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ORIGINAL STUDIES

Complex rehabilitation in patients with knee arthroplasty

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Abstract
Background. Osteoarthritis (OA) - a progressive and incurable joint disease – is the most prevalent form of arthritis and is a leading cause of disability, a problem that becomes more pronounced with age. Like in the entire medical world, in Romania, knee arthroplasty is the most commonly performed joint replacement procedure for advanced stages of knee osteoarthritis (KOA).

Aims. In the present study, we aim to highlight the role of a supervised and complete rehabilitation program (inpatient and home-based) in the recovery of the clinical and functional status of advanced stage KOA patients who underwent elective TKA. Probably, the judiciously chosen parameters of physical exercise will permit to perform the kinetic program in healthcare, regardless of location, for this type of patients.

Methods. The study was a randomized controlled trial including two groups of patients (SG-study group and CG-control group), homogeneous in terms of biographical, clinical and functional features. All patients were completely assessed - clinically, by imaging and functionally.

Results. Clinical and functional parameters had a signif cantly modif cation (knee ROM, total WOMAC scale, stif ness and functional WOMAC subscales) in patients who underwent the complex rehabilitation program.

Conclusions. A combination of exercise, physical rehabilitation measures and properly selected pharmacological treatment will greatly help the management of these patients. The signif cant improvement in perception of balance conf dence is welcome in controlling movement and gait in KOA patients with a well-f xed and well-aligned TKA.

Key words: knee arthroplasty, kinetic training, rehabilitation program

Introduction

Osteoarthritis (OA) - a progressive and incurable joint disease – is the most prevalent form of arthritis and is a leading cause of disability, a problem that becomes more pronounced with age (Kiliç et al., 2017). OA is found in almost 70% of the population aged over 60 years and the global prevalence is approximately 4%. Worldwide, there is a higher prevalence of OA among elderly women (Van Manen et al., 2012).

The primarily af ected joints in OA are the knee and the hip. The progression of the disease is inf uential on quality of life. This includes functional and social activities, body image, and emotional well-being (Kongtharvonskul et al., 2015).

Knee osteoarthritis (KOA) is the most common and complex multifactorial joint disease, def ned through three pathogenic aspects: local inf ammation, articular cartilage loss and subchondral bone remodeling, with proliferative changes in the surrounding bones (Henricsdotter et al., 2016). KOA causes considerable pain and disability and imposes a major economic burden not only on those af ected, but also on the whole society. For this reason, conservative treatments - weight reduction, medical treatment, rehabilitation programs (physiotherapy measures, regular exercises, occupational therapy, and orthotics) and lifestyle modif cations (patient self-management education, mind/body interventions) - are often recommended for patients with mild to moderate KOA to reduce pain and improve function (Cudejko et al., 2018). The same goals of end-stage KOA

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treatment (relieving pain and improving knee functions) are obtained through conventional surgery - total knee arthroplasty (TKA), widely used around the world (Kim et al., 2011). Like in the entire medical world (Howells et al., 2016), in Romania, knee arthroplasty is the most commonly performed joint replacement procedure for advanced stages of KOA. Total knee arthroplasty (TKA) is indicated for patients with severe KOA, characterized by: continued, severe and refractory knee pain often at night, decreased mobility and af ected activities of daily living, and imaging evidence of degenerative knee disease, when conservative options have been exhausted (Kim et al., 2011). So, in patients with severe KOA, TKA is aimed at restoring normal joint motion and mechanical features (alignment, restoring a normal Q angle, preserving the joint line), reducing pain, preventing further degenerative disease, returning the patient to full daily function, to work and recreational activities (Van Manen et al., 2012).

Although total knee arthroplasty is the proper surgical intervention for KOA (Iolascon et al., 2020), it is not always without complications (Healy et al., 2013; Bozic et al., 2014). Almost 20% of TKA patients experience unpleasant pain, caused by a wide variety of factors, and functional limitations (Beswick et al., 2012). Despite the positive consequences of TKA (self-reported functional ability and pain reduction), it does not eliminate all impairments (ascending / descending a f ight of stairs, strength and mobility def cits) when compared to age-matched individuals without knee pathology, with a socioeconomic impact (Losina et al., 2012; Ravi et al., 2012).

The integrated use of multimodal analgesic drugs and rehabilitation, specially adapted physical activity represents the cornerstone of postoperative pain control and self-reported function improvement in patients with KOA (Jones et al., 2015). Taking into consideration that functioning is the third health indicator, complementary to morbidity and mortality (Stucki et al., 2019), a rehabilitation program is essential for the health strategy that aims to optimize the function of persons experiencing or likely to experience a limitation in functioning (***, 2018), as patients with TKA. Fifteen years ago, one of the primary conclusions from the consensus conference of the National Institute of Health surrounding TKA was that “the use of rehabilitation services was one of the most understudied aspects of the perioperative management of patients following total knee replacement” and “there is no evidence supporting the generalized use of any specif c preoperative or postoperative rehabilitation interventions.” (***, 2004).

By now, medical studies have well demonstrated the following aspects:

- outcomes after TKA may be related to the type and intensity of postoperative rehabilitation that patients receive;

- optimal pain management generates a better and earlier functional rehabilitation after TKA and prevents chronic pain (Vergne-Salle, 2016);

- improvements in pain and functional performance are achieved with assistance from rehabilitation programs (Bade et al., 2010);

- traditional rehabilitation programs typically focus on improving knee strength (quadriceps muscle strength) and optimal range of movement, and improving gait and stair climbing (Westby & Backman, 2010).

The recovery of knee function in TKA patients following a traditional rehabilitation program is not complete, compared to healthy age-matched persons (Schache et al., 2016). The persistence of functional limitations and residual pain proves that an optimal rehabilitation program is required, with a consensus regarding the dif erent stages – early postoperative, inpatient and outpatient, home-training (Glassou et al., 2014; El Bitar et al., 2015). Furthermore, prior to surgery, patients with end-stage KOA presented lower limb muscle dysfunction (Hinman et al., 2010). The inpatient rehabilitation program is focused on early and safe kinetic exercises (El Bitar et al., 2015) to improve knee range of motion and knee muscle strengthening (Artz et al., 2015).

Objectives

The aim of our randomized control study is to compare the outcomes of a complete rehabilitation program with those of traditional rehabilitation programs in elderly patients with unilateral TKA for KOA. Before complete rehabilitation management of all studied TKA patients, we made a comprehensive assessment to establish appropriate goals and rehabilitation measures, in accordance with the current European League Against Rheumatism (EULAR) guidelines (Fernandes et al., 2013; Iolascon et al., 2020).

Hypothesis

In the present study, we aimed to highlight the role of a supervised and complete rehabilitation program (inpatient and home-based) in the recovery of the clinical and functional status of advanced stage KOA patients who underwent elective TKA. Probably, the judiciously chosen parameters of physical exercise will permit to perform the kinetic program in healthcare, regardless of location, for this type of patients.

Material and methods

We mention that we obtained the approval of the Ethics Committee of the University of Medicine and Pharmacy of Craiova No 61/22.03.2019 and a signed informed consent from all the subjects participating in our study. Our research was performed on 38 patients, all previously diagnosed with end-stage KOA.

Research protocol

Period and place of the research

We conducted our study during the period April 2019 - February 2020 in the Rehabilitation Department of the “Filantropia” Hospital Craiova.

Subjects and groups

The study was a randomized controlled trial including two groups of patients (study group – SG and control group – CG), homogeneous in terms of biographical and rheumatic disease features, each consisting of 19 patients (Table I).

Table I
The demographic data of the patients.

Group		Age (years)	Age / place		Female age	Male age
			Urban	Rural		
SG Study group 19 patients	Average	65.05	65.36	64.63	64.00	69.00
	St.dev.	6.20	5.95	6.91	5.93	6.32
	Minimum	56	58	56	56	61
	Median	64	64	62	62	70
	Maximum	70	76	75	76	75
CG Control group 19 patients	Average	66.42	66.27	66.63	65.93	68.25
	St.dev.	5.08	3.93	6.65	5.44	3.30
	Minimum	56	60	56	56	65
	Median	68	67	70	68	68
	Maximum	72	72	72	72	72

The inclusion criteria taken into account when designing the groups were:

- patients older than 50 years of age, diagnosed with severe primitive knee osteoarthritis according to the American College of Rheumatology, with primary unilateral TKA typically in the previous 10 days;
- absence of other joint replacement;
- patients with stable cardiovascular and respiratory function, with normal blood pressure and without unstable medical conditions;
- compliance with physical exercise during the healthcare program.

Our study design was a single-blinded randomized controlled trial (Fig. 1).

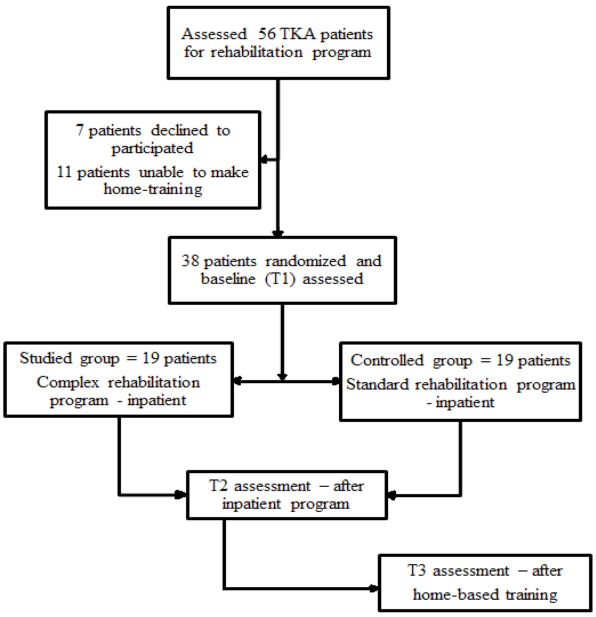

Fig. 1 – Diagram of our study.

We performed the patient randomization via the computer-generated list. Only the physical therapist knew the real allocation of each patient. The other members of the rehabilitation team and the patients had no information about the randomization. We respected the Recommendation for Interventional Trials (SPIRIT) guidelines (Chan et al., 2013).

Tests applied

We completed an initial clinical, laboratory (laboratory screening, imaging examination - radiography) and functional assessment. All tests applied are mentioned below.

The *clinical assessment* included:

- general physical examination (system examination including sensory evaluation);
- musculoskeletal examination – somatoscopic exam, systematic palpation of all areas of the knee, assessment of the range of motion (we used a goniometer), tenderness and stability and manual muscle testing of the lower limb muscles;
- exam in loaded bipodal, unipodal and sitting position;
- examination of balance and gait.

During the examination, we conducted *standard laboratory tests* and *radiological examination* of both knees (Fig. 2a - anteroposterior incidence and Fig. 2b - lateral incidence).

Fig. 2a – Anteroposterior incidence.

Fig 2b – Lateral incidence.

a) For *functional assessment*, we used:

- the VAS - Visual Analogue Scale (from 0 to 10, 0 = absence of pain and 10 = maximum pain score, other values between 0 and 10 are directly proportional to the intensity of pain, depending on the individual pain threshold);
- the WOMAC scale to assess the impact of knee disorder in performing activities of daily living (0-96, where 0 is maximum functional status and 96 is minimum, with maximum disruption of daily activities); we took into consideration two subscales of WOMAC questionnaire – WOMAC stif ness (0-8, where 0 is no stif ness and 8 is maximum stif ness), and WOMAC function (0-68, where 0 is no dif culty in function and 68 is the highest dif culty).

Outcomes for knee f exion, VAS, WOMAC scores were measured at admission to inpatient rehabilitation (T1), 3 weeks (T2), and 3 months (T3) after the commencement of rehabilitation. These time points were chosen to adequately measure the rate of improvement in all outcome measures.

The rehabilitation program was performed in two phases:

- the inpatient period; when patients had the ability to perform some kinetic tasks (mentioned in Table II), we considered them to be able to be discharged from hospital;
- a home-based program with bi-monthly supervision (Table III).

b) The healthcare objectives were adapted for all patients and rehabilitation phases:

- pain status control;
- controlling the inf ammatory process;
- restoring the mobility and stability of the knee;
- correcting the abnormal walking scheme, with recovery of normal walking;
- regaining motor control, optimal lower limb function.

c) The rehabilitation program was complex, based on non-surgical measures in both groups of patients, and included:

- pharmacological measures - analgesics, anti-inf ammatory drugs,
- non-pharmacological measures - educational, dietary, and hygienic, posture, physical (cryotherapy, magneto-therapy, neuromuscular electric stimulation - NMES for the quadriceps), massage and kinetic measures.

All patients of SG (study group) performed a complete rehabilitation program in contrast to the CG; more exactly, the standard rehabilitation program for CG was improved with some exercises (neuromuscular proprioception techniques - Kabat, Frenkel; closed-kinetic chain strengthening, such as ¼ squats, ¼ front lunges; complex gait training) to decrease muscle guarding, increase balance and return to functional daily activities. Each exercise session was supervised and performed twice daily, 5 days/week, 3 weeks. The a.m. kinetic program (5 minutes warm-up, 20 minutes ROM and progressive resistive exercises, 5 minutes cool-down) was preceded by neuromuscular electric stimulation - NMES for the quadriceps and a p.m. kinetic program (5 minutes warm-up, exercises for return to functional activities, 5 minutes cool-down), followed by 20 minutes of magnetotherapy.

Statistical processing

Statistical analysis was performed using Microsoft Excel (Microsoft Corp., Redmond, WA, USA), along with the XLSTAT add-on for MS Excel (Addinsoft SARL, Paris, France) and IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY, USA) for processing the data. To describe the numerical data used in the present study, we used the following statistical indicators: arithmetic mean and standard deviation, and spread indicators - minimum, maximum, median, quartiles (percentiles). None of the recorded data sets had a Gaussian distribution, therefore we had to use non-parametric tests. We used the Mann-Whitney test to compare the variables between the two groups, at all moments, and Friedman's test for paired data, in order to compare the results for each variable among the three evaluation moments, for each group.

Table II

Kinetic program for the inpatient rehabilitation program.

Components of the kinetic program applied for patients with knee arthroplasty between T1 and T2 evaluation period (SG = study group, CG = control group)

Objective		Rehabilitation components / Intermediate Exercise Program
Diminish pain and inf ammation	SG, CG	1. Pain modulation modalities – cryotherapy, medication 2. Cyriax massage
Increase knee range of motion	SG, CG	1. Heel slides in supine or sitting position to increase knee f exion 2. Lower extremity range of motion (ROM) → active assisted active (AA/AROM) exercises (supine and seated positions) 3. Patellar and tibiofemoral joint mobilizations 4. Stationary bike without resistance to increase f exion ROM
Increased dynamic joint Stability Muscle strength 3/5-4/5 Full weight bearing per implant status	SG, CG	1. Progressive passive / then active stretches to hamstrings, gastrocnemius, soleus, quadriceps within a pain-free range 2. Active straight-leg raises in f exion, abduction, adduction, extension 3. Gravity-assisted knee extension in supine (placing a towel roll under the ankle and leaving the knee unsupported) and in sitting position 4. Continue isometric quadriceps, hamstring, gluteal isometric exercises, then concentric and eccentric quadriceps exercises. 5. NMES for the quadriceps if poor quad contraction is present. 6. Pain-free progressive resisted exercises using ankle weights
	SG	1. Neuromuscular proprioception techniques (Kabat, Frenkel) to decrease muscle guarding, and increase balance 2. Agonist contraction to decrease muscle guarding, particularly in the quadriceps, and increase knee f exion. 3. Closed-kinetic chain strengthening, such as ¼ squats, ¼ front lunges
Maximize patients' mobility and functional independence Return to functional activities	SG, CG	1. Ambulation with use of an assistive device 2. Ascend and descend stairs, with assistive device. Gait training on stairs to engage the knee through 0 -110° of motion, optimal ROM to ambulate on stairs without compensations. Focus on eccentric quad control and stabilization in the stance phase. 3. Training the transfers and sitting and standing balance 4. Protected, progressive aerobic exercise, such as cycling without resistance, walking !!! Assistive devices are discontinued when the patient demonstrates adequate lower extremity strength and balance during functional activities
	SG	1. Complex gait training - weight shifting, tandem walking, lateral stepping over / around objects, obstacle courses, front and lateral step-ups, closed-kinetic chain activities

Table III
Home-based kinetic program.

Objective Example exercises		Home-based kinetic program – between T2 and T3 (SG = study group, CG = control group)	
		Exercise parameters	
Flexibility (ROM)	SG, CG	Active movement of lower limbs Stretching of calf muscles, hamstrings and quadriceps	Daily, 5 sets for each of the lower limb joints, from distal to proximal Daily, 5 sets of 6 seconds for each of the muscle groups
Muscle strength	SG, CG	Isometric contraction of vastus medialis oblique into the quadriceps and gluteus maximus muscles	Daily, 3 sets, 5 repetitions/set, 6 seconds for isometric contraction, 1 minute rest between contractions
		Isotonic contraction of leg f exor and leg extensor, quadriceps muscle, calf muscles	Daily, in antigravity position for each muscle, 2 sets, 10 repetitions/ set, 2 minutes rest between sets. Intensity equal to maximal voluntary contraction
Endurance	SG, CG	Cycling, walking, housework	Daily, 30 – 40 minutes. Intensity equal to submaximal voluntary contraction
ADL (functional activities)	SG, CG	Sitting to standing in chair, bed, other places Stair climbing Getting in and out of car	Daily
Control of movement and gait	SG	Frenkel exercises for the lower limbs Front and back cross-over stepping Tandem walking Eyes closed walking (supervised!)	3 per week

Table IV
Values for parameters in all patients.

Group		Study	Control	Study	Control	Study	Control
		T1		T 2		T3	
VAS	Average	7.21	7.63	4.89	5.05	3.16	3.26
	St.dev.	1.44	0.90	1.33	0.97	1.30	1.10
	C.V. (%)	19.93%	11.73%	27.15%	19.20%	41.24%	33.64%
	p value	p M-W = 0.358		p M-W = 0.797		p M-W = 0.940	
	Female	7.33±1.54	7.87±0.83	4.93±1.44	5.2±1.01	3.20±1.42	3.53±1.06
	Male	6.75±0.96	6.75±0.5	4.5±0.96	4.75±0.58	2.25±0.52	3±0.5
	Urban	7.45 ± 1.21	7.73 ± 1.10	5.18 ± 1.33	5.27 ± 1.10	7.45 ± 1.21	3.36 ± 1.29
	Rural	6.88 ± 1.73	7.5 ± 0.53	4.50 ± 1.31	4.75 ± 0.71	2.88 ±1.36	3.13 ± 0.83
ROM	Average	48.68	39.74	73.95	65.79	95.26	84.21
	St.dev.	6.20	6.34	7.18	7.86	9.20	5.07
	C.V. (%)	12.74%	15.96%	9.71%	11.95%	9.66%	6.02%
	p value	p M-W = 0.000		p M-W = 0.005		p M-W = 0.000	
	Female	50.00±6.27	48.00±6.26	74.00±7.84	66.33±7.5	96.00±10.04	85.00±4.63
	Male	43.75±2.5	38.75±7.5	73.75±4.79	63.75±7.5	92.5±5.0	81.25±6.29
	Urban	49.09 ±7.01	43.59 ±6.64	75.0 ± 8.37	65.91 ± 8.01	98.18 ± 9.52	84.55 ± 4.72
	Rural	48.13 ±5.30	43.53 ±6,23	74.5 ± 5,35	65.63 ± 8.21	91.25 ± 6.94	83.75 ± 5.87
t WOMAC	Average	56.26	60.26	43.84	49.11	34.84	41.37
	St.dev.	8.20	7.99	7.69	5.87	7.35	5.87
	C.V. (%)	14.58%	13.25%	17.54%	11.95%	21.10%	14.19%
	p value	p M-W = 0.087		p M-W = 0.039		p M-W = 0.003	
	Female	56.07±9.24	59.4±8.71	43.8±8.57	49.13±5.89	34.8±7.29	42.33±6.13
	Male	57.0±2.61	63.5±3.32	44.0±7.12	49.0±6.68	35.0±8.72	37.75±3.3
	Urban	55.64 ±10.69	58.45 ±7.31	42.73 ± 8.49	47.00 ±5.53	35.45 ± 8.47	39.82 ±6.15
	Rural	57.13 ± 2.9	62.75 ±8.68	45.38±6.67	52.00 ±4.84	34.00 ± 5.93	43.5 ± 5.07
s WOMAC	Average	5.16	5.00	3.21	3.79	1.79	3.00
	St.dev.	0.90	0.75	0.79	0.71	0.71	0.58
	C.V. (%)	17.42%	14.91%	24.52%	18.82%	39.86%	19.25%
	p value	p M-W = 0.436		p M-W = 0.017		p M-W = 0.000	
	Female	5.07±0.9	4.93±0.8	3.13±0.83	3.8±0.77	1.87±0.74	3.0±0.65
	Male	5.5±0.58	5.25±0.5	3.5±0.58	3.75±0.5	1.5±0.58	3±0.02
	Urban	4.73 ±0.9	4.82 ±0.75	3.18 ± 0.98	3.64 ±0.81	1.82 ±0.2	3.0 ±0.45
	Rural	5.75 ± 0.46	5.52 ±0.21	3.25±0.46	4.00 ±0.53	1.75 ± 0.71	3.0 ± 0.75
f WOMAC	Average	42.53	44.26	26.74	33.53	18.68	26.26
	St.dev.	6.96	6.85	6.40	5.99	5.68	6.30
	C.V. (%)	16.35%	15.49%	23.94%	17.88%	30.38%	23.98%
	p value	p M-W = 0.372		p M-W = 0.001		p M-W = 0.000	
	Female	43.07±7.73	43.0±6.78	27.47±6.96	32.27±5.73	19.33±6.08	26.57±6.81
	Male	40.5±2.08	49.0±5.42	24.0±2.71	38.25±4.99	16.25±3.3	27.0±4.55
	Urban	41.64±8.04	43.63±6.33	26.45±6.95	33.0±5.73	18.91±6.28	24.82±5.91
	Rural	43.75±5.39	45.5±7.78	27.13±6.01	34.25±6.67	18.38±5.13	28.25±6.65

Comparison between each recorded variable at each moment, for SG - Friedman's test $p < 0.0001$
Comparison between each recorded variable at each moment, for CG - Friedman's test $p < 0.0001$

C.V. (%) = coef cient of variation - the ratio of the standard deviation to the mean, expressed as percentage.
VAS = pain scale, ROM = range of motion for knee f exion, t WOMAC = total WOMAC scale score,
s WOMAC = stif ness subscale score, f WOMAC = functional subscale score, p M-W = p Mann-Whitney

Results

The two groups (SG - study group and CG – control group) were compatible in terms of structure. Comparing the age distribution for the two patient groups, with the Mann-Whitney test, no statistically signif cant dif erences were obtained (pMW=0.438).

For all variables, a highly signif cant improvement over time was observed (Table IV).

Comparing, at each moment, for each recorded variable, the study ant the control group, we made the following observations:

- VAS: at all moments, there was no statistical dif erence between the two groups; the average VAS scale values for subscales of patients (female/male, urban/rural) had a synchronic evolution, decreasing after the rehabilitation program, without signif cant dif erences;

- ROM: at all moments, there was a signif cant dif erence between the two groups; only patients of SG obtained an optimal f exion in the operated knee, over 90^0 range of motion, regardless of age, gender or background (Fig. 3).

- scores for WOMAC scale (t WOMAC or tW), and two subscales for stif ness (sWOMAC or sW) and function (f WOMAC or fW): initially, there was no dif erence between the groups (p M-W = 0.087 – for tW, p M-W = 0.436 – for sW, p M-W = 0.372 – for fW); for the second evaluation, there was a signif cant dif erence between the two groups (p M-W = 0.039 – for tW, p M-W = 0.017 – for sW, p M-W = 0.001 – for fW); for the third evaluation, there were signif cant and highly signif cant dif erences between the two groups (p M-W = 0.003 – for tW, p M-W = 0.000 – for sW, p M-W = 0.000 – for fW) (Fig. 4).

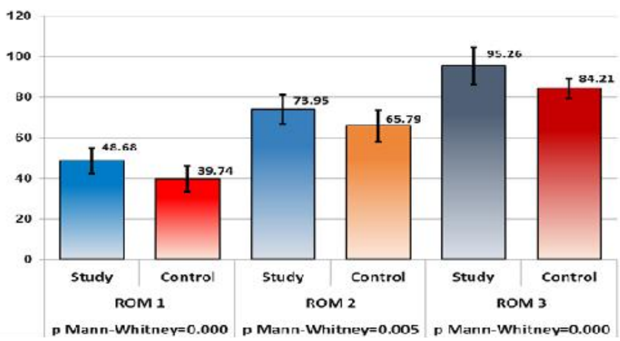

Fig. 3 – The mean values of ROM at all evaluation moments.

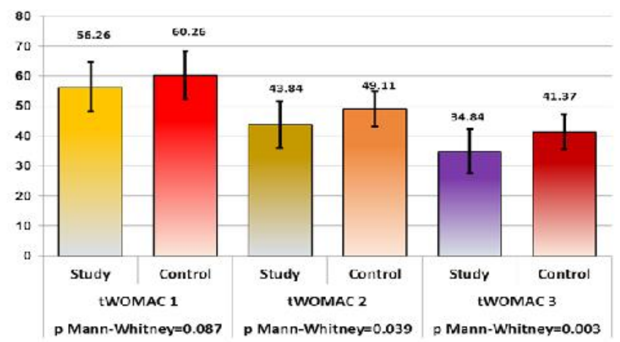

Fig. 4 – The mean values of total WOMAC scale score at all evaluation moments.

Discussions

Worldwide, a multidisciplinary approach to TKA patients is more and more implemented in clinical practice. Rehabilitation, including physiotherapy and exercise, is widely promoted after total knee replacement (Artz et al., 2015).

In our study, we proved the importance of a complete assessment and complex rehabilitation program (12 supervised and progressive exercises inpatient sessions, which started within the f rst postoperative month, and an 8 weeks home-based program) for quality of life in KOA patients. Published data for comprehensive evaluation and reassessment during regular follow-ups (Iolascon et al., 2020) argues the importance of functioning and correct patient management, in light of the interaction between patient's health capacity and environmental factors (Stucki & Bickenbach, 2017).

Our patients had no standard regarding the severity of symptoms in the indication of TKA. The decision for TKA is based on individual response to non-surgical treatment and was not conditioned by any other individual factor - age and weight.

Before and after intervention, we carefully decided the medication prescribed for pain and inf ammation, taking into consideration the compliance and adherence to drug treatments against the known adverse ef ects of each drug category (Stewart et al., 2018). All patients had painless status during and after the rehabilitation program. We did not mention any signif cant dif erences between the average VAS values in our patients. Pain perception improved in all our patients regardless of the applied rehabilitation measures. We respected the order in the program, to have the possibility of painless training. Magnetic therapy was indicated in order to reduce sympathetic tonus and control pain. Also, cryotherapy was optimally applied to control joint swelling and postsurgical joint inf ammation. None of our patients had a severe degree of pain. This is a frequently described subjective parameter for absence of proximal tibial tenderness after knee replacement (Simpson et al., 2009; Beswick et al., 2012).

The rehabilitation program was established in accordance with other clinical trials and reviews in which there are mentions of recommendations and benef ts of early supervised exercise therapy following TKA in the immediate postsurgical setting, with a heterogeneous group of exercises.

Our applied rehabilitation program included only two stages: an inpatient program and home-based training. We did not perform an outpatient program because, as mentioned in other trials, there was no dif erence in pain and functional outcomes between patients randomized to home-based and outpatient rehabilitation (Piqueras et al., 2013). Also, we considered the patient's f nancial possibilities to access the outpatient program for 2–3 weeks.

The components of the kinetic program performed in our patients were carefully chosen. We tried to apply an optimal inpatient physical therapy protocol. The dif erence between the kinetic programs in our patients is represented by neuromuscular proprioceptive exercises and complex gait training (inpatient phase) and Frenkel exercises for lower limbs with gait coordination exercises (home-based phase). Other exercises – mobilization and strengthening exercises, complemented by functional exercises – were identical and all parameters (intensity, duration, frequency) were based on patient progress.

Criteria for progression, and evidence of progression and compliance among patients were very important, as mentioned in other controlled clinical trials (Meier et al., 2008).

We considered that permanent supervised rehabilitation therapy may be effective in limiting some of the impairments following TKA. Several studies without direct oversight produced poor results (Pozzi et al., 2013). Bade et al. mentioned in their studies that more intensive rehabilitation, using progressive resistance exercise and functional strengthening, may substantially improve patient function without compromising safety (Bade et al., 2017). This conclusion is sustained by our results.

In SG, all patients had superior outcomes in functional performance and gait status compared with CG. This aspect is demonstrated by the values of ROM, total WOMAC and WOMAC subscale scores. Probably, performing coordination and agility exercises after the standard kinetic program - isometrics and active range of motion exercise with progression to weight-bearing exercise and daily activities – was effective and safe for lower limb function.

For ROM flexion there was evidence of improved flexion in all patients, with these observations:

- SG females had a higher percent of improvement at both evaluation moments after the rehabilitation programs than CG females (48% at T2 and 29% at T3 – for SG, 35% at T2 and 28% at T3 for CG);
- SG males had a higher percent of improvement only at T2 (68% compared with 64% in CG males); in the final evaluation, the differences were approximately equal, 26% for SG and 27% for CG);
- SG urban patients had a higher percent of improvement at both evaluation moments after the rehabilitation programs than CG urban patients (53% at T2 and 30% at T3 – for SG, 51% at T2 and 28% at T3 for CG);
- rural patients had approximately equal values of flexion improvements (50% at T2 and 26% at T3 – for SG, 50% at T2 and 27% at T3 for CG);
- SG patients had a higher percent of improvement in the final evaluation (28%) than CG patients (27%).

