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Original article

Age and the effect of exercise, nutrition and cognitive training on oxidative stress – The Vienna Active Aging Study (VAAS), a randomized controlled trial

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ABSTRACT

The purpose of this study was to investigated the effect of age – over or under life-expectancy (LE) – on six months resistance training alone or combined with a nutritional supplement, and cognitive training by analyzing markers for oxidative stress and antioxidant defense in institutionalized elderly, living in Vienna.

Three groups (n = 117, age = 83.1 ± 6.1 years) – resistance training (RT), RT combined with protein and vitamin supplementation (RTS) or cognitive training (CT) – performed two guided training sessions per week for six months. Oxidative stress, antioxidant defense and DNA strand breaks were analyzed and transformed into an "antioxidant factor" to compare the total effect of the intervention. Physical fitness was assessed by the 6-min-walking, the chair-rise and the handgrip strength tests.

We observed significant negative baseline correlations between 8-oxo-7.8-dihydroguanosine and handgrip strength (r = −0.350, p = 0.001), and between high sensitive troponin-T and the 6-min-walking test (r = −0.210, p = 0.035). RT and RTS groups, showed significant improvements in physical performance. Over LE, subjects of the RT group demonstrated a significant greater response in the "antioxidant factor" compared to RTS and CT (RT vs. RTS p = 0.033, RT vs. CT p = 0.028), whereas no difference was observed between the intervention groups under LE.

Six months of elastic band resistance training lead to improvements in antioxidant defense, DNA stability and oxidative damage, summarized in the "antioxidant factor", however mainly in subjects over their statistical LE. Consuming a supplement containing antioxidants might inhibit optimal cellular response to exercise.

The study was approved by the ethics committee of the City of Vienna (EK-11–151–0811) and registered at ClinicalTrials.gov, NCT01775111.

1. Introduction

The steadily increasing life-expectancy (LE) of humans living in developed countries and consequently the incidence of age-related diseases is already a challenge for the health system. Sarcopenia, the loss of muscle mass and function with aging, as well as the aging process itself, are strongly correlated to increased oxidative damage, which in turn is linked to typical age-related diseases such as cardiovascular disease, cancer, dementia and diabetes [1]. Especially elderly living in institutionalized facilities are experiencing a rapid decline of physical function often accompanied and partly caused by malnutrition and physical inactivity as soon as they change their living situation from "free-living" into a community-dwelling surrounding [2,3].

Resistance training, together with protein supplementation, seems to be most effective to increase muscle mass and strength in the elderly [4]. Especially the use of elastic bands has been shown to be an

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appropriate, versatile and effective tool to safely increase physical performance and muscle quality in older subjects [5–7]. Although there are official guidelines for conducting an effective and health-promoting resistance training program in the elderly [8], outcomes on parameters of oxidative stress and DNA damage after exercise are contradictory; either of improved but also of deteriorated mechanisms was reported [9,10]. Importantly, the acutely increased level of reactive-oxygen-species (ROS) caused by physical activity is an essential messenger to activate redox-sensitive pathways which ultimately improve antioxidant defense and DNA repair mechanisms [11,12]. Therefore the consumption of antioxidants could potentially influence optimal adaptation after exercise and should be considered carefully, especially in the elderly, where a low status of several micronutrients is common [2,13]. A sufficient availability of nutrients, especially antioxidant vitamins, such as vitamin C and E, is recommended to support antioxidant defense mechanisms. However, supplementing these nutrients, in too close proximity to an exercise stimulus, seems to restrain optimal adaptation of the redox-system [14,15]. Interestingly, the very oldest of our society, who are reaching an age beyond current statistical LE, demonstrate a lower incidence of age-related diseases, improved antioxidant defense, better DNA integrity and superior genome stability, although their physical fitness is still lower compared to those below LE [1,16]. This super-aging cohort urges deeper analyses to better understand their unique cellular resistance.

As exercise and nutrients intake seem to have an important effect on oxidative stress, antioxidant potential, DNA stability and physical fitness, it is of eager importance to investigate and optimize nutritional and exercise based strategies in the elderly to increase or at least keep strength and muscle mass until high age.

In the present study we hypothesized that after six months of strength training increased physical fitness improves resistance against oxidative stress as well as against oxidative damage in institutionalized elderly. Supplementing (antioxidant) vitamins and protein should further enhance this protective effect.

