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ORIGINAL ARTICLE

A single blind randomized controlled trial of global postural re-education: Cognitive effects on Alzheimer disease patients

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Abstract
Background and objectives: Based on the Alzheimer disease (AD) prevention and slowing down, this study has shown interest in evaluating the effects of Global Postural Reeducation (GPR) on the cognitiveness of individuals with AD. It is important to verify that by modifying and improving postural attitudes through GPR, a better concentration of cognitions in older people is achieved, increases self-awareness and proprioception in comparison with the effects of frequent therapies implemented in elderly centers.
Methods: A randomized controlled clinical trial with parallel assignment and single blind outcomes assessment analysis was deployed. 135 patients with AD (46 male and 89 female; average age = 80.7; SD = 5.32) were randomly allocated to either the GPR group or control group. The patients in GPR group underwent 2 weekly/30–40 min sessions each for a period of 24 week versus the control group that did not receive any specific therapy except of residences daily conventional protocol exercises. To evaluate the cognitivity of both groups were used the Mini Mental State Examination questionnaire (MMSE); for the depression were Geriatric Depression Scale (GDS) and Neuropsychiatric Inventory (NPI), for the quality of life was Quality of Life in Alzheimer's Disease (QoL-AD) and for the autonomy and equilibrium were Barthel Index (BI) and Tinetti Scale (TS).

Abbreviations: AD, Alzheimer's disease; GPR, Global Postural Reeducation; MMSE, Mini Mental State Examination; GDS, Geriatric Depression Scale; QoL-AD, Quality of Life in Alzheimer's Disease; BI, Barthel Index; NPI, Neuropsychiatric Inventory; TST, inetti Scale; NINCDS-ADRDA Criteria, National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association; T0, Pre Test; T1, Post Test.

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Results: The experimental group showed a significant increase in the cognitive abilities in the end of treatment compared with control one ($p < 0.005$). Beyond this, statistically significant results were achieved concerning the variables such as: quality of life, depression, neuropsychological symptoms, autonomy, and equilibrium ($p < 0.005$ in all cases) by comparing the difference between groups and effect size results.
Conclusion: This study demonstrates feasibility concerning GPR on individuals with AD.

Introduction

Because of the aging population, the emergence of Alzheimer's disease (AD) cases is growing rapidly, thus, AD is a concern for public health. Among the most studied risk factors is the decline of cognitive abilities which represent the progressive deterioration of intellectual functions. It has been noted that cognitive decline is a physiological process that occurs after the age of 70–80 as a result of brain cell aging.[1] This fact can be considered as a risk factor for the dementia if this phenomenon occurs before the above mentioned age, and especially if the other affected element is memory. As of today, some of the most effective strategies to combat dementia include vascular risk factor control, cognitive activity, physical activity etc.[2]

Based on the disease prevention and slowing down, this study has shown interest in investigating and evaluating the effects of physical activity on the cognitiveness and perception of individuals with AD. Physical activity is an extremely simple and economical therapy and tool, able to produce scientifically proven benefits.[3] Correspondingly, the practice of physical exercise can positively influence cardiovascular, respiratory, hormonal and neurological levels.[4] Meanwhile from the latest advances in neuro-imaging techniques, physical exercise has shown that structural and functional brain changes are noticeable.[5] Comparatively the connection of physical exercise with cognitive capability has been strengthened recently in respect of observational and epidemiological studies prospective.[6–9]

An effective therapy for the regeneration of muscular and articular tension, relaxation and anxiety management, psychosomaticity, and globality is the one developed from Philippe Emmanuel Souchard's named Postural Global Re-education (GPR).[10] This method has been developed since 1981 and is based on the formation of muscular kinetic glands that may be encountered with their cuts influenced by different individual behaviors, wrong postures, or psychological problems. The GPR's aim is prolonged muscle relaxation and contraction of antagonistic muscles by avoiding postural asymmetry. It is indicated for various diseases, such as morphological problems, articular problems, post traumatic problems, respiratory problems, neurological spastic problems and sporting problems. Moreover the existence of many studies supports the theoretical basis of this method and its clinical effectiveness.[11–13] Thus, specific exercises to improve muscle strength, mobility and joint stability, the sensory dysfunction that is reflected in the decrease of proprioception, are the core of rehabilitation. Furthermore, it is essential to educate the patient on its anxiety management concerning the need for the rest of life as well as on the importance of articular economy and relaxation.[14]

In this context the objective of this study is to evaluate the tolerability and efficacy of GPR in the improvement of such domains: physical, cognitive, psychological, behavioral and quality of life of patients with AD. Aiming to evaluate the postural benefits of the above mentioned technique we hypothesized its functional and psychological improvements despite the progressing disease and alteration of medication plan of elders with AD.