Our results differ from those of other studies, where benefits for ROM flexion were seen, particularly, after 6 months (Artz et al., 2015).

We established in our study a WOMAC – stiffness subscale because this sign is associated with more severe dissatisfaction. Even if the joint is not painful, a stiff knee related to surgery is very difficult to manage daily and therefore likely to be associated with important lower limb dysfunction (Beswick et al., 2012).

At both evaluation moments, after beginning the rehabilitation program, all SG patients had improvements in the scores of total WOMAC scale and stiffness and functional WOMAC subscales, regardless of age, gender or the environment of origin.

The kinetic measures performed (progressive passive / then active stretching, neuromuscular proprioception techniques) allowed to control the postsurgical knee stiffness. Our results sustain this affirmation: the improvement in the stiffness WOMAC score was better for SG (38% and 65%) than CG (25% and 30%) at both evaluation moments (T2 and T3). Gait training and correct posture in bed and chair were possible for our patients after both knee joints had stiffnessless status.

Physical function was measured using WOMAC-function subscale and total WOMAC score. As shown in Table IV, there was a significant difference in mean values between SG and CG, in the T2 and T3 assessments. The improvement of these two scores was better for SG (38% and 65% for functional WOMAC, 22% and 38% for total WOMAC score) than CG (25% and 30% for functional WOMAC, 19% and 31% for total WOMAC score), at both T2 and T3. The particular structure of the kinetic program applied to our SG patients explains these results, different from other clinical trials (Madsen et al., 2013).

Also, we did not start the inpatient rehabilitation program early after knee replacement; the functional performance was not lost in the following three months after TKA.

We consider that a complex and supervised kinetic program has similar effects to the early initiation of progressive resistance exercises and functional strengthening in limiting the extent of this knee function loss (Jakobsen et al., 2014).

One of the most important targets of our rehabilitation program, similarly to other studies (Meier et al., 2008), was to regain the strength of muscles around the knee and of the entire lower limb. All patients had a large decrease in quadriceps strength immediately after TKA, due to rest and previous hypotrophy due to pain status. This loss of strength generates functional impairments (Thomas & Stevens-Lapsley, 2012), so the recovery of muscle parameters is essential. We used in our rehabilitation program progressive exercise protocols, based on isometric and isotonic contractions. To optimally regain the quadriceps strength, we indicated NMES, which was well tolerated.

The role of this physical measure is known (Pozzi et al., 2013), but the aim of our study was not to elucidate the contribution of NMES to complete rehabilitation of TKA patients.

The stable bipodal posture and safety during the gait are two important biomechanics aspects in patients with TKA. We consider that a kinetic program should contain some special exercises for balance and gait. Over the first two weeks after surgical replacement, Kabat technique and Frenkel exercises for the lower limbs permit to decrease muscle guarding and increase balance. So, the patient has full trust to perform exercises to maximize functional independence and return to daily activities. This recovery objective is debated in several recent systematic reviews (Henderson et al., 2018) whose authors have demonstrated benefits of postoperative rehabilitation programs after TKA, but have questioned the quality of evidence supporting these benefits (Warwick et al., 2019).

The major role and benefit of the rehabilitation program after total joint replacement was to regain function and quality of life for patients, while decreasing hospital length of stay in the orthopedic clinic. Today the average of this indicator is 2 to 4 days (Keswani et al., 2016). So, all medical teams are focused on improving the surgical techniques, better pain management, faster mobilization, modif cations of rehabilitation protocols, and pathway directed care (Argensen et al., 2016).

Educational training is as important as the kinetic program. Preoperative and postsurgical education measures familiarize patients with the correct mode of daily training, especially in the home-based phase of the rehabilitation program (Peer et al., 2017), so their knowledge expectations after knee replacement can be fulf lled (Soeters et al., 2018).

The single negative aspect is the lack of large randomized trials with adequate methodology on rehabilitation for TKA patients, with a paucity and heterogeneity of results (Argensen et al., 2016; Sattler et al., 2019). Most studies are performed on patients who followed a complete rehabilitation program – inpatient, outpatient and home-based training. During the hospital stay, the main rehabilitation objectives were pain control, optimal knee mobilization and achievement of functional status. Regaining gait and balance is continued during home-based training (Oatis et al., 2014).

The limitation of our study is the absence of rehabilitation (preoperative physiotherapy and exercise programs), which should improve patient disposition at the time of surgery and may prepare patients for a better recovery after surgery (Wang et al., 2016).

We could not establish what type of preoperative program our patients performed, so we did not take into consideration this outcome. Probably, the best results in our study were obtained by those patients who attended the kinetic and adapted physiotherapy program.

One important aspect, certainly established and respected in our study, is the early application of the rehabilitation program after joint replacement, despite a lack of evidence for the optimal type, duration or frequency of measures to provide the best clinical outcomes (Sattler et al., 2019).

Conclusions

1. A multimodal and multidisciplinary therapeutic approach represents the gold standard for regaining function and quality of life in TKA patients.

2. A combination of exercise, physical measures and properly selected pharmacological treatment will greatly help the management of these patients.

3. The signif cant improvement in perception of balance conf dence improves movement control and gait in KOA patients with a well-f xed and well-aligned TKA.

4. The values obtained for knee f exion (ROM) and WOMAC were attributes of the control group, and to normative values, so we can conclude that our rehabilitation program had signif cant ef ciency in restoring the functional ability for patients, regardless of age and gender.

Conf icts of interests
No conf icts of interests.

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Ef ects of group physical therapy on the walking speed in patients with Parkinson's disease

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Abstract

Background. Parkinson's disease is a progressive neurologic disorder characterized by motor impairments which alter the walking capacity, and lead to reduced walking speed, decreased stride length and increased double support time. Physical therapy interventions are an important part of the non-pharmacological treatment for Parkinson's disease.

Aims. The purpose of this study was to assess whether there is a dif erent outcome regarding improvement of walking speed, when applying a physical therapy program in an individual or in a group manner.

Methods. A prospective, observational, cohort type study on 60 patients with Parkinson's disease was carried out between November 2014 - July 2017, in the Clinical Rehabilitation Hospital in Cluj-Napoca, Cluj county, Romania. Patients were randomly divided into 2 groups, and were prescribed either individual (1 patient and 1 physical therapist) or group physical therapy (6 patients and 1 physical therapist). The treatment protocol included 10 sessions of physical therapy, in the same room setting, and patients performed the same routine of exercises, except for the 3 breaks during the sessions in the group therapy for informal socialization. Walking speed was measured by two validated instruments, the 6-minute walk test and the 10-meter walk test, before and after treatment.

Results. There was an increase in both groups regarding gait speed after treatment (all $p<0.05$), except for the values obtained by the 6-minute walk test in the individual therapy group, which did not improve signif cantly. The 6-minute walk test scores after treatment showed signif cantly higher values of gait speed in the group therapy, compared to individual therapy ($p=0.002$).

Conclusions. Patients with Parkinson's disease could benef t more from a group physical therapy program, as gait speed increased signif cantly. The group approach facilitates interactions and is cost-ef ective, as it requires only one therapist and more patients.

Key words: Parkinson's disease, physical therapy, walking speed

Introduction

Parkinson's disease (PD) is a progressive neurologic disorder characterized by the cardinal motor signs of bradykinesia, tremors, rigidity, and postural instability. These motor impairments are the main reasons for alterations in the walking capacity that lead to decreased stride length, increased double support time, and reduced walking speed compared to healthy subjects (Morris et al., 2001; Sofuwa et al., 2005).

Gait disturbances are among the primary symptoms of PD and have a huge impact on a patient's quality of life, functionality and independence. The PD gait pattern is typically characterized by hesitant, shuf ing steps which are short and quick, f exed forward posture with limited natural arm swing and dif culty in initiating gait. Also, PD patients are unable to generate proper stride length, which they compensate by an increased gait cadence. As the disease progresses, movement is impaired and the walking pattern becomes slower (Jankovic et al., 2001; Morris et al., 1996).

Treatment for gait disturbances due to PD includes the standard drug regime, but in addition to this, non-pharmacological interventions are required to help manage the disease. Among them, the most common treatment

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prescribed for gait disturbances in PD is physical therapy (PT) (Giladi et al., 2001).

The PT program for gait rehabilitation in a patient with PD can consist of conventional PT or can be aided by dif erent sensory cues (auditory, visual). One of the most interesting features of PD, which was the basis of the cueing technique, is that patients are sometimes able to perform complex movements almost normally under certain conditions, despite the motor symptoms. The classic example is a patient with PD that will inexplicably freeze while walking through a doorway, but will have no trouble at all climbing a f ight of stairs (Giladi et al., 2001). This is why sensory cueing was implemented in PD treatment guidelines, as they appear to be a powerful way of stimulating and improving gait and walking speed, as shown in multiple studies (Rubinstein et al., 2002; Suteerawattananon et al., 2004; Herman et al., 2007).

Among the gait parameters, walking speed or gait velocity strongly correlates with functional ability and is a discriminating factor in determining the potential for rehabilitation (Perry et al., 1995; Goldie et al., 1996). Also, it has the ability to predict future health status and functional decline and has been used as a predictor and outcome measure across multiple diagnoses (Studenski et al., 2003; Purser, 2005; Brach, 2002; Meyer-Heim, 2007; Lee et al., 2007).

Short-distance walking speed tests are recommended clinical screening and monitoring tools of functional capacity and safety for all patients with disability (Fritz & Lusardi, 2009). The 10-meter walk test is commonly used to assess the walking speed, as it is easy to perform and it only requires a 20-m path that includes 5 m for acceleration and deceleration (Peters et al., 2013). The 6-minute walk test is used to measure the maximum distance that a person can walk in 6 minutes and is a useful instrument due to its ease of use (Stef en, et al., 2002).

Hypothesis

Besides motor symptoms, depression and social isolation are common f ndings in a PD population, resulting in a low quality of life (Herman et al., 2007). From a physical therapy point of view, treating PD patients as a group could be of further benef t than the classical one-on-one therapy in terms of functionality and/or well-being, but more research is needed in this area.

The objective of the present study was to assess whether there is a dif erent outcome regarding walking speed values when applying a PT program for PD patients, in an individual or in a group manner.

Material and methods

All subjects were informed of the characteristics of the study and were required to sign an informed consent document approved by the Ethics Committee of the "Iuliu Hatieganu" University of Medicine and Pharmacy (approval no. 130/11.04.2014). The study was registered on *clinicaltrials.gov* (NCT04187963).

Research protocol

a) *Period and place of the research*

The current study is prospective, observational, cohort type, and it was carried out during November 2014 - July 2017, in the Clinical Rehabilitation Hospital in Cluj-Napoca, Cluj county, Romania.

b) *Subjects and groups*

A total of 60 subjects diagnosed with typical, idiopathic PD participated in this study. All patients met the following inclusion criteria: (1) stable medication usage; (2) Hoehn and Yahr stage 2, 3 or 4; (3) ability to walk independently or by using an assistive walking device; (4) age 50 to 70 years; (5) no severe cognitive impairments (Mini-Mental State Examination - MMSE score, ≥24); (6) no other severe neurologic, cardiopulmonary or orthopedic disorders; and (7) not having participated in a PT or rehabilitation program in the previous 2 months.

The patients were randomly divided into 2 treatment groups: group physical therapy – GPT (n=30) and individual physical therapy – IPT (n=30). The treatment protocol for each group included 10 sessions of physical therapy, each 1.5 hour long, on a daily basis, for 2 weeks. All treatment sessions were conducted at the same time of the day throughout the study, in the morning, 60-90 minutes after intake of pharmaceutical treatment for PD. For the GPT, there were groups of 6 patients, supervised by 1 physical therapist. The group sizes were kept small to promote ef ciency and motivation. The patients undertaking IPT were alone with the physical therapist during the sessions. Both groups were treated in the same physical therapy room setting.

The rehabilitation protocol for IPT consisted of cardiovascular warm-up activities, stretching exercises, strengthening exercises, functional, gait and balance training, recreational games, and ended with relaxation exercises. In addition, the GPT protocol followed the exact same pattern, except for 5-10 minute breaks for informal socialization between participants, at the beginning of the session, mid-session and at the end of the session.

Also, both groups had access to external cues, which were applied during a variety of tasks and environmental situations, such as gait initiation and termination, heel strike and push-of , sideways and backwards stepping, walking while dual tasking, and walking over various surfaces and long distances. There is evidence in the literature to support each of the components contained in the intervention (Thaut et al., 1996; Schenkman et al., 1998; Scandalis et al., 2001; Dam et al., 1996; Mohr et al., 1996; Schenkman et al., 2000; Protas et al., 1996). In order to facilitate initiation and speed of movement, most activities employed visual and auditory cues as triggers. Visual cues were looking at and following the therapist's movements in the IPT group or the other group member's movements in the GPT group. A mirror was also used. Auditory cues were music with regular rhythm and verbal suggestions and reinforcement from the therapist in the IPT group, or from the therapist and other participants in the GPT group.

c) *Tests applied*

All patients were evaluated at the beginning and at the end of the physical therapy program. The evaluation included the 6-minute walk test and the 10-meter walk test. Gait speed for each participant was calculated as the ratio between the walked distance and the time unit, and it was measured in meters/seconds.

For each subject, all assessment sessions were performed in the morning, by the same person and all tests were performed in the same order, to control for variations in performance because of the medication cycle. All assessments were conducted in the "on" state for the subjects experiencing motor f uctuations.

d) *Statistical processing*

Patient data was entered in the Microsoft Of ce Excel 2010 program and statistical analysis was performed using MedCalc Statistical Software version 17.9.7 and SPSS for Windows, version 20. Quantitative data were tested for normality of distribution and expressed as mean±standard deviation or median and interquartile range (IQR), whenever appropriate. Qualitative data were expressed as frequency and percent. Comparison between groups was performed using the Student t-test, Mann-Whitney test or chi-square test, whenever appropriate. Correlations between two groups were tested using the Spearman's rho correlation coef cient. A p-value <0.05 was considered statistically signif cant.

Results

A total of 60 patients met the inclusion criteria, of which 31 were female and 29 were male. The mean age was 64.77 (± 4.65) years in the GPT group, and 64.43 (± 5.41) years in the IPT group, respectively. Based on the PD stage, in GPT, 20% of the patients were in stage 2, 56.6% were in stage 3 and 23.3% were in stage 4. In IPT, 16.6% of the patients were in stage 2, 63.3% were in stage 3 and 20% were in stage 4. There were no signif cant dif erences between groups based on gender, age, MMSE score, use of walking aid or PD stage (all p>0.05) (Table I).

Table I

Clinical characteristics of the patients included in the study.

n=60		Group PT (n=30)	Individual PT (n=30)	p-value
Gender	Female (n=31)	16	15	0.8
	Male (n=29)	14	15	
Age (years ± SD)		64.77 ± 4.65	64.43 ± 5.41	0.88
MMSE (score ± SD)		28.6 ± 1.59	28.13 ± 1.53	0.22
Walking aid (%)	Yes (n=40)	21 (52.5%)	19 (47.5%)	0.12
	No (n=20)	9 (45%)	11 (55%)	
PD stage (%)	2	6 (20%)	5 (16.6%)	0.7
	3	17 (56.6%)	19 (63.3%)	
	4	7 (23.3%)	6 (20%)	

There was an increase in both groups regarding gait speed after treatment (all p<0.05), as measured by the two instruments, except for the values obtained by the 6-minute walk test in the IPT group, which did not improve signif cantly (p=0.07) (Table II).

There were no dif erences between the 2 groups regarding initial gait speed, as measured by the 10-meter or 6-minute walk tests (all p>0.05). In the group therapy, the 10-meter walk test at normal speed showed higher gait speeds than in the individual therapy group, but it did not reach statistical signif cance (p=0.06). The 10-meter walk test at maximum speed showed no statistically signif cant dif erence between the treatment groups (p=0.72). The 6-minute walk test scores after treatment showed signif cantly higher values of gait speed in the group therapy compared to individual therapy (p=0.002) (Table III).

Table III

Comparison between groups before and after treatment

Gait speed (m/s)	Test	Group PT (n=30)	Individual PT (n=30)	p-value
BASELINE (mean ± SD)	10-meter walk - normal speed	0.89 ± 0.2	0.85 ± 0.15	0.51
	10-meter walk maximum speed	1.06 ± 0.2	1.05 ± 0.2	0.98
	6-minute walk	0.69 ± 0.11	0.66 ± 0.22	0.49
AFTER TREATMENT (mean ± SD)	10-meter walk - normal speed	1.06 ± 0.2	0.97 ± 0.16	0.06
	10-meter walk maximum speed	1.21 ± 0.21	1.18 ± 0.16	0.72
	6-minute walk	0.85 ± 0.13	0.72 ± 0.17	**0.002**

Discussion

It is now a known fact that rehabilitation is one of the most important parts of the multidisciplinary therapy approach to PD. One of the most af ected motor tasks in PD is gait, due to a def cit of internal rhythmic signals, which interferes with motor performance (Azulay et al., 1999). PD is the most common neurological disorder leading to gait disturbance and falls. Despite advances made regarding pharmacological treatments, gait and balance def cits still persist, and are associated with loss of independence and mobility and high costs for the healthcare systems. Therefore, rehabilitation approaches that complete the current pharmacological options are important to manage these problems (Grimbergen et al., 2004; Nieuwboer et al., 2007).

The positive ef ect of a physical therapy program on the motor and functional performance of patients with PD has been previously demonstrated in several studies (Formisano et al., 1992; Comelia et al., 1994; Schenkman et al, 1998). The main objective of physical therapy interventions is to decrease impairments and functional limitations evolving from the disease. This is achieved by teaching the patients strategies to bypass the basal ganglia – supplementary motor area circuit by "recruitment" of other areas in the

Table II

Dif erences in gait speed within groups before and after treatment.

Groups (n=60)	Group therapy (n=30)			Individual therapy (n=30)		
Test	10-meter walk test normal speed (m/s)	10-meter walk test maximum speed (m/s)	6-minute walk test (m/s)	10-meter walk test normal speed (m/s)	10-meter walk test maximum speed (m/s)	6-minute walk test (m/s)
Gait speed (m/s) mean ± SD (95% CI)	-0.17 ± 0.08 (95% CI [-0.2 – -0.14])	-0.16 ± 0.1 (95% CI [-0.19 – -0.12])	-0.16 ± 0.11 (95% CI [-0.2 – -0.12])	-0.11 ± 0.11 (95% CI [-0.15 – -0.07])	-0.13 ± 0.15 (95% CI [-0.19 – -0.07])	-0.06 ± 0.19 (95% CI [-0.13 – 0.01])
p-value	<0.05	<0.05	<0.05	<0.05	<0.05	0.07

brain, such as the premotor cortex. One of the interventions is the application of external cues and cognitive strategies for initiation of motor acts (Tamir et al., 2007). Literature data show that external stimuli (acoustic, visual and /or somatosensory) are able to modulate the motor pattern in PD, helping the patients to start and maintain a rhythmic motor task. Cued gait training represents a precious aid for managing motor symptoms in PD patients (Stolze et al., 2005). Cueing is def ned as using external temporal or spatial stimuli to facilitate gait initiation and continuation and to improve walking speed, step length and step frequency (Rubinstein et al., 2002; Lim et al., 2005a).

The inf uence of cueing has mainly been studied in single-session experiments in laboratory settings, and results show a short-term correction of gait parameters and gait initiation (Morris et al., 1996; Thaut et al., 1996; Lewis et al., 2000).

The purpose of the current study was to assess whether a group physical therapy program applied to patients with PD has more positive ef ects on gait speed when compared to an individual physical therapy program. The results show that both treatment interventions were ef ective in improving gait speed, as measured by the 6-minute walk test and the 10-meter walk test (all $p>0.05$), except for the gait speed in the 6-minute walk-test in the IPT group, which did not improve signif cantly ($p=0.07$). When comparing the two treatment groups, the GPT group showed higher gait speeds as measured by the 6-minute walk test ($p=0.002$) than the IPT group. This could be of importance for PD patients, as the 6-minute walk test scores are of importance in everyday life, due to its similarity to normal daily activities.

A study conducted by Gauthier (Gauthier et al., 1987) showed that patients with PD treated by occupational therapy within a group achieved more behavioral changes than an individual, more dependent client-therapist relationship would have achieved. This has shown that group therapy is well suited for patients with chronic degenerative diseases who are easily drawn into depression and social isolation.

Also, a more recent study showed that training as a group has long-term benef ts for people with PD. The positive and supportive environment provided by the group exercise program helped to improve attitudes, fostered optimism and was a positive force for the patients (Park et al., 2014).

In comparison to other studies with participants with PD at similar Hoehn & Yahr stages, tested while taking PD medications, the mean comfortable walking speed found in this study was close to that reported by Morris et al. (1996) and Brusse et al. (2005). However, it was considerably faster than previously reported by Stef en et al. (2008). The mean fast walking speed recorded by the group of participants in this study was also faster than the previously reported speeds (Lim et al., 2005b).

Certainly, any study involving patients with a degenerative, neurological disease and sometimes f uctuating symptoms has its limitations. However, our study was conducted with maximum scientif c rigor. The main limitations of the present study are the modest number of participants, the fact that the patients were selected from the same hospital setting and that only one gait parameter was assessed, as it did not require special equipment. But as said before and validated by dif erent authors, measurement of gait speed is a valid tool to emphasize the functional limitations of a patient with a neurological, degenerative disorder and to assess the outcomes of a rehabilitation program implemented. Also, it is important to see whether this type of GPT intervention has long-term positive ef ects on gait speed, and it should be further assessed in larger cohorts and multiple treatment centers in order to validate its potential.

Conclusions

1. A physical therapy program aided by the cueing techniques has a positive ef ect on gait speed. Patients with PD could benef t more from a GPT program, as gait speed increased more than in the IPT program.
2. The group provides in addition a supportive environment and facilitates interactions among peers. Also, the group approach is cost-ef ective, as it requires one therapist for 6 patients.
3. This therapy format is a necessity, since the number of patients with PD is increasing.

Conf icts of interests

No conf icts of interests.

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The ef ect of combined antipsychotic antidepressant treatment in experimental depression

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Abstract

Background. The use of atypical antipsychotics to increase the antidepressant pharmacological treatment in the experimental depressive disorder was analyzed.

Aims. We aimed to study experimentally, on a model of rat-induced depression, the ef ects of an atypical antipsychotic (Quetiapine) and major antidepressant (Agomelatine), associated with Omega-3 polyunsaturated fatty acids, on emotional and locomotor behavior and motor learning.

Methods. The animals were assigned to f ve groups as follows: G I – control animals; G II – animals with reserpine-induced depression; G III – animals with reserpine-induced depression, treated with Quetiapine; G IV - animals with reserpine-induced depression and treated with Quetiapine and Agomelatine; G V - animals with reserpine-induced depression, treated with Quetiapine, Agomelatine and supplemented with Omega-3 fatty acids, in which emotional and locomotor behavior were tested by the open f eld test, whereas motor and memory learning were tested by the Morris Water Maze Test.

Results. Thirty days later, the treatment with Quetiapine caused, in sedentary animals with reserpine-induced experimental depression, a decrease in excitability, involuntary mobility, in the learning ability and control, compared to control animals with depression. The co-treatment with Quetiapine and Agomelatine (a major antidepressant) in sedentary animals with reserpine-induced depression decreased excitability, increased involuntary mobility, learning ability, and its control after 30 days, compared to control animals with depression and those treated with Quetiapine. The co-treatment with Quetiapine, Agomelatine, and Omega-3 fatty acids supplements of sedentary animals with reserpine-induced depression caused a decrease in excitability and an increase in involuntary motility after 30 days, and an increase in the learning ability, decreasing its control over the group not supplemented with Omega-3 fatty acids.

Conclusions. The therapeutic combination used - antipsychotic and antidepressant, with and without the addition of Omega-3 fatty acids, has favorable neurobehavioral ef ects in experimental depression.

Key words: depression, Reserpine, Quetiapine, Agomelatine, Omega-3 fatty acids, open f eld test, Morris test

Introduction

Depression is considered the most common psychiatric disorder, but it also occupies an important place among non-psychiatric disorders. It is a multicausal af ective disorder by changing the mood. The treatment of depression can be done by using pharmacological and non-pharmacological methods.

Pharmacological treatment is aimed at augmentation strategies, therapeutic combinations, therapeutic conversion, and obtaining superior results to monotherapy.

Therapeutic combinations aim to increase therapeutic ef cacy, accelerate the onset of the antidepressant ef ect, and the possibility of continuing the administration of the initial antidepressant (Goldberg, 2001; Gheorghe, 2007; Prelipceanu, 2011). At the same time, an augmentation strategy to increase the pharmacological ef ect and the ef ectiveness of the antidepressant is its association with an atypical antipsychotic or another antidepressant. Numerous

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studies have observed the ef ect of co-treatment with an atypical antidepressant and antipsychotic in treatment-resistant depression:

- Paroxetine and Fluoxetine - Risperidone (Nelson, 2003)
- Citalopram - Risperidone (Rapaport et al., 2006)
- Fluoxetine - Olanzapine (Shelton., 2006)
- Fluoxetine, Citalopram, Paroxetine, Sertraline - Ziprasidone (Papakostas et al., 2007)
- Fluoxetine – Clozapine (Todorović et al., 2019)
- Escitalopram, Mitrazapine – Risperidone (Kamińska et al., 2018)
- Venlafaxine – Aripripazole (Ratajczak et al., 2018)
- Escitalopram – Ziprasidone (Papakostas et al., 2015)

Aims

We aimed to study experimentally, on a model of rat-induced depression, the ef ects of an atypical antipsychotic (Quetiapine) and major antidepressant (Agomelatine), associated with Omega-3 polyunsaturated fatty acids, on emotional and locomotor behavior and motor learning.

Hypothesis

The use of atypical antipsychotics to increase antidepressant pharmacological treatment led us to analyze their association in experimental depressive disorder.

Material and method

The studies were conducted in the Experimental Research Laboratory of the Physiology Department of "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, with the approval of the Bioethics Committee and the Sanitary Veterinary Authority Cluj-Napoca regarding the protection of animals used for experimental and scientif c purposes.

Research protocol

a) *Period and place of the research*

The studies were performed on white male Wistar rats, aged 4 months, with a weight of 200-250 g, from the animal facility of the "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca. Throughout the duration of the research, 1 Aug 2019 - 30 Sept 2019, the animals were kept under adequate *vivarium* conditions: temperature, humidity, lighting, feeding and hydration. At the end of the experiment, the animals were euthanized with ketamine.

b) *Subjects and groups*

The animals were assigned to f ve groups (G) (n = 10 animals/group), as follows:

- G I - witness - control animals, which are administered physiological saline 5 ml/kg body weight/day for 14 days
- G II - animals with reserpine-induced depression: 1 mg/kg body weight/24 hours IP for 14 days
- G III - animals with reserpine-induced depression and treated with Quetiapine 5 mg/kg body weight/24 hours IP, for 14 days, after the induction of depression
- G IV - animals with reserpine-induced depression and treated with Quetiapine 5 mg/kg body weight/24 hours IP and Agomelatine 1 mg/ kg body weight/24 hours IP, for 14 days, after the induction of depression
- G V - animals with reserpine-induced depression, treated IP with Quetiapine 5 mg/kg body weight/24 hours IP and Agomelatine 1 mg/ kg body weight/24 hours IP, and supplemented with Omega-3 fatty acids, 30 mg/kg body weight/24 hours by oropharyngeal gavage, for 14 days, after the induction of depression

c) *Tests applied*

The research calendar, by objectives, days and tests applied, included:

- induction of depression T_0-T_{14} by reserpine (the preparation used was Reserpinum, Sigma) (Arora & Chopra, 2013; Ruiz et al., 2018)
- treatment program T_{15}-T_{30} with Quetiapine, or Quetiapine + Agomelatine, or Quetiapine + Agomelatine + Omega-3 fatty acids administration (the preparations used were Seroquel^R for Quetiapine, produced by Astra Zeneca^R UK Limited; Valdoxan for Agomelatine, produced by Les Laboratoires Servier; Omega-3 fatty acids produced by Ozone Laboratories Pharma S.A)
- control of depression based on the Tail Suspension Test (TST), for antidepressant activity (Steru et al., 1985)
- control of therapy - T_{30} by the Open Field Test (OFT), according to Denenberg & Whimby (1963), to test spontaneous emotional and locomotor behavior, hyperactivity, exploring behavior in an open space and induced anxiety.
- The Morris Water Maze Test (MWM) (1981) was used for spatial learning and memory based on water navigation. The learning and control values, expressed in seconds, indicate the learning and memory ability. The time points analyzed were days 0-T_0, 14-T_{14} and 30-T_{30}.

d) *Statistical processing*

Statistical analysis was performed with StatsDirect v.2.7.2 software. The results were graphically represented using Excel application (Microsoft Of ce, 2010).

