

# Exercise Training is Beneficial for Alzheimer's Patients

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## Key words

- activities of daily living
- physical activity
- elderly
- resistance training
- neurological disease

## Abstract

Decreased ability to perform activities of daily living (ADLs) associated with deterioration in physical capacity are key determinants of the poor quality of life and loss of independence of patients with Alzheimer's disease (AD). The purpose of this study was to determine the effects of a 12-week training program (including resistance, flexibility, joint mobility and balance/coordination exercises) for Spanish patients with AD on their i) overall functional capacity (muscle strength and flexibility, agility and balance while moving, and endurance fitness), and ii) ability to perform ADLs. Using a randomized block design,

16 patients were assigned to a training (mean [SD] age: 76 [4] yrs) or control group (73 [4] yrs) (n = 8 subjects [3 male, 5 female] per group). The results showed significant improvements after training ( $p < 0.05$ ) in upper and lower body muscle strength and flexibility, agility and dynamic balance, and endurance fitness (using the Senior Fitness test), gait and balance abilities (with subsequent decrease in risk of falls) (Tinetti scale) and in the ability to perform ADLs independently (Katz and Barthel scores). No changes ( $p > 0.05$ ) were found in the control group over the 12-week period. Exercise training could be included in the overall medical/nursing care protocol for patients with AD.

## Introduction

Alzheimer's disease (AD) is the most common neurological disorder that accompanies the ageing process, demonstrating a growing prevalence in Western countries as life expectancy keeps increasing. It is projected that, unless a cure or prevention is found, AD will affect 14 million people in the United States by the year 2040 [5]. AD is a degenerative brain disease resulting in progressive mental deterioration with disorientation, memory disturbance and confusion, all of which can interfere with the ability to perform activities of daily living (ADLs) [12]. This is a crucial problem for this subpopulation as the loss of their ability to cope with ADLs is the main factor affecting their quality of life [3], institutionalization [16], risk of death [35], and also increases the burden for the caregiver and community [28]. A growing number of studies have linked AD with physical deterioration and reduced muscles mass, resulting in higher risks of falls and fractures, decline in mobility, or poorer quality of life and further loss of independence [9, 21, 34].

Despite the well-established benefits of exercise training in the functional capacity of the elderly [2, 26], comparatively little research has focused on patients with AD. Rolland et al. [31] showed using a noncontrolled design that a 7-week program of endurance exercise training (walking, bicycling) reduced nutritional and behavioral complications and risk of falls in AD patients. Teri et al. [32] demonstrated that a home-based exercise training (performed over a 3-month period) combined with teaching caregivers behavioral management techniques improved physical health and depression in patients with AD [32]. Most recently, Rolland et al. [30] reported the effectiveness of a simple exercise training program (1 hour twice weekly) over a one-year period in attenuating the decline in the ability of these patients to perform ADLs. To the best of our knowledge, this is the only study that has assessed the effects of exercise training on the ability of patients with AD to perform ADLs. Rolland and co-workers included some resistance (strength) training exercises of the lower extremities, yet with no external loads, i.e., repeated stand ups from a chair or lateral elevation of the legs in a

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standing position. Resistance exercise should however be an integral component of any exercise training program in chronically diseased individuals [11]. Indeed, increased muscle mass and strength induced by resistance training result in an attenuated cardiovascular stress response to any given load during ADLs because the load now represents a lower percentage of the maximal voluntary contraction [24]. On the other hand, although both short and long term training studies add important, complementary information to the body of knowledge in the field, relatively short-term controlled training studies (i.e.,  $\leq 3$  months) have a practical advantage. By reporting the early benefits of exercise, indeed, they support the rationale for patients with AD to enter into training programs as soon as possible.

It was therefore the purpose of this study to determine the effects of a relatively short-term (12-week), combined training program (including resistance, joint mobility and coordination exercises) for patients with AD on their i) overall functional capacity (muscle strength and flexibility, agility and balance while moving, and endurance fitness), and ii) ability to perform ADLs.

