©Journal of Sports Science and Medicine (2014) **13,** 597-603
http://www.jssm.org

Case report

Resistance Training with Instability in Multiple System Atrophy: A Case Report

Carla Silva-Batista ✉[1], Hélcio Kanegusuku [1], Hamilton Roschel [1], Eduardo O. Souza [1], Telma F. Cunha [1], Gilberto C. Laurentino [1], Manoel N. Jr [2], Marco T.De Mello [3], Maria E.P. Piemonte [4], Patrícia C. Brum [1], Claudia L. Forjaz [1], Valmor Tricoli [1] and Carlos Ugrinowitsch [1]

[1] School of Physical Education and Sport; University of São Paulo, São Paulo, Brazil; [2] Division of Rheumatology, School of Medicine, University of São Paulo, São Paulo, Brazil; [3] Center for Psychobiology and Exercise Studies, Federal University of São Paulo, São Paulo, Brazil; [4] Department of Physical Therapy, Faculty of Medical Science, University of São Paulo, São Paulo, Brazil

Abstract

This case report assessed quality of life, activities of daily living, motor symptoms, functional ability, neuromuscular parameters and mRNA expression of selected genes related to muscle protein synthesis and degradation in a patient with Multiple System Atrophy (MSA). The patient underwent resistance training with instability devices (*i.e.,* bosu, dyna disk, balance disk, Swiss ball) for six months twice a week. After the six months training, the patient's left and right quadriceps muscle cross-sectional area and leg press one-repetition maximum increased 6.4%, 6.8%, and 40%, respectively; the patient's timed up and go, sit to stand, dynamic balance, and activities of daily living improved 33.3%, 28.6%, 42.3%, and 40.1%, respectively; the patient's severity of motor symptoms and risk of falls decreased 32% and 128.1%, respectively. Most of the subscales of quality of life demonstrated improvements as well, varying from 13.0% to 100.0%. mRNA expression of mechanogrowth factor and mammalian target of rapamycin increased 12.7-fold and 1.5-fold, respectively. This case report describes likely the first nonpharmacological therapeutic tool that might be able to decrease the severity of motor symptoms and risk of falls, and to improve functional ability, neuromuscular parameters, and quality of the life in a patient with MSA.

Key words: Exercise training, risk of falls, motor symptoms, cross-sectional area.

Introduction

Multiple System Atrophy (MSA) is a sporadic neurodegenerative disorder characterized by a variable combination of parkinsonism and cerebellar features, autonomic, and urinary dysfunction, and pyramidal signs (Quinn and Wenning, 1996). It usually affects people at middle age, and its prevalence is estimated at 4.6 cases per 100.000 people. The most dominant symptom exhibited by the patient allows classifying MAS. When cerebellar dysfunction is the most prominent feature the disease is categorized as MSA cerebellar ataxia. When Parkinson's disease-like movement dysfunction is the most prominent feature (*i.e.,* rigidity, bradykinesia, and postural instability) the disease is categorized as MSA parkinsonism subtype (Quinn and Wenning, 1996).

Patients with MSA present not only a functional incapacity but also a greater severity of motor symptoms when compared with patients with Parkinson's disease (Tison et al., 2002). They also exhibit muscle weakness (van de Warrenburg et al., 2007; Rivest et al., 1990) with consequent impaired muscle performance (Wedge, 2008) and loss of balance (Tison et al., 2002). When these factors are combined, they contribute to the increase in the risk of falls (Tison et al., 2002). Tison et al. (2002) observed that falls were tenfold more frequent in patients with MSA (20%) than in patients with Parkinson's disease (2%).

Importantly, information about an evidence-based treatment in MSA is largely lacking (Jecmenica-Lukic et al., 2012). Clinical practice suggests that most patients are poorly responsive to pharmacological treatment (*e.g.,* dopaminergic drugs) (Tison et al., 2002). In this context, non-pharmacological strategies able to mitigate the MSA-induced symptoms are in great need.

Instability is a mode of exercise in which the individual performs exercises having most of his bodyweight supported on instability devices (*e.g.,* bosu, dyna disk, balance disk and Swiss ball) (Behm et al., 2010). This mode of exercise has been effective in ameliorating spinal mobility, dynamic balance, and functional ability in a frail elderly population (Granacher et al., 2012) by providing a great challenge to balance and motor control. Additionally, it has been recently shown that a low- to moderate-intensity conventional resistance training program was able to improve the functional ability, balance, and muscle performance in a patient with MSA (Wedge, 2008).