Results

A. *The Tail Suspension Test (TST)* (Table I)

In the statistical analysis of the values of *the tail suspension test (TST)*, the following were noticed:

- considering *the 4 rat groups* studied
  - o at moment T_0 – statistically signif cant dif erences between at least two of the groups ($p < 0.05$)
  - o at moments T_{14} and T_{30} – highly statistically signif cant dif erences between at least two of the groups ($p < 0.001$)
- considering the *3 time moments* studied
  - o in group I – the absence of statistically signif cant dif erences between the studied moments ($p > 0.05$)
  - o in groups II, III, IV– highly statistically signif cant dif erences between at least two of the moments ($p < 0.001$)

In the statistical analysis of TST values, the following were observed for *unpaired samples:*

- at moment T_0 – statistically signif cant dif erences between groups IV-V ($p < 0.05$) and very statistically signif cant dif erences between groups III-V ($p < 0.01$)
- at moment T_{14} – statistically signif cant dif erences between groups II-V ($p < 0.05$), highly statistically signif cant dif erences between groups I-II, I-III, III-IV, III-V ($p < 0.001$)
- at moment T_{30} – highly statistically signif cant dif erences between groups I-II, I-III, I- IV, II-V, III- IV, III-V ($p < 0.001$)

In the statistical analysis of TST values, the following were observed for *paired samples*:

- in group I –the absence of statistically signif cant dif erences between the time moments (p > 0.05)
- in group II – very statistically signif cant dif erences between T_0-T_{14}, T_{14}-T_{30} (p < 0.01) and highly statistically signif cant dif erences between T_0-T_{30} (p < 0.001)
- in group III – highly statistically signif cant dif erences between T_0-T_{14}, T_0-$T_{30,}$ T_{14}-T_{30} (p < 0.001)
- in group IV – very statistically signif cant dif erences between T_{14}-T_{30} (p < 0.01) and highly statistically signif cant dif erences between T_0-T_{14}, T_0-T_{30} (p < 0.001)
- in group V – highly statistically signif cant dif erences between T_0-T_{14} (p < 0.001) and very statistically signif cant dif erences between T_0-$T_{30,}$ T_{14}-T_{30} (p < 0.01)

B. *The Open-Field Test (OFT)* (Tables II and III)

In the statistical analysis of the values of the *Open Field test-excitability score*, considering the *4* studied *groups of rats* (except the control group), highly statistically signif cant dif erences between groups at moments T_0, T_{14} and T_{30} (p <0.0001) were noticed.

In the statistical analysis of the values of the *Open Field test-motility score***,** considering the *4* studied *groups of rats* (except the control group), highly statistically signif cant dif erences between groups at moments T_0, T_{14} and T_{30} (p <0.0001) were noticed.

In the statistical analysis of the values of the *Open Field test in unpaired samples*, the following were noticed regarding:

- excitability score

o at moment T_0 – statistically signif cant dif erences between groups I-III, II-III (p < 0.05), very statistically signif cant dif erences between groups III-IV, IV-V (p < 0.01), and highly statistically signif cant dif erences between groups I-V, II-V, III-V (p < 0.001)

o at moment T_{14} – highly statistically signif cant dif erences between groups I-II, I-IV, I-V, II-III, II-IV, II-V, III-V (p <0.001)

o at moment T_{30} – statistically signif cant dif erences between groups I-II (p < 0.05), and highly statistically signif cant dif erences between groups I-IV, I-V, II- IV, II-V, III-IV, III-V (p < 0.001)

- motility score

o at moment T_0 – highly statistically signif cant dif erences between groups I-III, I-IV (p < 0.001)

o at moment T_{14} – very statistically signif cant dif erences between groups III-IV (p < 0.01), and highly statistically signif cant dif erences between groups I-II, I-III, I-IV, I-V, II-III, II- IV, III-V, IV-V (p < 0.001)

o at moment T_{30} – very statistically signif cant dif erences between groups II-III, II-IV (p < 0,01), and highly statistically signif cant dif erences between groups I-II, I-III, I-IV, II-V, III-V, IV-V (p < 0.001).

In the statistical analysis of the values of the *Open Field test in paired samples* (T_0-T_{14}, T_0-T_{30}, T_{14}-T_{30}), the following were noticed regarding:

- excitability score

o in group II – statistically signif cant dif erences between T_0-T_{30} and T_{14}-T_{30} (p < 0.05), and highly statistically signif cant dif erences between T_0-T_{14} (p < 0.001)

o in group IV – statistically signif cant dif erences between T_{14}-T_{30} (p < 0.05), and very statistically signif cant dif erences between T_0-T_{14} and T_0-T_{30} (p < 0.01)

Table I

Comparative analysis for TST values in the studied groups and statistical signif cance.

Moment	Group	Mean	SE	Median	SD	Min	Max	Statistical significance (p)											
T0	I	3	0,2582	3	0,8165	2	4	II-III-IV-V		T0	0,0218	T0-T14-T30		I	0,6624	IV	< 0,0001		
	II	2,7	0,2603	3	0,8233	1	4			T14	< 0,0001			II	< 0,0001	V	< 0,0001		
	III	2,6	0,2667	3	0,8433	1	4			T30	< 0,0001			III	< 0,0001				
	IV	2,8	0,3266	3	1,0328	1	4		T0-T14	0,75		T0-T14	0,002		T0-T14	< 0,0001		T0-T14	< 0,0001
	V	3,8	0,2906	4	0,9189	2	5	I	T0-T30	0,4609	II	T0-T30	< 0,0001	III	T0-T30	< 0,0001	IV	T0-T30	< 0,0001
T14	I	3,1	0,2333	3	0,7379	2	4		T14-T30	0,6875		T14-T30	0,0027		T14-T30	0,0002		T14-T30	0,0013
	II	12	0,4714	12	1,4907	10	14		T0-T14	< 0,0001									
	III	24,1	0,8750	24	2,7669	20	29	V	T0-T30	0,002									
	IV	18,5	0,6009	18,5	1,9003	16	22		T14-T30	0,002									
	V	10,5	0,4014	10	1,2693	9	13	T0				T14				T30			
T30	I	3,3	0,2603	3,5	0,8233	2	4	I-II	0,5894	II-IV	0,9192	I-II	< 0,0001	II-IV	< 0,0001	I-II	< 0,0001	II-IV	0,5879
	II	15,4	0,5617	15,5	1,7764	12	18	I-III	0,4228	II-V	0,011	I-III	< 0,0001	II-V	0,0262	I-III	< 0,0001	II-V	< 0,0001
	III	22	0,7454	21,5	2,3570	19	27	I-IV	0,8103	III-IV	0,641	I-IV	< 0,0001	III-IV	< 0,0001	I-IV	< 0,0001	III-IV	< 0,0001
	IV	16	0,9309	16	2,9439	12	21	I-V	0,0823	III-V	0,007	I-V	< 0,0001	III-V	< 0,0001	I-V	< 0,0001	III-V	< 0,0001
	V	8,1	0,3786	8	1,1972	7	11	II-III	0,841	IV-V	0,0345	II-III	< 0,0001	IV-V	< 0,0001	II-III	< 0,0001	IV-V	< 0,0001

Table II

Comparative analysis for the values of the Open Field test – excitability score and statistical signif cance.

Moment	Group	Mean	SE	Median	SD	Min	Max	Statistical significance (p)											
T0	I	8,5	0,3727	9	1,1785	7	10	II-III-IV-V		T0	< 0,0001	T0-T14-T30		I	-	IV	< 0,0001		
	II	8,6	0,3399	9	1,0750	7	10			T14	< 0,0001			II	0,0002	V	< 0,0001		
	III	9,9	0,4069	10	1,2867	7	11			T30	< 0,0001			III	0,1753				
	IV	7,6	0,4989	7,5	1,5776	4	9		T0-T14	-		T0-T14	0,0007		T0-T14	0,1563		T0-T14	0,0039
	V	5,1	0,4333	5	1,3703	3	7	I	T0-T30	-	II	T0-T30	0,0234	III	T0-T30	0,25	IV	T0-T30	0,002
T14	I	-	-	-	-	-	-		T14-T30	-		T14-T30	0,0195		T14-T30	0,9453		T14-T30	0,0313
	II	11,8	0,5121	11,5	1,6193	10	14		T0-T14	0,0418									
	III	8,9	0,4333	9	1,3703	7	11	V	T0-T30	0,156									
	IV	4,8	0,3887	4,5	1,2293	3	7		T14-T30	0,938									
	V	4,1	0,3786	4	1,1972	2	6	T0				T14				T30			
T30	I	-	-	-	-	-	-	I-II	0,9501	II-IV	0,1683	I-II	0,0001	II-IV	< 0,0001	I-II	0,0192	II-IV	< 0,0001
	II	9,9	0,2769	10	0,8756	9	11	I-III	0,021	II-V	< 0,0001	I-III	0,5336	II-V	< 0,0001	I-III	0,3927	II-V	< 0,0001
	III	9	0,4216	9	1,3333	7	11	I-IV	0,2307	III-IV	0,0017	I-IV	< 0,0001	III-IV	< 0,0001	I-IV	< 0,0001	III-IV	< 0,0001
	IV	3,3	0,2603	3,5	0,8233	2	4	I-V	< 0,0001	III-V	< 0,0001	I-V	< 0,0001	III-V	< 0,0001	I-V	< 0,0001	III-V	< 0,0001
	V	4,1	0,2769	4	0,8756	3	5	II-III	0,0211	IV-V	0,0018	II-III	0,0004	IV-V	0,2134	II-III	0,1434	IV-V	0,0873

Table III

Comparative analysis for the values of the Open Field test – motility score and statistical signif cance.

Moment	Group	Mean	SE	Median	SD	Min	Max
T0	I	34,4	1,2927	33	4,0879	30	42
	II	34,4	1,2667	33,5	4,0056	30	42
	III	9,4	0,5207	9	1,6465	8	12
	IV	9,4	0,4522	9,5	1,4298	8	12
	V	9,1	0,6403	9	2,0248	6	12
T14	I	-	-	-	-	-	-
	II	25,6	0,5416	25,5	1,7127	23	28
	III	12,3	0,4955	12,5	1,5670	10	14
	IV	15,2	0,6633	15	2,0976	13	20
	V	25,2	1,1235	27	3,5528	20	29
T30	I	-	-	-	-	-	-
	II	18,2	0,5121	18	1,6193	16	21
	III	20,9	0,7219	20,5	2,2828	18	24
	IV	21,8	1,0088	21,5	3,1903	17	28
	V	32,4	0,7483	32,5	2,3664	28	36

Statistical significance (p)

II-III-IV-V		T0-T14-T30	
T0	0,0002	I	-
T14	< 0,0001	II	< 0,0001
T30	< 0,0001	III	< 0,0001
		IV	< 0,0001
		V	< 0,0001

Group	T0-T14	T0-T30	T14-T30
I	-	-	-
II	< 0,0001	< 0,0001	< 0,0001
III	0,0098	0,002	< 0,0001
IV	0,002	0,002	< 0,0001
V	< 0,0001	< 0,0001	0,0003

T0				T14				T30			
I-II	> 0,9999	II-IV	< 0,0001	I-II	< 0,0001	II-IV	< 0,0001	I-II	< 0,0001	II-IV	0,0052
I-III	< 0,0001	II-V	< 0,0001	I-III	< 0,0001	II-V	0,7535	I-III	< 0,0001	II-V	< 0,0001
I-IV	< 0,0001	III-IV	0,9482	I-IV	< 0,0001	III-IV	0,0025	I-IV	< 0,0001	III-IV	0,4775
I-V	< 0,0001	III-V	0,7684	I-V	< 0,0001	III-V	< 0,0001	I-V	0,1972	III-V	< 0,0001
II-III	< 0,0001	IV-V	0,7108	II-III	< 0,0001	IV-V	< 0,0001	II-III	0,0069	IV-V	< 0,0001

Table IV

Comparative analysis for Morris test values – learning score, control and statistical signif cance.

Moment		Group	Mean	SE	Median	SD	Min	Max
Learning	T0	I	262,56	3,439	262,33	10,875	242,92	281,83
	T14	II	372,63	2,326	371,75	7,356	361,25	383,92
		III	369,73	3,056	368,42	9,663	355,00	382,25
		IV	346,17	4,241	346,92	13,413	321,83	365,58
		V	350,81	3,742	350,13	11,835	332,00	368,58
	T30	II	376,27	3,376	376,88	10,676	352,83	388,58
		III	360,70	4,262	362,92	13,479	336,67	380,08
		IV	312,17	4,140	314,00	13,091	286,25	331,67
		V	270,72	8,015	271,88	25,347	231,25	309,58
CTRL	T0	I	85,43	2,384	88,00	7,539	74,00	98,33
	T14	II	22,90	0,965	22,33	3,051	20,33	31,00
		III	20,53	0,995	21,17	3,147	15,33	24,33
		IV	17,93	0,796	17,00	2,518	15,33	22,33
		V	11,07	0,325	10,83	1,028	10,00	12,67
	T30	II	15,07	0,730	14,33	2,308	12,67	21,00
		III	19,47	0,777	19,83	2,456	15,00	23,00
		IV	17,03	0,429	17,67	1,356	15,00	18,67
		V	8,20	0,311	7,83	0,984	7,33	10,33

Statistical significance (p)

Learning			CTRL		
T14	II-III-IV-V	< 0,0001	T14	II-III-IV-V	< 0,0001
T30		< 0,0001	T30		< 0,0001

Learning T14		Learning T30		CTRL T14		CTRL T30	
I-II	< 0,0001	I-II	< 0,0001	I-II	< 0,0001	I-II	< 0,0001
I-III	< 0,0001	I-III	< 0,0001	I-III	< 0,0001	I-III	< 0,0001
I-IV	< 0,0001	I-IV	< 0,0001	I-IV	< 0,0001	I-IV	< 0,0001
I-V	< 0,0001	I-V	0,3677	I-V	< 0,0001	I-V	< 0,0001
II-III	0,4599	II-III	0,0103	II-III	0,2538	II-III	0,0012
II-IV	< 0,0001	II-IV	< 0,0001	II-IV	0,0005	II-IV	0,0093
II-V	0,0001	II-V	< 0,0001	II-V	< 0,0001	II-V	< 0,0001
III-IV	0,0003	III-IV	< 0,0001	III-IV	0,0563	III-IV	0,0404
III-V	0,001	III-V	< 0,0001	III-V	< 0,0001	III-V	< 0,0001
IV-V	0,4226	IV-V	0,0002	IV-V	< 0,0001	IV-V	< 0,0001

T14-T30	II	III	IV	V
Learning	0,4786	0,0787	0,0001	< 0,0001
CTRL	0,002	0,4506	0,9102	0,002

Learning - CTRL	II	III	IV	V
T14	0,002	< 0,0001	< 0,0001	0,002
T30	0,002	< 0,0001	0,002	0,002

o in group V – statistically signif cant dif erences between T_0-T_{14} ($p < 0.05$)

- motility score

o in group II – highly statistically signif cant dif erences between T_0-T_{14}, T_0-T_{30} and T_{14}-T_{30} ($p < 0.001$)

o in group III – very statistically signif cant dif erences between T_0-T_{14} and T_0-T_{30} ($p < 0.01$), and highly statistically signif cant dif erences between T_{14}-T_{30} ($p < 0.001$)

o in group IV – very statistically signif cant dif erences between T_0-T_{14} and T_0-T_{30} ($p < 0.01$), and highly statistically signif cant dif erences between T_{14}-T_{30} ($p < 0.001$)

o in group V – highly statistically signif cant dif erences between T_0-T_{14}, T_0-$T_{30,}$ and T_{14}-T_{30} ($p < 0.001$)

C. *The Morris Test* (Table IV)

In the statistical analysis of the values of the *Morris test*, the following were noticed**:**

- considering the *4 rat groups* studied (except the control group) in the learning period

o at moments T_{14} and T_{30} – highly statistically signif cant dif erences between at least two of the groups ($p < 0.001$)

- considering the *4 rat groups* studied (except the control group) in the control period

o at moments T_{14} and T_{30} – highly statistically signif cant dif erences between at least two of the groups ($p < 0.001$).

In the statistical analysis of the values of the *Morris test* in the learning period, the following were noticed in *unpaired samples:*

- at moment T_{14} – highly statistically signif cant dif erences between groups I-II, I-III, I- IV, I-V, II-VI, III-IV ($p < 0.001$), very statistically signif cant dif erences between groups III-V ($p < 0.01$)

- at momentT_{30} – highly statistically signif cant dif erences between groups I-II, I-III, I- IV, II-V, III-IV, III-V, IV-V ($p < 0.001$), and statistically signif cant dif erences between groups II-III ($p < 0.05$).

In the statistical analysis of the values of the *Morris test* in the learning period, the following were noticed in *paired samples:*

- at moment T_{14} – highly statistically signif cant dif erences between groups I-II, I-III, I-IV, II- IV, II-V, III-IV, III-V, IV-V ($p < 0.001$)
- at moment T_{30} – highly statistically signif cant dif erences between groups I-II, I-III, I- IV, I-V, II-V, III-V, IV-V ($p < 0.001$), very statistically signif cant dif erences between groups II-III, II-IV ($p < 0.01$), and statistically signif cant dif erences between groups III-IV ($p < 0.05$).

In the statistical analysis of Morris test values, the following were noticed in *paired samples between T_{14}-T_{30}:* highly statistically signif cant dif erences for group V ($p <0.001$) in the learning period, and very statistically signif cant dif erences for groups II and V in the control period.

In the statistical analysis of Morris test values, the following were noticed in *paired samples between the learning period and the control period:*

- in groups II and V – very statistically signif cant dif erences ($p < 0.01$) at moments T_{14} and T_{30}
- in group III – highly statistically signif cant dif erences ($p < 0.001$) at moments T_{14} and T_{30}
- in group IV – highly statistically signif cant dif erences ($p < 0.001$) at moment $T_{14,}$ and very statistically signif cant dif erences ($p < 0.01$) at moment T_{30}

Discussions

Our results regarding the experimental pharmacological model of induction of depression in animals (Manea et al., 2019) using Reserpine, obtained in group II, show in the TST test the onset of depressive behavior from moment T_0, compared to control animals (G I), and its signif cant increase after 14 days of administration (T_{14}) and at 30 days (T_{30}). Depression induced in sedentary animals sets in quickly and is long-lasting.

Administration of Quetiapine in experimental depression

Quetiapine (Seroquel^R) is an atypical neuroleptic (a non-conventional antipsychotic), which by metabolization gives rise to an active compound, norquetiapine. Both substances have moderate af nity for receptors D_1, D_2 and 5-HT_{2A} (antagonistic action) and α1, α2, Ach. It acts on the dopaminergic, serotonergic and noradrenergic systems. Because it dissociates rapidly from D_2 receptors, it has a reduced risk of extrapyramidal side ef ects or hyperprolactinemia (Prelipceanu, 2011; Buzoianu, 2016).

Indications: schizophrenia, bipolar depressive af ective disorder, major depressive episodes in patients who have responded suboptimally to antidepressant monotherapy, insomnia.

In group III, with Reserpine-induced depression and treatment with Quetiapine, an atypical antipsychotic, the following were found compared to the untreated group (G II):

- signif cant decreases in excitability at T_{14}
- signif cant decreases in involuntary motility at T_{14}, followed by increases at T_{30}
- signif cant increases in learning at T_{30}
- signif cant increases in learning control at T_{30}

Administration of Quetiapine and Agomelatine in experimental depression

Agomelatine (Valdoxan) is an antidepressant with a serotonergic and serotonergic/melatonergic modulating action. It is a melatonin analogue, which acts as an agonist directly on MT_1 and MT_2 receptors and a selective serotonin antagonist on 5-HT_{2b} and 5-HT_{2c} receptors (Prelipceanu, 2011; Buzoianu, 2016).

Indications: depression, major depressive disorder, circadian rhythm regulation and increased duration and quality of physiological sleep, epilepsy.

It stimulates the lateral entorhinal cortex and the hippocampal dorsal subiculum by the action of c-FOS expression, which explains its antidepressant therapeutic ef ect.

It increases the level of the hippocampal neurotrophic factor.

It prevents anxiety, depressive behavior in depressed rats.

It modulates the acute inf ammatory response by acting as a mediating antidepressant.

In group IV, with Reserpine-induced depression and co-treatment with Quetiapine – an atypical antipsychotic, and Agomelatine – an antidepressant, the following were noticed compared to the untreated group (G II):

- signif cant decreases of excitability at T_{14} and T_{30}
- signif cant decreases of involuntary motility at T_{14}, followed by signif cant increases at T_{30}.

Administration of Quetiapine and Agomelatine, and supplementation with Omega-3 polyunsaturated fatty acids

Essential fatty acids (EFAs) are lipids that the body cannot synthesize, but must be provided through food. They can be dif erentiated, depending on the position of the f rst double bond (omega) in the hydrocarbon chain in polyunsaturated fatty acids (PUFAs), into 2 classes:

- class n=3 ($C_{18:3}$): α-linolenic acid, docosahexaenoic acid, and eicosapentaenoic acid
- class n=6 ($C_{18:2}$): linoleic acid, cis-linoleic acid, and γ-linoleic acid (Dobreanu, 2010).

The sources of PUFA – Omega-3 are seaweed (spirulina), trout, sardines, salmon, tuna, herring, anchovies, cod, shrimp, minnows, f sh and vegetable oils such as f ax seeds, hemp, chia; canola, nuts, peanuts, soybeans, hazelnuts, almonds.

The PUFA – Omega-3 ef ects are numerous (Lieberman & Bruning, 2005; Goldman, 2009; Palacios-Pelaez, 2010; García-Alonso et al., 2012; Wylde, 2013; Zungo et al., 2014; Manea, 2014; Pérez et al., 2018).

a) Cellular functions: af nity for membrane phospholipids and redistribution of PUFA n=6, maintenance of cellular homeostasis, activation of antioxidant enzymes, chemical messengers, release of arachidonic acid, and biosynthesis of prostaglandins and thromboxanes, antiplatelet agents, neutrophil chemotaxis, anti-mitogen to epithelial and macrophage cells.

b) Sanguine ef ects: anticoagulant, antif brinolytic, decrease of triglycerides, increase of HDL cholesterol.

c) Systemic ef ects: cardiovascular (hypotensive, heart rate regulation, restoration of arterial elasticity in the elderly), anti-inf ammatory, antimicrobial, antiviral, anti-allergic, antitumor, strengthens the immune system.

Therapeutic uses

- psychiatric illnesses: depression, schizophrenia, dyslexia, hyperactivity disorders, aggression in children, behavioral disorders, stabilization of mental mood;
- cardiovascular diseases: atherosclerosis, risk of stroke, heart attack;
- inf ammatory and allergic diseases;
- autoimmune diseases: herpes, multiple sclerosis;
- psoriasis, dermatitis, diabetes, colds, breast, colon and lung cancer;
- weight loss.

Co-treatment with Quetiapine and Agomelatine and addition of Omega-3 fatty acids in experimental depression determine, compared to the not supplemented group IV:

- signif cant decreases of excitability at T_{14} and T_{30}
- signif cant increases of involuntary motility at T_{14} and T_{30}
- signif cant increases of learning capacity at T_{30}
- signif cant decreases of learning control at T_{14} and T_{30}

Our data are in agreement with those communicated by Perez et al. 2018 regarding the improvement of the learning and memory capacity in rats, after the administration of Omega-3 fatty acids.

Conclusions

1. Treatment with Quetiapine - an atypical antipsychotic - causes after 30 days, in sedentary animals with reserpine-induced experimental depression, a decrease in excitability and involuntary motility, in the learning capacity and its control, compared to control animals with depression.
2. Co-treatment with Quetiapine and Agomelatine - a major antidepressant - in sedentary animals with reserpine-induced depression, leads to a decrease in excitability, an increase in involuntary motility, in the learning capacity and its control after 30 days, compared to control animals with depression and those treated with Quetiapine.
3. Co-treatment with Quetiapine and Agomelatine and Omega-3 fatty acid supplements in sedentary animals with reserpine-induced depression cause after 30 days a decrease in excitability, an increase in involuntary motility, an increase in the learning capacity and a decrease in the learning control, compared to the group not supplemented with Omega-3 fatty acids.
4. The therapeutic combination used – an antipsychotic and an antidepressant, with and without the addition of Omega-3 fatty acids, has favorable neurobehavioral ef ects in experimental depression.

Conf icts of interest

Nothing to declare.

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Changing body composition in a group of amateurs who practice constant physical activity

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Abstract

Background. Over the years, most f tness gyms have introduced dif erent programs of physical exercise for groups (eg. Aerobics, TRX, step aerobics). In order to avoid accidents, it is important to personalize and monitor these programs by a professional gym instructor.

Aims. The aim of this study is to evaluate the association between activity plans, individual food intake and body composition.

Methods. A prospective analytical study was conducted during February-March 2019 in Târgu-Mureș, Romania. The study sample was represented by 35 subjects from a f tness gym that practices physical activity in groups. The data required for the study were collected using a foot-to-foot bioimpedance scale, a plicometer, a tape measure and a 3-day food journal.

Results. The subjects had an average intake of 19.92% proteins, 37.87% fat and 42.90% carbohydrates. Statistical correlations were noticed between the intake of proteins and the abdominal skinfold (p=0.03). Other associations were visible between the intake of fats and the waist measurement (p=0.009), along with correlations between the intake of carbohydrates and the triceps skinfold (p=0.002).

Conclusions. The connection between inadequate physical activity, with high intensity, and an unbalanced nutritional plan (high in proteins but low in carbohydrates) will lead to a minor change in body mass because of dehydration.

Key words: physical activity, f tness, dehydration, proteins, body composition

Introduction

A balanced diet along with daily physical exercise is important to achieve a healthy lifestyle and therefore a proper body development. According to the World Health Organization, every individual should perform at least 300 minutes of physical exercise every week in order to gain superior medical benef ts (1). The main health benef ts are usually related to a reduced risk for developing coronary heart dysfunctions, higher blood pressure, metabolic syndrome, colon or breast cancer, along with depression. All these benef ts can be favored by a daily physical exercise program of low to medium exercise intensity applicable in all sex and age groups (2). However, the literature study introduces new therapeutic methods for obese individuals, which act on understanding the fundamental causes of excessive weight gain (***, 2004).

Daily physical exercise increases caloric intake and therefore daily macro-micronutrient intake. As seen in the literature, active individuals exceed 0.8 g proteins/kg due to the desire to develop active body tissue (Stensel et al., 2017), whereas further increasing carbohydrate and limiting fat intake. As a result, the risk of exceeding the energy requirements increases, causing a positive energy balance and also an increase in body weight. Such energy intake measures, adopted frequently, can result from high-intensity physical exercise in groups with low exercise capacity. Ulbrich et al. (2016) conf rmed that both high intensity and low intensity physical exercise can improve quality of life in patients with heart failure, while other papers reported similar results over healthy individuals. Yet, low exercise capacity and high exercise intensity can lead to important negative changes in energy metabolism. Of the main changes, an increased respiratory exchange ratio (RER) can be seen early and therefore, an increased carbohydrate metabolism while limiting the use of fat as an energetic compound (Ramos-Jiménez, 2008). In such cases, improper anthropometric changes are described through an increased fat mass and total body weight.

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Over the years, most f tness gyms have introduced dif erent physical activity programs intended for specif c groups. Of these, the most common are aerobics, total body resistance exercises (TRX) and step aerobics. In order to avoid injuries and to achieve the physical goal set for each individual, it is important for this programs to be personalized and monitored by professional individuals (Jordan et al., 2018). Therefore, the purpose of our study was to evaluate the association between physical activity, individual food intake and changes in body composition.

Material and methods

The research was initiated after obtaining the approval of the Ethics Committee of Scientif c Research, the necessary data being collected after obtaining the written consent of all study participants.

Research protocol

a) Period and place of the research

A prospective analytical study was conducted during February-March 2019 in Târgu-Mureș, Romania. The study was performed after obtaining the gym manager's consent to conduct the study in the gym and each subject's consent for data collection.

b) Subjects and groups

The following inclusion criteria were applied: healthy females and males, without any medical problems, engaged in a physical f tness group, having a permanent residence in Târgu-Mureș.

The exclusion criteria were: no subject under the age of 18, without a permanent residence in Târgu-Mureș, suf ering from chronic illness af ecting physical development, with the presence of a pathology restricting physical exercise.

The study sample was represented by 35 subjects from a f tness gym that practices physical exercises in groups, both females and males being included in this study.

c) Tests applied

- Anthropometric and food related data

The data required for the study was collected using a foot-to-foot bioimpedance scale (Tanita BC-1000 Japan with a max capacity of 200 kg and an accuracy of 0.1 kg) and food journals. A plicometer and a tape measure were used to collect anthropometric data such as biceps, triceps, abdominal, subscapular skinfolds along with hip and waist circumferences. The measurements were taken at the beginning and the end of the study, with the subjects in a standing position with their back straight, without clothes.

The food jurnal was completed for a 3-day period, having the objective to collect the following data: number of meals - including snacks, serving period, serving type, food type and quantity, along with the daily water intake. All the data were used to determine daily energy intake and therefore macronutrient and micronutrient consumption.

- Physical exercise analysis

The f tness plan was described everyday for a whole week by a gym representative. The training volume was 60 minutes/day, and the equivalent of 300 minutes/week. The training was conducted over f ve days per week and two days of rest. The group training intensity dif ered by the type of physical exercises: high intensity (full body workout, plyometric, accelerator), medium intensity (kettlebell training, TRX, back & base) and low intensity (yoga and dumbbell training). During a 4-week program, these types of exercises were repeated 2 to 3 times.

d) Statistical processing

GraphPad Prism 6.0. was used to statistically analyze this data. Standard deviation (±SD) along with the variation coef cient (CV%) and median were used for the descriptive statistical analysis. The D'Agostino Pearson omnibus normality test was used to evaluate the normality of data. We considered the P value of <0.05 as statistically signif cant with a range of conf dence of 95% (95% CI).