## Methods



### Subjects

Sixteen patients (10 female, 6 male) participated in this study and were assigned to either a training ( $n = 8$ ; 3 m, 5 f; mean  $\pm$  SD age, body mass and height of  $76 \pm 4$  yrs,  $70.2 \pm 14.1$  kg and  $164.9 \pm 13.0$  cm) or control group ( $n = 8$ ; 3 m, 5 f;  $73 \pm 4$  yrs,  $66.7 \pm 9.5$  kg and  $161.1 \pm 7.9$  cm) following a randomized block, controlled (single blind) design (i.e., to remove the potential confounding effect of gender on physical capacity, before group assignment the patients were divided in two blocks according to their gender). Informed consent was obtained from each participant's closest relatives and the study was approved by the local Human Investigations Committee (Universidad Europea de Madrid, Spain). After the corresponding geriatrician provided consent, subjects from a residential nursing home (Residencia Los Nogales) were deemed eligible for the study if they met each of the following conditions: 1) diagnosed by a trained geriatrician with AD [25] of low-medium grade, i.e., score ranging between 18–23 in the Spanish, validated version for the general geriatric population [18] of the Mini-Mental Status Examination (MMSE) [10]; 2) to have lived in the nursing home for at least 4 months; and 3) free of neurological (other than AD), vision, muscle or cardio-respiratory disorders. The patients' MMSE score before entering the study averaged  $20.1 \pm 2.3$  (training group) and  $19.9 \pm 1.7$  (control group).

### Tests measurements and procedures

All the training sessions and evaluations (including familiarization sessions) of subjects' functional capacity (Senior Fitness test), ability to perform ADLs (Katz ADL score and Barthel ADL index) and gait and balance abilities (Tinetti scale) that are described below were performed inside the aforementioned nursing home.

Before ("baseline") and after the 12-week period corresponding to the training protocol, we performed the following evaluations in the two groups. The *Senior Fitness test*, which is composed of a battery of tests, was used to evaluate the functional capacity of the patients, including the following items [29]: 1) muscle dynamic strength endurance of the legs (30-s chair stand test) and of the upper body (arm curl test using a 2.3 kg [5 pound] weight

for women and a 3.6 kg [8 pound] weight for men); 2) flexibility of the lower (chair sit-and-reach test) and upper body (back scratch test); 3) speed, agility and balance while moving (8-foot up-and-go test); and 4) aerobic endurance (2-minute step test). Besides indicating overall functional capacity, these items are of practical applicability as they are involved in common ADLs such as getting up from a chair, lifting, bending, or stretching. Before the baseline tests, all the items of the Senior Fitness test were preceded by 5 familiarization sessions for all the subjects (spread over a 2-week period) that finished with repeated tests showing significant ( $p < 0.01$ ), high ( $r \geq 0.97$ ) intra-class correlation coefficients for all types of tests. For each subject and test, we took the highest value of the repeated tests.

We used the Katz ADL score [15] and the Barthel ADL index [22] to assess patient's ability to perform ADLs. The *Katz ADL scale* includes six items (eating, transferring from bed to chair, walking, using the toilet, bathing, and dressing) each of which is scored with 0 (i.e., unable to perform the activity without complete help), 0.5 or 1.0 (= able to perform the activity with little help or without any help, respectively) [15]. A sum-score (ranging from 0 to 6) is given for each patient.

The *Barthel index* is an instrument widely used to measure the capacity of a person for the execution of ten basic activities in daily life, obtaining a quantitative estimation of the subject's level of independency [7,22]. The ten items include: eating, transferring from bed to chair, using the toilet, bathing/showering, personal hygiene (tooth brushing, shaving, etc.), dressing, walking, stair climbing, and bowel and bladder control. Each individual item is scored with 0 (i.e., unable to perform without complete help or fecal/urine incontinence), 5 (i.e., able to perform the activity with little help or only accidental fecal/urine incontinence) or 10 (i.e., able to perform without any help or total fecal/urine continency). The sum-score ranges from 0 (i.e., totally dependent) to 100 (totally independent).

