Background and aims

Gait impairment and consecutively reduced mobility are typical features of idiopathic Parkinson´s disease (PD) and atypical parkinsonian disorders (APDs). However, these features develop earlier and are more pronounced in APDs such as Parkinson variant multiple system atrophy (MSA-P) [1]. The emergence of gait disorders with instability, freezing and falls represents a major motor milestone in the natural history of parkinsonian syndromes indicating a transition to sustained disability and reduced quality of life. Impaired physical activity and sedentary behavior are associated with reduced walking bouts and increased time spent in sitting or lying posture [2], resulting in disabling consequences for daily life activities and therefore creating a vicious cycle, which is linked to higher mortality rate also in normal elderly people [3]. On the contrary, increased activity levels can sustain independence, delay onset of decline and lower fall risk [4, 5]. A special characteristic of MSA patients is their resistance to dopaminergic therapy. Also in PD patients that typically benefit from dopaminergic treatment, in advanced stages, where gait impairment is increasing, dopaminergic intervention becomes less effective. Importantly, for gait impairment in PD non-pharmacological interventions are more and more recognized as complementary treatment options [6]. Up to now, many exercise-based interventions are available for PD, ranging from community exercises like dancing and tai chi to complex computer-based training options and the scientific evidence for their efficacy is growing [6-8]. For instance, Cusso et al. described the positive impact of physical activity on motor as well as non-motor symptoms[8] and there is strong evidence that freezing of gait can be effectively overcome using cueing strategies[9]. As extensively described by Bloem et al., many domains of physical therapy (PT) have been evaluated as interventions in PD, including exercise, strength training, balance and gait training and also a combination of them, with promising effects. In 2014, the European Physiotherapy Guideline for Parkinson´s Disease was developed and provides practical and evidence-based information for physiotherapists but also for physicians [10, 11]. A multidisciplinary approach seems to provide the best benefit for parkinsonian gait disorders. A few small-sized studies examined efficacy of diverse PT strategies in classical Progressive Supranuclear

Palsy (PSP) patients[12]. However, to this point there is no study that addressed PT in MSA-P (or cerebellar variant MSA=MSA-C) patients. Up to now, it remains unknown whether a referral to physiotherapists should be considered and, still, which kind of physical therapy should be recommended for MSA patients. This aspect represents an unmet need for MSA, even more as pharmacological treatment is not effective to overcome motor symptoms. To address these questions, the present study aimed to explore the effects of PT for patients with MSA. The study prospectively investigated the effectiveness of two forms of PT for improving MSA associated gait disorders and sedentary life style using clinical rating scales (CRS) and sensor-based gait analysis as clinical outcome measures.

Subjects and Methods

Between June 2017 and June 2018, 20 not-demented patients having either a diagnosis of MSA of parkinsonian type (probable MSA-P n=10) [13] or of idiopathic Parkinson´s disease (IPD n=10) [14] were enrolled in the outpatient clinic of the Department of Neurology at the, Austria. Additional inclusion criteria consisted of age 30-80 years, stable doses of dopaminergic replacement therapy and orthostatic hypotension (OH) pharmacological/non-pharmacological treatment for at least three weeks prior to recruitment, ability to walk unassisted, no hearing or visual problems interfering with walking or testing. Exclusion criteria consisted of non-PD related gait impairments (e.g. spinal or orthopedic surgery, spasticity, stroke, neuropathy, myelopathy, hydrocephalus), diagnose of severe dementia, Hoehn and Yahr stage 4 or 5, recent surgery, deep brain stimulation, unstable coronary disease, history of freezing of gait and severe motor fluctuations. Intervention protocol was standardized and falls frequency was monitored during the intervention period to ensure participants´ safety. The study flow chart is represented in the figure 1. Every visit in-hospital was performed by an expert neurologist and consisted on clinical rating scales, patients´ questionnaires and instrumented gait analysis. Physical tests were performed immediately after every study visit by a blinded-physiotherapist and consisted in standardized physical tests. Motor parts of MDS-UPDRS (for all patients) and of UMSARS (for MSA patients) were rated by a blinded neurologist. Walking