Results

Following statistical analysis, we noticed a signif cant dif erence in the subjects' body weight. The f rst measurement median value was 67.47 kg and the second measurement value was 64.02 kg (Fig. 1). A lower weight dif erence for the second month can be observed in Table 1 (p=0.024).

Table I

Statistical data regarding the weight of subjects between and after 1 month of training.

Indicators	First measurement (kg)	Last measurement (kg)
Minimum value	41.20	40.90
Maximum value	103.8	96.10
Median	64.70	59.50
Mean	67.47	64.02
SD	14.96	14.20
Variation coef cient %	22.18	22.18

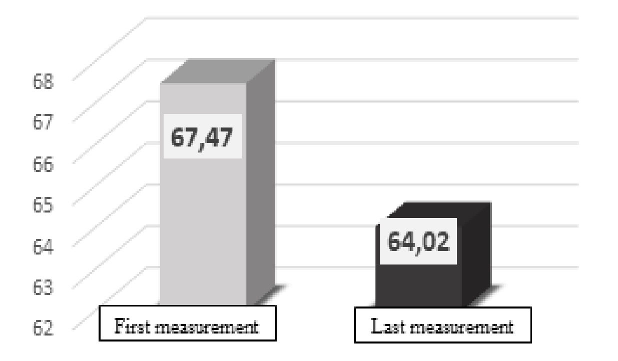

Fig. 1 – Weight measurements - graphic representation of the means (kg).

Regarding the skinfold measurement (biceps=SFb, abdominal=SFabd, subscapular=SFsp), we observed a signif cant dif erence in the subscapular skinfold, as further detailed in Table II.

A signif cant dif erence was seen compared to hip measurement values. During the f rst measurement, the average value was 98.69 cm versus 94.71 cm during the second measurement. An important dif erence was noticeable between the two check-ups (p=0.009); the dif erence between the average values was ±7.71 cm. These dif erences can be viewed in Table III.

Table II

Descriptive statistical data regarding the subjects' skinfold measurements (mm).

Indicators	SFb1*	SFb2**	SFt1	SFt2	SFabd1	SFabd2	SFsp1	SFsb2
Minimum value	3.10	2.80	4.00	6.40	5.60	5.10	5.40	6.70
Maximum value	19.20	14.50	24.70	19.70	25.70	22.90	21.30	20.40
Median	7.50	6.80	11.60	11.65	17.60	15.00	11.20	8.02
Mean	8.53	7.13	13.06	11.53	16.74	14.96	12.59	11.11
±SD	4.25	2.80	4.77	3.30	6.02	5.75	4.11	3.89
p value	0.36		0.17		0.06		0.02	
Variation coef cient %	49.89	39.37	36.54	28.64	35.98	38.48	32.67	35.05

**1=the f rst measurement; **2=the last measurement*

Table III

Statistical data regarding hip measurements

Indicators	Hip circumference - 1	Hip circumference - 2
Minimum value	88 cm	70 cm
Maximum value	116 cm	114 cm
Median	98 cm	97,5 cm
Mean	98.69 cm	94.71 cm
±SD	7.71 cm	10.11 cm
Variation coef cient %	7.82 cm	10.67 cm

**1=the f rst measurement; **2=the last measurement*

Regarding body composition, more specif cally considering the fat tissue and the muscle tissue, there were no signif cant statistical data dif erences, with a dif erential p value of 0.08 for the fat tissue and 0.15 for the muscular tissue. Furthermore, the hydration level did not record any signif cant dif erences (p=0.19). From the data illustrated in Table IV it can be seen that the subjects were in an average state of dehydration.

Table IV

Statistical data regarding the % of water deposits in the body.

Indicators	Water deposits - 1	Water deposits - 2
Minimum value	43.60%	42.20%
Maximum value	63.40%	65.50%
Median	54.00%	54.40%
Average	53.27%	53.65%
±SD	5.38%	5.70%

**1=the f rst measurement; **2=the last measurement*

Figure 2 shows the level of hydration of the sample group (% of water from the body weight).

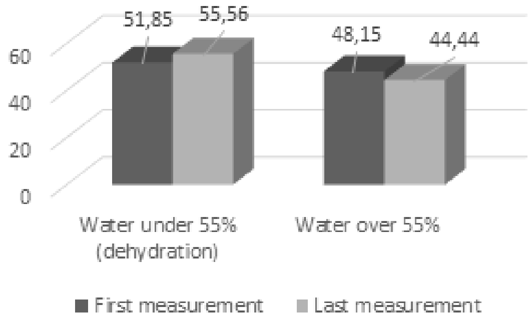

Fig. 2 – Graphic representation of the hydration level (% from the sample)

When statistically evaluating the food journals, signif cant dif erences were noticed among the general recommendations of macronutrient intake per day: proteins - 15%, carbohydrates - 55%, fat - 30%. Analyzing the data, the subjects had an average intake of 19.92% ± 4.18 SD proteins (p=0.006), 37.87% ± 10.18 SD fat (p<0.001) and 42.90% ± 11.50 carbohydrates (p<0.001).

Analyzing the association between the intake of macronutrients and anthropometric measurements, signif cant statistical correlations were noticed between the intake of proteins and the abdominal skinfold (p=0.03). Other associations were visible between the fat intake and the waist measurement (p=0.009), along with carbohydrate intake and the triceps skinfold (p=0.002). There were no statistical changes when analyzing the association between macronutrients and other anthropometric measurements (Table V).

Table V

Statistical data regarding the associations between anthropometry and macronutrient intake.

Measurements	Measurements-protein association		Measurements-fats association		Measurements-carbohydrates association	
	p value	Spearman r	p value	Spearman r	p value	Spearman r
% of fat tissue	0.8944	-0.04	0.5824	-0.18	0.5094	-0.22
% of muscular tissue	0.8944	0.04	0.5824	0.18	0.5094	0.22
Kilograms	0.9151	-0.03	0.3296	-0.32	0.7683	0.10
Biceps skinfold	0.7293	-0.11	0.9153	0.03	0.7899	-0.09
Triceps skinfold	0.1433	0.47	0.0665	0.57	0.0028	-0.80
Abdomen skinfold	0.0388	0.62	0.8627	0.05	0.2275	-0.39
Scapular skinfold	0.5926	0.18	0.7287	0.11	0.1591	-0.45
Hip circumference	0.8399	0.06	0.0877	0.53	0.3284	-0.32
Waist circumference	0.4149	-0.27	0.009	0.74	0.6091	-0.17

Discussions

According to the study results, a signif cant weight loss was seen in the study group. Low intensity physical exercise can improve energy metabolism due to a lower respiratory exchange ratio, a lower heart rate and an increased fat metabolism use (Purdom et al., 2018).

According to Christense et al. (2018), in order to lose weight, a hypocaloric diet is needed along with daily physical exercise. During physical exercise with an intensity of over 70% of HRmax, glycogen becomes the main energy fuel. Post-workout glycogen synthesis is increased in order to enhance post-exercise recovery. According to Starling et al. (1997), after 2h cycling training (with 65% of HRmax intensity), a diet rich in carbohydrates leads to a 93% muscular glycogen restoration, while a diet poor in carbohydrates leads to only 13% deposit restoration (Murray & Rosenbloom, 2018). The low carbohydrate diet seen in our sample will lead to the body's incapacity to restore the glycogen in muscular deposits (Starling et al., 1997).

According to the main theoretical recommendations, a regular diet consists of 15% proteins, 50-55% carbohydrates and 30-35% fats (Jensen et al., 2011). A low protein intake will lead to weight loss due to muscular protein usage as a substrate for gluconeogenesis. (Longland et al., 2016). A weight loss diet plan should be f rst of all hypocaloric and low/medium in fat, high/normal in proteins and low/medium in carbohydrates. Analyzing our subjects' food journals, it was concluded that their diet was high in proteins, high in fats and low in carbohydrates. Although there were important changes in the body weight, there were fewer changes in the fat tissue, which may bring into question other factors that favored body weight loss.

During muscular glycogenolysis, glycogen is decomposed into pyruvate in order to provide enough energy to sustain physical activity. During muscular contractions, more specif cally during aerobic contractions, pyruvate is decomposed into carbon dioxide and water (Martin & Tarcea, 2015). Due to a low carbohydrate intake, our subjects may have a slower muscular glycogen restoration and a false weight loss due to low intramuscular water deposits (Tero-Vescan et al., 2013).

The purpose of a diet plan rich in proteins is to increase the muscle mass. Furthermore, with an adequate ratio of carbohydrates, it helps restoring the body's glycogen which was oxidized (Zajak et al., 2014). Carbohydrate intake leads to increased postprandial glycemia, which causes the pancreas to release insulin. This mechanism will help amino acids to enter through active transport inside the striated muscle f bers for protein synthesis (Martin & Tarcea, 2015). Although the subjects of the present study had a protein rich diet, this did not lead to a signif cant increase in their muscle mass.

From the results of this study it can be seen that pre- and post-workout hydration is inadequate. The subjects' average intake of water was 1.6 L/day. According to the literature, an optimal restoration presumably needs the intake of 150% of the lost water (Jensen et al., 2011). Peacock et al. (2011) suggest that it is very important to drink water before and after workout. As we also concluded in this study, the participants were in a state of dehydration at the beginning of a new workout. Furthermore, according to Bilsborough & Mann (2006), a high protein intake requires a high water intake. An inadequate intake of water in our sample group will eventually lead to the dehydration of the subjects.

Engaging into physical exercise of dif erent intensity levels is not enough to achieve signif cant changes in the body composition. A well planned diet is as important as the physical exercises performed. Respecting the nutritional plan of ered alongside the workout plans may lead to positive changes for the subject and also for his/her exercise performance.

Conclusions

1 The activity plans that were proposed to the subjects were not personalized and not adapted to their endurance.

2. An inadequate physical activity plan along with an unbalanced nutritional plan (high in proteins but low in carbohydrates) can lead to a slight change in body mass due to dehydration.

Conf icts of interest

There are no conf icts of interest.

Acknowledgments

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How can transcranial direct current stimulation inf uence sports exercises for normal or high-level practitioners

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Abstract

Background. When transcranial direct current stimulation (tDCS) was reintroduced as a non-invasive brain stimulation technique, it had been known for more than 50 years that the main mechanism of action was the sub-threshold regulation of neuronal membrane potential, which depended on changing the cortical excitability and activity through the current f ow of the target neuron. In this review we concentrated on the progress made for tDCS in the last few years in sports, which so far has partially found entrance into the design of clinical studies, and on results obtained in recently conducted clinical pilot studies.

Aims. Our objective was to analyze the ef ects of tDCS în sport exercises, for normal or high-level practitioners.

Methods. We performed a literature review în dif erent databases: PubMed, Web of Science, SCOPUS, SportDiscus, Google Scholar. Full text articles that used tDCS for exercise performance improvement in athletes were included (only articles in English were found). We searched for articles available in each database until 15 January 2018. We used articles published in journals, randomized sham controlled trials comparing anodal stimulation and cathodal stimulation to a sham / control for performance in isometric, isokinetic or dynamic strength exercise and whole-body exercise.

Results. We included 23 studies that met our selection criteria, in which tDCS produced changes in cycling training for: the whole body (9 articles), for muscle strength in isometric exercise (7 articles), for maximal isometric voluntary contraction (MIVC) (2 articles), for isokinetic exercises (3 articles) and during dynamic exercise (2 articles).

Conclusions. The anodal stimulation (a-tDCS) on the motor cortex (M1) had better results than sham stimulation especially for cycling exercises; consequently, more studies and attempts of dif erent montages are needed. Interest in tDCS is constantly growing, as evidenced by the growing number of studies in recent years. Consequently, positive results will appear more and more with the discovery of optimal stimulation parameters. In other words research must continue for this therapy of the future to become a consistent therapeutic alternative, especially in performance athletes.

Key words: transcranial direct current stimulation (tDCS or HD-tDCS), exercise, fatigue, athletic performance, non-invasive brain stimulation (NIBS).

Introduction

About 20 years ago, transcranial direct current stimulation (tDCS) was reintroduced as a non-invasive brain stimulation (NIBS) technique (Priori et al., 1998; Nitsche & Paulus, 2001). Its main mechanism of action is the sub-threshold regulation of the neuronal membrane potential, which depends on changing cortical excitability and activity through the current f ow of the target neuron (Purpura & McMurtry, 1965). Other biological ef ects of electric f elds may also be relevant (changes in neurotransmitters, ef ects on glial cells and microvessels, regulation of inf ammatory processes). Transcranial direct current stimulation (TDCS) is an accepted technique because of its potential impact on the brain activity of healthy subjects; it has attracted more and more attention and the patient populations. tDCS is a non-invasive, portable, easy-to-use, safe, well tolerated method (Batsikadze et al., 2013; Okano et al., 2015), (Prateek et al., 2006) using an economical technology, with a weak direct current DC (up to 2 mA current for tens of minutes) applied to the scalp to modulate cortical excitability (Nitsche et al., 2001; Nitsche et al., 2003a). Traditionally, the anode is placed close to the nominal targets (anodal tDCS, a-tDCS), which is assumed to increase neuronal excitability, plasticity, while placing the cathode near the nominal target (cathodal tDCS, c-tDCS) is assumed to have the opposite ef ect (Nitsche et al., 2001; Nitsche et al., 2003b). The clinical ef cacy of tDCS has been shown in a variety of diseases, such as post-stroke

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exercise rehabilitation and depression (Fregni et al., 2005; Fregni et al., 2006; Hummel et al., 2005).

Here we will concentrate on the progress made for tDCS over the last few years in sports, which so far has partially found entrance into the design of clinical studies, and on results obtained in recently conducted clinical pilot studies. It is known that sports performance is af ected by various physical, physiological and psychological factors (McCormick et al., 2015; Breil et al., 2010; Pearson et al., 2006). Especially in sports, alternatives have always been looked for to improve human function (Schubert et al., 2013); some athletes even use illegal drugs for this purpose (Săvulescu et al., 2003). In recent years, the focus has shifted to the brain and to how performance may be limited or improved. The brain plays an important role in establishing fatigue and sports performance (Noakes et al., 2012). In this case, several centrally-acting performance modif ers have been shown to have an impact on sports performance (Noakes et al., 2012).

There are multiple brain areas that may be involved in exercise regulation or limitation; therefore, the reasons for using tDCS to enhance performance may vary. However, most studies on exercise and athletic performance fail to provide clear or unambiguous assumptions about why placing electrodes at specif c locations to excite or inhibit a given brain area improves athletic performance. Although this is not an extensive list, some of these areas include the main motor cortex (M1), prefrontal cortex (PFC), island cortex (IC) and supplementary motor area (SMA).

More and more researchers are interested in the potential role of tDCS in improving performance and there has been an increase in the past few years. Cogiamanian et al. (2007) provide the f rst proof that tDCS can delay fatigue. They show that tDCS greatly reduces the fatigue ef ect of exercise in healthy individuals and is signif cantly extended by 50% compared with M1, the TTE of the isometric contraction of the elbow f exor muscle after no stimulation. Later, Okano et al. (2015) also show that a-tDCS (for IC on the left) improves cycling performance by 4% (i.e. maximum power output and TTE) in national level road cyclists. These results are further supported, although there can be dif erent montages of electrodes and performance measurements (Abdelmoula et al., 2016; Vitor-Costa et al., 2015; Nitsche et al., 2008).

Although some studies using tDCS showed a positive performance improvement (Okano et al., 2015; Cogiamanian et al., 2007; Abdelmoula et al., 2016; Vitor-Costa et al., 2015), others failed to reproduce positive results (Barwood et al., 2016). The mixed f ndings may be due to protocol changes such as placement of electrodes, current intensity and density, the type of exercise test used, participant's physical or activity adaptation level, and sample size. Similarly, the usage time of tDCS is also inconsistent because studies have used tDCS before, during testing and during training.

These early studies with positive results (Okano et al., 2015) have stimulated business and consumer interest in tDCS' athletic performance, including elite levels.

Several submissions and literature reviews suggest that tDCS is an ef ective improvement method for performance (Davis et al., 2013; Colzato et al., 2017; Park et al., 2017), including discussions about its fairness and ethical use in sports, for example as a "neuro-doping" technique (Davis et al., 2013; Colzato et al., 2017; Angius et al., 2017), as some authors debate this moral mode of using tDCS in sports (Park et al., 2017), and other modes of recommended anti-doping regulators list tDCS as an illegal strategy to enhance performance in sports (Park et al., 2017). Therefore, it is a call on researchers to determine the biomarkers used by tDCS in order to be able to test their use in competition or out of competition (e.g. anti-doping test) (Park et al., 2017).

Hypothesis

In this review article, we synthesized the necessary information regarding the ideal parameters in order to improve sports performance using a non-invasive transcranial stimulation therapy. There are numerous studies conducted in various pathologies and the vast majority highlight the benef ts of this new medical therapy.

Methods

Research protocol

a) Period and place of the research

We performed a literature review in dif erent databases: PubMed, Web of Science, SCOPUS, SportDiscus, Google Scholar. Full text articles that used tDCS for exercise performance improvement in athletes were included (only articles in English were found). We searched for articles available in each database until 15 January 2018.

For the eligibility criteria we used published articles in journals, randomized sham-controlled trials comparing anodal stimulation and cathodal stimulation to a sham / control for performance in isometric, isokinetic or dynamic strength exercise and whole-body exercise.

b) Subjects and groups

For each included article, we extracted data regarding the sample size and characteristics (age, sex, level of physical activity, f tness or training, and type of exercise training), the number and reasons for dropout, intervention characteristics (electrode location, current intensity density, and duration), side and adverse ef ects.

c) Test applied

For the outcome, we extracted the following data (absolute values): (a) transthoracic echocardiogram (TTE) during whole-body dynamic exercise and isometric exercise for major muscle groups and (b) maximal isometric, isokinetic, and dynamic muscle strength.

Results

A total of 1612 records were screened and the qualif cation of 29 full texts was evaluated. The most common causes excluded during the screening phase were studies involving patient-related health conditions (such as multiple sclerosis, stroke, Parkinson's disease, Alzheimer's disease) as well as the elderly and adolescents.

We included 13 studies, involving 245 participants in qualitative comprehensive research, and 10 studies involving 228 participants in quantitative comprehensive research. The number of studies included in this review is mainly due to the stimulated area (i.e. PFC, M1, TC) and results (e.g. isometric, isokinetic, dynamic muscle strength or TTE, sprint, time trial, peak power output in cycling) and we were unable to perform quantitative synthesis.

The references included in the article are from the period 1965 to January 2018.

A comprehensive summary of the characteristics of the included studies on the impact of tDCS in improving athletic performance can be found in the following Table I. All included studies were randomly grouped, of which 11 (84.6%) were cross-over studies and 2 (15.4%) were parallel studies. Ten studies (76.9%) had a sham condition or group as comparators, 2 studies (15.4%) had both sham stimulation and control, while one study (7.7%) had only the control group serving as a comparator. Nine studies (69.3%) performed only a-tDCS, while 4 (30.7%) studies applied both a-tDCS and c-tDCS. The current intensity applied was 1.5 or 2 mA and the current density (mean ± SD) was 0.104 ± 0.110 mA / cm² (from 0.043 to 0.44 mA / cm²), with a duration of 15.1 ± 4.8 minutes (from 10 to 20 min).

The study evaluated both men and women, with an average ± SD sample size of 14.4 ± 5.7 (6 to 24 participants) per study, a median of 12 years, ages from 17 to 42 years, and dif erent levels of physical activity or f tness.

Regarding the timing of tDCS, 8 studies (61.5%) applied tDCS before exercise, 2 studies (15.4%) applied tDCS in sports, and one study (7.7%) applied tDCS before and during exercise, one study (7.7%) applied tDCS to repeated training, and one (7.7%) during sports training. The ef ect of tDCS on improving exercises was assessed in 8 studies (61.5%), where muscle strength performance was evaluated, of which 4 studies (30.8%) used isometric, 2 (15.4%) constant speed, 2 (15.4%) dynamic power exercise. Four studies (30.8%) evaluated the ef ect of tDCS on improving whole-body cycling performance.

The most stimulated area was M1 (n = 16; 72.5%), but there were also studies on the stimulation of dorsolateral PFC (n = 2; 9.1%), left TC (N = 3; 13.6%), as well as M1 and lateral PFC (n = 1; 4.5%).

tDCS can improve whole-body performance in cycling training

We found that a-tDCS followed by a constant-load cycling exercise would increase TTE. Although the signif cant ef ect found to be benef cial for a-tDCS did not have signif cant heterogeneity (Chi² = 0.45, P = 0.80, I² = 0%) in a study by Vitor-Costa et al. (2015), a disproportionate body weight (84.8%) was presented in the analysis.

c-tDCS has no ef ect on the arrival time in physical exertion during constant load cycling exercise. Vitor-Costa et al. (2015) found no heterogeneity this time (Chi 2 = 0.03, P = 0.87, I 2 = 0%), and there was also a disproportionate weight (94.9%).

Other four studies used tDCS to enhance whole-body cycling. However, due to dif erent brain regions and / or other types of exercise tests performed, this could not be quantitatively synthesized.

tDCS was used to improve muscle strength during isometric exercise

Compared with sham stimulation, the application of a-tDCS before exercise had no ef ect on isometric muscle strength of the upper or lower limbs.

Especially for the upper limbs, signif cant heterogeneity was found (Chi 2 = 11.51, P = 0.009, I 2 = 74%). Similarly, compared with sham stimulation, application of a-tDCS during exercise had no signif cant ef ect on isometric muscle strength.

Due to the evaluation of dif erent muscles or the use of repeated tDCS training, two studies were not included in the quantitative synthesis.

When Hazime et al. (2017) applied a-tDCS to the M1 of handball players, it was found that the amount of maximal isometric voluntary contraction (MIVC) of the shoulder internal and external rotator muscles during tDCS remained unchanged (MD = 0.10 N / Kg; 95% CI = -0.05 N / Kg to 0.25 N / Kg and MD = 0.10 N / Kg; 95% CI = 0.00 N / Kg to 0.20 N / Kg), but increased by 30 minutes (both MD = 0.20 N / Kg; 95% CI = 0.05 N / Kg to 0.35 N / Kg) and 60 minutes (MD = 0.20 N / Kg. After stimulation, both 95% CI = 0.05 N / Kg to 0.35 N / Kg. Frazer et al. (2016) evaluated the ef ect of applying a-tDCS on M1 for four consecutive days and reported a signif cant improvement in wrist f exor MIVC, 8% compared to 3% for sham stimulation.

tDCS was used to improve muscle strength during isokinetic exercise

Only three studies analyzed the ef ect of tDCS on isokinetic strength. Because they stimulated dif erent brain regions, a quantitative synthesis was not possible. Two of the studies used similar tDCS parameters (2 mA, 20 minutes, 0.057 mA / cm²), isokinetic exercise assessments (2-3 sets, performed 5 and 10 times in knee extensors at 60º.s-1) and samples (physically active men).

tDCS was used to improve muscle strength during dynamic exercise

Only two studies evaluating the ef ect of tDCS on dynamic muscle strength were found. Latari et al. (2016), before conducting the second 10-time maximum elbow f exor test (i.e. up to 10 repetitive workloads), applied a-tDCS and c-tDCS (2 mA, 0.057 mA / cm² for 20 minutes) to the trained men, and found that the number of repetitions after a-tDCS was signif cantly higher than that of sham tDCS (MD = 4.28; 95% CI = 2.56 to 6.00). Interestingly, c-tDCS reduced the number of repetitions compared to sham tDCS (MD = -2.52; 95% CI = -3.75 to -1.28). Hendy & Kidgel (2014) applied only a-tDCS and a-tDCS combined with sham in the non-dominant hand M1 alone to perform resistance exercises in the dominant hand. The authors report that a single a-tDCS exercise is associated with resistance exercise, which can increase the maximum voluntary dynamic strength of untrained limb wrist extensors compared to sham stimulation + resistance exercise and a-tDCS alone, but its 95% CI MD has not conf rmed its positive ef ect (MD = 0.46 kg; 95% CI = -2.00 kg to 2.92 kg; MD = 0.56 kg; 95% CI = -2.01 kg to 3.13 kg) (Hendy & Kidgel, 2014).

Table I
Stimulation parameters from the included studies.

Study Information					Sample		tDCS set-up			
Authors	**Design**	**Exp**	**Exercise type**	**Exercise protocol**	**a**	**Training status**	**Anode or Cathode Return electrode**	**Intensity (mA)**	**Density (mA/cm2)**	**Duration (Min)**
Abdelmoula et al., 2016	Cross	1	Isometric strength	35% of MIVC of elbow f exion	11 (8M/3W)	N/D	Left M1 Right Shoulder	1.5	0. 043	10
Cogiamanian et al., 2007	Parallel	1	Isometric strength	35% of MIVC of elbow f exion	24 (10M/14W)	N/D	A Left M1 Right Shoulder	1.5	0. 043	10
Authors	Parallel	2	Isometric strength	35% of MIVC of elbow f exion	24 (10M/14W)	N/D	C Left M1 Right Shoulder	1.5	0. 043	10
Kan et al., 2013	Cross	1	Isometric strength	30% of MIVC of elbow f exion	15 M	N/D	Right M1/ Right Shoulder	2.0	0. 083	10
Radel et al., 2017	Cross	1	Isometric strength	35% of MIVC of elbow f exion	22M (13M/9W)	N/D	A C2 and C 4cm around (HD-tDCS 4x1)	2.0	N/D	N/D
Authors	Cross	2	Isometric strength	35% of MIVC of elbow f exion	22M (13M/9W)	N/D	HD-tDCS (A) AF4 and (C) 4 cm around	2.0	N/D	N/D
Williams et al., 2013	Cross	1	Isometric strength	20% of MIVC of elbow f exion	18 (9M/9W)	9 active/ 9 low active	Right M1 Fp2	1.5	0. 043	<= 20
Hazime et al., 2017	Cross	1	MIVC	Shoulder internal/external rotations	8 (W)	Handball athletes	C3/C4 Fp2/Fp1	2.0	0. 057	20
Frazer et al., 2016	Cross	1	MIVC	Wrist f exors	14 (6M/8W)	N/D	Left C3 Fp2	2.0	0. 08	20
Maeda et al., 2017	Parallel	1	Isokinetic strength	5 reps of eccentric knee extension/f exion	24 (12M/12W)	N/D	M1 Shoulder	2.0	0. 08	10
Montenegro et al., 2015	Cross	1	Isokinetic strength	10 reps of knee extension/f exion	14 (M)	Trained in RT (>=6 months)	Left M1 Fp2	2.0	0. 057	20
Sales et al., 2016	Cross	1	Isokinetic strength	5 reps of knee extension	19 (M)	Physically active	T3 Fp2	2.0	0. 057	20
Hendy et al., 2014	Cross	1	Dynamic strength	1RM wrist extension	10 (5M/5W)	N/D	Right M1 Fp1	2.0	0. 08	20
Lattari et al., 2016	Cross	1	Dynamic strength	10RM elbow f exion	10 (M)	Trained in RT (>=6 months)	F3 Fp2	2.0	0. 057	20
Angius et al., 2018	Cross	1	Cycling	TTE at 70% PP	12 (8M/4W)	Recreationally active	A both M1/ shoulders	2.0	0. 057	10
Authors	Cross	2	Cycling	TTE at 70% PP	12 (8M/4W)	Recreationally active	A both M1/ shoulders	2.0	0. 057	10
Angius et al., 2015	Cross	1	Cycling	TTE at 70% PP	9 (M)	Recreationally active	Right M1/F4	2.0	0. 17	10
Barwood et al., 2016	Cross	1	Cycling	20 km time trial	6 (M)	Physically active	T3/Fp2	1.5	0. 43	20
Authors	Cross	2	Cycling	TTE at 75% PP	8 (M)	Physically active	T3/Fp2	2.0	0. 44	20
Lattari et al., 2016	Cross	1	Cycling	TTE at 100% PP	11 (M)	Moderately active	F3/Fp2	2.0	0. 057	20
Okano et al., 2015	Cross	1	Cycling	Incremental maximum	10 (M)	Athletes (cyclists)	T3/Fp2	2.0	0. 057	20
Vitor-Costa et al., 2015	Cross	1	Cycling	TTE at 80% PP	11 (M)	Physically active	A both M1/ Inion	2.0	0. 056	13
Authors	Cross	2	Cycling	TTE at 80% PP	11 (M)	Physically active	C both M1/ Inion	2.0	0. 056	13

Discussions

In this review article we included 13 studies with a total of 245 participants, and we studied the ef ects of tDCS on athletic performance. In the stimulation protocols that we found for a-tDCS applied on M1 cortical area in cycling, there was weak evidence, but a separate study strongly inf uenced the results, in contrast with c-tDCS which did not signif cantly af ect the results. In addition, for the tested protocol, a-tDCS applied before or during exercise did not show a signif cant ef ect on the isometric muscle strength of the upper or lower extremities. These studies present mixed results related to the application of a-tDCS to isokinetic muscle strength. Before or during the dynamic muscle strength test, only two studies using a-tDCS applied to PFC and M1 also showed mixed results.