We assessed all participants' gait and balance abilities using the *Tinetti scale* [33]. This is a simple, easily administered test that measures a patient's gait and balance. The test is scored on the patient's ability to perform specific tasks related to both abilities. For gait evaluation, the subject stands with the examiner, walks across the room, first at "usual" pace, then back at "rapid, but safe" pace (utilizing usual walking aids) and the following tasks are scored (0, 1 or 2): initiation of gait, step length and height, step symmetry, step continuity, path, trunk sway and walking stance. For balance evaluation, the subject is seated in a hard, armless chair and the following maneuvers are tested (score 0, 1 or 2): sitting balance, getting up, attempts at getting up, immediate standing balance (first 5 seconds), standing balance, "nudged", eyes closed, turning 360 degrees and sitting down. The maximum sum-score of both gait and balance components is 28 points. Patients who score below 24 are at risk for falls, and the risk of falling is high with a score below 19.

### Training protocol

The intervention included a total of 36 programmed training sessions, i.e., three weekly sessions (Monday-Wednesday-Friday) of  $\sim 75$  min duration each over a 12-week period (end-January to end-March 2007). Each patient was recruited from his room by the exercise scientist (see below) before the start of the session, which was performed in a room inside the nursing home. Exercises began at individualized, very light intensities. Music (from the patients' youth years) accompanied each session [30]. Each session was supervised by an exercise scientist

(different than the one performing the pre- and post-intervention evaluations) working with groups of 4 patients and started and ended with a very light 15-min warm-up and 15-min cool-down period, respectively, consisting of walking without reaching breathlessness (on an inside walking trail) and “gentle” stretching exercises for all major muscle groups. The core portion of the training session was divided into joint mobility, resistance, and coordination exercises that were consistently performed in the aforementioned order. Joint mobility exercises focused on shoulder, wrist, hip, knee and ankle joints. Resistance training included nine exercises with elastic medium-resistance bands (3 sets of 15 repetitions each) engaging some of the major muscle groups: chest, biceps, triceps, shoulder, knee extensors, abductor and adductor muscles, and calf muscles. All exercises were performed through the full range of motion normally associated with correct technique for each exercise. Stretching exercises of muscles involved in an exercise were performed at the end of each set of resistance exercises. Coordination exercises were performed with foam balls of gradually decreasing size over the program, e.g., bouncing a ball with both hands, tossing and catching a ball, etc.

Participants assigned to the control group received routine nursing/medical care and did not perform any type of programmed physical activity, except those activities necessary for daily living, e.g., normal ambulation inside the nursing home.

### Statistical analysis

Statistical analyses were performed with the Statistical Package for Social Sciences (SPSS) 14.0 software (SPSS Inc., Chicago, IL, USA). We used a two-factor (group, time) ANOVA with repeated measures to assess the training effects on the patients' functional capacity (Senior Fitness test, Tinetti scale) and ability to perform ADLs (Barthel ADL index). The Tukey test was applied post hoc. For the Katz ADL score (which has a maximum possible score value of 6) we used the nonparametric Mann-Whitney U test to compare baseline and post-intervention values, respectively, between the two groups.