A few studies have demonstrated that the combination of instability and regular resistance training increases the challenge imposed to the neuromuscular system and, therefore, may enhance motor control, and functional and neuromuscular gains in young adults (Kibele and Behm, 2009). When properly adapted, the combination of instability with conventional resistance training emerges as an appealing adjunct therapeutic approach that may alleviate the MSA-related effects and improve the quality of life of these individuals. Furthermore, although there is no information in the literature with respect to skeletal muscle atrophy in patients with MSA, the hampered muscle performance (Wedge, 2008) and muscle weakness (van de Warrenburg et al., 2007, Rivest et al., 1990) may be indicative of impaired muscle plasticity in response to exercise. In this regard, several studies have investigated the molecular responses (*e.g.* atrophy and hypertrophy related mRNA gene expression) to different modes of exercise and its relation to phenotypical (*i.e.,*

Received: 23 December 2013 / Accepted: 27 February 2014 / Published (online): 01 September 2014

Figure 1. Initial (left) and final (right) phase of motion in the leg press exercise performed with bosu under the feet and balance disc under the seat.

muscle cross-sectional area) adaptations (Murton and Greenhaff, 2013) but not in patients with MSA.

Therefore, the purpose of this current case report was to assess quality of life, motor symptoms, functional ability, activities of daily living, risk of fall, neuromuscular parameters and mRNA expression of selected genes related to muscle protein synthesis and degradation in a patient with MSA before and after resistance training with instability.

Methods

Patient´s characteristics prior to the training

A 79-year-old man (weight = 55 kg, height = 1.70 m, peak oxygen uptake [VO_{2peak}] = 10.1 $mL \cdot kg^{-1} \cdot min^{-1}$ - assessed by a maximal graded test on a cycloergometer) presented six years of sleep disorders, urinary incontinence, fatigue, muscle weakness and Parkinson's disease-like symmetrical onset motor symptoms (akinesia, bradykinesia, rigidity and postural impairment) and a poor response to dopaminergics drugs. The diagnosis for probable MSA was performed by a neurologist through magnetic resonance imaging and confirmed by the predominant striatonigral degeneration in the absence of cerebellar dysfunction, presence of cardinal features including parkinsonism, and symptoms of autonomic failure (Quinn and Wenning, 1996). The neurologist classified the severity of Parkinson's disease-like symptoms as Hoehn and Yahr stage 4 (Goetz et al., 2004). The patient has been treated with levodopa-prolopa (ranged from 100 $mg \cdot d^{-1}$ to 500 $mg \cdot d^{-1}$) and with pramipexole (ranged from 0.50 $mg \cdot d^{-1}$ to 150 $mg \cdot d^{-1}$) for five years. The patient presented neither dementia (as assessed by the Mini Mental State Examination (Bertolucci et al., 1994) [score 30]) nor depression (as assessed by the Geriatric Depression Scale (Almeida and Almeida, 1999) [score 2]). However, three months prior to the intervention, he presented a rapid progression of the motor symptoms, reduction of the bodyweight from 65 kg to 55 kg, reported a rather extensive history of falls (11 times during this period) and was unable to perform any activities of daily living without the help of a cane.

Training protocol

The program of resistance training with instability was performed twice a week (Mondays and Thursdays) during 24 weeks for a total of 48 sessions performed. The patient was tested and trained in the clinically "on" state (fully medicated) during the morning time within 1.5 hours of taking his last dose of the dopaminergic drug. Each training session lasted between 40 and 50 min, and started with a 10-min warm-up on a bicycle ergometer (20 to 40 rpm). The resistance training with instability consisted on the combination of conventional external load lower-limb resistance training machines (*i.e.,* leg press and plantar flexion) and free exercise (*i.e.,* half-squat) with unstable devices (*i.e.,* balance pad, dyna discs, balance discs, bosu, and Swiss ball). The unstable devices were placed between the patient's base of support (*i.e.,* the body area responsible for sustaining most of his body weight and/or on the point of force application) and the resistance training machines for each individual exercise. Figure 1 depicts an example of the combination of resistance exercise with the unstable device. The progression of the training protocol (i.e., load and instability) throughout the six months of the intervention is shown in Table 1. Exercise loads were incremented whenever the patient was able to perform two consecutive sessions with the

Table 1. Protocol of resistance training with instability throughout the six months of intervention.