The synthesis shows that a-tDCS has a signif cant ef ect when M1 area is stimulated, and this fact can improve TTE during cycling for about 93 seconds, which shows that a-tDCS can actually improve performance and be used for this purpose before training and / or competition. Because cycling performance can be improved, even by a small percentage, around 1-2%, it can be a key issue in terms of high competitive performance such as the

Olympics because those milliseconds, seconds can make the dif erence between the 1st place and the 2nd place. However, it should be noted that only three studies evaluated actual athletes (Okano et al., 2015, Hazime et al., 2017), other studies included samples with varying levels of physical activity and health status (from individuals with low to active levels), which may have af ected the changes in the results. In addition, although most studies are conducted with a small sample size and it is almost impossible to obtain lots of info, it is worth noting that the cost-ef ectiveness of tDCS seems to be benef cial, especially considering that there were no adverse ef ects. In addition, the wider community's use of tDCS outside the professional setting may produce uncertain results due to electrode placement, contact, impedance and current intensities. It should be noted that only two studies used tDCS to improve the performance of repeated training, four of which (Frazer et al., 2016) for seven times, and the safety of tDCS in daily use needs to be evaluated, for example before / during training. Therefore, the wide application of tDCS outside the laboratory should be considered with caution, such as in commercial equipment, until clear scientif c evidence supports its safety and ef ectiveness.

The review of isometric muscle exercise shows that there is no signif cant dif erence between a-tDCS and sham stimulation in the upper and lower limbs, when a-tDCS is applied before and during exercise. In addition, in order to fatigue the isometric contraction of the elbow f exors, signif cant heterogeneity was detected in the results of the included studies. Importantly, the percentage of MIVC in studies that use isometric muscle strength as a result is surprisingly low, between 25% and 38%. Future research should consider using higher-intensity exercise to better represent the sports environment, for example, in f ghting sports involving isometric movements, such as judo or wrestling. So far, the existing evidence has not supported the use of a-tDCS to improve isometric muscle strength performance.

Regarding isokinetic muscle strength performance, available research stimulated dif erent brain regions and found opposite results. One study improved the isokinetic strength of the knee extensors by a-tDCS applied to the left TC. Another study found no dif erence in a-tDCS applied to M1.

Interestingly, only two studies involving dynamic strength exercises showed opposite results. A single a-tDCS before exercise can improve the maximum number of repetitions of elbow f exion (Lattari et al., 2016) and the single strength training associated with a-tDCS will not change the maximum strength of the contralateral wrist extensor muscles compared to strength training alone or a-tDCS (Hendy & Kidgel, 20140).

It should be noted that the methodological aspects of tDCS may have an impact on the stimulation ef ect, and this must be considered in future studies using tDCS for performance enhancement. In recent years, the adoption of computational forward models of brain currents has increased because it provides a deeper understanding of brain current patterns, and in some cases, even challenges simplif ed electrode placement based on "classic" assumptions. In general, the application of tDCS using large electrode pads (called "conventional" tDCS) will cause brain currents to spread and therefore exhibit low focus, and the peak intensity is usually not on the nominal target.

To overcome this limitation, "high-def nition" tDCS (HD-tDCS) uses an array of smaller electrodes arranged in various conf gurations, including a 4x1 ring HD-tDCS montage. Compared with the traditional tDCS, HD-tDCS has better focus, and has a precise gyroscopic stimulation (Kuo et al., 2012), and the potential amplitude and duration may be greater (Kuo et al., 2012). Unfortunately, there are only two studies that tested HD-tDCS to improve performance, but the results did not show signif cant improvements in isometric contraction of elbow f exors and knee extensors. Regarding the tDCS mechanism, it is assumed that the positive charge applied by a-tDCS will cause sub-threshold depolarization and c-tDCS hyperpolarization due to its negative charge. This hypothesis produced the "classical" polarity-dependent ef ects of tDCS (i.e. a-tDCS excitation and c-tDCS inhibition), and thus inferred that the role of tDCS would be mediated by changes in neuronal excitability. Studies in non-human animals suggest that tDCS-induced changes in neuronal excitability may be due to the phosphorylation of α-amino-3-hydroxy-5-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptor and its transport from the cytosol to the synapse (Staf ord et. al., 2018).

In the context of motion, researchers have used tDCS based on the "classic" polarity-related assumption. However, only one study actually found that the performance of c-tDCS after dynamic strength exercise decreased signif cantly (Lattari et al., 2016), while other studies showed no change in performance (Cogiamanian et al., 2007; Vitor-Costa et al., 2015; Nitsche et al., 2008). Our research shows that c-tDCS has no adverse ef ect on riding performance, but shows a clear trend to improve riding performance. This result is consistent with previous experimental studies by Batsikadze et al. (2013), who found that 2 mA of c-tDCS on M1 for 20 minutes can increase cortical excitability instead of reducing cortical excitability; therefore, future research needs to determine that hypothetical changes in brain regions have actually occurred. Ideally, the proposed tDCS montage ef ect should be tested before testing the ef ect of excitability changes on athletic performance.

Neuromodulation ef ects of tDCS can be monitored using electroencephalography (EEG) combined with near infrared spectroscopy (NIRS). With these control tools tDCS montage should be personalized to increase the possibility of causing performance changes. However, no studies have tested the ef ect of anatomical changes on tDCS in athletic performance. In addition, studies have shown that the baseline level of motor function af ects the after ef ects of tDCS. Therefore, people with lower functional baseline levels showed (greater) improvement after tDCS, while people with higher functional levels showed lower improvements or no change in performance. However, these studies were conducted with good motor skills (that is, playing musical instruments). It is still necessary to test the ef ect of tDCS on individuals with dif erent exercise levels (such as running, cycling, weightlifting, or resistance to weightlifting).

Regarding tDCS montages, most studies have focused on M1, while less attention has been paid to other aspects, such as dorsolateral PFC, left TC, and lateral prefrontal cortex. As already mentioned in the introduction, various parts of the brain are involved in athletic performance. In short, the principle of stimulating M1 is to increase its excitability, so that the connection between M1, the thalamus and the island cortex (IC) can be used to extend the driving force of nerves to active muscles and delay central fatigue or changes caused by the exercise induced pain process, which will increase performance by reducing pain.

Following this review, we cannot recommend a certain montage for the electrodes, but it seems that tDCS on the M1 brain area gave the best results. On the one hand, existing research shows protocol heterogeneity, on the other hand, the theoretical optimal dose of tDCS has not been fully explored (for example, current intensities of 2 mA); in actual training, several weeks of repeated courses may be used; therefore, the existing dosage plan should be regarded as a pilot, rather than as an optimized plan.

Conclusions

Anodal stimulation (a-tDCS) on the motor cortex (M1) had better results than sham stimulation, especially for cycling exercises.

When comparing anodal stimulation (a-tDCS) with sham stimulation in the isometric muscle strength of the upper and lower limbs, no significant improvement was found.

To test the presumed effect of tDCS on athletic performance, future research should try to personalize the tDCS protocol, such as using a computational model with single MRI data to define the most effective electrode placement (including the reference electrode) to achieve a given goal.

It is necessary to establish some recommendations / protocols regarding the installation, duration, current intensity, and also the recurrence of the stimulation sessions regarding the physical training (e.g. before training, during training, before competition).

Probably investigating the usage of a current intensity higher than 2mA will be able to deliver better results in terms of achieving athletic performance.

For the given results, especially the use of HD-tDCS can give better results.

The wide application of tDCS outside the laboratory should be considered with caution, such as in commercial equipment, until clear scientific evidence supports its safety and effectiveness.

The results obtained from this review reflect the good trend of this therapy, tDCS, in improving sports performance; even if the results do not provide a major plus, it is important that they exist and for high-level athletes improving performance through this kind of brain stimulation, even if only by 1-2%, can make major differences in sports competitions.

Interest in tDCS is constantly growing, as evidenced by the growing number of studies in recent years. Consequently, positive results will appear more and more with the discovery of optimal stimulation parameters; in other words, research must continue for this therapy of the future to become a consistent therapeutic alternative.

Conflicts of interest

Nothing to declare.

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Is there a link between physical activity, body mass index, Finnish Diabetes Risk Score (FINDRISC) and blood pressure?

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Abstract
Background. Physical activity is one of the essential pillars of a healthy lifestyle and one of the important tools that can signif cantly improve general health condition. Constant exercise favorably inf uences 7 out of 10 most common chronic diseases.
Aims. The aim of the study was to analyze the associations between anthropometric data, physical activity, blood pressure and the Finnish Diabetes Risk Score (FINDRISC) in a group of Romanian adults.
Methods. The present research represents a cross-sectional observational pilot study, which includes a group of 95 subjects from Argeş County. The study was conducted between May and June 2019. We calculated the FINDRISC score to estimate the risk of patients to develop diabetes in the next 10 years using 2 dif erent validated questionnaires, focused on lifestyle aspects and nutritional status.
Results. In our study, FINDRISC was signif cantly associated with waist circumference, waist/hip ratio and body mass index. No correlations were found with subjects' interest for health, physical activity and rest. However, we noticed that patients who spend more time resting weekly have a lower FINDRISC and subjects who rarely exercise have a higher FINDRISC.
Conclusions. There was a link between abdominal circumference, abdomen / hip ratio, BMI and age, blood pressure and FINDRISC score. Our study proves the importance of a healthy lifestyle, BMI and blood pressure for preventing cardiovascular and metabolic diseases such as diabetes.
Key words: Finnish Diabetes Risk Score (FINDRISC), diabetes, physical activity, lifestyle, blood pressure

Introduction

Physical activity is one of the essential pillars of a healthy lifestyle and one of the important tools that can signif cantly improve general health condition. (1) Constant exercise favorably inf uences 7 out of 10 most common chronic diseases (2). According to the World Health Organization (3), overweight and obesity are responsible for 5% of global mortality. Furthermore, lack of physical activity is the fourth risk factor for global mortality (approximately 6% of deaths worldwide), followed by high blood pressure (13%), tobacco use (9%) and elevated serum blood glucose (6%) (3).

Globally, it is observed that children, young people, as well as adults are increasingly replacing physical activity with a sedentary lifestyle. Sedentary lifestyle condition is associated with various psychological problems and an increased risk for cardiovascular and metabolic diseases (D'Isanto et al., 2017; Al-Nakeeb et al., 2015; Monteiro et al., 2019).

The benef ts that physical activity of ers consist of decreasing mortality of any cause, by improving the general physical condition. It also decreases the risk of developing cardiovascular disease, high blood pressure, type 2 diabetes, lipid prof le disorders, and the appearance of neoplasms in the genitourinary and digestive systems. Exercise improves bone metabolism, promotes a normal body weight, reduces the risk of anxiety and depression, and improves cognitive function, sleep or quality of life (Wahlich et al., 2020; Meader et al., 2017).

Objectives

The aim of the study was to analyze the associations between anthropometric data, physical activity, blood pressure and the Finnish Diabetes Risk Score (FINDRISC score).

Hypothesis

Our hypothesis was that patients who allocate less time for physical activity have a higher risk of developing

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diabetes in the next ten years, higher values of the body mass index and blood pressure, and there is a connection between obesity, sedentarism, diabetes and arterial hypertension.

Methods

Research protocol

All data were collected after obtaining the approval of the Ethics Committee and the consent of each participant in the study.

a) Period and place of the research

Our research was based on a cross-sectional observational pilot study, which included a group of 95 patients from Argeș County, interviewed in the Family Medicine of ce. The study was conducted between May and June 2019. The data were collected with the approval of the family physician, and with the subjects' consent.

The inclusion criteria were: minimum age 18 years, and no history of chronic diseases. The exclusion criteria were as follows: patients diagnosed with diabetes or other chronic/acute pathologies that may inf uence physical development.

The data collected included: age, gender, weight, height, abdominal circumference and gluteal circumference. Based on the collected data, the Body Mass Index (BMI) was calculated using the formula weight (kg) / height^2 (m^2). We interpreted the BMI results as follows: under 18.49 - underweight, 18.50 - 24.99 normal weight, 25.00 - 29.99 overweight, over 30 - obesity. We considered normal values for the abdomen / hip ratio < 0.90 for men and < 0.85 for women (1); (4).

Two questionnaires ("Assessment of nutritional status and lifestyle risk factors") of 38 and 25 items related to eating habits and food preferences, cof ee consumption, alcohol, smoking, stress level, physical activity, medical history were used to assess the nutritional status and lifestyle. We used the Finnish Diabetes Risk Score (FINDRISC) for estimating the risk of patients to develop diabetes in the next ten years. FINDRISC studies were a random sample based on the National Population Register, from North Karelia, Kuopio, and South-Western Finland in 1987, and another independent sample from the Helsinki-Vanraa region in 1992 (Lindström & Tuomilehto, 2003).

b) Subjects and groups

Our study included 95 adults, 59 (62.11%) women and 36 (37.89%) men, aged between 21 and 78 years. The data from Tables I and II illustrate the relationship between the demographic data of our patients and their BMI, FINDRISC score and blood pressure. The average BMI values were 26.66 ± 4.87.

Table I

Demographic data of the study group.

Indicators	Patients	Gender		Residence	
	N	Female	Male	Urban	Rural
Body mass index					
Underweight	1 (1.05%)	1 (1.69%)	0	1 (1.85%)	0
Normal weight	37 (38.95%)	27 (45.76%)	10 (27.78%)	26 (48.15)	11 (26.83%)
Overweight	37 (38.95%)	20 (33.90%)	17 (47.22%)	20 (37.04%)	17 41.46%)
Obesity	20 (21.05%)	11 (18.64%)	9 (25%)	7 (12.96%)	13 (31.71%)
The FINDRISC risk					
Below	33 (34.73%)	24 (40.68%)	9 (25%)	18 (33.33%)	15 (36.59%)
Slightly high	31 (32.63%)	20 (33.90%)	11 (30.56%)	20 (37.04%)	11 (26.83%)
Moderate	18 (18.95%)	10 (16.95%)	8 (22.22%)	8 (14.81%)	10 (24.39%)
High	13 (13.68%)	5 (8.47%)	8 (22.22%)	8 (14.81%)	5 (12.20%)
Blood pressure					
Optimal	20 (21.05%)	11 (20.37%)	9 (21.95%)	11 (20.37%)	9 (21.95%)
Normal	26 (27.37%)	17 (31.48%)	9 (21.95%)	17 (31.48%)	9 (21.95%)
Highly normal	20 (21.05%)	11 (20.37%)	9 (21.95%)	11 (20.37%)	9 (21.95%)
Hypertension	29 (30.53%)	15 (27.78%)	14 (34.15%)	15 (27.78%)	14 (34.15%)

Table II

Demographic data of the study group.

Indicators	Age (years)					
	≤20	21-30	31-40	41-50	51-60	> 60
Body mass index						
Underweight	0	0	1 (14.29%)	0	0	0
Normal weight	0	3 (75%)	4 (57.14%)	13 (48.15%)	6 (26.09%)	11 (32.35%)
Overweight	0	1 (25%)	1 (14.29%)	13 (48.15%)	12 (52.17%)	10 (29.41%)
Obesity	0	0	1 (14.29%)	1 (3.70%)	5 (21.74%)	13 (38.24%)
The FINDRISC risk						
Below	0	3 (60%)	5 (41.67%)	14 (51.85%)	7 (30.43%)	4 (11.76%)
Slightly high	1 (100%)	2 (40%)	7 (58.33%)	7 (25.93%)	9 (39.13%)	12 (35.29%)
Moderate	0	0	0	6 (22.22%)	4 (17.39%)	8 (23.52%)
High	0	0	0	0	3 (13.04%)	10 (29.41%)
Blood pressure						
Optimal	0	0	4 (57.14%)	7 (25.93%)	6 (26.09%)	3 (8.82%)
Normal	0	4 (100%)	2 (28.57%)	13 (48.15%)	2 (8.70%)	5 (14.71%)
Highly normal	0	0	1 (14.29%)	6 (22.22%)	6 (26.09%)	7 (20.59%)
Hypertension	0	0	0	1 (3.70%)	9 (39.13%)	19 (55.88%)

c) Tests applied

We used two questionnaires to evaluate the nutritional status and lifestyle risk factors. The main questions related to physical activities were: "How much time do you give for weekly rest?", "How much time do you spend resting daily?", "How often do you exercise?", "What kind of exercise do you do?", "Do you perform at least 30 minutes of daily exercise at work/in your spare time/at home?", "Does a change of 2.5 kg in your weight af ect your way of life?**"**. Regarding the attitude of patients to health, they answered the following questions: "Do you know the caloric value of the common products?", "Have you ever tried to apply preventive measures for hereditary diseases (related to food, physical activity)?"

We calculated the FINDRISC score to estimate the risk of patients to develop diabetes in the next 10 years. We followed the answers to 8 questions: age, BMI, waist circumference, daily physical activity, frequency of daily consumption of vegetables and fruits, use of antihypertensive drugs, personal history of hyperglycemia, history of type 1 and 2 diabetes. Values below 7 indicate a low risk of developing diabetes in the next 10 years, values between 7 and 11 slightly high risk, between 12 - 14 moderate risk, between 15 - 20 high risk and very high risk over 20. The questionnaire was validated in several studies both in the original form and in the simplif ed formula (Omech et al., 2016; Vandermissen & Godderis, 2015; Makrilakis et al., 2011; Soriguer et al., 2012; Conceicao et al., 2020; Munoz-Gonzalez et al., 2019; Winlker et al., 2013; Grasdalsmoen et al., 2019; Jayawardana et al., 2017a).

d) Statistical processing

For statistical analysis we used GraphPad InStat software (Version 3.06). For quantitative variables (BMI, age, blood pressure, FINDRISC score, anthropometric measurements), we performed descriptive statistics, using the mean and standard deviation for variables with Gaussian distribution (BMI, FINDRISC, age) and the median, minimum and maximum for variables with non-Gaussian distribution (BP, abdominal circumference, abdomen-hip ratio). We applied the Pearson correlation test for parametric data and Spearman for nonparametric data to see if the values of abdominal circumference, abdomen / hip ratio and BMI correlated with age, blood pressure and FINDRISC score. For qualitative variables (patients' responses to the questionnaires) we applied extended contingency tables, and statistical interpretation was performed against the statistical signif cance threshold p ($p < 0.05$ statistically signif cant).

Results

The mean FINDRISC score was 8.947 + 5.009. The median systolic blood pressure (SBP) value was 130 mmHg, with a minimum of 90 mmHg and a maximum of 170 mmHg, and the median diastolic blood pressure (DBP) value was 80 mmHg, with a minimum of 55 mmHg and a maximum of 100 mmHg.

We analyzed the interest of the subjects in health, physical activity and rest. There was no statistically signif cant association between BMI and the daily rest, the exercise frequency, the time spent for physical activity (less or more than 30 minutes per day), the type of physical activity and how a 2.5 kg change in body weight af ected the patients ($p > 0.05$). BMI was statistically signif cantly associated with the weekly rest ($p = 0.0335$). Normal and overweight patients allocate 1-2 days of weekly rest in a higher percentage, and a smaller number of them rarely make time for rest. More than half of obese patients allocate 2 days per week for rest (Fig. 1).

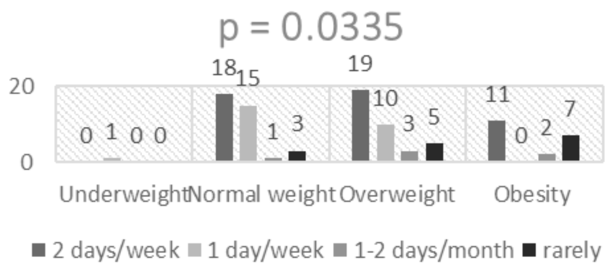

Fig. 1 – The association between Body Mass Index and weekly rest.

We observed a statistically signif cant association between BMI and patients' response to questions about whether they knew the caloric value of the common products ($p = 0.0030$) and whether they had ever tried to apply methods for preventing hereditary diseases related to food and physical activity ($p = 0.0296$). Most patients answered the two questions negatively, but we found that overweight patients knew the caloric value of common products and tried to apply preventive methods regarding hereditary diseases in a higher percentage than the other groups.

Concerning the link between the interest in health, physical activity, rest and the risk of developing diabetes in the next ten years, we observed that the FINDRISC was not associated with any of the patients' responses ($p > 0.05$). However, we noticed that patients who spent more time resting weekly had a lower FINDRISC and subjects who rarely exercised had a higher FINDRISC. Instead, we observed that BP values were associated with the time given to daily rest ($p = 0.0012$) and weekly rest ($p = 0.0475$). Hypertensive patients allocated more time for both daily and weekly rest, and those with normal BP values allocated time for weekly, but not daily rest. There was no statistically signif cant association with other variables ($p > 0.05$).

Regarding the anthropometric measures, we compared the values of the abdominal circumference, the abdomen / hip ratio and BMI with age, SBP and DBP values, and FINDRISC score, respectively. We observed that between these variables there were statistically signif cant positive correlations (Table III).

Discussions

In our study, we did not identify a statistically signif cant association between BMI values and patients' responses to the daily rest time, frequency and type of exercise, duration of physical activity, and how a 2.5 kg change in body weight af ected them. BMI values were associated with the weekly resting time ($p = 0.0335$). Grasdalsmoen

Table III

Correlations between anthropometric measures, age, blood pressure and the FINDRISC score.

Indicators		**Waist circumference**	**Waist/hip ratio**	**Body mass index**
Age	r value	0.3900	0.2716	0.3876
	CI (95%)	0.1987 to 0.5527	0.07407 to 0.4486	0.2018 to 0.5465
	p value	**< 0.0001**	**0.0078**	**0.0001**
SBP	r value	0.5780	0.2106	0.4888
	CI (95%)	0.4210 to 0.7013	0.003346 to 0.4005	0.3131 to 0.6321
	p value	**< 0.0001**	**0.0405**	**< 0.0001**
DBP	r value	0.4659	**0.1752**	**0.3542**
	CI (95%)	0.2862 to 0.6140	0.03339 to 0.3692	0.1585 to 0.5232
	p value	**< 0.0001**	0.0895	**0.0004**
FINDRISC	r value	0.6951	**0.3777**	**0.5804**
	CI (95%)	0.5698 to 0.7888	0.1906 to 0.5383	0.4291 to 0.7001
	p value	**< 0.0001**	**0.0002**	**< 0.0001**

SBP=Systolic blood pressure; DBP= Diastolic blood pressure

et al. (2019) showed in a study conducted on 3 large groups of subjects that there is a causal relationship between physical activity, overweight and obesity (Grasdalsmoen et al., 2019). Similarly, Jayawardana et al. (2017a) showed in a study of 2469 men that an increased level of physical activity was associated with a reduced likelihood of being obese (p = 0.0122) (Jayawardana et al., 2017a). Another study shows similar results, with low levels of physical activity being signif cantly associated with an increased BMI (p = 0.002) (Karunanayake et al., 2020).

The FINDRISC score was not signif cantly associated with any of the answers to questions related to physical activity and lifestyle attitudes in our study. However, we observed that patients who devoted more time to weekly rest had a low risk of developing type 2 diabetes. Subjects who rarely exercised had a moderate or high risk of developing diabetes in the next ten years. Clinical studies have demonstrated the importance of lifestyle in the prevention of type 2 diabetes, the measures of changing some unhealthy daily habits having favorable long-term ef ects (Lindrstom et al., 2010). It has been observed that replacing sedentary behavior with physical activity, even of low intensity, can contribute to improving serum blood glucose levels, reducing the incidence of diabetes, and even improving BP values (Egan, 2017; Hamilton et al., 2014).

In the present research, BP was associated with daily (p = 0.0012) and weekly rest (p = 0.0475). Subjects with optimal and normal blood pressure allocated 1-2 days a week for rest. Hypertensive patients allocated more time for daily and weekly rest. BP was not associated with the other variables studied. However, we noticed that hypertensive patients preferred physical work, while normotensive patients chose walking or running, and only a small number of patients chose both physical activity and other types of exercise.

A considerable number of studies have shown the benef ts of exercise on hypertension, reducing both SBP and DBP. Exercise has been shown to be an essential element of lifestyle in primary prevention and hypertension treatment (Hegde et al., 2015). Ahmadi-Abhari et al. (2017) showed that reducing the time spent in front of television or other sedentary leisure activities, as well as increasing the frequency of sports activities can have benef cial ef ects on the circulatory system, slowing down the aging of blood vessels. Physical inactivity is associated with the risk of developing cardiovascular disease. In a study of 22,476 participants aged 30 to 64 years with no history of cardiovascular disease, Zhang et al. (2020) found a high risk of developing cardiovascular disease in overweight or obese patients compared to those with a BMI <25 kg / m^2.

In this study, there was no statistically signif cant link between FINDRISC score, blood pressure values and interest in health. However, patients at moderate-high risk of developing diabetes over the next ten years appear to pay more attention to the prevention of genetically predisposed but lifestyle-inf uenced diseases.

We found in our study that blood pressure values and FINDRISC score correlated positively with anthropometric measurements. In other words, the higher the values of abdominal circumference, abdomen / hip ratio and BMI, the higher the BP values and the higher the risk of developing diabetes in the next ten years. Similar results were shown by the study conducted by Jayawardana et al. (2017b), who found that both SBP and DBP were correlated statistically signif cantly with age, abdominal circumference and BMI. They did not identify signif cant correlations between blood pressure values and the intensity of physical activity.

There are several limitations of this study related to the relatively small number of participants and their inequality, being divided into groups according to BMI, FINDRISC score and blood pressure values. However, we mention that this was a pilot study and that we are considering a study on a larger cohort starting from the present research.

Conclusions

1. Normal weight subjects have a lower risk of developing diabetes in the next ten years.
2. Patients with a moderate or high risk of developing diabetes in the next ten years prefer physical work and not sport activities.
3. There is a link between abdominal circumference, abdomen / hip ratio, BMI, age, blood pressure and FINDRISC score. Patients with higher BMI values have a higher risk of developing diabetes in the next ten years.
4. Our study proves the importance of lifestyle, BMI and blood pressure for preventing cardiovascular and metabolic diseases such as diabetes.

Conf icts of interest

There are no conf icts of interest.

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The impact of physical activity on body fat and self-esteem in adult women

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Abstract

Background. An active life entails many physical, social, and psychological benef ts, and there is a direct proportionality between physical activity and life expectancy. According to the 2018 Special Eurobarometer, the proportion of Europeans who have never exercised or played a sport continues to grow.

Aims. Through this study we aimed at analyzing the ef ect of physical activity programs on the percentage of body fat and self-esteem in adult women.

Methods. The participants selected in the study were 89 adult women aged 23 to 57, the average age being 31.62 (SD = 6.60). Anthropometric measurements were made, and questionnaires were applied to collect data and interpret them according to the Rosenberg Self Esteem Scale. The data thus obtained were statistically processed using IBM SPSS 23.0 software, by performing descriptive analysis, checking distribution and means comparison.

Results. Between the means of body fat percentages, calculated before and after subject's participation in the physical training program, the dif erences were quite signif cant (t = 30.765, df = 88, p =.000), the outcome ef ect being quite substantial (d = 3.26). Signif cant dif erences were also recorded in the assessment of self-esteem (SE) before and after participation in the intervention programs (z = -7.910, df = 88, p =.000, d = -.84).

Conclusions. The study found that the ef ect of the participation of some adult women in the physical activity programs consisted of a decrease in the percentage of their body fat and subsequently an increase in self-esteem.

Key words: physical activity, self-esteem, body fat, adult women

Introduction

The human body was conceived for motility and needs regular physical activity not only for optimal functioning, but also to reduce the risk of developing a disease. According to Physical Activity Guidelines (1), physical activity has been def ned as "any bodily movement produced by the contraction of skeletal muscle that increases energy expenditure above a basal level." An active life entails many physical, social, and psychological benef ts, and there is a direct proportionality between physical activity and life expectancy. Nowadays, active populations tend to live longer than inactive ones.

Sedentary lifestyle is a risk factor for the development of many chronic diseases, including cardiovascular disease (CVDs), one of the leading causes of mortality in the world. A low intensity of physical exertion, or its absence, is the main cause of the increase in the proportion of body fat in all individuals, regardless of the social category. Due to the galloping technology, there has been a sharp decrease of physical ef ort required to carry out daily household chores, for moving from one place to another, and even for practicing recreational activities (including those involving a physical exertion component).

According to the Special Eurobarometer 2018 (3), a survey in which 28,031 subjects participated showed that in 2017 the share of Europeans who have "never exercised or played a sport continues to increase. Almost half of Europe's population (46%) never exercise or play a sport, while 14% rarely do so. In contrast, 40% of Europeans exercise or practice a sport with a certain regularity, of which 7% regularly exercise or play a sport. Compared to 2013, the share of those who never exercise or play a sport increased by 4 p.p. (i.e. from 42% to 46%), while the percentage of those who rarely do so decreased from 17% to 14%. This shows that the long-term trend has continued from 2009, when 39% of respondents declared they never perform physical activity".

According to the Prospective Studies Collaboration (***, 2009), both a sedentary lifestyle and obesity are responsible for a considerable part of health problems and mortality rate. The largest ongoing study, which examines

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the link between obesity and mortality, covering nearly one million adults in Europe and North America, shows that mortality rises sharply along with the increase of Body Mass Index (BMI) and as soon as individuals exceed the 25 kg/m^2 threshold, the lower limit of the overweight category.

The European Health Interview Survey of 2014 (2) reveals that almost 1 in 6 adults in the EU is considered obese. The share of overweight and obesity increases with age, a model being valid for women in all European countries: the older they are, the higher the share of overweight and obese people. This increase can also be observed in Romania: in the 18-24 age group, the percentage of obese persons was 1.2%; in the 25-34 age category, 4.8%; in the 35-44 age group, 7.2%; in the 45-64 age group, 12.6%; in the 65-74 age group, 16.0%; and in the 75+ age group, 11.4%.