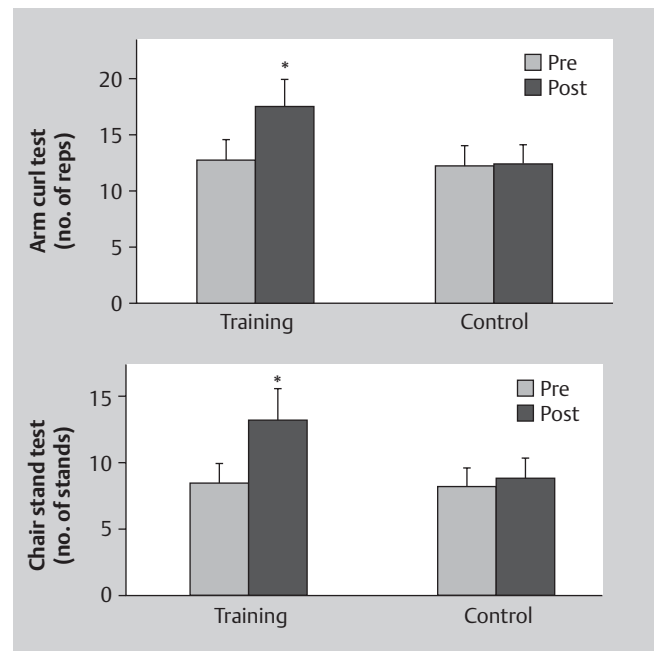
Results are expressed as mean  $\pm$  SD and the level of statistical significance was set at 0.05. The  $\eta^2$  statistic provided estimates of the effect sizes.

### Results

Adherence to training averaged 98.9% (individual values of 100% in five subjects and 97% in three subjects). In all subjects, one Friday session had to be performed on Saturday due to a previously planned leisure trip with all patients of the nursing home. Reasons for missing one of the 36 originally planned training sessions in three patients were fever, mild hyperglycemia and dizziness due to a recent change in medication, respectively. No major adverse effect and no major health problem were noted in the subjects of both groups over the 12-week period. Although no follow-up was systematically conducted in the study participants after the second battery of tests, subjects in the training group were satisfied with the results of the study and reported that they would like to continue a similar training program.

#### Overall functional capacity: Senior Fitness test

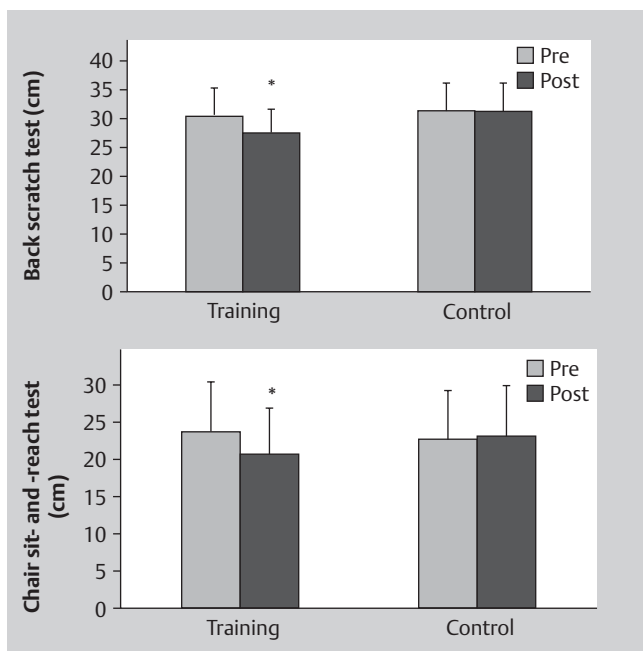
No significant difference ( $p > 0.05$ ) was found between the two groups at baseline in muscle strength endurance of upper (arm curl test) and lower limbs (chair stand test) (● Fig. 1). A signifi-



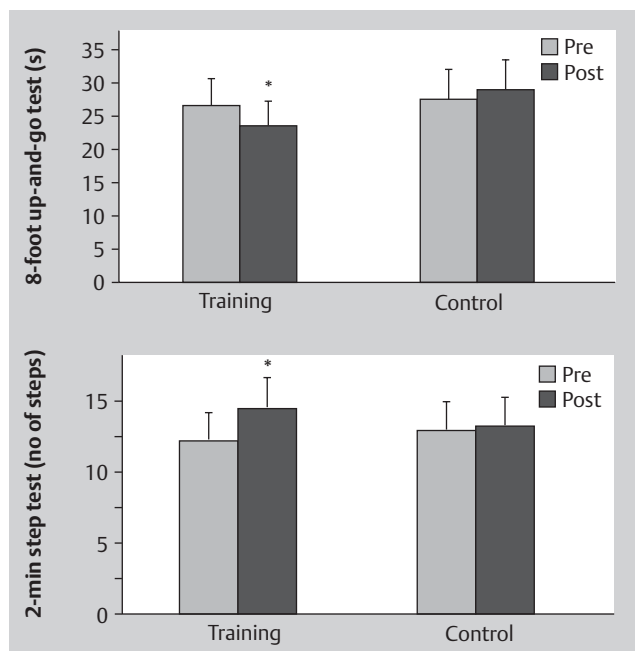
**Fig. 1** Results (mean  $\pm$  SD) of upper (arm curl test) and lower limb muscle strength endurance (30-s chair test). Symbol: \*  $p < 0.05$  for pre- vs. post-intervention values within the training group.