Months	Sets	RM	Exercises
1	2-3	10-12	Half-squat (balance pad - feet and Swiss ball - back), leg press and plantar flexion (balance pad - feet and balance disc - seat);
2	3	8-10	Half-squat (dyna discs - feet and Swiss ball - back), leg press and plantar flexion (dyna discs - feet and balance disc - seat);
3-4	3-4	8-10	Half-squat (balance disc - feet and Swiss ball - back), leg press and plantar flexion (balance disc - feet and seat);
5-6	4	6-8	Half-squat (bosu - feet and Swiss ball - back), leg press and plantar flexion (bosu - feet and balance disc - seat).

RM = repetition maximum. An interval of at least 90s was guaranteed between sets and exercises.

same load. The progression in the unstable device was included in the training program from less unstable to more unstable. All of the training sessions were monitored by at least two investigators.

Data collection

Quadriceps muscle cross-sectional area (CSA) was obtained through magnetic resonance imaging (Signa LX 9.1, GE Healthcare, Milwaukee, WI, USA). CSA images were obtained at 50% of the segment length with 0.8-cm slices for three seconds. The pulse sequence was performed with a view field between 400 and 420 mm, time repetition of 350 milliseconds, eco time from 9 to 11 milliseconds, two signal acquisitions, and a reconstruction matrix of 256 × 256. The images were transferred to a workstation (Advantage Workstation 4.3, GE Healthcare, Milwaukee, WI, USA) to determine quadriceps CSA. In short, the segment slice was divided into the following components: skeletal muscle, subcutaneous fat tissue, bone and residual tissue. Then the left and right thigh CSA was assessed by computerized planimetry (de Souza et al., 2012).

Maximum dynamic strength test (one repetition maximum [1RM]) was assessed in the 90° leg-press exercise according to procedures followed the guidelines of the American Society of Exercise Physiologists (Brown and Weir, 2001). The patient performed three familiarization sessions to achieve 1RM stabilization (variation between two subsequent sessions was less than 5%), with the testing procedures separated by, at least, 48 hours. In short, patient started with a general warm-up consisting of a 10-min warm-up on a bicycle ergometer (20 to 40 rpm). Then, a specific warm-up routine of eight repetitions at 50% of estimated 1RM followed by a set of three repetitions at 70% of estimated 1RM was performed. Warm-up sets were separated by a 2-min interval. After the completion of the second set, patient rested for three minutes before the beginning of the test. Testing included single attempts at progressively heavier weights until the 1RM was identified, which typically required three to five attempts. A three-minute interval was allowed between attempts and strong verbal encouragement was provided during the attempts.

Dynamic balance, functional gait and mobility were assessed using timed up and go test (Podsiadlo and Richardson, 1991). The patient performed three familiarization sessions with the testing procedures separated by, at least, 48 hours. The patient was timed while he rose from an arm chair (approximate seat height 46 cm), walked at a comfortable and safe pace to a line on the floor three metres away, turned and walked back to the chair and sat down again. The patient wore his regular footwear and used his customary walking aid (cane).

Lower extremity strength was assessed using the timed stands test (Newcomer et al., 1993). A straight-backed chair without arms, with a seat height of 45 cm, was used in this test. The patient was seated in a position which allowed him to place his feet on the floor with knees flexed to slightly over 90° so that his heels were somewhat closer to the chair than the back of the knees. The arms were crossed over the chest and the rose was from full sitting position all the way up to standing.

Risk of fall was assessed by the Biodex balance system (Biodex Medical Systems - SD, USA). The patient performed three familiarization sessions with the testing procedures separated by, at least, 48 hours. The patient performed five 20-second trials in the level 8 (ranging from 2 to 12) of difficulty. The average of the five trials (overall balance index of anterior-posterior and medial-lateral directions) was registered. Higher values indicate increase in the risk of falls (Sieri and Beretta, 2004).

Dynamic balance was assessed using the Berg Balance Scale, which has been validated to assess the balance of patients with Parkinson's disease. A score below 46 indicates the risk of falls (Qutubuddin et al., 2005).

Activities of daily living and motor severity were assessed by section II and III, respectively, of the Unified Parkinson Disease Rating Scale (UPDRS). The UPDRS has been considered by the Movement Disorders Society to be the gold standard assessment for patients with Parkinson's disease (Goetz et al., 2008). Thus, as our patient presented Parkinson's disease-like movement dysfunctions, we opted to use the UPDRS to assess activities of daily living and motor severity. UPDRS's lower scores indicate better performance in the activities of daily living (section II) and decrease of motor severity (section III).

