed depression-related dissimilarities in healthy and Parkinsonian gait patterns. Considering the associations between gait and depression these data might aid the development of exact clinical diagnoses, to conduct more efficient rehabilitation training for gait disturbances.

During goal-directed movement, proprioception, that is the localization of the body and its parts to each other and to the environment, defines the body schema's function and has an important role in this study as well. The impairment of the proprioceptive system that is connected to the basal ganglions defines gait patterns in PD patients. In the case of PD patients, the dysfunction of proprioception is observable, that is the assessment of the placement of various limbs toward the body and the ground show a deficit. Based on our results, it is evident that a healthy proprioception has a significant importance in keeping the joints in place and in coordinated movement, these in turn define the function of the body schema. We can observe dysfunctions of general sensomotry integration and proprioception in PD patients, moreover, the impaired basal ganglions have a defining role in structuring and commanding movement and posture.

4) II. Examination: Multisensory integration and age-dependent sensitivity to body representation modification induced by the rubber hand illusion

4.1 Participants, Methods and Analysis

One hundred and one right-handed volunteers were invited from a larger population, from a community-based Facebook group and pensioners' clubs of the local town. The junior adult group involved fifty individuals (mean = 27.7 years, SD = 4.6, minimum = 20, maximum = 41; male/female: 28/22) and senior adult group involved fifty-one persons (mean = 65.9, SD = 5.8, minimum = 56, maximum = 72; male/female 26/25) groups. Participants belonging to the junior group were employed, and the senior group consisted of retired people. The recruitment criteria: Mini-Mental State Examination (MMSE) (Folstein et al. 1975; Feher et al. 1992) was conducted for the senior adults (minimum requirement score 23). On the total sample, the handedness was checked by the Edinburgh Handedness Inventory (Oldfield 1971) (minimum criterion for right hand were 70% or higher) and by self-report, and no participant had any previous psychiatric or acute somatic illness or experience with RHI. Each participant was blind to the hypothesis tested by the study. Participation was voluntary, but participants received a small fee (equivalent to 10USD) for their participation. The study was conducted according to the principles of the Declaration of Helsinki and approved by the Regional Research Ethics Committee of the Medical Center at the University of Pecs.

Rubber hand illusion induction

In our arrangement, participants were seated on a chair with their arms resting on a table with the palm facing down. The experimenter was standing opposite to the participants. Three experimental conditions were used: pretest condition (no stroking), illusion induction condition (synchronous stroking) and no illusion induction condition (asynchronous stroking). In the synchronous and the asynchronous conditions, a realistic-looking artificial left hand was placed on the right of the participant's real left hand. A standing screen was placed between the artificial and the real hand to prevent participants from seeing their own left hand. Three outcome measures were applied to describe the rate of RHI: proprioceptive drift, ownership of the rubber hand and disownership of the real hand (Longo et al. 2008). The proprioceptive drift involves a pointing error between the spatial location of the real hand and the rubber hand. The ownership and disownership are assessed by self-report scales.

Proprioceptive drift

The change in the perceived position of the participants' left hand was assessed by a procedure elaborated by Lopez et al. (2012). A ruler was placed in front of the participants, who were asked to put their right index finger somewhere on the front part of the ruler. Then, after having instructed the participants to close their eyes, the experimenter removed the standing screen and
positioned the ruler 13 cm up the table. While the participants' eyes were closed, there were asked to indicate the perceived position of the left index finger by drawing their right index finger on a ruler to the location, where they felt it was exactly above the tip of their left index finger. The extent of the proprioceptive drift was defined by the distance between the participant's posttest and pretest scores of location (in cm). Lower scores indicated bigger pointing errors, that is, participants perceived that their real arm's location was nearer to the rubber hand.