cant main group (i.e., between groups) ( $F_{(1,14)} = 12.90$ ;  $p = 0.003$ ; effect size [ $\eta^2$ ] = 0.480), time (i.e., within groups) ( $F_{(1,14)} = 81.28$ ;  $p < 0.001$ ;  $\eta^2 = 0.853$ ) and interaction (group  $\times$  time) effect ( $F_{(1,14)} = 73.15$ ;  $p < 0.001$ ;  $\eta^2 = 0.839$ ) was found for the arm curl test. We also observed a main group ( $F_{(1,14)} = 9.66$ ;  $p = 0.008$ ;  $\eta^2 = 0.408$ ), time ( $F_{(1,14)} = 81.64$ ;  $p < 0.001$ ;  $\eta^2 = 0.854$ ) and interaction effect ( $F_{(1,14)} = 48.74$ ;  $p < 0.001$ ;  $\eta^2 = 0.777$ ) for the chair stand test. In both arm curl ( $p < 0.05$ ) and chair stand tests ( $p < 0.05$ ), post hoc analysis revealed that post-intervention values were significantly higher than baseline values in the training group whereas no changes were observed in controls ( $p > 0.05$ ). No significant difference ( $p > 0.05$ ) was found between the two groups at baseline in flexibility of upper (back scratch test) and lower body (chair sit-and-reach test) (● Fig. 2). We found no significant main group effect for the back scratch test ( $F_{(1,14)} = 0.471$ ;  $p = 0.504$ ;  $\eta^2 = 0.033$ ), though a significant time ( $F_{(1,14)} = 42.89$ ;  $p < 0.001$ ;  $\eta^2 = 0.754$ ) and interaction effect existed ( $F_{(1,14)} = 36.04$ ;  $p < 0.001$ ;  $\eta^2 = 0.720$ ). For the chair sit-and-reach, no significant main group effect was observed ( $F_{(1,14)} = 0.037$ ;  $p = 0.850$ ;  $\eta^2 = 0.003$ ), though a significant time ( $F_{(1,14)} = 24.31$ ;  $p < 0.001$ ;  $\eta^2 = 0.635$ ) and interaction effect existed ( $F_{(1,14)} = 40.18$ ;  $p < 0.001$ ;  $\eta^2 = 0.742$ ). In both back scratch ( $p < 0.05$ ) and chair sit-and-reach tests ( $p < 0.05$ ), post hoc analysis revealed that post-intervention values were significantly lower than baseline values in the training group (e.g., in the chair sit-and-reach test, a decreased distance [cm] between fingers and toes of the extended leg means increased flexibility). In contrast, no differences were found in controls ( $p > 0.05$ ).

No significant difference ( $p > 0.05$ ) was detected between the two groups at baseline in agility and dynamic balance (8-foot up-and-go test) test and aerobic endurance (2-min step test) (● Fig. 3). We found no significant main group effect for the 8-foot up-and-go test ( $F_{(1,14)} = 1.69$ ;  $p = 0.214$ ;  $\eta^2 = 0.108$ ), though we observed a significant time ( $F_{(1,14)} = 6.24$ ;  $p = 0.026$ ;  $\eta^2 =$



**Fig. 2** Results (mean  $\pm$  SD) of upper (back scratch test) and lower body flexibility (chair sit-and-reach test). Symbol: \*  $p < 0.05$  for pre- vs. post-intervention values within the training group. Note that a decrease in the post-training values of test results denotes an actual performance improvement, i.e., improved flexibility.