performance was captured using a sensor-based gait analysis system (eGAIT), consisting of wearable SHIMMER 2 sensors laterally attached to the posterior lateral portion of both shoes. Patients were asked to perform standardized walking tests on a 10 m long corridor in the hospital at: a) self-paced comfortable speed b) fast self-paced speed c) slow self-paced speed d) counting aloud backwards while walking at self-paced speed (dual task) and e) 2-minute walking at self-paced comfortable speed.

Straigth strides were automatically detected and used for spatio-temporal gait parameters calculation.

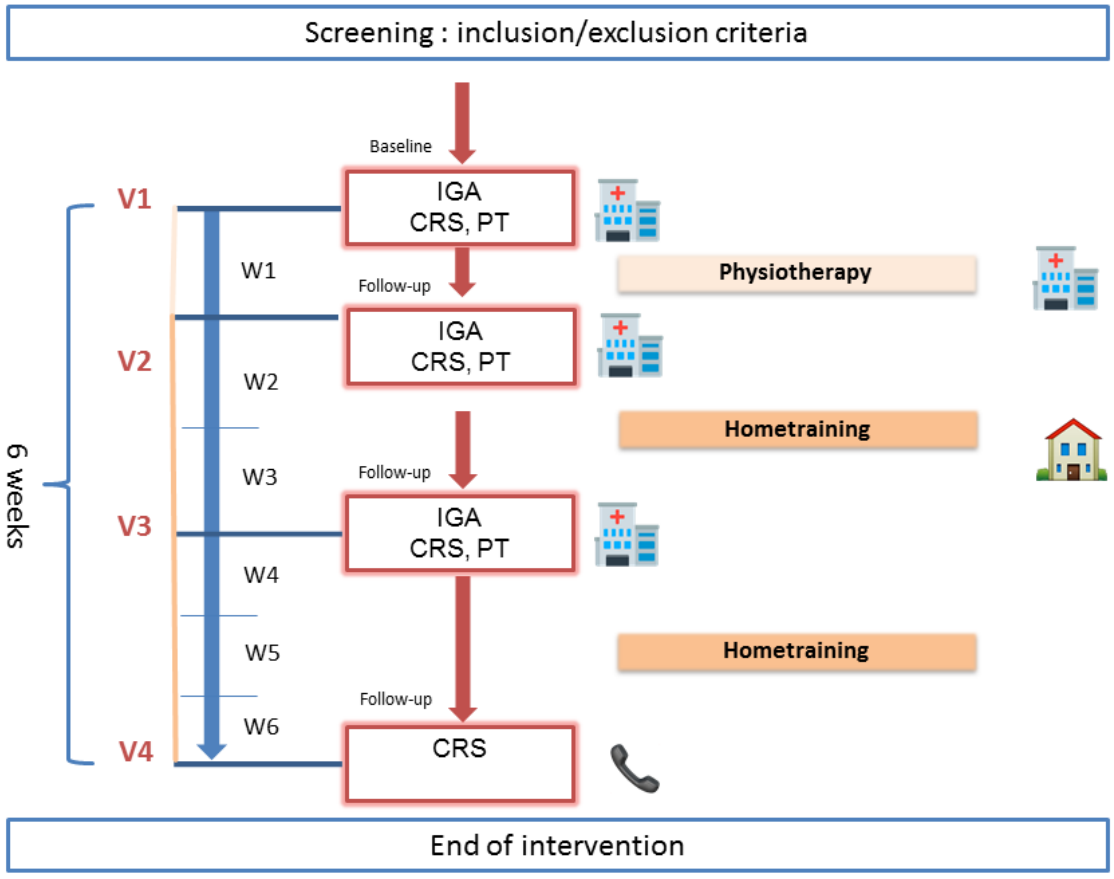

Figure 1: study flow chart. Testing was performed at three different time points in-hospital and was structured as follows: baseline at day 0, the first posttest (visit 1) immediately after the first week of intervention (day 5) and the second posttest (visit 2) after three weeks of intervention (day 19). A one long-term phone interview to assess quality of life and motor/non-motor symptoms was performed after 6 weeks of intervention (day 40).
V: Visit; W: Week; IGA: Instrumented Gait Analysis; CRS: Clinical Rating Scales; PT: Physical Tests