Physical exercise practiced outdoors or in gyms, in winter or summer, in any form whatsoever, brings substantial benef ts to the human body. According to Sonstroem (1998), there are many individual, social and environmental factors that inf uence mental health, including self-esteem. Self-esteem is a term used in psychology to express the degree of positivity of individuals towards themselves.

Self-esteem is an assessment we make about ourselves that can take many forms (global or multidimensional, mood or disposition, personal or collective). For example, Rosenberg (1979) distinguishes between high self-esteem (positive) and low self-esteem (negative). He def nes self-esteem as a complex cognitive and af ective synthesis and considers that self-esteem dictates the better or worse attitude of an individual towards himself/herself. Most psychologists def ne self-esteem as the overall assessment of self-worth as a person.

Physical activities can be ways in which practitioners become more aware of their personal worth and can fulf ll their potential. Sports practitioners have a positive perception of how they look and feel. There are studies that suggest that one way to improve self-esteem is to exercise, since physical activity has an important contribution to improving one's mental and physical health. According to Mansour et al. (2013), by improving mobility and ef ectiveness, physical exercise has positive ef ects on self-esteem. Findlay & Bowker (2009) mention that top athletes reach a high level of competitiveness, an athletic body and a high degree of self-esteem compared to non-athletes. According to Megakli et al. (2015), a 12-week exercise program, containing aerobic and endurance exercise, has the potential to improve physical self-perception and self-esteem in obese women

In a two-year prospective study, Elavski (2010) examined the physical activity model and self-esteem in a sample of 143 middle-aged women. The results of the study support the hierarchical and multidimensional structure of self-esteem and indicate that middle-aged women can improve the way they perceive their physical condition and attractiveness by continuously participating in physical activity, increasing self-ef cacy and maintaining their BMI within a healthy range.

Our study was conducted to analyze the ef ect of physical activity on the percentage of body fat and self-esteem in adult women who regularly participate in workouts in gyms.

Hypotheses

In this study we started from the following hypotheses:

a) A physical activity program practiced by adult women for 12 months will have the ef ect of reducing the percentage of body fat and increasing self-esteem;

b) The type of physical activity practiced can inf uence the reduction of the body fat percentage and the self-esteem score.

Materials and methods

Research protocol

a) *Period and place of the research*

The research took place for 12 months, i.e. between January 2016 and January 2017, in two gyms in the city of Oradea, the subjects participating in three physical training sessions per week.

b) *Subjects and groups*

The study was attended voluntarily by 89 adult women, clients of some gyms in Oradea, aged between 23 and 57, the average age being 31.62 years (SD = 6.60). Depending on the type of physical activity practiced, the sample was divided into 5 groups: circuit group (18 subjects), softball group (18 subjects), f tball group (18 subjects), aerobics group (18 subjects) and tae-bo group (17 subjects).

c) *Tests applied*

The subjects were assessed for fat percentage and self-esteem before and after participating in the training program. In order to assess the percentage of body fat, skinfold thickness measurement was made using a Digital Body Fat Caliper, and the percentage of body fat was calculated based on the measurement of f ve skinfolds (biceps, subscapular, abdominal, suprailiac or f ank and thigh), using the formula below (Cordun, 2011):

Body fat% = (sum of 5 skinfolds (mm) x 0.15) + 5.8 + body surface area) m^2;

BSA = body surface area was calculated using the Du Bois nomogram.

To assess subjects' self-esteem, a survey was conducted using the Rosenberg Self-Esteem Scale related questionnaire. The purpose of the questionnaire was to f nd the answer to the question whether self-esteem is inf uenced by physical activity or not. Subjects had to write down all the answers and had 10 minutes at their disposal. The questionnaires were anonymous, and the consent of each person included in the survey sample had been previously given.

Interpretation of the self-esteem scale related questionnaire results

This scale was developed to measure the overall sense of self-worth and self-acceptance. The questionnaire includes 10 items with 4 possible answers ranging between "I totally disagree with…" (1 point) and "I totally agree with…" (4 points). Items 2,5,6,8,9 are quoted in reverse order. Scores that can be obtained by the participants range between 10 and 40 points, where a low score indicates a low self-esteem. When rating the results, the values ranging between 10-16 points indicate a low self-esteem level for the respondents; between 17-33 points indicate an average self-esteem level; 34-40 points indicate a high self-esteem level.

d) *Statistical processing*

Descriptive statistical analysis of the collected data was performed, normal distribution was tested and comparisons between the average scores recorded were made. Statistical information processing was done using IBM SPSS, version 23.0. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to test the normal distribution. In the case of data with normal distribution, the t (Student) test was used to compare the averages of the paired variables, and in the case of values with uneven distribution or ranks, the Wilcoxon signed-rank test was used. For the analysis of three or more groups, the ANOVA test was employed in the case of data with normal distribution, or the non-parametric Kruskal-Wallis test in the case of values with uneven distribution or ranks. The signif cance threshold for the tests used was α = 0.05 (5%), 0.01 (1%) or 0.001.

Results

To process the data collected after performing the measurements and applying the "Self-esteem scale" related questionnaire, the distribution of the recorded scores was verif ed (Table I).

Considering the results of the Kolmogorov-Smirnov test, the data recorded concerning the percentage of body fat were normally distributed, while in the case of self-esteem, data were not normally distributed. Consequently, in order to verify the signif cance of the dif erences between the averages of the results from the initial test (T1) and those from the f nal test (T2), the parametric tests were used in the f rst case and the non-parametric tests in the latter case.

Table I

Distribution of body fat (BF) and self-esteem (SE) before and after participation in the intervention program (N = 89).

Variables	Tests of Normality					
	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
BF (%) T1	.082	89	.199	.984	89	.351
BF (%) T2	.060	89	.200*	.991	89	.833
SE T1	.099	89	.031	.953	89	.003
SE T2	.139	89	.000	.916	89	.000

a. t-test; b. Wilcoxon signed ranks test

Table II

Signif cance of dif erences between average body fat (BF) and self-esteem (SE) scores in the subjects included in the study (N = 89).

Pair variables	Mean	Std. Deviation	Std. Error Mean	t[a]/z[b]	df	Sig. (2 tailed)	d
BF (%) T1 -	22.8806	2.42151	.25668	30.765	88	.000	3.26
BF (%) T2	17.8679	1.90217	.20163				
SE T2 -	22.69	7.717	.818	-7.910[b]	88	.000	-.84
SE T1	27,20	6.719	.712				

a. t-test; b. Wilcoxon signed ranks test

According to Table II, in the subjects (N = 89) participating in a 12-month training program in gyms, the percentage of body fat decreased, and the self-esteem score increased. As regards the averages of the body fat percentage, calculated before and after the participation in trainings, the dif erences were signif cant (t = 30.765, df = 88, p = .000), the size of the ef ect being substantial (d = 3.26). Signif cant dif erences were also recorded in the average scores recorded in the self-esteem (SE) assessment before and after participation in the intervention programs (z = -7.910, df = 88, p = .000, d = -.84).

Table III

ANOVA test for comparing the means of the body fat percentage (BF) by type of physical activity and time of assessment.

ANOVA

Time	Variable		Sum of Squares	df	Mean Square	F	Sig.
T1	BF (%)	Between Groups	6.320	4	1.580	.260	.903
		Within Groups	509.687	84	6.068		
		Total	516.006	88			
T2	BF (%)	Between Groups	29.861	4	7.465	2.173	.079
		Within Groups	288.547	84	3.435		
		Total	318.407	88			

Since the sample was divided into f ve groups, depending on the type of physical activity performed, the comparison of group averages/means was performed using ANOVA and Kruskal Wallis tests, depending on the distribution of data. In this way, it was checked whether there were signif cant dif erences between the mean percentage of body fat tissue or self-esteem, depending on the type of physical activity performed and the time of measurement (Tables III and IV).

Although at the end of the study the whole sample was found to have a reduced percentage of body fat and increased self-esteem, in both cases the dif erences between the means recorded in the f ve groups were not signif cant (F = .260, sig. = .903 for T1 and F = 2.173, sig. = .079 for T2; respectively χ2 = 1.029, sig. = .905 for T1 and χ2 = 1.859, sig. .762 for T2).

Table IV

Kruskal Wallis test to compare self-esteem (SE) means by type of physical activity and time of assessment.

Test Statistics[a,b]

Time	Variable	Chi-Square (χ^2)	df	Asymp. Sig
T1	SE	1.029	4	.905
T2	SE	1.859	4	.762

a. Kruskal Wallis Test
b. Grouping Variable: Type of physical activity performed

To assess the inf uence of the type of physical activity on the percentage of body fat and self-esteem, the means recorded in each group of subjects at the two time moments of the study were compared. The analysis of the distribution following the application of the Shapiro-Wilk test revealed that the scores recorded for the percentage of body fat variable were normally distributed, and the scores recorded for the self-esteem variable were not normally distributed (Table I). Consequently, the comparison of the means of the body fat variable was performed using the t-test for paired samples (Table V), and the comparison of the means of self-esteem was made using the Wilcoxon test (Table VI).

Table V

Comparison of the mean percentage of body fat (BF) before and after the intervention program according to the type of physical activity performed by the subjects.

Paired Samples Test[a]

Physical activity type	Pair BF	Paired Dif erences					t	df	Sig. (2 tailed)	d
		Mean	Std. Deviation	Std. Error Mean	95% Conf dence Interval of the Dif erence					
					Lower	Upper				
Circuit	BF T1 - BF T2	5.709	1.560	.3677	4.933	6.485	15.526	17	.000	3.77
Softball	BF T1 - BF T2	5.161	1.188	.2800	4.570	5.752	18.427	17	.000	4.46
Fitball	BF T1 - BF T2	5.378	2.110	.4974	4.328	6.427	10.811	17	.000	2.62
Aerobic	BF T1 - BF T2	4.377	1.153	.2716	3.803	4.950	16.109	17	.000	3.91
Tae-Bo	BF T1 - BF T2	4.405	1.094	.2654	3.843	4.968	16.595	16	.000	4.15

Table VI

Comparison of self-esteem (SE) means before and after the intervention program by type of physical activity performed by the subjects.

Test Statistics[a,b]

Type of physical activity	Pair	Z	Asymp. Sig. (2-tailed)	Ef ect size r
Circuit	Self-esteem T2 - Self-esteem T1	-3.729[c]	.000	-.90
Softball	Self-esteem T2 - Self-esteem T1	-3.732[c]	.000	-.91
Fitball	Self-esteem T2 - Self-esteem T1	-3.480[c]	.001	-.84
Aerobic	Self-esteem T2 - Self-esteem T1	-3.753[c]	.000	-.91
Tae-Bo	Self-esteem T2 - Self-esteem T1	-3.188[c]	.001	-.80

a. Type of physical activity = Circuit, Softball, Fitball, Aerobic, Tae-Bo; b. Wilcoxon Signed Ranks Test; c. Based on negative ranks.

Table VII

Means and standard deviation in body fat percentage and self-esteem by group and time of measurement.

Descriptive Statistics[a]

Variables and Time	**Circuit** (N=18)	Softball (N=18)	Fitball (N=18)	Aerobic (N=18)	Tae-Bo (N=17)
	Mean (StDev)	Mean (StDev)	Mean (StDev)	Mean (StDev)	Mean (StDev)
BF (%) T1	23.17 (2.88)	22.47 (2.65)	22.85 (2.23)	22.76 (1.73)	23.17 (2.66)
BF (%) T2	17.47 (1.82)	17.30 (1.99)	17.47 (1.36)	18.39 (1.21)	18.76 (2.61)
BF % T1 – T2	5.71 (1.06)	5.16 (0.67)	5.38 (0.87)	4.38 (0.51)	4.41 (0.06)
SE T1	21.72 (7.31)	22.61 (7.06)	24.17 (8.17)	21.89 (6.38)	23.06 (9.97)
SE T2	28.28 (7.26)	27.67 (6.13)	27.50 (6.58)	25.72 (6.40)	26.82 (7.66)
SE T2 – T1	6.56 (-0.05)	5.06 (-0.94)	3.33 (-1.59)	3.83 (0.02)	3.76 (-2.31)

The data in Table V, which presents the results obtained when comparing the average percentage of body fat, show that in all groups performing physical activity the dif erences between the mean scores recorded at the two time moments of the study were signif cant and the ef ect size was quite substantial. We obtained the same f ndings following the review of the results obtained after applying the Wilcoxon test for the self-esteem variable (Table VI).

Discussions

According to Sziva et al. (2009), aging results in a change in body composition - a gradual increase in weight and body fat percentage, while lean body mass (LBM) decreases. These negative changes in the human body composition can lead to metabolic syndrome, physical exercise being recommended as a mediator for the positive change in human body composition (Theodorakopoulos et al., 2017).

In our study, following participation in the physical training programs in gyms, it can be seen that for the entire sample included in the study the body fat percentage decreased by 5.01%, i.e. from 22.88 to 17.87% (Table II). Dif erentiated by type of physical activity, the decreases in the body fat percentage of the participants were as follows: circuit group - 5.71%, f tball group - 5.38%, softball group - 5.16%, tae bo group - 4.41% and aerobics - 4.38% (Table VII). However, although there were dif erences between the averages/mean results of the subjects included in the f ve groups, the ANOVA analysis shows that they were not signif cant (see Table 3 above); thus, it can be concluded that the type of physical activity performed is not decisive in reducing the body fat percentage.

Bicer (2013) found that the average self-esteem increased as an ef ect of aerobic exercise practiced for 12 weeks by a group of students; before the intervention it was 33.21% and after the intervention it increased to 36.32%, which allowed to conclude that self-esteem is positively inf uenced by physical exercise.

In a study conducted on 300 subjects aged 20-60, which analyzed the relationship between physical activity and self-esteem, Sani et al. (2016) estimated, using a pattern, that physical activity is directly and indirectly associated with self-esteem.

In a comparative study conducted on 84 students, Mousavi & Pour (2016) concluded that participation in an aerobic exercise program for 8 weeks contributed to increased self-esteem.

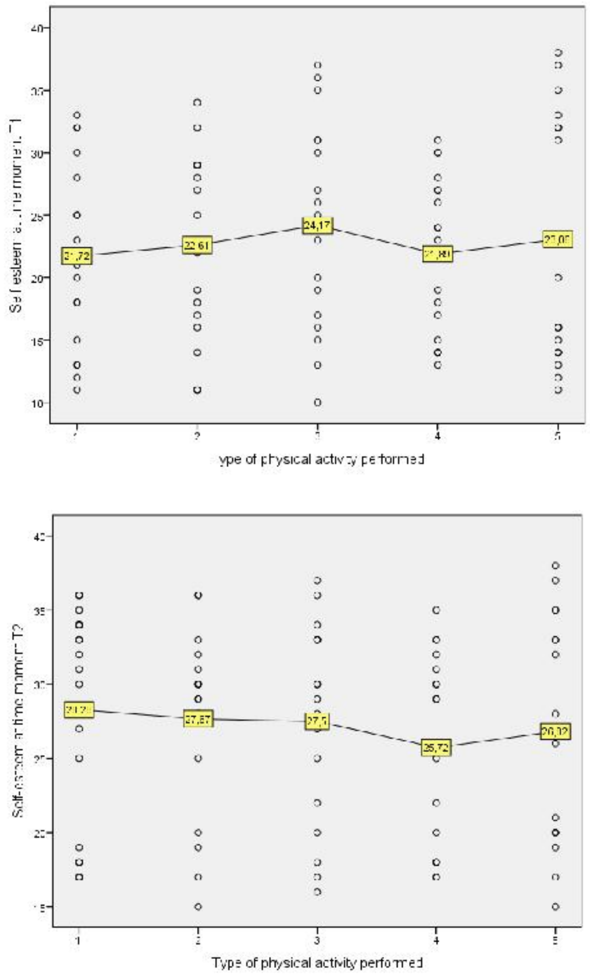

Fig. 1 – Dispersion diagram and interpolation line of self-esteem score means by type of physical activity and assessment time.

Similar results were obtained in our study, self-esteem increasing by 4.51 p.p., from 22.69 p.p. at the beginning of the physical activity program to 27.20 at its end (Table II), this indicator being maintained at a medium level. Increases in the f nal self-esteem score were also found in the physical activity groups (Fig. 1), the highest increase being recorded in the circuit group (6.56 p.p. – from 21.72 to 28.28) and the lowest improvement in the f tball group (3.33 p.p. – from 27.17 to 27.50). However, according to the data presented in Table IV above, the dif erences between the groups were not signif cant ($\chi2 = 1.859$, df = 4, p = .762), which means that self-esteem is not inf uenced by the type of physical activity practiced, only regular physical training being important.

Conclusions

1. In the sample of adult women participating in our study, physical activity performed for 12 months, three times a week, led to a decrease in body fat percentage and an increase in self-esteem, validating the hypothesis that physical activity positively inf uences the two dependent study variables.
2. Regarding the ef ect of the type of physical activity on the two reviewed aspects, the study reveals that the dif erences between the average scores recorded at the beginning of the study and those recorded at its end are not signif cant, which means that physical activity practice and not the type of physical exercise practiced is important.

Conf icts of interest

The authors hereby state that there is no conf ict of interest involving this study.

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Eye-hand relationship of proprioceptive motor control and coordination in children 10–11 years old

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Abstract

Background. Eye-hand coordination refers to the capacity to use the vision skill to guide hand movements and is vital not only in sports activities but also in everyday life and jobs.

Aims. Our investigation tried to identify statistically signif cant variations between 110 children, aged 10–11 years old, from f ve dif erent schools in Targu Mures - Romania, who practice or not sports activities, comparing genders, and also correlating those who practice predominantly arm or leg sports.

Methods. As a research method, we used the hand-eye coordination test and also examined the obtained data with professional statistical programs.

Results. The results showed that between genders there is a statistically signif cant dif erence with better results in the eye-hand coordination test in the male gender. Also, a statistically signif cant dif erence was found between those who practiced sport and those who did not, and also between genders. No statistical dif erence was found between predominantly leg and arm sports.

Conclusions. The conclusions of our investigation highlighted a statistically signif cant dif erence between the numbers of executions in the female gender compared with males and also between the median number of executions in students who practice sports and those who do not, and between the average number of executions for the female and male gender for those who practice sports.

Key words: eye-hand coordination; balance; motor activities.

Introduction

Recent studies in visual attention prove that this cognitive process allows fundamental data, from dissipated and various visual scenes, and worthless data to be sifted through (McMains & Kastner, 2009).

The eye-hand coordination quality which is characterized by the usage of vision cognitive perception that implies leading hand movements such as apprehending and reaching is fundamental for upper limb dexterity (Crawford et al., 2004). This process demands the implication of many cognition elements such as the visual apparatus, the lower and upper extremities of the body to make controlled, fast reactions and accurate movements (Shandiz et al., 2018).

The eye-hand coordination process takes place in an organized manner that implies, f rst of all, the visual f nding of the focused object or target, then the process of focusing attention on that target, followed by the perceptual recognition of its location, the cognitive process, and the scheme of reaching the target, and f nally the excitation of the extremity muscular system for initiating the movement process (Gao et al., 2010).

In other words, eye movements are interconnected with lower extremity movements, as the eyes start and f nish their process of recognition faster than the hands (Carey, 2000). The coordination malfunction is described as any dif culty or restriction at the level of motor coordination that results in a low level of anticipated performance, relying on the patient's chronological age (Coetzee & Pienaar, 2013).

As presented in some research investigations (Ellison, 2015), the prompt reaction time of the visual system regarding the eye-hand movement is issued by the

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fulfillment of assignments that requires numerous findings and resulting motor movements (Laby et al., 2018).

The capacity of motor coordination consists of binding the nervous and musculoskeletal systems that produce a fast, precise, and well-balanced motor reaction which can be evaluated by measuring and comparing the reaction time of the eye-hand or eye-foot coordination skill (Corbin et al., 2000; Lopes et al., 2012). Agility skill refers to the rapidly changing position and direction of the body through space, having high parameters of rapidity and also being very precise. This experience of physical activity during early childhood can create a predisposition for an active lifestyle later in youth and adulthood (Barnett et al., 2009).

Some studies on gymnasium students discovered a significant link among maximum cardiorespiratory fitness (VO_2max), the procedure of cognition, specific attention skill, and visual memory, which was affiliated with basal ganglia and activation of the prefrontal and parietal cortices (Chaddock et al., 2012). Other researchers found that the dorsal striatum is mainly responsible for cognitive control responses, which can positively affect aerobic fitness (Chaddock et al., 2010). Every motor activity or aerobic workout can contribute to the children's cognitive level of performance.

It was found that short periods of intense coordination exercise, up to 10 minutes, can develop the concentration and attention level of children from gymnasium school compared to a regular PE class with the same duration (Budde et al., 2008).

Scientific papers concentrate their attention on analyzing eye-hand coordination influence as phenomenological, using a drift-diffusion framework, which implies the first movement as a development to a fixed limit (Ratcliff & Van Dongen, 2011; Ratcliff et al., 2016), to recommend two opposite sets of rules and methods for highlighting the eye-hand coordination skill. For utilizing a double task paradigm with a reduced RT correlation (Dean et al., 2011), it was observed that taking individually the eye and hand movement development is more efficient.

Other scientists (Gopal & Murthy, 2015) utilized a quick and simultaneous reach task to highlight that a usual accumulator with a hand-specific peripheral delay had main attributes to generate a high level of coordinated eye-hand movements. The coordination condition can be explained as an issue or malfunction in motor coordination that is manifested in poor performance, also being associated with the patient's chronological age (Coetzee & Pienaar, 2013).

Skills such as visual attention, eye-hand coordination, and balance were considered in the specific modern literature in terms of general knowledge, mainly in investigation papers that monitored the effects of exercises on this feature (Udermann et al., 2004; Hardy et al., 2011; Mohammadi et al., 2012). Eye-hand coordination represents one of the system's capacities for re-evaluating information for controlling the upper limbs of the body, helping in tasks such as writing or successfully catching a ball (Natarajan & Malliga, 2011).

In other scientific papers (Williams et al., 1999) it was found that athletes use perceptual tools to improve the level or shorten the eye-hand visual reaction time, even planning and modeling the responses to specific visual information. Those panning models that focused on other experiences than sportive enabled athletes to select pre-programmed motor actions and allowed them to foretell and choose the appropriate model, so they were not merely reacting.

It was discovered that visual-motor coordination has a too high value in executing basic movements in motor activity and cardiorespiratory fitness in young athletes (Wilson et al., 2013). In the essential learning of motor skills, having high levels of performance in unusual motor actions implies more perceptual and cognitive strain in moving (Kerick et al., 2004).

The first phase of visual perception is the visual-motor integration of objects and events that are evaluated and is the basis of cognitive operations (Goodale, 1998). As part of the usual youth development, the system of visual perceptual function has a good development at the age of three and five years, stabilizes at the age of seven and nine years, and can develop up to the age of about ten years (Case-Smith, 2010).

Visual-motor coordination is essential in acquiring visual information from the environment, about objects coming during sports practice (e.g. a ball), requiring a high level of eye-hand coordination for players so they can rapidly react to the external stimuli with efficiency and also improve their adaptation movements needed for specific situations on the field (Przednowek et al., 2019).

Objectives

The study aimed to analyze the hand-eye coordination capacity of youth regarding gender, practicing sports activities, and practicing predominantly leg sports or predominantly arm sports.

The main objective of our research was to analyze the hand-eye coordination capacity of youth from five schools and to identify whether there are significant statistical differences between those who practice sports activities and those who do not, between boys and girls, and also between those who practice predominantly leg sports compared with those that practice predominantly arm sports.

Hypothesis

The research started from the assumption that children who practice sports activities have a superior level of hand-eye coordination compared to those who do not practice sports.

Material and methods

Research protocol

This investigation was performed under the Declaration of Helsinki (2013) and authorized through the Ethics Committee of the "Lucian Blaga" University in Sibiu before the commencement of the study. It also met the ethical standards for Sport and Exercise Science Research.

In the process of investigation during the research, the European Union regulations regarding the privacy of personal information were respected and an agreement was signed with every legally responsible person of our subjects from the experiment sample, given that our subjects were under 18 years old and are considered minors in our country. All the participants in the investigation agreed to participate voluntarily and had the possibility to end their involvement at any time, without any consequence. The participants' documented informed consent was received through an instructed and independent person.

a) *Period and place of the research*

The investigation took place in five gymnasium schools from Târgu Mureş, Romania: "Romulus Guga" Gymnasium School, "Dr. Bernady Gyorgy" Gymnasium School, "Mihai Viteazu" Gymnasium School, "Dacia" Gymnasium School, "Rakoczi Ferenc II" Roman Catholic Theological High School, in partnership with the "George Emil Palade" University of Medicine, Pharmacy, Science, and Technology of Targu Mures, over a 3-month period starting on 1 February 2019, and ending on 31 May 2019.

b) *Subjects and groups*

The experiment sample consisted of 110 children aged 10–11 years, 60 girls and 50 boys, 50 of them practicing sports, and 60 playing no sports.

The exclusion criterion used in the investigation was the health confirmation document certifying the appropriate level of health for sports practice. Students that did not have the paper were excluded from the research. Also, another criterion was that the participants in the study had to fit in the age range of 10–11 years and be gymnasium students at the investigated schools.

The investigation procedure objective was to track the capability of children's vision process to organize the data obtained with their eyes with the main aim to manage, guide, and coordinate hands in catching a ball tossed to the wall.

c) *Tests applied*

The protocol of the experiment required the children to throw a tennis ball with their right hand against the wall and catch it with the left hand, and then switch, throw it with the left hand and catch it with the right hand for 30 seconds. The evaluator counted the maximum number of catches in 30 seconds (Mackenzie, 2009).

d) *Statistical processing*

Statistical analysis included descriptive statistics (frequency, percentage, 95% confidence interval, mean, median, standard deviation), and inferential statistics. The Shapiro-Wilk test was implemented to determine the normal distribution of the analyzed data series. For the comparison of means, the t-Student test was applied for unpaired data and the ANOVA test, the Mann-Whitney test and the Kruskal-Wallis test, non-parametric tests, for comparing the medians. The significance threshold chosen for the p-value was 0.05. Statistical evaluation was conducted using the GraphPad Prism, the trial variant.

Results

Regarding gender distribution, 54.55% were females, and 45.45% were males (Table I).

Table I

Gender frequency.

Gender distribution	Frequency	Percentage	95% confidence interval
Female gender	60	54.55%	44.77%-64.07%
Male gender	50	45.45%	35.93%-55.23%
Total	110	100.00%	-

Considering sports practice distribution, 50 of the study participants practiced sports, and 60 never played any sports (Table II).

Table II

Sports practice frequency.

Practice sport/do not practice sports	Frequency	Percentage	95% confidence interval
Practice sports	50	45.45%	35.93%-55.23%
Do not practice sports	60	54.55%	44.77%-64.07%
Total	110	100.00%	-

Taking into consideration the type of practiced sport, the majority of the study participants played basketball (30.00%), football and handball (22.00%) (Table III).

Table III

Practiced sport.

Practiced sport	Frequency	Percentage	95% confidence interval
Basketball	15	30.00%	17.86%-44.61%
Basketball, Handball, Swimming, Ballet	1	2.00%	0.05%-10.65%
Dance	4	8.00%	2.22%-19.23%
Football	11	22.00%	11.53%-35.96%
Gymnastics	1	2.00%	0.05%-10.65%
Handball	11	22.00%	11.53%-35.96%
Field Hockey	1	2.00%	0.05%-10.65%
Swimming	3	6.00%	1.25%-16.55%
Volleyball	3	6.00%	1.25%-16.55%
Total	50	100.00%	-

Regarding the schools, the majority of the study participants were selected from "Romulus Guga" Gymnasium School and "Dr. Bernady Gyorgy" Gymnasium School (Table IV).

Table IV

School attended.

Attended school	Frequency	Percentage	95% confidence interval
"Romulus Guga" Gymnasium School	25	22.73%	15.28%-31.70%
"Dr. Bernady Gyorgy" Gymnasium School	25	22.73%	15.28%-31.70%
"Mihai Viteazu" Gymnasium School	20	18.18%	11.47%-26.67%
"Dacia" Gymnasium School	20	18.18%	11.47%-26.67%
"Rakoczi Ferenc II" Roman Catholic Theological High School	20	18.18%	11.47%-26.67%
Total	110	100.00%	-

In the whole group, the average number of executions was 7.327±5.069 (Table V).

Table V

Number of exercises - descriptive statistics.

Statistical interpretation	**Number of exercises**
Number of values	110
Minimum	0.0
25% Percentile	3.000
Median	6.000
75% Percentile	11.00
Maximum	22.00
Mean	7.327
Std. Deviation	5.069
Std. Error	0.4833
Lower 95% CI of mean	6.369
Upper 95% CI of mean	8.285

When comparing gender, we observed a lower mean of the number of executions in females (5.100±3.606) than in males (10.00±5.303) and a higher mean of the number of executions in those who practiced sports (11.38±4.337) than in those who never practiced any kind of sports (3.950±2.514) (Table VI).

For the Mann-Whitney test, p <0.05, we found a statistically signif cant dif erence between the median number of executions in the female and male gender.

Also, for the Mann-Whitney test, p <0.05, we observed a statistically signif cant dif erence between the median number of executions in those who practiced and did not practice sports.

Using the t-Student test, p> 0.05, we discovered no statistically signif cant dif erence between the mean number of executions in those practicing sports predominantly with their arms and those practicing sports predominantly with their legs. Predominantly arm sports: basketball, handball, and volleyball. Predominantly leg sports: football, grass hockey, dance, gymnastics, and swimming.