**Fig. 3** Results (mean  $\pm$  SD) of agility and dynamic balance (8-foot up-and-go test) and aerobic endurance (2-minute step test). Symbol: \*  $p < 0.05$  for pre- vs. post-intervention values within the training group. Note that a decrease in the time to perform the 8-foot up-and-go test (s) denotes an actual performance improvement, i.e., improved agility and dynamic balance.

0.308) and interaction effect ( $F_{(1,14)} = 36.78$ ;  $p < 0.001$ ;  $\eta^2 = 0.724$ ). No significant main group effect was observed for the 2-min step test ( $F_{(1,14)} = 0.034$ ;  $p = 0.856$ ;  $\eta^2 = 0.002$ ), though a significant time ( $F_{(1,14)} = 14.00$ ;  $p = 0.002$ ;  $\eta^2 = 0.500$ ) and interaction effect existed ( $F_{(1,14)} = 8.96$ ;  $p = 0.010$ ;  $\eta^2 = 0.390$ ). In the training group, post hoc analysis of the 8-foot up-and-go and 2-min step tests revealed that post-intervention values were significantly lower and higher, respectively, than baseline values ( $p < 0.05$ ). In contrast, no changes were observed in controls ( $p > 0.05$ ).

#### Gait and balance abilities (Tinetti scale)

The results of the Tinetti scale (which scores both participants' gait and balance and subsequent fall risk) [33] are shown in **Fig. 4**. No significant difference ( $p > 0.05$ ) was found between the two groups at baseline. No significant main group effect was found ( $F_{(1,14)} = 2.27$ ;  $p = 0.154$ ;  $\eta^2 = 0.140$ ), though a significant time and interaction effect existed (for both effects:  $F_{(1,14)} = 45.13$ ;  $p < 0.001$ ;  $\eta^2 = 0.887$ ). Post hoc analysis revealed that post-intervention values were significantly improved in the training group ( $p < 0.05$ ) whereas no improvement was observed in controls ( $p > 0.05$ ).

#### ADLs tests

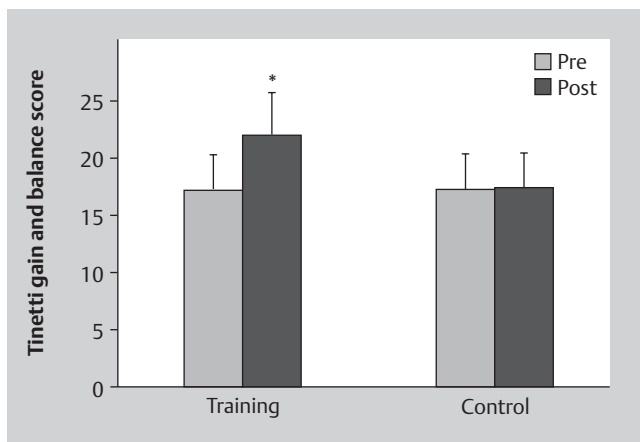
The results of the nonparametric Mann-Whitney U test showed no significant differences at baseline between the two groups ( $p > 0.05$ ) in the Katz ADL score, whereas they revealed significantly higher score values in the training group compared with controls in the post-intervention evaluation ( $p = 0.019$ ) (**Fig. 5**, upper panel).

The results of the Barthel ADL scale are shown in **Fig. 5**, lower panel. No significant difference ( $p > 0.05$ ) was found between the

two groups at baseline. A significant main group ( $F_{(1,14)} = 14.89$ ;  $p = 0.002$ ;  $\eta^2 = 0.515$ ), time and interaction effect was found (for the two latter effects:  $F_{(1,14)} = 89.60$ ;  $p < 0.001$ ;  $\eta^2 = 0.865$ ). Post hoc analysis showed that post-intervention values were significantly improved in the training group ( $p < 0.05$ ) whereas no differences existed in controls ( $p > 0.05$ ).