Quality of life was assessed by the Parkinson's disease questionnaire (PDQ-39) (Souza et al., 2007). PDQ-39's lower scores indicate better quality of life.

Muscle samples were obtained from the vastus lateralis of the patient's most affected leg (left) using the percutaneous biopsy technique (Neves et al., 2012) at baseline and approximately 48 hours after the last training session. All of the biopsies were performed after a 10-h overnight fasting period. The patient was asked to record and reproduce his meals for a 48-h period before each muscle biopsy and he was offered a standard breakfast approximately two hours before the procedure (~311 kcal; 63.5% carbohydrates, 21.8% proteins, and 14.7% fat). All of the biopsies were performed at the same time of the day. The mRNA expression of mechanogrowth factor (MGF), mammalian target of rapamycin (mTOR), atrogin-1, and muscle RING finger-1 (MuRF-1) were quantified using real-time polymerase chain reaction on the basis of current methodology (Bustin et al., 2009).

The evaluators were blinded to the treatment. The patient received a verbal explanation of the possible benefits, risks, and discomforts associated with the case report and signed an informed consent before participating in the case report. This case report was approved by the Ethical Advisory Committee from the School of Physical Education and Sport, University of Sao Paulo (approval number - 2011/12).

Results

The training protocol was well tolerated by the patient. No adverse effects were reported during the trial and adherence to the protocol was high (98% attendance). The

Table 2. Effects of six month resistance training with instability on quadriceps muscle cross-sectional area and one repetition maximum (1RM) leg press in a patient with Multiple System Atrophy.

	Baseline	Post-trial Period
Left quadriceps cross-sectional area (mm^2)	4071	4354
Right quadriceps cross-sectional area (mm^2)	4117	4418
1RM leg press (kg)	30	50

patient's medication did not changed during the entire protocol.

After the trial, the quadriceps muscle CSA from both legs increased similarly (6.4% and 6.8% for the left and right legs, respectively). The patient showed a 40% improvement in the leg-press 1RM. (Table 2). The functional ability showed improvements in all of the tests. The performance on the timed up and go and timed stands tests was improved by 33.3% and 28.6%, respectively. The Berg balance scale showed an improvement in dynamic balance of 42.3%. The risk of fall improved by 128.1%. Performance of activities of daily living as assessed by part II of the UPDRS - which includes functions such as walking, hygiene, clothing, changing position in bed and incidence of falls - showed an improvement of 40.1%. The severity of motor symptoms, as assessed by part III of the UPDRS, improved by 32% Additionally, the rigidity, alternating movements of hands, leg agility, arising from chair, gait, postural instability, posture and bradykinesia were the symptoms that contributed most to the score (33 points) in this scale before the training protocol. Importantly, these symptoms were decreased after the exercise training protocol (Table 3). Most of the PDQ-39 showed lower values after the intervention. The specific reductions were: 65.0% for mobility, 50.0% for activities of daily living, 13.0% for emotional well-being, 100.0% for cognition, and 100.0% for bodily discomfort. However, the items stigma, social support, and communication, were not altered. The molecular assays revealed an increase in both the MGF and mTOR mRNA expression (12.68- and 1.51-fold increase, respectively). In contrast, atrogin-1 mRNA expression was reduced (1.66-fold), whereas MuRF-1 mRNA expression was only slightly reduced (1.32-fold).

Discussion

This case report showed that six months of resistance training with instability may improve neuromuscular parameters, functional ability, activities of daily living, motor symptoms, and quality of life in a patient with MSA. Additionally, our data suggests that the changes in muscle morphology and function may be partially explained by MGF and mTOR up-regulation and atrogin-1 down-regulation.

To the best of our knowledge, this is first study to evaluate the effects of the resistance training with instability in a patient with MSA. Moreover, this is the first report of positive changes in the MSA-related effects, and consequently in the quality of life of this patient after a non-pharmacological treatment.

Our functional ability findings are in accordance with previous data from the literature. Wedge (2008) examined the efficacy of a low- to moderate-intensity conventional resistance training program in one patient with MSA (68-year-old). The program consisted of 2-3 sets of 8-10 repetitions for lower limb muscles, two times a week for 22 weeks. However, the study was limited to the evaluation of functional ability and severity of motor symptoms. The author reports improvements in the timed up and go and the timed single-limb stance test (42.8% and 100%, respectively), as well as an improvement in the performance oriented mobility assessment (POMA) test by 8.0%. Importantly, the author reports no change on the severity of motor symptoms (score of the UPDRS part III). Our data expands the notion that a resistance training program with instability may be beneficial to other parameters such as the severity of motor symptoms, quality of the life, activities of daily living, and muscle morphology and function in patients with MSA.