Methods

Study design

A single blind assessment in the randomized controlled trial in parallel groups was conducted through a masked evaluator during 6 months with pre–post tests (T0–T1) executed at a baseline and after 24 weeks of treatment, by having in focus the evaluation of GPR therapy effects on cognitive, proprioceptive, depressive, autonomy, gait and life quality of the above mentioned subjects. Concretely, the study protocol was registered in Clinical Trial Registry of the U.S. National Institute of Health (*Clinical Trials.gov Identifier: NCT03732053 retrospectively registered).*

Participants

A total of 135 subjects with AD in the mild or moderate phase participated in the study during December 2016–July 2017 period from which 90 pertain to research group and the rest to the control one. The examined subjects were selected in the senior residences of Tirana (Albania), Murcia and Malaga (Spain) according to the NINCDS-ADRDA criteria,[15] based on the medical documentation of dementia with differential diagnosis of AD aged between 67 and 92 years. These data are shown in the Fig. 1 flow chart. All participants signed the informed consent and their family members were also informed concerning the purpose of the study. Correspondingly the data were provided by a referential physical therapist for each center that was in charge of including or excluding patients who performed the above mentioned technique. Then the collected results were given to a single external evaluator who provided the study 'data-pool'.

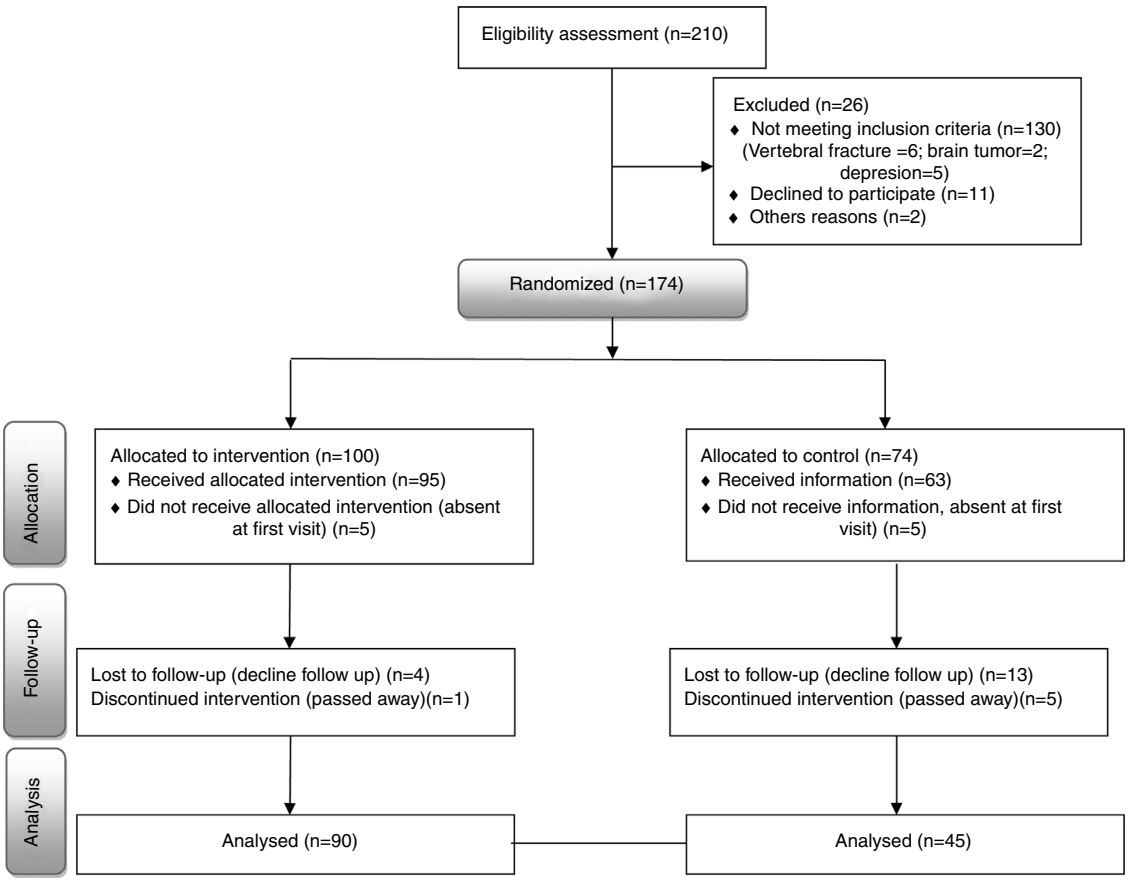

Figure 1 Flow chart of participants.