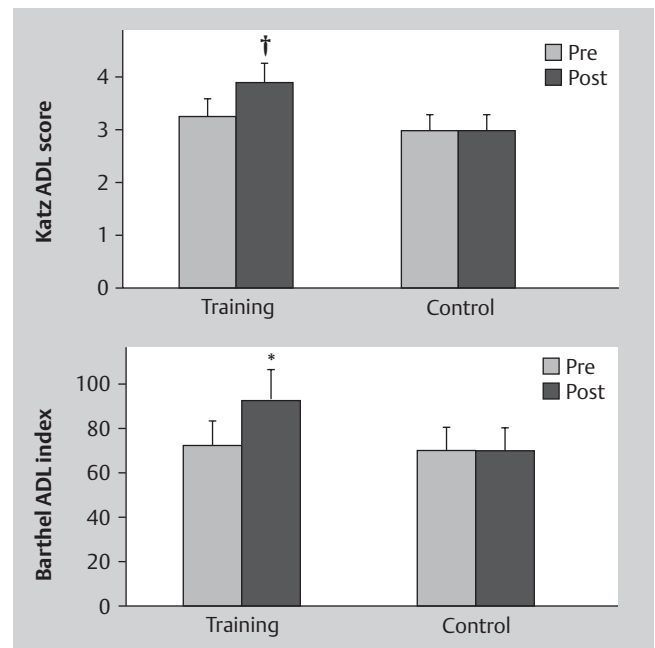
#### Discussion

The main finding of our study was that a relatively short-term (12-week) training program for patients with AD (over 70 yrs of age) combining resistance, joint mobility and coordination exercises entirely performed in a nursing home dwelling with inexpensive equipment, significantly improved their overall functional capacity, i.e., muscle strength, flexibility, agility and coordination while moving (which in turn reduces fall risk) and endurance fitness, with an associated improvement in their ability to perform ADLs independently, e.g., walking, getting up from a chair, transferring from bed to chair, bathing, or dressing. Our data are in agreement with previous research in the field showing the overall health benefits of exercise interventions for patients with AD [19,30,31] and for the elderly (>65 years of age) in general [26]. The improvements observed here after 12 weeks are not population specific as comparable increases have been observed in the functional performance of healthy, sedentary elderly after a 12-week training intervention [1,8]. The efficacy of our training program, which combined resistance, joint mobility and coordination exercises, was reflected by the fact that not only did it attenuate the decline in the patients' ability to perform ADLs, as shown by the study by Rolland et al. [30]: it actually improved such ability significantly over the 12-week



**Fig. 4** Results (mean  $\pm$  SD) of the Tinetti gait and mobility test. Symbol: \*  $p < 0.05$  for pre- vs. post-intervention values within the training group.

period, as reflected by the results of the Katz and Barthel scores, e.g., sum-score of 93 in the Barthel score at post-training, and thus close to 100 (= "total independence" in performing ADLs). The improvement seen here after a 12-week intervention vs. the attenuated decline previously reported after a longer, one-year intervention [30] might be due, at least partly, to the fact that Rolland et al. [30] largely focused on "aerobic" training (i.e., half of the session devoted to walking exercises) whereas here we likely placed a greater emphasis on exercise capabilities that are crucial in ADLs, such as flexibility, neuromuscular coordination and strength of some major muscle groups. Training-induced improvements in such capabilities have important consequences in daily living, i.e., they improve gait-joint kinematics though an increased dynamic range of motion (ROM) in the ankle joint, with a subsequent decrease in fall risk [6]. In this regard, the Tinetti score at baseline was clearly below 19 points (that is, indicating a high risk for falls) in both groups, but after the training program (mean score of  $22 \pm 3$  at post-training) it approached the threshold (= 24 points) above which the risk for falls is negligible and reached the 19–24 score interval (within which the risk of falls persists but is not high anymore) [33]. To our knowledge, only a recent relevant study [30] assessed the effects of exercise training on these patients' ability to perform ADLs. The novelties of our study are the following: we showed that shorter duration programs (i.e., 12 weeks here vs. 1 year in the study by Rolland et al. [30]) are sufficient to induce significant improvements in patients' functional performance and independence during ADLs, which strengthens the rationale for patients with AD who live in nursing homes to enter training programs as soon as possible given the early benefits that can be obtained with this intervention. Thus, not only do exercise training interventions have a low cost-to-benefit ratio in chronic, debilitated patients [20]: relatively early improvements are also possible. We also included resistance exercises (with elastic medium resistance bands) involving some of the main muscle groups in each of the three weekly training sessions. Resistance exercise should be an integral component of any exercise training program in chronically diseased individuals [11]. Indeed, increased muscle strength induced by resistance training results in an attenuated cardiovascular stress response to any given load during ADLs because the load now represents a lower percentage of the maximal voluntary contraction [24]. On