Regarding the muscle strength and mass data, our results are similar to those observed in patients with Parkinson's disease (Dibble et al., 2006) or in healthy elderly population (Wallerstein et al., 2012). Dibble et al. (2006) reported increases in quadriceps CSA and muscle strength (6% and 24%, respectively) after 12 weeks of high-intensity resistance training in patients with Parkinson's disease. Wallerstein et al. (2012) demonstrated a 6.1% and 42.7% increase in quadriceps CSA and strength, respectively, after 16 weeks of high-intensity resistance training in healthy older individuals. In the present study, our patient showed comparable increases in both quadriceps CSA (6.4% and 6.8%) and strength (40%). The increase in muscle mass and strength was paralleled by the improvement in functional ability. After training, our patient was able to perform the mobility tests without any assistance (including the use of a cane) and his falling episodes were reduced to zero during the 6-month training

Table 3. Effects of six month resistance training with instability on functional ability (timed up and go, timed stands, Berg balance scale, and fall risk tests), activities of daily living (Unified Parkinson's Disease Rating Scale [UPDRS section II], and motor symptoms (UPDRS section III) in a patient with Multiple System Atrophy.

	Baseline	Post-trial Period
Timed-up-and-go (s)	0	9
Timed-stands (repetitions)	0	7
Berg balance scale (score)	30	52
Fall risk test (score)	12.3	5.4
UPDRS part II (score)	28	20
UPDRS part III (score)	33	25

period and the severity of motor symptoms were greatly reduced after the intervention. Collectively, the aforementioned benefits may have influenced the results of both the functional ability and quality of life of the patient, as observed through the change in the PDQ-39 items.

Although, there is no information in the literature with respect to skeletal muscle atrophy in patients with MSA, three months prior to the training our patient presented reduction of the bodyweight from 65 kg to 55 kg and was unable to perform any activities of daily living without the help of a cane. Collectively, these factors combined with the central nervous system and motor dysfunction resulting from MSA could have possibly contributed to the high prevalence of falls verified in the patient in the three-month period before the commencement of the trial. In chronic diseases such as cancer, heart failure and diabetes, reductions in bodyweight and functional inability are associated with loss of muscle mass and consequently with skeletal muscle atrophy, which may impair patient recovery and reduce independence and quality of life (Foletta et al., 2011). Moreover, patient's muscle alteration is corroborated by the reduction in atrogin-1 mRNA expression (40%), a muscle-specific ubiquitin ligase involved in the last step of protein labeling before degradation by the ubiquitin-proteasome system and known to be required for skeletal muscle atrophy (Bodine et al., 2001). Interestingly, the MuRF-1 gene expression did not follow the same pattern. Despite the fact that atrogin-1 and MuRF1 are both E3 ligases and important markers for skeletal muscle atrophy, they have different substrates for degradation and, hence, they can be stimulated by different signaling pathways depending on the disease or condition associated to atrophy (Foletta et al., 2011).

In respect of the protein-synthesis related genes, the increase in quadriceps CSA was paralleled by an increase in MGF mRNA expression (92.1%), which has shown to be up regulated in response to mechanical overload, and to be associated with muscle hypertrophy (Lambert et al., 2008). Similarly, we observed an increase in mTOR gene expression (33.4%), a downstream protein of several activators, including the MGF, which has also been associated with resistance training induced muscle hypertrophy (Lambert et al., 2008). However, further studies should investigate the mechanisms underlying the skeletal muscle adaptations in response to training in patients with MSA.

It is important to emphasize that the data from the present study does not allow causal conclusions on the effects of this mode of exercise in MSA. Therefore, caution should be exercised when interpreting our findings as they cannot be generalized to the entire MSA population. However, the interesting findings herein warrant further investigation on the effects of this type of intervention with a more robust experimental approach (*i.e.,* a randomized controlled trial with adequate statistical power). In addition, our case report suggests that high complexity exercise interventions may be very beneficial to individuals with impaired motor control and function.

Conclusion

This case report describes an innovative nonpharmacological therapeutic strategy that may be able to counteract some of the decline in the quality of life, activities of daily living, motor symptoms, functional ability, and neuromuscular parameters in MSA. Further randomized controlled trials and larger cohort studies are needed in order to establish the efficacy and safety of this training mode in MSA patients.