Preliminary data

Patient characteristics	PD n = 10 mean (range) median (IQR)*	MSA-P n = 10 mean (range) median (IQR)*	P value
Age at examination (years)	74.5 (65-77)*	55.5 (54.5-60)*	< 0.05
Gender (m:f)	5 : 5	4:6	n.s.
Disease duration (years)	9.5 (4.5-15.2)*	4 (2.7-6.2)*	< 0.05
Clinical rating scales			
Hoehn Yahr	2.7 (2-3)*	3 (2.7-3)*	n.s.
MDS-UPDRS I	8 (3-20)*	12.70 (5-17)*	<0.05
MDS-UPDRS II	6.3 (0-19)*	20.5 (9-37)*	< 0.05
MDS-UPDRS III	23.6 (9-46)*	33.4 (16-71)*	< 0.05
UMSARS I		19.7 (11-32)*	
UMSARS II		20.5 (8-43)*	
Quality of life	**PD**	**MSA-P**	**P value**
PDQ-39	3.8 (1.5-10.5)*	6.7 (2.1-10.1)*	< 0.05
Physical examination			
Berg Balance Scale (value)	52.7 (43-56)*	45.2 (6-55)*	< 0.05

Timed up and go (s)	9.2 (5.1-12.6)*	16.1 (7.10-58.40)*	< 0.05
10 m walking test (s)	7.5 (5.3-10.3)*	9 (5.1-14.1)*	n.s.
Tandem Gait without side steps (%)	100	10	< 0.05
Stopped riding (%)	0	90	< 0.05
Cognitive assessment			
MoCA	24.8 (22-30)*	27.6 (22-30)*	n.s.

Table illustrates patients´ characteristics. Normal distributed variant are expressed in mean (range), while non-normal distributed variables are expressed as median and interquartile range (IQR). PD: Parkinson´s Disease. MSA-P: Multisystematrophy of parkinsonian type. MDS-UPDRS: MDS-Unified Parkinson's Disease Rating Scale. UMSARS: Unified Multiple System. Atrophy Rating Scale. PDQ-39: 39-item Parkinson's Disease Questionnaire. MoCA: Montreal Cognitive Assessment.