**Fig. 5** Results (mean  $\pm$  SD) of the ability to perform activities of daily living ADLs: Katz score (upper panel) and Barthel index (lower panel). Symbols: †  $p < 0.05$  for the between-group comparison at post-intervention (using the nonparametric Mann-Whitney U test), \*  $p < 0.05$  for pre vs. post-intervention values within the training group.

the other hand, participants in our study underwent a thorough familiarization period before performing the baseline evaluations, especially the strength tests included in the Senior Fitness test battery. A familiarization period allows to eliminate learning effects and to assess the reliability of pre-training tests, both of which are necessary to accurately determine the effects of training on human muscle strength [13]. An additional methodological strength from our study was that all training sessions were directly supervised by an investigator (exercise scientist), a procedure that has been shown to be important in obtaining maximal gains during strength training compared to unsupervised programs [23]. Our findings are of potential clinical relevance as the loss of the ability to cope with ADLs is the main determinant of the quality of life of patients with AD [3], institutionalization [16], risk of death [35], and also burden for the caregiver and community [28]. Alzheimer's disease is commonly associated with physical deterioration and reduced muscles mass, resulting in higher risks of falls and fractures, decline in mobility or poorer quality of life and further loss of independence [9,21,34]. Another clinically relevant finding of our study (together with that of Rolland et al. [30]) is the fact that the ability of patients with AD to cope with ADLs cannot only be increased by an improvement in cognitive function, as previously suggested [17,27]: their ability to perform ADLs can also be increased relatively early by improving their physical capacity, irrespective of the development of their mental capabilities. This is an important finding to support per se the systematic introduction of physical activity programs in patients with AD. In this regard, although the results of cohort studies show that physical activity is associated with better cognitive function and less cognitive decline in later life in healthy humans, more evidence is needed (based on randomized clinical trials) to clearly demonstrate that physical activity may signifi-

cantly reduce the risk of dementia and AD [17]. On the other hand, the training-induced gain in patients' muscle strength was of practical applicability, as reflected by their improved ability to perform lower-body functional living tasks that involve rapid movements as rising from a chair (i.e., the chair stand test). Important physical abilities such as balance, coordination, maximal strength and the ability to generate torque are performance determinants in the aforementioned functional task [13]. Performance during this type of task is indeed impaired by ageing-induced decline in joint function (relative to hip, knee, and ankle torque) and/or decrease in the ability to recover balance after perturbation or to carry out time-critical actions requiring moderate-to-substantial strength [13]. Finally, adherence to our training program was nearly 100%, showing the feasibility of this type of exercise intervention and how well it is tolerated by patients.

In summary, a relatively short-term (12-week) training program for patients with AD including resistance, joint mobility and coordination exercises significantly improved their overall functional capacity and their ability to perform ADLs independently. We suggest that, until a cure or prevention is found for this disease, this type of simple and inexpensive intervention could be included in the overall medical/nursing care protocol for these patients.

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