Acknowledgements

The authors thank Diagnósticos das Américas S/A (DASA) for the magnetic resonance images, Center for Psychobiology and Exercise Studies and Associação Brasil Parkinson. Carlos Ugrinowitsch and Carla Silva-Batista are supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (CU: 2012/03056-4 & CSB: 2013/04970-4, respectively). Carlos Ugrinowitsch, Eduardo Oliveira de Souza and Valmor Tricoli are supported by CNPq (CU 304205/2011-7, EOS: 152658/2011-5 & VT: 304814/2010-5, respectively). No conflicts of interest, financial or otherwise, are declared by the authors.

References

Almeida, O.P. and Almeida, S.A. (1999) Reliability of the Brazilian version of the ++abbreviated form of Geriatric Depression Scale (GDS) short form. *Arquivos de Neuro-psiquiatria* **57,** 421-426.

Behm, D.G., Drinkwater, E.J., Willardson, J.M. and Cowley, P.M. (2010) The use of instability to train the core musculature. *Applied Physiology, Nutrition and Metabolism* **35,** 91-108.

Bertolucci, P.H., Brucki, S.M., Campacci, S.R. and Juliano, Y. (1994) The Mini-Mental State Examination in a general population: impact of educational status. *Arquivos de Neuro-psiquiatria* **52,** 1-7.

Bodine, S.C., Latres, E., Baumhueter, S., Lai, V.K., Nunez, L., Clarke, B.A., Poueymirou, W.T., Panaro, F.J., Na, E., Dharmarajan, K., Pan, Z.Q., Valenzuela, D.M., Dechiara, T.M., Stitt, T.N., Yancopoulos, G.D. and Glass, D.J. (2001) Identification of ubiquitin ligases required for skeletal muscle atrophy. *Science* **294,** 1704-1708.

Brown, L.E. and Weir, J.P. (2001) ASEP procedures recommendation I: accurate assessment of muscular strength and power. *Journal of Exercise Physiology online* **4,** 1-21.

Bustin, S.A., Benes, V., Garson, J.A., Hellemans, J., Huggett, J., Kubista, M., Mueller, R., Nolan, T., Pfaffl, M.W., Shipley, G.L., Vandesompele, J. and Wittwer, C.T. (2009) The MIQE guidelines: minimum information for publication of quantitative real-time PCR experiments. *Clinical Chemistry* **55,** 611-622.

De Souza, E.O., Tricoli, V., Paulo, A.C., Silva-Batista, C., Cardoso, R.K., Brum, P.C., Bacurau, A.V., Laurentino, G., Neves-Jr, M., Aihara, A.Y. and Ugrinowitsch, C. (2012) Multivariate analysis in the maximum strength performance. *International Journal of Sports Medicine* **33,** 970-974.

Dibble, L.E., Hale, T.F., Marcus, R.L., Droge, J., Gerber, J.P. and Lastayo, P.C. (2006) High-intensity resistance training amplifies muscle hypertrophy and functional gains in persons with Parkinson's disease. *Movement Disorders* **21,** 1444-1452.

Foletta, V.C., White, L.J., Larsen, A.E., Leger, B. and Russell, A.P. (2011) The role and regulation of MAFbx/atrogin-1 and MuRF1 in skeletal muscle atrophy. *Pflugers Archiv* **461,** 325-335.

Goetz, C.G., Poewe, W., Rascol, O., Sampaio, C., Stebbins, G.T., Counsell, C., Giladi, N., Holloway, R.G., Moore, C.G., Wenning, G.K., Yahr, M.D. and Seidl, L. (2004) Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: status and recommendations. *Movement Disorders* **19,** 1020-1028.

Goetz, C.G., Tilley, B.C., Shaftman, S.R., Stebbins, G.T., Fahn, S., Martinez-Martin, P., Poewe, W., Sampaio, C., Stern, M.B., Dodel, R., Dubois, B., Holloway, R., Jankovic, J., Kulisevsky, J., Lang, A.E., Lees, A., Leurgans, S., Lewitt, P.A., Nyenhuis,

D., Olanow, C.W., Rascol, O., Schrag, A., Teresi, J.A., Van Hilten, J.J. and Lapelle, N. (2008) Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. *Movement Disorders* **23,** 2129-2170.

Granacher, U., Lacroix, A., Muehlbauer, T., Roettger, K. and Gollhofer, A. (2012) Effects of Core Instability Strength Training on Trunk Muscle Strength, Spinal Mobility, Dynamic Balance and Functional Mobility in Older Adults. *Gerontology* **59,** 105-113.