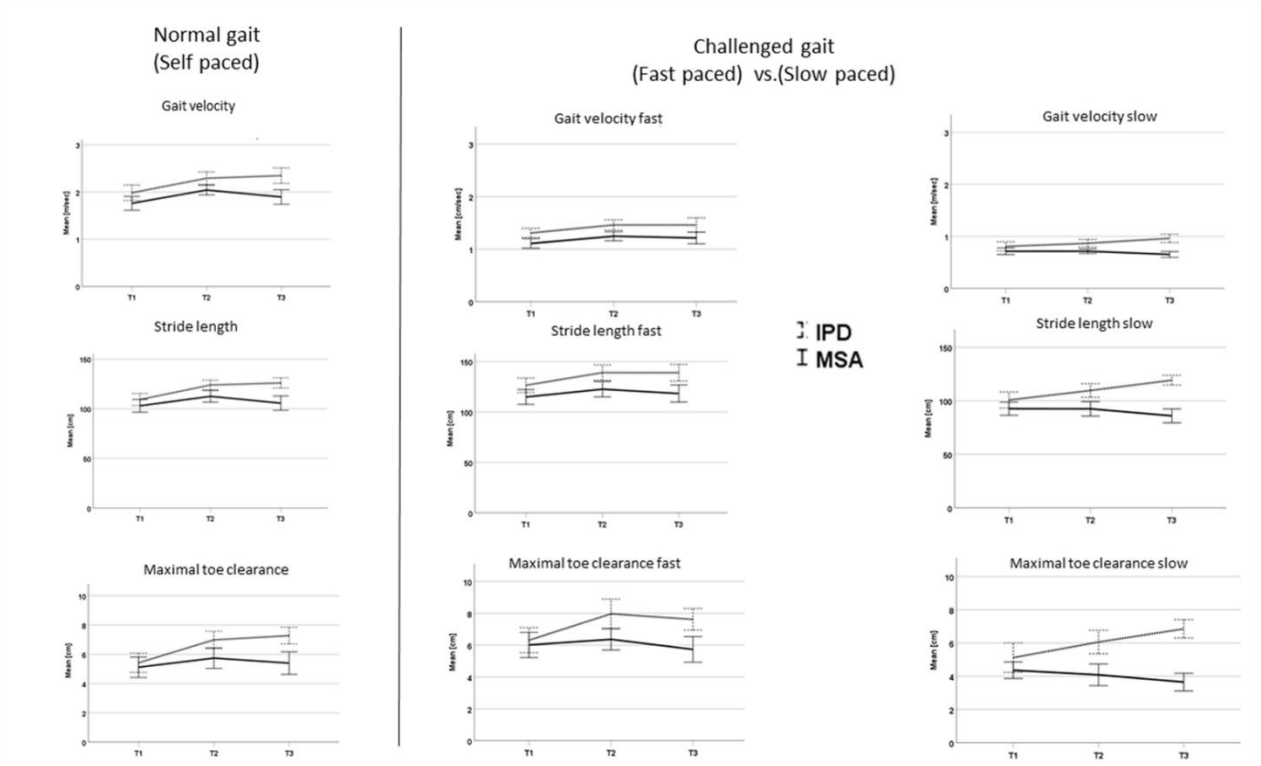

Figure 2: IGA based gait parameters. T1, T2, T3: Timepoint 1, 2, 3. IPD: Parkinson´s Disease. MSA: Multisystem atrophy.

Conclusions and outlook

Our study addressed the primary research question whether MSA patients can benefit from a standardized physiotherapy based on guidelines for PD. Additionally, the study aimed to investigate whether physiotherapy effects are sustainable. The most important clinically relevant finding was that gait of MSA patients is improving after an intensive in-hospital in-patient physiotherapy program. Thinking further, this finding after such a short treatment duration is even surprising in relation to the motor impairment of MSA patients. Still, most of these therapeutic effects were not significantly worsening after a low-dose unsupervised in-home training program. However, our data indicate a tendency not to maintain the same improvement levels showed after an intensive physiotherapy in-hospital. Therefore, an intensive in-patient in-hospital physiotherapy seems to be a more effective intervention than a low-dose in-home training. There are several possible explanations for this result. Firstly, it may be hypothesized that patients at home without supervision of an expert are not performing the training program properly. Secondly, it may reflect that patients do not have enough time during the 5-day long in-hospital physiotherapy to learn properly the training program and being able to reproduce it correctly at home. Another possible explanation is the lack of compliance and adherence to the training plan.

The current study was the first-ever assessment of physiotherapy in MSA patients. Further studies are needed to confirm and implement our results. For patients with PD, there is strong evidence that the introduction of an activity coach in the intervention plan, who guides patients towards a more active lifestyle through periodic coaching sessions enhances patients´ motivation and promotes physical activity [15]. Therefore, an activity coach may educate patients about the benefits and the importance of physical activity, may help to overcome any perceived barriers to engaging in physical activity and set systemic goals, therefore improving patients´ motivation, well-being and levels of independence.

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