Procedure

Before starting the experimental phase, participants went through a short pretest session. They were asked to point to the location of the index finger of their left hand with their right hand with eyes closed on a scale placed over the desk near to the real hand to define the baseline point before inducing RHI. The experimental phase consisted of two blocks corresponding to the two experimental conditions: synchronous and asynchronous stimulation on their own left hand and on the rubber hand. Two blocks were applied in random order, while the visual perception of the left hand was inhibited by a folding screen. Both the synchronous and the asynchronous block contained 2-min ''stroking periods''. The pattern and the frequency (1 Hz) of stroking were predetermined in both conditions by the use of a metronome that guided the experimenter over an earphone. In the asynchronous condition, the seen stroking was followed by a felt, but not seen stroking with 1 s lag. The stroking in both conditions touched to each finger and to dorsum manus, except the thumb. There were 5-min pauses between the synchronous and asynchronous experimental blocks. After the stroking period, the proprioceptive drift was assessed. Subsequently, participants were asked to fill in a questionnaire consisting of test items concerning ownership and disownership statements.

Data analysis

According to the outcome scores of RHI in both synchronous and asynchronous conditions, the ownership and disownership scores and the proprioceptive drift were tested for normal distribution. The Kolmogorov–Smirnov test yielded significant deviations from normality for ownership and disownership, while proprioceptive drift showed normal distribution. Therefore, the nonparametric Mann–Whitney U test was performed to compare the two age groups for each RHI measures. To decrease the familywise error rate, the reported significances were adjusted by the Bonferroni method. In addition, the Wilcoxon rank test was used within the age groups to analyze the within-subjects difference between the synchronous and asynchronous conditions. A gender-based comparison for all RHI scores did not show any differences (asynchronous ownership $Z = -1.3$; asynchronous disownership $Z = -2.09$; synchronous ownership $Z = -0.2$; synchronous disownership $Z = -0.7$; asynchronous proprioceptive drift $t = -1.1$; synchronous proprioceptive drift $t = 0.4$).

4.2 Results

A Wilcoxon rank test was conducted for the synchronous and asynchronous conditions, in the total sample and separately for the two age groups. A significant difference was found between the two stroking conditions in the total sample for each measure (ownership, disownership, proprioceptive drift). The same analysis within the two age groups yielded similar results, except for disownership scores, where, after Bonferroni correction, the rate of difference showed only a tendency in the elderly group. That is, the difference between the synchronous and asynchronous conditions reached significance in both age groups for each of the three measures, but in the elderly group, the differences in disownership experiences were only limited The pairwise comparision within each group showed a vivid response to the synchronous visuo-tactile stimulation, but the articulation of the disownership experience and the proprioceptive drift scores were relatively limited in the case of the senior adults. These findings indicate that the synchronous multimodal stimulation evoked the expected RHI, but the magnitude of response is moderate in any outcome scores of RHI in senior's group. In the next step of analysis, the ownership and disownership RHI vividness index, the total score for the ownership and disownership experiences and the behaviorally defined proprioceptive drift scores were compared between junior and senior groups. These analyses yielded significant differences between the age groups for the ownership (junior

mean = 15.9 ± 23.26; senior mean = 6.4 ± 14.53; Z = -3.69, p = 0.001), total score for experiences in RHI (junior mean = 22.75 ± 22.21; senior mean = 9.2 ± 20.75; Z = -3.57, p = 0.001), and moderated differences for the disownership scores (junior mean = 6.4 ± 11.82; senior mean = 2.8 ± 8.04; Z = -1.661, p = 0.097), but proprioceptive drift has no found similar differences (junior mean = -0.2 ± 7.40; senior mean = -0.8 ± 7.12; Z = -0.51, p = 0.61 ns.). However, after the Bonferroni correction, only ownership index and the total RHI experience score remained significant. These findings suggest that the senior adults showed significantly lower scores compared to junior adults on RHI-related experiences, in particular on feelings of ownership. The scores on the behaviorally measured proprioceptive drift did not point to differences between groups.