2. Methods

The presented data are part of the Vienna Active Ageing Study, which is a multidisciplinary project between the Centre for Sport Science and University Sports, the Faculty of Life Sciences, the Research Platform Active Ageing (all University of Vienna), the Karl Landsteiner Institute for Remobilization and Functional Health (Institute for Physical Medicine and Rehabilitation) and the Curatorship of Viennese Retirement Homes.

2.1. Subjects

Over a time period of 6 months (July 2011 - Jannuary 2012) 117 institutionalized elderly women and men (aged 65–98 years), were recruited from five different senior residencies in the area of Vienna (Curatorship of Viennese Retirement Homes) (Fig. 1). The subjects were mentally (Mini Mental State Examination ≥ 23) and physically (Short Physical Performance Battery > 4) able to participate in this training intervention study. They were sedentary (less than one hour of physical activity or exercise per week) and free of severe diseases that would contra-indicate medical training therapy or measurement of physical performance, including cardiovascular diseases, diabetic retinopathy and regular use of cortisone-containing drugs. Inclusion and exclusion criteria have been described in detail by Oesen et al. [6]. The health condition of all study subjects was assessed by specialists in internal medicine and gerontology. Written informed consent was obtained from all participants before entry into the study in accordance with the Declaration of Helsinki. Subjects were not allowed to take part in any exhausting physical activity within 2 days before the blood sampling and fitness test. All participants followed their medication protocols as prescribed by their physicians. If supplements were consumed before entering the study, details on further intake were discussed with their physicians.

2.2. Study design

The present study design was decribed previously in Franzke et al. [17]. Briefly, study participants were randomly assigned into three intervention groups – cognitive training (CT), resistance training (RT), RT + supplement (RTS) – and matched for gender in a randomized, controlled, observer-blind design. At baseline (T1), after three (T2) and after six months (T3) blood samples were taken as well as physical and functional tests were performed. The current study was conducted to investigate the effect of six months elastic band resistance training, either with or without consuming a supplement containing macro- and micro-nutrients on markers of oxidative stress (malondialdehyde), antioxidant potential (uric acid, ferric reducing ability potential, superoxide dismutase, catalase, glutathione peroxide) and oxidized DNA/RNA (DNA strand breaks, 8-oxo-7.8-dihydro-2′-deoxyguanosine, 8-oxo-7.8-dihydroguanosine) in Austrian institutionalized elderly. With respect to the old age of our subjects (almost 60% were older than their statistical LE [18]) we further analyzed whether there was a different response between subjects over LE compared to subjects at or under LE.

2.3. Resistance training

The resistance training groups (RT and RTS) received two weekly sessions of resistance training, conducted on two non-consecutive days and were supervised by a sports scientist. Training attendance was recorded every session. Exercises were conducted using elastic bands, chairs and own body weight - for detailed training program see supplement of Oesen et al. [6]. The progressive resistance training protocol was designed based on the guidelines of the American College of Sports Medicine for resistance training with older subjects [8]. The about one hour lasting workout consisted of an initial 10 min warm up, a 30–40 min strength training for the main muscle groups (legs, back, abdomen, chest, shoulder and arms) and a 10 min cool down. The participants were motivated and controlled to adapt the resistance of the elastic band (shorter or stronger band) to keep exercise intensity within an effective range. After completing the initial phase of 4 weeks, where one set of 15 repetitions was performed, the intensity and volume has progressively been increased from two sets of light exercises to two sets of heavy resistance.

2.4. Resistance training and supplementation

The RTS group performed the same exercises together with the RT group and additionally received a liquid supplement every morning, as well as directly after each training session. Each drink supplied a total energy of 150 kcal and contained 20.7 g protein (56 energy (En)%, 19.7 g whey protein, 3.0 g leucine, > 10 g essential amino acids), 9.3 g carbohydrates (25 En%, 0.8 BE), 3.0 g fat (18 En%), 1.2 g roughage (2 En%), 800IU (20 µg) of vitamin D, 250 mg calcium, vitamins C, E, B6 and B12, folic acid and magnesium (FortiFit, NUTRICIA GmbH, Vienna, Austria). The intake of the nutritional supplement was controlled at breakfast as well as after the training sessions.

2.5. Cognitive training

The CT groups served as our control group and performed coordinative or cognitive tasks [19] two times per week, equally to the frequency of the RT and RTS groups. This was done to minimize the "bias" of being part of a social group activity.

Participants of all groups were instructed to maintain their regular food intake, which was controlled by food diaries.