Jecmenica-Lukic, M., Poewe, W., Tolosa, E. and Wenning, G.K. (2012) Premotor signs and symptoms of multiple system atrophy. *Lancet Neurology* **11,** 361-368.

Kibele, A. and Behm, D.G. (2009) Seven weeks of instability and traditional resistance training effects on strength, balance and functional performance. *Journal of Strength and Conditioning Research* **23,** 2443-2450.

Lambert, C.P., Wright, N.R., Finck, B.N. and Villareal, D.T. (2008) Exercise but not diet-induced weight loss decreases skeletal muscle inflammatory gene expression in frail obese elderly persons. *Journal of Applied Physiology* **105,** 473-478.

Murton, A.J. and Greenhaff, P.L. (2013) Resistance exercise and the mechanisms of muscle mass regulation in humans: acute effects on muscle protein turnover and the gaps in our understanding of chronic resistance exercise training adaptation. *International Journal of Biochemistry Cell Biology* **45,** 2209-2214.

Neves, M., Jr., Barreto, G., Boobis, L., Harris, R., Roschel, H., Tricoli, V., Ugrinowitsch, C., Negrao, C. and Gualano, B. (2012) Incidence of adverse events associated with percutaneous muscular biopsy among healthy and diseased subjects. *Scandinavian Journal of Medicine Science in Sports* **22,** 175-178.

Newcomer, K.L., Krug, H.E. and Mahowald, M.L. (1993) Validity and reliability of the timed-stands test for patients with rheumatoid arthritis and other chronic diseases. *Journal of Rheumatolology* **20,** 21-27.

Podsiadlo, D. and Richardson, S. (1991) The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *Journal of the American Geriatrics Society* **39,** 142-148.

Quinn, N.P. and Wenning, G.K. (1996) Multiple system atrophy. *Advances in Neurology* **69,** 413-419.

Qutubuddin, A.A., Pegg, P.O., Cifu, D.X., Brown, R., Mcnamee, S. and Carne, W. (2005) Validating the Berg Balance Scale for patients with Parkinson's disease: a key to rehabilitation evaluation. *Archives of Physical Medicine and Rehabilitation* **86,** 789-792.

Rivest, J., Quinn, N. and Marsden, C.D. (1990) Dystonia in Parkinson's disease, multiple system atrophy, and progressive supranuclear palsy. *Neurology* **40,** 1571-1578.

Sieri, T. and Beretta, G. (2004) Fall risk assessment in very old males and females living in nursing homes. *Disability and Rehabilitation* **26,** 718-723.

Souza, R.G., Borges, V., Silva, S.M. and Ferraz, H.B. (2007) Quality of life scale in Parkinson's disease PDQ-39 - (Brazilian Portuguese version) to assess patients with and without levodopa motor fluctuation. *Arquivos de Neuro-psiquiatria* **65,** 787-791.

Tison, F., Yekhlef, F., Chrysostome, V., Balestre, E., Quinn, N.P., Poewe, W. and Wenning, G.K. (2002) Parkinsonism in multiple system atrophy: natural history, severity (UPDRS-III), and disability assessment compared with Parkinson's disease. *Movement Disorders* **17,** 701-709.

Van De Warrenburg, B.P., Cordivari, C., Ryan, A.M., Phadke, R., Holton, J.L., Bhatia, K.P., Hanna, M.G. and Quinn, N.P. (2007) The phenomenon of disproportionate antecollis in Parkinson's disease and multiple system atrophy. *Movement Disorders* **22,** 2325-2331.

Wallerstein, L.F., Tricoli, V., Barroso, R., Rodacki, A.L., Russo, L., Aihara, A.Y., Da Rocha Correa Fernandes, A., De Mello, M.T. and Ugrinowitsch, C. (2012) Effects of strength and power training on neuromuscular variables in older adults. *Journal of Aging and Physical Activity* **20,** 171-185.

Wedge, F. (2008) The impact of resistance training on balance and functional ability of a patient with multiple system atrophy. *Journal of Geriatric Physical Therapy* **31,** 79-83.

Key points

- Six months of resistance training with instability alleviate the MSA-related effects and improve the quality of life in a patient with MSA.
- High complexity exercise intervention (i.e., resistance training with instability) may be very beneficial to individuals with impaired motor control and function as MSA patients.
- Caution should be exercised when interpreting our findings as they cannot be generalized to the entire MSA population and they do not allow establishing causal conclusions on the effects of this mode of exercise on MSA.