4.3 Discussion

In the present study, we found evidence for age-related differences in multimodal integration, while participants met a rubber hand illusion where the visuo-tactile and visuo-proprioceptive stimuli were manipulated. First, the analyses showed that the synchronous multimodal stimulation elicited a rubber hand illusion both in junior and senior groups. The rate of ownership, disownership, and proprioceptive drift was higher after the synchronous stimulation than in the asynchronous condition. Second, the between-group analyses conducted for the ownership index, the disownership index and the total score for experiences in RHI in senior groups comparing with juniors revealed lower ownership index and total score for experiences in RHI, but age-dependent disownership and proprioceptive drift difference were not significant. Our results are consonant with former research findings and indicate that in both the junior and senior groups the RHI can be detected. Comparing with the asynchronous condition the synchronous stimulation results a significant gain for the integration of multimodal stimuli. In addition, our presented analyses pointed to special differences of how the RHI-induced multimodal integration is controlled by participants of different ages. Results in condition wherein visuo-tactile sensations were dominated
indicated less vivid rubber hand-related ownership and total score for experiences in RHI in the senior group. Further, in the condition wherein the visuo-proprioceptive stimuli (proprioceptive drift) were pronounced the gain in multimodal integration remained nearly equivalent in the groups. These results on proprioceptive drift support our hypothesis, that the adaptation to conflicting visuo-proprioceptive stimulation remains relatively productive in lifespan, while results in ownership and the total score for experiences in RHI showed a less vivid response to RHI induction in senior adults. These experiences indicated that when the rubber hand and the real hand were stimulated synchronously, participants experienced as if their limb would separate from their body representation, while the rubber hand was embodied.

Considering our results, we concluded that the perceptual vividness and the rate of agency over the limb are lower in the senior than in the junior group. More specifically, a lessened activity of ownership and total vividness score for RHI that contained limited interoceptive awareness may be the source of declined scores in the senior group. Senior individuals can be characterized by limited attentional focus, high tactile discriminatory threshold and low visual acuity. This sensory decline might play a role in sensitivity to react to synchronous visual, tactile and proprioceptive information. Consequently, senior participants compared to junior adults experience less vivid rubber hand illusion in visuo-tactile condition. We have to suggest that this agerelated declining in RHI may be considered as a mark of decline in the natural adaptation of self-perception to the rapidly changing face, body shape and appearance. The principal aim of multimodal integration is to test the temporal and spatial synchronicity and assure the semantic congruence of the context. The decline of perceptual and cognitive functions in

aging is compensated with focused and more selective attentional functions. The organization of attention allocation and multisensory integration shifts from the posterior brain areas toward anterior networks. In aging, in line with this attentional shift and multimodal integration capacity enhancements, the perception tends to slow down, while the temporal and space windows of the integrated stimuli become wider.

In the present study, tactile stimulation was applied to form an ecological likelihood relationship between two similar objects. The proprioceptive stimulus dominated on the visually separated real hand. The target of the visual attention in the participant's peripersonal space was the rubber hand without proprioceptive stimuli. Our presented results support the role of multimodal integration in the rubber hand-induced situation, both in one's own body ownership and the proprioceptive drift. But the betweengroup comparison showed that the proprioceptive component of multimodal integration remains unchanged across the lifespan. In contrast, when the attention focused on the visual stimulus that was separated from the proprioceptive one, body ownership experiences decreased in the senior group. Both the consciousness of body ownership and the associated real hand loss experiences decreased in the senior group indicating that the salience of the visual modality decreased among rival body-related modalities.

This conclusion supports the validity of the posterior–anterior attentional shift hypothesis for senior, in which the high background noise in parallel stimulus channels is limited by a conceptual anterior-type data processing and as a consequence, the visual information channel remained, in part, unattended. Neuroimaging evidence indicates that separate processes are involved in ownership experiences and in the proprioceptive drift. The multimodal stimulation differs in ownership, disownership (that related to visuo-tactile) and proprioceptive drift (related to visuo-proprioceptive) stimulation. Currently, the number of studies to describe multimodal integration in the elderly is limited, so the exact nature of the visual sensitivity decreasing in the order of multimodal integration remains open for investigation in this age group. Our presented results propose one of the possible lines of interpretation concerning the role of multimodal integration in the limited plasticity of body representation in the senior adults. In sum, we examined the age-related differences in outcome measures of rubber hand illusion. The results indicated that when visuo-tactile stimuli synchronously presented, the gain in multisensory integration decreased. In contrast in the case of visuo-proprioceptive synchronous presentation, the efficiency of multisensory integration remained unchanged across the lifespan.