For the t-Student test, p <0.05, we found a statistically signif cant dif erence between the mean number of executions for the female and male gender for those practicing sports.

Also, using the Mann-Whitney test, p> 0.05, we discovered no statistically signif cant dif erence between the median number of executions in females practicing sports predominantly with their arms contrasted with those practicing sports predominantly with their legs.

Using the t-Student test, p> 0.05, we observed no statistically signif cant dif erence between the mean number of executions in males practicing sports predominantly with their arms and those practicing sports predominantly with their legs.

Table VII

Comparison between schools regarding the number of executions of those not practicing sports.

School attended	**Number of executions**	**Value of p**
"Romulus Guga" Gymnasium School	7.960±4.218 (8.00)	
"Dr. Bernady Gyorgy" Gymnasium School	12.04±5.564 (12.00)	
"Mihai Viteazu" Gymnasium School	4.850±3.602 (4.00)	<0.0001
"Dacia" Gymnasium School	5.550±4.236 (4.00)	
"Rakoczi Ferenc II" Roman Catholic Theological High School	4.900±3.024 (4.00)	

Table VIII

Comparison between schools regarding the number of executions of those practicing sports.

Schools attended	**Number of executions**	**Value of p**
"Romulus Guga" Gymnasium School	11.15±2.734 (11.00)	
"Dr. Bernady Gyorgy" Gymnasium School	16.00±3.783 (16.00)	
"Mihai Viteazu" Gymnasium School	9.000±2.309 (8.00)	<0.0001
"Dacia" Gymnasium School	9.375±3.462 (10.00)	
"Rakoczi Ferenc II" Roman Catholic Theological High School	7.750±2.765 (8.50)	

Table VI

Number of exercises - descriptive statistics.

	Female gender	**Male gender**	**Value of p**
Number of executions	5.100±3.606 (4.00) Practice sports	10.00±5.303 (10.00) Do not practice sports	*<0.0001
Number of executions	11.38±4.337 (11.00) Predominantly arm sports	3.950±2.514 (3.00) Predominantly leg sports	*<0.0001
Number of executions	11.57±4.470 (11.00) Females practicing sports	11.10±4.229 (10.50) Males practicing sports	0.7134
Number of executions	8.696±2.867 (9.00) Females practicing arm sports	13.67±4.086 (13.00) Females practicing leg sports	<0.0001
Number of executions	8.941±2.947 (9.00) Males practicing arm sports	8.000±2.757 (8.00) Males practicing leg sports	*0.3770
Number of executions	15.00±3.764 (14.00)	12.43±4.108 (12.00)	0.1032

* Mann-Whitney test

Discussion

In a recent study, it was found that the influence of particular sets of exercises with specialized focus on cognitive performance can be very efficient (Chang et al., 2012). Taking into account the literature from a particular exercise that focused on visual attention development, it can be seen that visual attention can be developed through web-based training (Scanlon et al., 2007). By observing the investigation results, it can also be concluded that highly specialized exercises can improve the level of hand-eye coordination skills. Also, other conclusions of the related investigation proved that eye-hand coordination effects on balance skills in swimming training also have positive effects on hand-eye coordination (Hsu et al., 2010).

Other research investigations on hand-eye coordination in table tennis players concluded that improving this skill can raise the level of performance of those athletes compared with others that do not train this skill (Paul et al., 2011).

Substantial gains through brain training exercises are the possibility of moving the legs and arms through a variety of combinations, catching and tossing objects, and at the same time, developing visual perception and hand-eye coordination (Demirakca et al., 2016).

In recent studies (Ellison et al., 2014), researchers use the Sports Vision Trainer program for analyzing and assessing the eye-hand and visual-motor reaction time ability. The results of the investigation highlighted the high-retest validity values (with a value of r = 0.82 to 0.89), showing that the testing system is a valid method to assess the eye-hand visual-motor reaction time.

Other researchers (Wells et al., 2014) reported their experimentation of eye-hand visual-motor assessment with the program Dynavison D2 for measuring the reaction time of athletes. The conclusions of their investigation highlighted the increased viability of this device, after using three attempts for an acquaintance before the final assessment.

Taking a look at other inquiries having visual attention development and brain exercise as a primary purpose, it was found that in this domain of visual training, significant progress has been made in the direction of hand-eye coordination in youth university students (Du Toit et al., 2011).

Recent research has discovered a new set of visual training skills termed “eyerobic”, which consists of exercises for female football players allowing an excellent development of balance and hand-eye coordination in the experiment group compared with the control group (McLeod, 1991).

Conclusions of other investigations highlighted the idea that using brain exercises can positively affect visual attention in high-level athletes (Vural, 2016).

In an article (Ciufreda, 2011) contributing to the ideas of Ando et al., it was discovered that the hand-eye capacity and the visual-motor reaction time can be developed through training for short periods; this process of training affects the central and peripheral visual skill and has durability at least for a short period.

The problem of brain workout exercises and their contribution to hand-eye coordination are analyzed by many modern scientific studies showing that those activities are focused on simultaneous moves that provide substantial variation of movement, improving hand-eye coordination for short to medium periods of training time, comparing the results with those of the control group. However, in some investigations, the parameter of dynamic balance and visual attention did not develop significantly over short periods of training time (Cetin et al., 2018).

Some specialists also tried to stimulate the noise effector-specific system (Gopal & Murthy, 2015) and the distinct interacting accumulators model (Dean et al., 2011) in developing the temporal part of the hand-eye coordination skill, in the pursuit of finding significant differences comparing the computational structure that eye-hand coordination in the dual and search task may affect the purpose of the central executive system (Seeley et al., 2007; Sridharan et al., 2008), which enables the athlete to pass from an ordinary to a separate accumulators model and in the opposite direction.

Other findings linked hand-eye coordination and visual-motor skill regarding their response time systems to being trainable and developed. Using the particular designed Sports Vision Trainer, researchers found out that this device has a 25% rate of progress and that the potential of development of hand-eye coordination on the visual-motor reaction time can also bring a high level of performance in different sports such as baseball or others that involve working with the hands and the visual system (Zupan et al., 2006).

Conclusions

1. The conclusions of our investigation highlighted a statistically significant difference between the median number of executions in females compared with the male gender in the eye-hand coordination test.
2. Also, we observed a statistically significant variation between the median number of executions in those practicing and those not practicing sports and between the mean number of executions for the female and male gender for those practicing sports.
3. No statistical difference was found by comparing the mean number of executions of those practicing sports predominantly with their arms and those practicing sports predominantly with their legs, the executions of females and males practicing sports predominantly with their arms compared to those practicing sports predominantly with their legs.
4. The conclusions of the investigation showed that males have better hand-eye coordination than females and also, those practicing sports registered more correct executions compared with those not practicing sports, proving that sports activities can improve skills such as balance and eye-hand coordination.

Conflicts of interest

Nothing to declare.

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Prosthetics and rehabilitation in lower limb amputees

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Abstract

Background. It is considered relevant to contextualize the health care process to amputated people since the hospitalization until the acquisition of the prosthesis to adapt to the new living condition and determine the bioethical aspects involved in this process. In that sense, the research question in this study was: how did health care to people submitted to limb amputation take place from the perspective of bioethical analysis? And the study objectives were: to analyze the care delivered by health professionals throughout the amputation process from the perspective of the amputees and discuss the health care process for amputated people from the perspective of bioethical analysis.

Aims. The overall objective of the standards and guidelines is to establish a basis for the provision of a service of excellence to the amputee population with equity of access throughout the Romania. It also aims to assist clinical governance and service development with standards presented in a format easily accessible for audit purposes.

Methods. A qualitative, descriptive and exploratory study was conducted through semi-structured questionnaires with 175 people undergoing amputation in the period 2008-2020, in SC. Theranova Protezare SRL in Romania. The objectives were to analyze the care provided by health professionals throughout the amputation process in the perspective of the amputee patient; and discuss the process of health care to the person with amputation in the bioethical analysis perspective. Data were analyzed according to content analysis. Three thematic categories emerged: the process of amputation; team performance and rehabilitation. Bioethics permits ref ection on the care provided to amputees and problematizes the relationship of the health care process with support available through public health policies. The professional involved in this process has to take responsibility for putting the process in practice and interdisciplinary is essential for the recovery of the amputated patient.

Results. It was verif ed that the causes leading to amputation can be triggered by a chronic illness as well as by trauma, the latter determined by external causes. Despite dif erent motives for the amputation, however, the care process is the same. In other words, based on the statements, it can be inferred that, despite the stakeholders' dif erent ages and needs, both end up in the same health care context: slow and fragmented.

Conclusions. In addition, in the interval of almost twelve years since they were submitted to the respective amputation, a precarious situation of physical, social and economic independence was evidenced. In short, these qualitative research results do not permit generalizations but questions: is these people's right to socio-professional integration being guaranteed? The question is: the amputated people and/or the health team's lack of knowledge, or the disorganization of the health care process?

Key words: amputation, health professionals, bioethics, assistance to health, public health policy

Introduction

The loss of a lower limb has severe implications for a person's mobility, and ability to perform activities of daily living (Brasil, 1999). This negatively impacts on their participation and integration into society (Instituto Brasileiro de Geograf a e Estatística, 2010). The ultimate goal of rehabilitation after limb loss is to ambulate successfully with the use of a prosthesis (Ministério da Saúde, 2010) and to return to a high level of social reintegration. Prosthetic rehabilitation is a complex task that ideally requires input from a transdisciplinary rehabilitation team. However, most often internationally, physiotherapists are in charge of the physical rehabilitation process (Vargas, 2013a).

To the extent that the bioethics of protection and intervention attempt to grant visibility to the equality/inequality or equity/inequity among people, they can provide competent support to make them understand their rights and claim them (Garrafa, 2012). "The right to health needs to combine the protection of individual autonomy and the collective provision of means to put that right in practice" (Alvarsson, 2012).

Hypothesis

Starting from the idea that the prosthesis manufacturing process and the management of patients with amputations should start as soon as possible, we wanted to f nd out some data about the information patients receive, the way and the

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duration of the recovery process, the time required to obtain funding from the national Health Insurance (C.A.S.), we included in the questionnaire a series of questions to give us a broader picture of these def ning elements. The most important and decisive decisions in this whole prosthesis manufacturing process must be made on the basis of the clearest and most comprehensive information possible in all that means amputation, recovery, life after amputation, possibilities and limitations in everyday life, which is why it is important for patients and their relatives to have this information so that they can make the best decisions.

Material and methods

a) *Period and place of the research*

A qualitative, descriptive and exploratory study was conducted through semi-structured questionnaires with 175 people undergoing amputation in the period 2008-2020, in SC. Theranova Protezare SRL in Romania.

b) *Subjects and groups*

To select the participants, the 268 preselected records were contacted personally, if contact was possible, they were asked whether they accepted to participate in the research or not. These participants represent a retrospective study of amputees who were served by Theranova. Therefore, a declaration from an ethics entity was not necessary. GDPR policy has been followed to the extent that the participating persons gave their consent, they have not been nominalized and they cannot be identif ed in any way. From this group 175 of whom accepted to participate in the study.

c) *Tests applied*

The research participants signed the Informed Consent Form, which authorized the investigation of the patient history and the participation in a semi structured questionnaire which was digitally recorded. The title of our questionnaire is: “Prosthesis evaluation questionnaire for persons with lower limb amputations: Assessing prosthesis-related quality of life” author Jaco Du Plessis

d) *Statistical processing*

Demographic and clinical characteristics of patients were analyzed and no formal hypothesis was tested. Discrete variables are presented as count and frequency (%). All the data were processed and grouped using Microsoft Excel 2016.

Results

Out of the total of 175 completed questionnaires, it is highlighted that 71% of the respondents are male and only 29% female (Fig. 1).

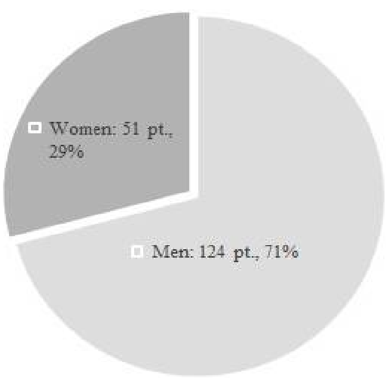

Fig. 1 – Distribution by gender.

Regarding the level of amputation, 135 people (77%) have thigh amputations (transfemoral) compared to 37 people (37%) with leg amputation (transtibial) and the dif erence is the amputations of the upper limbs, forearm and arm (Fig. 2).

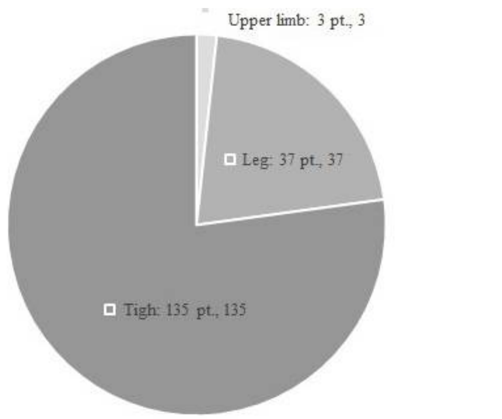

Fig. 2 – Distribution on amputation levels.

A small percentage of only 3% are patients with bilateral amputations, 52% are amputated on the left side and 45% on the right side (Fig. 3).

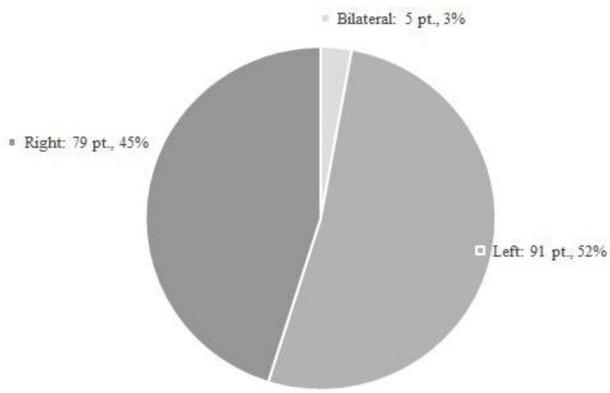

Fig. 3 – Distribution on the amputated side.

The causes of amputations are represented in a higher percentage of diseases (arteriopathy, diabetes, infections, tumors) 84%, followed by amputations due to accidents 12% and only 7% are congenital cases (Fig. 4).

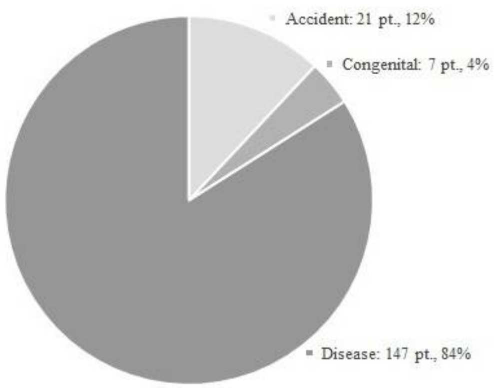

Fig. 4 – Distribution according to the reason for amputation.

From the point of view of the age of those involved in completing the questionnaires, 89 people were aged between 41-65 years, 48 people were over 65 years old, young adults aged 26-40 were 28, young people between 18-25 years old were only 8 in number and 2 people were under 18 years old (Fig. 5).

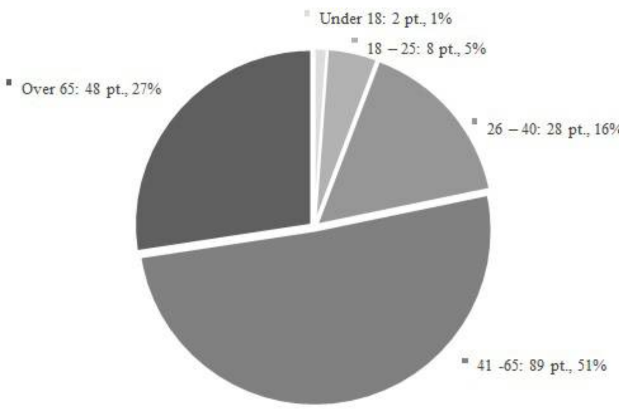

Fig. 5 – Distribution by age categories.

Of the 175 participants in the survey, 96 are retirees, 60 are employees, 5 are entrepreneurs, 12 are unemployed and 2 are students (Fig. 6).

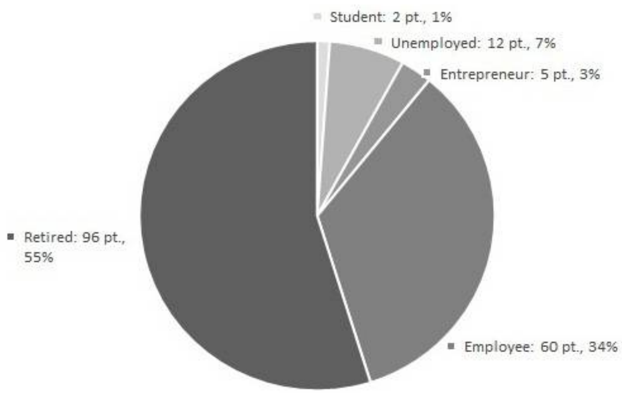

Fig. 6 – Distribution by occupation.

Patients in urban areas represent 64.8% those in rural areas 35.2%. 131 people have secondary education, 33 have higher education and 11 of them have education under 10 classes (Fig. 7).

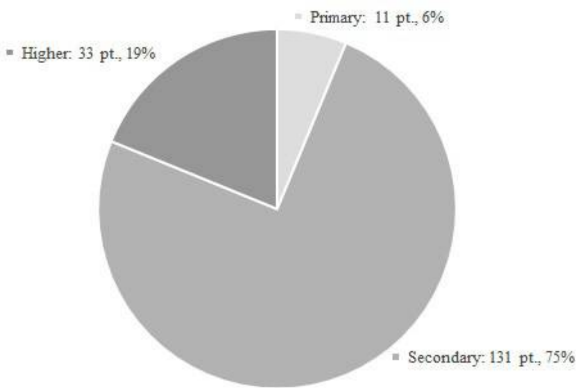

Fig. 7 – Distribution of patients according to studies.

Given that the vast majority of patients suf ering from amputations are retirees whose family income is provided only by pension or social benef ts, the costs involved in the prosthetic manufacturing process are a decisive factor when choosing the prosthesis model to be made (Fig. 8).

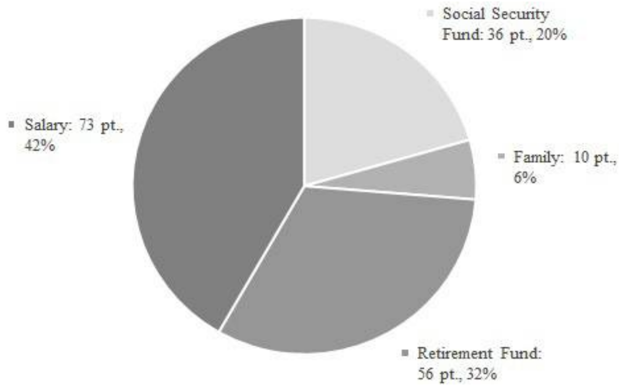

Fig. 8 – Distribution of income sources.

For this reason, the role of state f nancial support through the health insurance system is important even if the amount of money of ered by this insurance system is not the desired one, but for many patients it is the only way they can get a prosthetic device that can give them the chance for a recovery and social reintegration. Of the answers given by respondents out of the total number of people who received f nancial aid from the National Health Insurance (C.A.S.) 15% obtained the decision in one year, 32% waited between 6 and 12 months to obtain the decision from C.A.S., 26% obtained the decision within 3-6 months, 14% within 3-6 months, 6% within one month and 4% had to wait more than a year to obtain the decision from C.A.S., while 3% did not use C.A.S. support (Fig. 9).

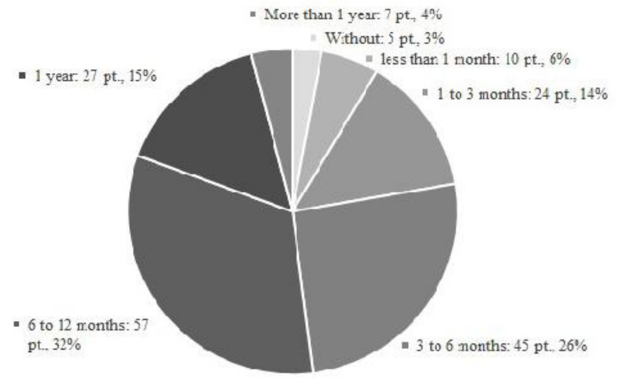

Fig. 9 – The waiting time for receiving the approval from C.A.S.

Another question we have asked patients was whether they wanted a more rudimentary prosthesis for which the costs would be fully covered by the C.A.S. or something more ef cient, which of course involves additional costs on behalf of the patient but also of ers a higher comfort in terms of prosthesis wear. From the answers received, it is clear that the vast majority of patients would like something better, although in many cases they are limited to what the health system of ers them due to the lack of funds needed to cover additional expenses (Fig. 10).

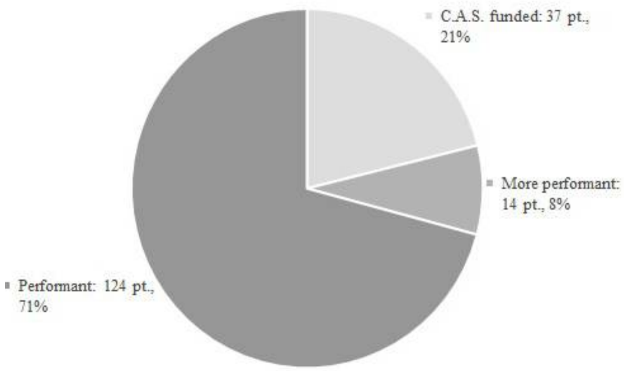

Fig. 10 – Patients preference for prostheses.

All those who chose the prosthesis option paid by the state subsidy cited as a reason the lack of money needed to purchase a better prosthesis.

Fig. 11 shows us the number of patients who have benefited or not from psychological counseling.

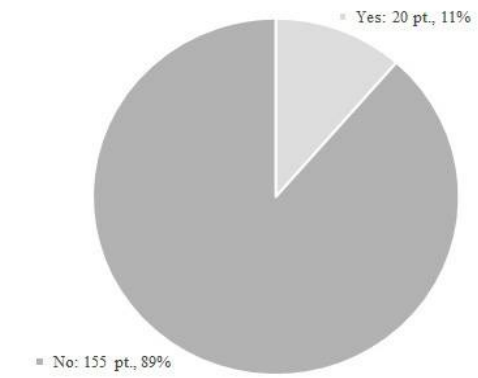

Fig. 11 – Psychological recovery.

Another important thing to note is that only 20% of patients answered positively to the question of whether they benefited from a recovery process compared to the 80% who did not mention such a thing (Fig. 12).

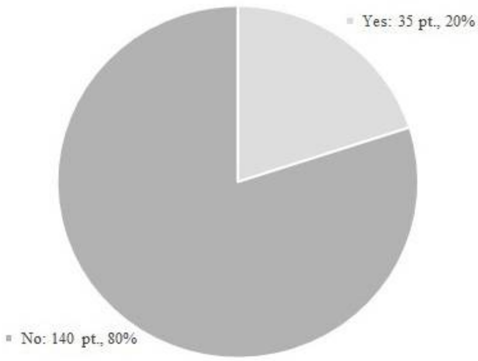

Fig. 12 – Participating in a recovery process.

The statistical data from the completed questionnaire show us a satisfactory result when we talk about the period of time that passes from amputation to the first prosthesis. A fairly good percentage (24%) say that they manage to buy their first prosthesis in less than 6 months after amputation, followed by a period between 6 and 12 months in a percentage of 40%. Those who manage to do this about 6 months after amputation end up representing 11%. The percentage of patients who end up waiting a year or even more than two years to be able to buy their first prosthesis is present but quite small of 1%, 3% and 4% respectively (Fig. 13).

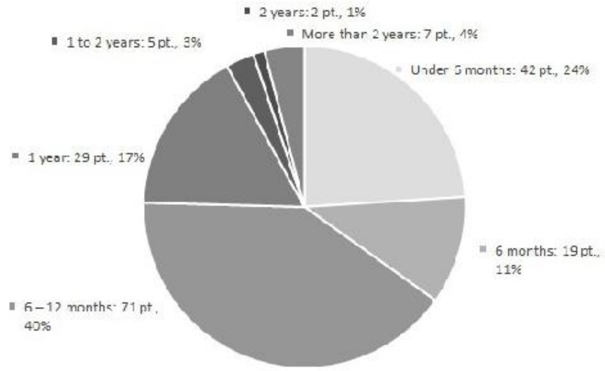

Fig. 13 – Time period from amputation to first prosthesis.

Table I

Demographic and financial data.

Characteristic		Patients n (%)
Gender	Males	124 (71)
	Women	51 (29)
Age (years)	< 18	2 (1)
	18-25	8 (5)
	26-40	28 (16)
	41-65	89 (51)
	> 65	48 (27)
Occupation	Student	2 (1)
	Entrepeneur	5 (3)
	Unemployed	12 (7)
	Employee	60 (34)
	Retired	96 (55)
Studies	Elementary	11 (6)
	High School	131 (75)
	University or higher	33 (19)
Income	Family	10 (6)
	Social Security	36 (21)
	Salary	73 (42)
	Retirement Fund	56 (32)

Table II

Amputation and prosthesis data.

Characteristic		Patients n (%)
Amputation level	Upper limb	3 (2)
	Leg	37 (21)
	Thigh	135 (77)
Amputation side	Right	79 (45)
	Left	91 (52)
	Bilateral	5 (3)
Favorite prostheses, dependin on the price	C.A.S. funded	37 (21)
	Performant	124 (71)
	More performant	14 (8)
Waiting time from amputation to prosthesis	None	42 (24)
	< 1 month	19 (11)
	1-3 months	71 (41)
	3-6 months	29 (17)
	6-12 months	5 (3)
	1 year	2 (1)
	> 1 year	7 (4)

Table III
Recovery data.

Characteristic		Patients n (%)
Psychological recovery	Yes	20 (11)
	No	155 (89)
Participating in a recovery process	Yes	35 (20)
	No	140 (80)

Even if the number of patients who completed the questionnaires is only a small sample compared to the number of patients who annually would undergo a prosthetic manufacturing process, we consider that the results of analysis and data processing are a good starting point for future evaluation at the national level with an even greater number of patients. The information obtained will provide us with the necessary basis for establishing conclusions that we hope will bring a new approach to the entire prosthetic process in our country with the involvement of all personnel involved in decision taking in all areas of activity that are an integral part of this process.

Discussion

The study findings with regard to sex and amputation cause indicate what the other studies also evidence. That is, men and the baseline disease DM predominate with regard to amputation. DM is a risk factor for amputation (Alvarsson et al., 2012; Holman et al., 2012; Andrews et al., 2013).

As observed, the participants' education level is low, based on which it is considered that knowledge deficits, especially in the male population, about the importance of health promotion and disease prevention, influences self-care (Fontes et al., 2011) actions and their "competence" to contextualize their rights in the health care process. The research participants, whether married or not, live with their family, legitimizing it as support for health promotion and disease prevention.

The feelings triggered by the imminent amputation are similar in the people going through this situation. After all, both are confronted with a new living condition, besides the duality between the need for the surgery and the "refusal" to lose part of themselves (Gabarra et al., 2009). Hence, accepting that the amputation is the best option is not easy, as the way the people see themselves in society changes, giving rise to countless problems. The patients are wounded for the situations triggered with regard to their new condition; they are not prepared to discern what is ideal to establish better living conditions.

Permitting the practice of autonomy means offering information on the best conducts to be taken; it means inserting the patients in the care process; it means knowing how to listen to them, knowing their weaknesses and providing for tools for them to feel capable and responsible for their recovery. Thus, the respect for autonomy is related to enabling the person to move beyond their concept of dependence (Vargas et al., 2013b). It should be underlined, however, that so-called autonomous persons can also make mistakes in their decisions made, as the conditions experienced at the moment of the decision directly interfere in their actions.

It is believed that clarifying the risks and benefits of care delivery avoids any bottleneck in the conduct taken. It is fundamental for the patients to know the pros and cons of the care performed, so as not to create mistaken expectations regarding that care (Magalhães et al., 2013).

The multidisciplinary activity results in greater safety with regard to the decision made, permitting greater benefits for the people considered as risk groups. The professionals' experience and the available technological apparatus are aspects considered in the care strategies adopted, in accordance with the complexity of the lesion (Magalhães et al., 2013).

The health professionals should acknowledge the needs of the patients submitted to the amputation, so that the orientations provided influence the short, medium and long-term recovery and, hence, the prevention of health problems associated with the amputation. The care the team provides should move beyond the physical and prosthesis focus; after all, in the course of the entire amputation process, psychological and social interventions are also essential (Liu et al., 2010).

The people who receive care sometimes do not know that that care is a right and not a favor granted by the person who provides it. In that sense, one of the participants praises the health team's activities. It can be inferred, however, that compliments for the professionals' care evidence the patients' lack of knowledge of their right to high-quality care.

The bioethics of protection is one way to reflect on the functioning of the public health system structure, in which the State is responsible for resource management, social control and qualified human resources (Gomes, 2012) and for providing/developing techniques aimed at reducing the stakeholders' disabilities (Vargas, 2013a).