AUTHORS BIOGRAPHY

Carla SILVA-BATISTA

Employment

Member of the Research Group of Neuromuscular Adaptations to Strength Training, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.

Degree

PhD student

Research interests

Methods of training and neuromuscular and functional adaptations in neurodegenerative disease and aging.

E-mail: csilvabatista@usp.br

Hélcio KANEGUSUKU

Employment

Member of the Exercise Hemodynamic Laboratory, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.

Degree

PhD student

Research interests

Methods of training and cardiovascular adaptations in special populations.

E-mail: helciokng@usp.br

Hamilton ROSCHEL

Employment

Prof. at the Department of the Sport and Coordinator of the Research Group of Neuromuscular Adaptations to Strength Training, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.

Degrees

PhD, Dr Habil

Research interests

Therapeutic effects of physical exercise, neuromuscular adaptations and sports nutrition

E-mail: hars@usp.br

Eduardo Oliveira de SOUZA

Employment

Member of the Research Group of Neuromuscular Adaptations to Strength Training, School of Physical Education and Sport of University of São Paulo, São Paulo and Prof. at the Paulista University (UNIP) Brazil.

Degree

PhD student

Research interests
Methods of training and neuromuscular adaptations to strength training
E-mail: desouza.eo@gmail.com

Telma Fátima CUNHA
Employment
Member of the Laboratory of Cellular and Molecular Physiology of Exercise, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.
Degree
PhD student
Research interests
Physical exercise and cellular and molecular physiology
E-mail: telma_21@yahoo.com.br

Gilberto Cândido LAURENTINO
Employment
Prof. at the Paulista University (UNIP) and Member of the Research Group of Neuromuscular Adaptations to Strength Training, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.
Degree
PhD
Research interests
Methods of training and neuromuscular adaptations
E-mail: gclkgs@yahoo.com.br

Manoel NEVES Jr
Employment
Rheumatologist and Member of the Research Group of Neuromuscular Adaptations to Strength Training, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.
Degree
PhD
Research interests
Rehabilitation and sports medicine
E-mail: manoelneves@gmail.com

Marco Túlio de MELLO
Employment
Prof. at the Department of Psychobiology and Coordinator of the Center for Psychobiology and Exercise Studies, Federal University of São Paulo, São Paulo, Brazil.
Degrees
PhD, Dr Habil
Research interests
Physical exercise, sleep disorders, and sports performance
E-mail: tmello@demello.net.br

Maria Elisa Pimentel PIEMONTE
Employment
Prof. at the Department of Physical Therapy and Coordinator of the Laboratory of Sensorymotor Learning, University of São Paulo, São Paulo, Brazil.
Degrees
PhD, Dr Habil
Research interests
Physical therapy, Parkinson's disease, learning sensorymotor and attention.
E-mail: elisapp@usp.br

Patricia Chakur BRUM
Employment
Prof. at the Department of the Biodynamics of Human Movement and Coordinator of the Laboratory of Cellular and Molecular Physiology of Exercise, School of Physical Education and Sport of University of São Paulo, Brazil.
Degrees
PhD, Dr Habil
Research interests
Physical exercise, cardiovascular adaptations and cellular and molecular physiology
E-mail: pcbrum@usp.br

Claudia Lúcia FORJAZ
Employment
Prof. at the Department of the Biodynamics of Human Movement and Coordinator of the Exercise Hemodynamic Laboratory, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.
Degrees
PhD, Dr Habil
Research interests
Physical exercise and cardiovascular adaptations
E-mail: cforjaz@usp.br

Valmor TRICOLI
Employment
Prof. at the Department of Sport and Coordinator of the Research Group of Neuromuscular Adaptations to Strength Training, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.
Degrees
PhD in Exercise Science
Research interests
Methods of training, neuromuscular adaptations and sports performance
E-mail: vtricoli@usp.br

Carlos UGRINOWITSCH
Employment
Prof. at the Department of Sport and Coordinator of the Research Group of Neuromuscular Adaptations to Strength Training, School of Physical Education and Sport of University of São Paulo, São Paulo, Brazil.
Degrees
PhD in Exercise Science
Research interests
Strength training methods, neuromuscular adaptations and sports performance
E-mail: ugrinowi@usp.br

✉ **Carla Silva-Batista**
School of Physical Education and Sport; University of São Paulo, São Paulo, Brazil