4) Common discussion of two examination

Based on our studies it is evident that the structuring of walking built upon the proprioceptive system is subject to change depending on the affective state. Depression in general decreases walking speed in both PD patients and healthy people. Cadence and stride length is further decreased with depressed PD patients. The slowdown encountered during goal-directed locomotion is compensated by increased cadence and shorter stride length, but only in PD patients with depression. Aside from all this it is evident that the multimodal integration stays the same to some degree with the advancement of age, the body schema based proprioceptive system being one of its main components.

Based on this a significant role can be occupied by the methods discussed during the theoretical background segment and which are all available locally; cognitive behavioral therapy, psychotherapy and music therapy, these may support the betterment of movement patterns by enhancing the patient's emotional state. It seems that the body schema, which is the system of posture and movement based on proprioception, can be enhanced through a better emotional state.

For treatment of the impairment affecting the proprioceptive system, which greatly influences the function of the posture and movement defining body schema, many suggestions are given nowadays by professional teams. A fledging field is robotics, which too was discussed in the section about theoretical background, supporting positive change somatosensory processes, cadence and stride length during neurorehabilitation. While discussing methods related to posture and movement, we must also mention the use of various consoles, which can enhance the proprioceptive system and cognitive processes. All these methods can be used to mend the proprioceptive systems of both PD patients and healthy older individuals.

Proprioceptive training is getting more and more emphasis these days through the betterments of coordination skills, sense of balance, assessments of temporal and spatial localizations of body positions, kinesthetic sense and accuracy of movement patterns. Through the improvement of static and dynamic balance situations, that comprise the basis of proprioceptive training, the perception of given body parts' position in space and the movement patterns can be improved as well. Furthermore, proprioceptive training entails active movement/balance drills, passive movement, somatosensory stimulation or the improvement of the multimodal sensory system. With this knowledge we can mention the possible inclusion of the two methods presented in the dissertation into rehabilitation. It is evident that with the aforementioned training, the proprioceptive system can be enhanced, both in PD patients and in healthy individuals. Through this the goal-directed locomotion survey method of PD patients is able to be included in the clinical rehabilitation procedures. We can gather important information from gait diagnostics, in relation to movement organization, body awareness, and visual-spatial localization. The method of the rubber hand illusion too illustrates that we can gather information about the function of the proprioceptive system. The improvement of body position perception and the multisensory integration that creates the body schema – body image through this and other similar methods, where body awareness may be improved may become usable in the neurorehabilitational practice. All of these processes determine the organization of the sensomotory system led by the multimodal integration which comprise the body schema.

5) List of Publications

Publications related to the thesis

1. <u>Kincses P</u>, Kovács N, Karádi K, Kállai J (2015) A Parkinson-kór biopszichoszociális ellátásának kritikus kérdései. Orvosi Hetilap. 156:(12) pp. 472-478.
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2. Kállai J, Hegedüs G, Feldmann Á, Rózsa S, Darnai G, Herold R, Dorn K, <u>Kincses P</u>, Csathó Á, Szolcsányi T (2015) Temperament and psychopathological syndromes specific susceptibility for Rubber Hand Illusion. Psychiatry Research. 229: pp. 410-419.
   IF: 2.466

3. Kállai J, **Kincses P,** Lábadi B, Dorn K, Szolcsányi T, Darnai G, Hupuczi E, Janszky J, Csatho (2017) A Multisensory integration and age-dependent sensitivity to body representation modification induced by the rubber hand illusion. Cognitive Processing. 18:(4) pp. 349-357.
   IF: 0.974

4. **Kincses P**, Kovács N, Karádi K, Feldmann Á, Dorn K, Aschermann Zs, Komoly S, Szolcsányi T, Csathó Á, Kállai J (2017) Association of Gait Characteristics and Depression in Patients with Parkinson's Disease Assessed in Goal Directed Locomotion Task. Parkinsons Disease. Paper 6434689. 7 p.
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   IF: 3.139

Publications not-related to the thesis

1. Bereczkei T, Papp P, **Kincses P**, Bodrogi B, Perlaki G, Orsi G, Deák (2015) A The neural basis of the Machiavellians' decision making in fair and unfair situations. Brain and Cognition. 98: pp. 53-64.