In the study participants' reports, it is highlighted that interdisciplinary actions are a problem. The amputated people see the professionals in an isolated manner; the function of each is acknowledged, but not the perceived importance of interdisciplinary care. Nevertheless, in a multidisciplinary team's care process, when acting in an interdisciplinary manner, communication is more effective and, consequently, the patients' recovery and rehabilitation process can be more satisfactory (Andrews et al., 2013; Latlief et al., 2012; Schoeller et al., 2013).

Knowing how to listen is essential; this conception is also articulated with the professionals' attitudes and work conditions.

As observed, the precarious infrastructure, associated with nonchalant care, leads to inappropriate care delivery, infringing on the rights of the people who need it. Health professionals are educators who should promote health and prevent diseases and complications, reducing the problems that affect the vulnerable society (5). Therefore, it is the duty of the State to offer a qualified and valued team and guarantee infrastructure and quality. Nevertheless, simply presenting policies is not sufficient, but means are needed to execute them. Rights have been gained through the constitution and they have to be respected.

Hence, questions are raised on the State's responsibility in resource management. In 2012, the Care Network for Disabled People was created, which offers financial incentives for specialized rehabilitation care centers, with a view to guaranteeing access to the people who need the service (Sena et al., 2012).

The reports showed that, when care is provided in an isolated manner, the expected outcome may not be evidenced. Therefore, it is considered that a treatment plan centered on the person should be comprehensive and developed from the start of the rehabilitation process (3, 5) Rehabilitation should be planned even before the amputation, because the team understands the importance of the early establishment of rehabilitation.

According to one study, health professionals, particularly in primary care, feel unprepared to deliver care to disabled people, especially people who were amputated, showing the lack of knowledge on the importance of rehabilitation (Baena & Soares, 2012). The National Health Promotion Policy determines that primary health care should solve most of the health needs evidenced by the population (5).

In that perspective, it is considered that a knowledgeable health team can plan, organize, develop and assess actions that grant better living conditions (Mattioni et al., 2011) to wounded people (5). Nevertheless, the professionals' lack of preparation is evidenced, which exacerbates avoidable situations, turning the recovery process even slower than expected (Baena & Soares, 2012; Mattioni et al., 2011)

The study also evidences the team's lack of experience in comprehensive care to amputated people and their relatives. These individuals f gure among the people who display multifactorial consequences due to the new living condition which, by itself, turns into a challenge for the professionals involved in care (Baena & Soares, 2012; Mattioni et al., 2011).

As regards the acquisition of the prosthesis, it should be reminded that, in the state where the study was developed, there is only one referral center for rehabilitation, which is unable to attend to the demand. This problem directly inf uences the rehabilitation process of amputated people. After all, care planning should be centered on the patient's social wellbeing and developed at the start of the rehabilitation process (3)

Conclusions

1. The study permits ref ecting on care for amputated people from a bioethical perspective, considering that studies on this theme focus the discussion on the stakeholders' characteristics, the professionals' care and the amputated people's experience. In other words, in Romania, no previous studies are available that analyzed the bioethical aspects of the health care process for amputated people.

2. Therefore, it was considered that the bioethics of protection and intervention is a productive possibility for the process of ref ecting on the care delivered to amputated people. It is highlighted that both contribute to the detailed arguments on several and dif erent subsidies deriving from public health policies that can intervene in the quality of care delivery and transform the people submitted to the amputation or not, enabling them to ref ect on their rehabilitation and new living condition.

3. In addition, in the interval of almost twelve years since they were submitted to the respective amputation, a precarious situation of physical, social and economic independence was evidenced. In short, these qualitative research results do not permit generalizations but questions: is these people's right to socio-professional integration being guaranteed? The question is: the amputated people and/or the health team's lack of knowledge, or the disorganization of the health care process?

4. Studies are needed that focus on the activities of amputated people, observing whether they readapt to the new living condition and develop a high-quality life or not. As evidenced, the professionals' activities in the course of the care process to disabled people are relevant for their rehabilitation to the "new life". Based on these professionals' perspective, the care network should be acknowledged that is established for care of disabled people.

Conf icts of interests

Nothing to declare.

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CASE REPORTS

Periarticular calcium pyrophosphate deposition disease in a young patient: a case report

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Abstract

Background. Calcium pyrophosphate deposition disease (CPPD) is an arthropathy that af ects the synovium and periarticular tissues. More often, persons aged over 50 years old suf er from this disease. CPPD pathogenesis is not yet completely understood. In younger patients, the suspicion of familial predisposition or a metabolic disease is raised. Imaging tests and aspirate analysis from tendon in optical microscopy are essential for establishing an accurate positive diagnosis.

Case presentation. We report a case of a 45-year-old female patient, without signif cant personal pathological history, with atypical periarticular location of calcium pyrophosphate deposition in the supraspinatus tendon. This deposition was evidenced by X-ray and ultrasound, and then conf rmed by the analysis of the aspirate from the tendon, in optical microscopy. The patient received nonsteroidal anti-inf ammatory drugs, physiotherapy of the shoulder, local inf ltration with betamethasone and lidocaine, with a favorable evolution.

Conclusions. This case is a rare one due to the following particularities: the patient has an age below the average age for this pathology; the atypical location of a single calcium pyrophosphate deposition in the supraspinatus tendon, a tendon that is usually correlated with hydroxyapatite deposition. The presented case highlights the importance of imaging examinations and aspirate analysis using optical microscopy in establishing the positive diagnosis of calcium pyrophosphate deposition disease.

Key words: calcium pyrophosphate deposition disease, supraspinatus tendon, imaging tests, optical microscopy, young patient

Background

Calcium pyrophosphate deposition disease (CPPD) is an arthropathy that af ects the synovium and, more rarely, periarticular tissues (Rosales-Alexander et al., 2014). CPPD pathogenesis is not yet completely understood, but it is known that the f rst stage in the development of the disease is represented by the formation of calcium pyrophosphate crystals, especially in the cartilage pericellular matrix and to a lesser extent, in non-cartilaginous tissues (Rosenthal & Ryan, 2016).

CPPD is rarely found under the age of 50 (Neame, 2003). Studies have shown that aging is a major risk factor, so that after the age of 50, the disease incidence increases signif cantly. Under the age of 45, the suspicion of familial predisposition or a metabolic disease is raised (Felson, 1989).

The clinical presentation of CPPD includes four phenotypes: acute (self-limited synovitis, previously known as "pseudogout"), chronic, associated with arthrosis, and asymptomatic. The term "chondrocalcinosis" refers to cartilage calcif cation evidenced by imaging methods or histological examination (Zhang et al., 2011; Abhishek, 2016; Tedeschi et al., 2019). Periarticular location is more rarely reported in the literature, the described cases occurring in the tendons of the triceps,

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quadriceps, gastrocnemius muscles, in the Achilles tendon, and to a lesser extent, in the shoulder rotator cuf tendons (Steinbach, 2004).

CPPD diagnosis is conf rmed by aspirate analysis which should evidence weakly positively birefringent crystals of rhomboid or rectangular shape, unlike the monosodium urate crystals in the form of needles with negative birefringence observed in gout (Rosales-Alexander et al., 2014; Iqbal et al., 2019).

Case presentation

A 45-year-old female patient, without signif cant personal pathological history, presented in April 2016 to the ambulatory service of the Clinical Rehabilitation Hospital for mixed pain in the left shoulder (at rest and during exercise), starting six weeks before. The patient had not performed sustained physical ef ort that might have been correlated with the development of symptoms, and had no trauma to the left shoulder. After administration of nonsteroidal anti-inf ammatory drugs (NSAIDs) and analgesics, pain persisted and worsened towards the end of March.

On clinical examination, an increase in pain during movement and limited mobility were observed, with pain worsening when regaining the initial position, and internal and external rotation impossible to perform.

The patient was informed about her health condition, the medical interventions proposed and associated risks, as well as about diagnosis, treatment and prognosis. According to Romanian legislation, the patient's written informed consent was obtained.

Left shoulder X-ray evidenced the presence of periarticular calcif cations anatomically corresponding to the supraspinatus tendon/subacromial-subdeltoid bursa (Fig. 1).

Fig. 1 – Left shoulder X-ray in anteroposterior view indicates periarticular calcif cation (a relatively well delimited, homogeneous mass, yet having a cloud-like appearance, supporting the subacute/chronic nature).

Left shoulder ultrasound of the supraspinatus tendon showed in longitudinal and transverse view a hyperechoic, inhomogeneous and well delimited area of 1.9 cm by 1.33 cm, with subacromial subdeltoid impingement syndrome. Power Doppler ultrasound indicated no vascularization. (Fig. 2).

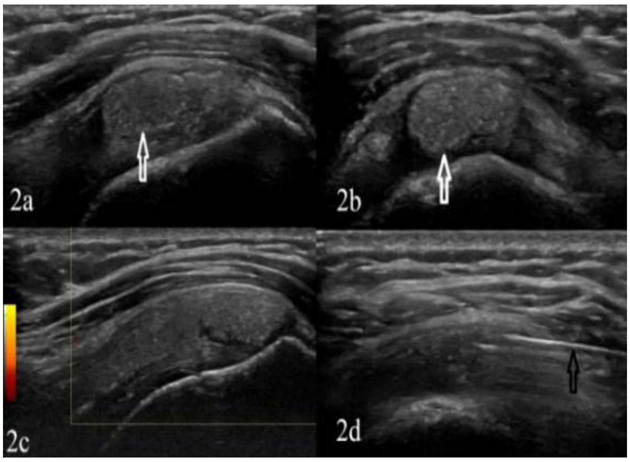

Fig. 2 – Ultrasound image of the supraspinatus tendon acquired in longitudinal and transverse view; **2a, 2b.** Hyperechoic, inhomogeneous, well-def ned area; **2c.** Power Doppler ultrasound showing no vascularization; **2d.** The puncture needle during intratendinous calcif cation aspiration (black arrow).

Biologically, mild inf ammatory syndrome was observed (1 h ESR = 20 mm/h, 2 h ESR = 38 mm/h). Laboratory tests did not identify a metabolic cause for CPPD.

Diagnosis was conf rmed by the analysis of the aspirate from the supraspinatus tendon. Macroscopically, it had a white-yellowish, chalky, f occulent appearance (Fig. 3a). Microscopically, the material was processed by paraf n embedding. In routine staining, the material was formed by amorphous eosinophilic deposits, with small or even large dystrophic basophilic calcif cations, without association of inf ammatory inf ltrate. In Congo red staining, no amyloid deposits were detected. Histological appearance suggested supraspinatus tendon chondrocalcinosis. The bacteriological examination of the aspirate was negative.

Polarized light optical microscopy using Alizarin red staining evidenced birefringent rectangular crystals (Fig. 3b), indicating the diagnosis of calcium pyrophosphate deposition disease. For this staining procedure, the following stages were performed: display of the aspirate on the slide, 10% formol f xation for 1 minute, application of 0.5% alizarin solution for 5-20 minutes, incubation of the slide at 40-50°, dehydration with acetone for 30 seconds and with a mixture of acetone and xylene in equal parts for 30 seconds. Transmission electron microscopy evidenced crystals about 0.5 μm long (Fig. 3c).

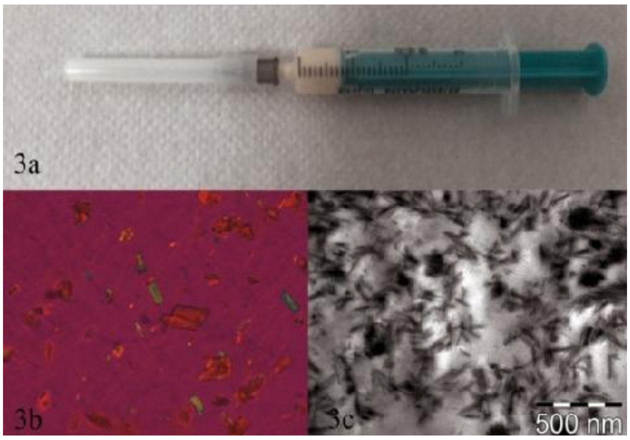

Fig. 3 – 3a. Macroscopic white-yellowish, chalky appearance of the aspirate; 3b. Polarized light optical microscopy using Alizarin red staining evidences positively birefringent rectangular crystals; 3c. Electron microscopic image with crystals of variable sizes (TEM x 80,000).

Locally, betamethasone and lidocaine were concomitantly administered. In addition, the patient received nonsteroidal anti-inf ammatory injections, physiotherapy of the shoulder, kinesiotherapy and massage of the paravertebral cervical spine and left shoulder.

Evaluation of the patient after one month evidenced improvement of pain (on the visual analogue scale from the initial value of 8 to 3) and of shoulder range of motion (active abduction improved from 55 degrees to 110 degrees).

Discussion

It is known that CPPD is rare among persons younger than 50 years of age; its presence under the age of 45 raises the possibility of familial predisposition or a metabolic disease (hemochromatosis, hyperparathyroidism, hypomagnesemia, Wilson's disease, hypothyroidism, gout, acromegaly) (Joshi et al., 2017**).** Given that laboratory tests were negative for a metabolic cause in a patient without a suggestive family history, the presented case can be included in the category of sporadic, rare cases in the literature (Zhang et al., 2011).

In the second place, periarticular involvement is rarely found in the case of CPPD. The literature describes the involvement of the triceps muscle tendons and Achilles tendon (Steinbach, 2004), as well as of the quadriceps and gastrocnemius muscles (Yang et al., 1996). A particularity of the case is therefore the location in the supraspinatus tendon, usually correlated with hydroxyapatite deposition (Chiou et al., 2009; Pereira et al., 2015).

The presented case highlights the importance of imaging examinations and aspirate analysis in establishing the diagnosis of CPPD. Compared to the nodular appearance of the calcium hydroxyapatite deposition, intratendinous calcif cation with calcium pyrophosphate deposition disease is linear or punctate (Steinbach, 2004). The imaging characteristics of this case are however particular compared to the ones found in the literature, also considering that ultrasound assessment detected hyperechoic spots in the supraspinatus tendon of other patients with CPPD disease (Filippucci et al., 2013; Filippou et al., 2018).

Since the aspirate contained tissue (supraspinatus tendon), Alizarin red staining was used to identify calcium pyrophosphate crystals. Routine hematoxylin-eosin staining has a low probability of evidencing birefringent crystals because of the reagent dissolution of the crystals. Studies have proven that using Alizarin red staining does not af ect crystals (Yamakawa et al., 2003).

The primary "take-away" lesson from this case presentation is that CPPD can occur in rare locations, such as the supraspinatus tendon, in young patients, despite the absence of a familial predisposition or a metabolic disease; imaging tests and aspirate analysis are essential for establishing an accurate positive diagnosis.

Conclusions

1. In the case of atypical localization of calcif cations, we should not exclude the calcium pyrophosphate deposition disease.
2. In this case, paraclinical investigations proved to be highly useful in establishing the etiopathogenetic diagnosis and the therapeutic conduct.

Conf icts of interest
There are no conf icts of interest.

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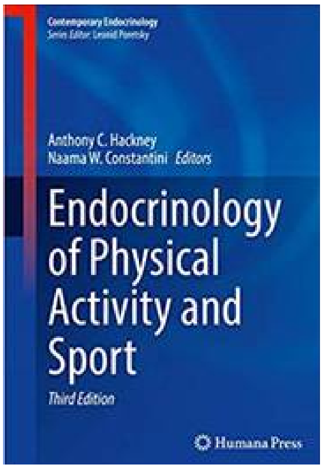
RECENT PUBLICATIONS

Book reviews

Endocrinology of Physical Activity and Sport. Third Edition
Editors: Anthony C. Hackney, Naama W. Constantini
Publisher: Springer, 2020
597 pages; price: €166.39 (paper) / €128.89 (eBook)



After about 20 years from its first publication, at the end of last February, a third edition of the book initially entitled *Sports Endocrinology* was launched by Springer, this time both the two editors and the title being the same as on the occasion of the second appearance.

In their brief preface, the two editors mention that no more than five years have passed from the second edition to the current one. An unusually short period for two successive editions of such a voluminous scientific book in our opinion, which shows both the interest of the topic and the rapid knowledge accumulation in the field. The last reason represents in fact the plausible explanation that among others, the recently released book contains 40 extra pages and two more chapters than the precedent one; 30 instead of 28.

The very complex bidirectional relationship between exercise and the endocrine system has always been of constant scientific interest. However, this interest has dramatically increased over the last decades as a consequence of the steeply growing incidence of obesity and diabetes, along with more and more convincing evidence that regardless of how it is performed, exercise could be particularly helpful for the prevention and treatment of the respective epidemics.

It is sufficient to just have a look at this book's table of contents to understand that the impressive team of no less than 44 contributors – illustrious international experts indeed – have addressed all the critical issues involved in understanding endocrinology and hormonal workings with respect to exercise and sport. And this not only regarding sport for health, but also professional sport, i.e. sport for performance and medals. So that we can undoubtedly say that we are facing a comprehensive encyclopedic text, an up-to-date synthesis of the essential endocrinology topics in the areas of sports medicine, kinesiology, and sports science.

That this work is a really exhaustive one is also proven by the fact that it contains chapters addressing the general aspects of the interrelation and interconditionality between exercise and the endocrine system, as well as chapters which refer to the situation when individuals make an effort of too high volume, intensity, and frequency in pursuing athletic performance. For that purpose, even aspects related to the so-called overtraining and overreaching are treated and clarified.

Otherwise, as expected, most of the topics contained in the previous edition are also present here. It is the case of the chapters dedicated to the effects of exercise on the hypothalamic-pituitary-adrenal axis, on the growth hormone-insulin-like growth factor-I axis, on thyroid function, on diabetes, and on the male and female reproductive systems. Other sections that are maintained are those addressing circadian endocrine physiology, the impact of exercise on the hormonal system of children and older adults, hormones, exercise and bone, or the interrelations between exercise and the immune and endocrine systems, etc. The brand new chapters of this edition present the endocrine implications of relative energy deficiency in sport (17), the role of hormones on exercise-induced muscle hypertrophy (21), metabolic syndrome, hormones, and exercise (29), and the effects of exercise and training on appetite-regulating hormones in obese individuals (30).

Considering the great complexity of the endocrine system itself, the fact that each of the endocrine structures and functions is not only involved in exercise, but is also acutely and chronically influenced by it, that the text presented this time represents the most complete and up-to-date compilation on the topic of "endocrinology of physical education and sport", which is intended for so many current and future professionals in health/medicine and sport, we feel entitled to sustain, without any fear of mistake, that it represents a real editorial event in sports sciences.

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FOR THE ATTENTION OF CONTRIBUTORS

The subject of the journal

The journal has a multidisciplinary nature oriented toward biomedical, health, exercise, social sciences f elds, applyable in activities of physical training and sport, so that the dealt subjects and the authors belong to several disciplines in these f elds. The main rubrics are: “Original studies” and “Reviews”.

The Journal is aimed at adapting the prof le of the journal to scientif c contemporaneity in the f eld of medical and pharmaceutical sciences and interdisciplinary integration with health, physical activity and biopsychosocial rehabilitation.

The journal will have the same contents: editorials, original articles, review articles, case reports, recent publications, events. The journal is open for publication to all members of the national and international scientif c community and of ers the possibility to promote young people involved in research, along with top researchers in the above mentioned f elds.

Regarding “Reviews” the main subjects that are presented are: oxidative stress in physical ef ort; mental training; psycho-neuroendocrinology of sport ef ort; physical culture in the practice of the family doctor; extreme sports and risks; emotional determinatives of performance; the recovery of patients with spinal column disorders; stress syndromes and psychosomatics; olympic education, legal aspects of sport; physical f tness/exercise in the elderly; psychomotricity disorders; high altitude sportive training; f tness; biomechanics of movements; EUROFIT tests and other evaluation methods of physical f tness; adverse reactions of physical f tness; sport endocrinology; depression in sportsmen/women; classical and genetic drug usage; Olympic Games etc.

Among articles devoted to original studies and researches we are particularly interested in the following: the methodo¬logy in physical education and sport; inf uence of some ions on ef ort capacity; psychological prof les of students regarding physical education; methodology in sport gymnastics; the selection of performance sportsmen.

Other articles approach particular subjects regarding dif erent sports: swimming, rhythmic and artistic gymnastics, hand¬ball, volleyball, basketball, athletics, ski, football, f eld and table tennis, wrestling, sumo.

The authors of the two rubrics are doctors, professors and educators, from universities and preuniversity education, trai¬ners, scientif c researchers etc.

Other rubrics of the journal are: the editorial, editorial news, reviews of the latest books in the f eld and others that are presented rarely (inventions and innovations, universitaria, preuniversitaria, forum, memories, competition calendar, portraits, scientif c events).

We highlight the rubric “The memory of the photographic eye”, where photos, some very rare, of sportsmen in the past and present are presented.

Articles signed by authors from the Republic of Moldova regarding the organization of sport education, variability of the cardiac rhythm, the stages of ef ort adaptability and articles by some authors from France, Portugal, Canada must also be mentioned.

The main objective of the journal is highlighting the results of research activities as well as the permanent and actual dissemination of information for specialists in the f eld. The journal assumes an important role regarding the achievement of necessary scores of the teaching staf in the university and pre university education as well as of doctors in the medical network (by recognizing the journal by the Romanian College of Physicians), regarding didactic and professional promotion.

Another merit of the journal is the obligatory publication of the table of contents and an English summary for all articles. Frequently articles are published in extenso in a language with international circulation (English, French).

All the content of the journal is available immediately upon publication and is Open Access.

The Editorial Board of the Health, Sports & Rehabilitation Medicine journal informs its collaborators and readers that access to the journal is open and free. The journal does not have article processing or submission charges.

The journal is published quarterly and the works are accepted for publication in English language. The paper is sent by e-mail at the address of the editorial staf . The works of contributors that are resident abroad and of Romanian authors must be mailed to the Editorial staf at the following address:

Health, Sports & Rehabilitation Medicine
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Website: www.jhsrm.org

Objectives

Our intention is that the journal continues to be a route to highlight the research results of its contributors, especially by stimulating their participation in project competitions. Articles that are published in this journal are considered as part of the process of promotion in one’s university career (accreditation that is obtained after consultation with the National Council for Attestation of Universitary Titles and Diplomas).

We also intend to encourage the publication of studies and research, that include original relevant elements especially from young people. All articles must bring a minimum of personal contribution (theoretical or practical), that will be highlighted in the article.

In the future we propose to accomplish criteria that would allow the promotion of the journal to superior levels according international recognition.

THE STRUCTURE AND SUBMISSION OF ARTICLES

The manuscript must be prepared according to the stipulations of the International Committee of Medical Journal Editors (http://www.icmjee.org).

The number of words for the electronic format:

– 4000 words for original articles;

– 2000 words for case studies;

– 5000-6000 words for review articles.

Format of the page: edited in WORD format, A4. Printed pages of the article will be numbered successively from 1 to the f nal page.

Font: Times New Roman, size 11 pt.; it should be edited on a full page, with diacritical marks, double spaced, respecting equal margins of 2 cm.

Illustrations:

The images (graphics, photos etc.) should be numbered consecutively in the text, with arabic numbers. They should be edited with SPSS or EXCEL programs, and sent as distinct f les: „f gure 1.tif", „f gure 2. jpg", and at the editors demanding in original also. Every graphic should have a legend, written **under** the image.

The tables should be numbered consecutively in the text, with roman numbers, and sent as distinct f les, accompanied by a legend that will be put above the table.

PREPARATION OF THE ARTICLES

1. Title page: includes the title of article (maximum 45 characters), the name of authors followed by surname, work place, mail address of the institute and mail adress and e-mail address of the f rst author. It will follow the name of article in the English language.

2. Abstract: For original articles a summary structured like this is necessary: (Background, Aims, Methods, Results, Conclusions), of maximum 250 words, followed by 3-8 key words (if is possible from the list of established terms). All articles will have a summary in the English language. Within the summary (abstract) abbreviations, footnotes or bibliographic references should not be used.

Background, Aims. Description of the importance of the study and explanation of premises and research objectives.

Methods. Include the following aspects of the study: Description of the basic category of the study: of orientation and applicative. Localization and the period of study. Description and size of groups, sex (gender), age and other socio-demographic variables should be given. Methods and instruments of investigation that are used.

Results. The descriptive and inferential statistical data (with specif cation of the used statistical tests): the dif erences between the initial and the f nal measurement, for the investigated parameters, the signif cance of correlation coef cients are necessary. The specif cation of the level of signif cance (the value p or the dimension of ef ect d) and the type of the used statistical test etc are obligatory.

Conclusions. Conclusions that have a direct link with the presented study should be given.

Orientation articles and case studies should have an unstructured summary (without respecting the structure of experimental articles) to a limit of 150 words.

3. Text

Original articles should include the following chapters which will not be identical with the summary titles: *Introduction* (General considerations), *Hypothesis, Materials and methods* (including ethical and statistical informations), *Results, Discussions* results, *Conclusions* and suggestions. The conclusions should be formulated brief y, without comments extracted from the research, and numbered. Other type of articles, as orientation articles, case studies, Editorials, do not have an obligatory format. Excessive abbreviations are not recommended. The f rst abbreviation in the text is represented f rst in extenso, having its abbreviation in parenthesis, and thereafter the short form should be used.

Authors must undertake the responsibility for the correctness of published materials.

4. References

The references should include the following data:

For articles from journals or other periodical publications the international Vancouver Reference Style should be used: the name of all authors as initials and the surname, the year of publication, the title of the article in its original language, the title of the journal in its international abbreviation (italic characters), number of volume, pages.

Articles: Pop M, Albu VR, Vişan D et al. Probleme de pedagogie în sport. Educaţie Fizică şi Sport 2000; 25(4):2-8.

Books: Drăgan I (coord.). Medicina sportivă, Editura Medicală, 2002, Bucureşti, 2002, 272-275.

Chapters from books: Hăulică I, Bălţatu O. Fiziologia senescenţei. In: Hăulică I. (sub red.) Fiziologia umană, Ed. Medicală, Bucureşti, 1996, 931-947.

Starting with issue 4/2010, every article should include a minimum of 15 bibliographic references and a maximum of 100, mostly journals articles published in the last 10 years. Only a limited number of references (1-3) older than 10 years will be allowed. At least 20% of the cited resources should be from recent international literature (not older than 10 years).

Peer-review process

In the f nal stage all materials will be closely reviewed by at least two competent referees in the f eld (Professors, and Docent doctors) so as to correspond in content and form with the requirements of an international journal. After this stage, the materials will be sent to the journal's referees, according to their prof les. After receiving the observations from the referees, the editorial staf shall inform the authors of necessary corrections and the publishing requirements of the journal. This process (from receiving the article to transmitting the observations) should last about 4 weeks. The author will be informed if the article was accepted for publication or not. If it is accepted, the period of correction by the author will follow in order to correspond to the publishing requirements.

In order to check the quality of articles submitted for publication, the Health, Sports & Rehabilitation Medicine journal applies the method of single-blind peer review (the identity of reviewers, but not authors, is kept anonymous).

Conf ict of interest

The authors must mention all possible conf icts of interest including f nancial and other types. If you are sure that there is no conf ict of interest we ask you to mention this. The f nancing sources should be mentioned in your work too.

Specif cations

The specif cations must be made only linked to the people outside the study but which have had a substantial contribution, such as some statistical processing or review of the text in the English language. The authors have the responsibility to obtain the written permission from the mentioned persons with the name written within the respective chapter, in case the readers refer to the interpretation of results and conclusions of these persons. Also it should be specif ed if the article uses some partial results from certain projects or if these are based on master or doctoral theses sustained by the author.

Ethical criteria

The Editors will notify authors in due time, whether their article is accepted or not or whether there is a need to modify texts. Also the Editors reserve the right to edit articles accordingly. Papers that have been printed or sent for publication to other journals will not be accepted. All authors should send a separate letter containing a written statement proposing the article for submission, pledging to observe the ethics of citation of sources used (bibliographic references, f gures, tables, questionnaires).

For original papers, according to the requirements of the Helsinki Declaration, the Amsterdam Protocol, Directive 86/609/EEC, and the regulations of the Bioethical Committees from the locations where the studies were performed, the authors must provide the following:

- the informed consent of the family, for studies in children and juniors;
- the informed consent of adult subjects, patients and athletes, for their participation;
- malpractice insurance certif cate for doctors, for studies in human subjects;
- certif cate from the Bioethical Committees, for human study protocols;

certif cate from the Bioethical Committees, for animal study protocols.

The data will be mentioned in the paper, in the section Materials and Methods. The documents will be obtained before the beginning of the study. Will be mentioned also the registration number of the certif cate from the Bioethical Committees.

Editorial submissions will be not returned to authors, whether published or not.

FOR THE ATTENTION OF SPONSORS

Requests for advertising space should be sent to the Editors of the “Health, Sports & Rehabilitation Medicine” journal, 1, Clinicilor St., 400006, Cluj-Napoca, Romania. The price of an A4 full colour page of advertising for 2012 will be EUR 250 and EUR 800 for an advert in all 4 issues. The costs of publication of a logo on the cover will be determined according to its size.

Payment should be made to the Romanian Medical Society of Physical Education and Sports, CIF 26198743. Banca Transilvania, Cluj branch, IBAN: RO32 BTRL 0130 1205 S623 12XX (RON).

SUBSCRIPTION COSTS

The “Health, Sports & Rehabilitation Medicine” journal is printed quarterly. The subscription price is 100 EUR for institutions abroad and 50 EUR for individual subscribers outside Romania. For Romanian institutions, the subscription price is 150 RON, and for individual subscribers the price is 120 RON. Note that distribution fees are included in the postal costs.

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