   IF: 2.399

Presentations related to thesis

1. Kállai J, **Kincses P**, Lucza T, Kovács N, Weintraut R, Aschermann Zs, Komoly S, Karádi K (2015) Testséma és téri tájékozódási zavarok Parkinson betegségben szenvedő személyeknél. A Magyar Pszichológiai Társaság XXIV. Országos Tudományos Nagygyűlése: Eger, 2015 május 28-30.

2. **Kincses P**, Kovács N, Lábadi B, Csathó Á, Dorn K, Szolcsányi T, Kállai J (2015) A gumikéz illúzió által indukált testséma és testkép disszociációs érzékenység az életkor vonatkozásában. A Magyar Pszichológiai Társaság XXIV. Országos Tudományos Nagygyűlése: Eger, 2015 május 28-30.

3. **Kincses P**, Kovács N, Karádi K, Feldmann Á, Lucza T, Kállai J (2015) A perceptuo-motoros rendszer klinikai validitásának vizsgálata Parkinson-kóros személyekkel. XIV. Magatartástudományi Napok: A pszichoszomatika modern szemlélete. Az orvostanhallgatók egészsége. Konferencia helye, ideje: Pécs, 2015 június 11-12.

Presentations not-related to thesis

1. Darnai G, Szolcsányi T, Kállai J, Hegedüs G, **Kincses P**, Kovács M, Simon E, Nagy Zs, Janszky J (2015) A testészlelés befolyásolása hangingerekkel a „láthatatlan kéz illúzióban". XIV. Magatartástudományi Napok: A pszichoszomatika modern szemlélete. Az orvostanhallgatók egészsége. Konferencia helye, ideje: Pécs, 2015 június 11-12.

2. Szolcsányi T, Darnai G, **Kincses P**, Hegedüs G, Janszky J, Kállai J (2015) Can bodily self-perception be modified by auditory signals? Sound-induced proprioceptive drift in the invisible hand illusion. Ciprus 19th Conference of the European Society for Cognitive Psychology, 2015. szeptember 17-20., Paphos, Cyprus

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4. Darnai G, Szolcsányi T, Hegedüs G, **Kincses P**, Kállai J, Janszky J (2014) Sound-induced proprioceptive changes in the invisible hand illusion. 11th Alps Adria Psychology Conference. Pécs, Magyarország: 2014 szeptember 18-20.

5. János Kállai, Gábor Hegedüs, Ádám Feldmann, Sándor Rózsa, **Péter Kincses**, Virág Pulai, Zsófia Bacskai, Tibor Szolcsányi (2014) Psychopathological syndrome specific susceptibility for rubber hand illusion. 11th Alps Adria Conference. Pécs, Magyarország: 2014 szeptember 18-20.

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7. Bodrogi B, Deák A, Papp P, **Kincses P**, Bereczkei T (2013) Machiavellista személyek érzelemszabályozási folyamatainak idegrendszeri korrelátumai. Magyar Pszichológiai Társaság XXII. Országos Tudományos Nagygyűlés: Budapest, Magyarország, 2013 június 5-7.

8. Darnai G, Perlaki G, Szolcsányi T, Hegedűs G, **Kincses P**, Plózer E, Altbäcker A, Janszky J (2013) A gumikéz illúzió és a kérgi aktivitás (előtanulmány), Neuroimaging Workshop Pécs - 2013

9. Darnai G, Szolcsányi T, **Kincses P**, Perlaki G, Hegedüs G, Janszky J, Kállai J (2013) A gumikéz illúzió indukciója során aktív ideghálózatok: fMRI vizsgálat. Magyar Pszichológiai Társaság XXII. Országos Tudományos Nagygyűlés: Konferencia helye, ideje: Budapest, Magyarország, 2013 június 5-7.

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14. Papp P, Bodrogi B, **Kincses P**, Oláh-Szijjártó L, Deák A, Bereczkei T (2011) Hideg fejjel? Machiavellista személyek információ-feldolgozási folyamatainak idegrendszeri korrelátumai: fMRI vizsgálat MAKOG XIX., KAPOSVÁR, 2011. JANUÁR 27-29.,

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