The study was validated and approved by the Ethics Committee of Catholic University of Murcia (N° 6573) in full compliance with ethical standards of the Committee on Human Experimentation of the institution in which the examinations were done as well as with the ones of Helsinki Declaration of 1975, as revised in 2008.

Inclusion criteria

older than 40 years of age, clinical diagnosis of Alzheimer Disease, either gender, intellectual disability, cognitive impairment, able to autonomously perform daily activities, no presence of any other neurological and psychological disease.

Exclusion criteria

Spondylolisthesis, fibromyalgia, previous back surgery, vertebral fracture, presence of brain tumors, presence of psychiatric disease, depression symptoms or ictus.

Neither inclusion nor exclusion criteria were changed during the trial.

Outcome measures

Primary outcomes: cognitive abilities measurements

The cognitive evaluation was performed by using the standardized neuro-cognitive test MMSE. Since the latter is a simple and effective tool able to monitor the cognitive abilities of a healthy person, and furthermore to assess the behavioral evolution of a subject affected by dementia of Alzheimer type:

1. Mini Mental State Examination (MMSE).[16] The version of 30 elements was used to obtain a global measure of cognitive function. Concretely, it allows obtaining a global score of the level of cognitive impairment by evaluating different cognitive areas: spatio-temporal orientation, memory, executive functions, language (repetition, comprehension, oral and written denomination) and practice-constructive abilities (referring to such evaluation: less than 5 points/terminal phase, 9–11 points/dementia, 12–22 points/deterioration, 23–26 points/pathological suspicions, 27–30 points/normal state).

Secondary outcomes: quality of life, depression, autonomy and equilibrium

Afterwards, patients underwent the following functional tests:

1. Quality of Life in Alzheimer's Disease (QoL-AD).[17] It consists in 13 elements referring to the perception that patients have concerning various aspects of their life: mood, health, cognition, environment and functional capacity. The estimated range of scores is 13–52, were higher scores indicate a better life quality.

2. The Geriatric Depression Scale (GDS).[18] The version of 15 articles was used, which given its length can be validly and reliably resolved by patients themselves in the quality of a self-report questionnaire aiming to investigate the possible presence of depressive symptoms. This questionnaire is specifically designed for elderly people and is widely used for the evaluation of depressive symptomatology in geriatric age since 1980. It scores from 0 (positive to depressive symptoms) to 15 (negative to depressive symptoms).
3. Barthel Index (BI).[19] It is used to measure performance in the basic activities of daily life. This index provides an indicative score concerning the possibility of eating, dressing, managing personal hygiene, bathing, using the toilet, moving from the chair to the bed and back again, walking slowly, up and down the stairs, control defecation and urination (scored 15, 10, 5, or 0). The maximum score is assigned if the patient performs the task in a completely independent manner. While the maximum score used is 100 points and refers to the patient's independence in all basic daily living activities.
4. Neuropsychiatric Inventory (NPI).[20] This test includes 12 symptoms scored according to the phenomenon severity and frequency. It is an instrument specifically designed for the assessment of psycho-behavioral disorders in individuals with cognitive impairment. For each individual scale, correspond one of the 12 neuropsychiatric syndromes and finally by multiplying the frequency and gravity the total score is achieved (scored from 0 to 12); since each scale is composed of multiple questions, it must be multiplied the frequency and severity for each question by considering the highest value as the syndrome score. The overall score is obtained by summing the symptoms total scores (product of frequency and severity). The score range is 0–144.
5. Tinetti Scale (TS).[21] The equilibrium subscale has been applied, which consists in 7 elements and has a score between 0 and 13. Highest scores indicate a better balance. It is a valid and important means of rehabilitation used in the hospital, nursing homes and private studios with the purpose of assessing the patients balance and path.

Complementary study variables:
These variables are specified by the subject of research itself or by data obtained through medical team or clinic files. They reflect that kind of data which cannot be collected through standardized tests. In this regard the first group of independent variables includes: gender, level of education, Alzheimer's phase, daily training (as: aerobic exercise, walking, and arts/animations, refer to Table 1).

a. Randomization

As previously mentioned, the selected residential centers are in significant distances from each other and to easily manage as well as to avoid study errors, a separate encoding (A, B, C, D) was allocated to them, which is further followed with a specific patient code. Participants are assigned through a simple randomization into experimental and controlled groups by an external assistant according an automatic software procedure. All participants received 48 treatment sessions scheduled on special days, 2 days a week, for 24 weeks. Subsequently the results were collected by a verbal external evaluator concerning participants' treatment distribution.

b. Experimental intervention

The intervention implemented to the experimental group patients with AD was the GPR postural therapy which lasted about 30–40 min in repeated sessions of 2 meetings per week pursued as per 6 months respectively by making 48 sessions in total. It consists in a global neck pompage, relaxed lying patient associated with deep diaphragmatic breathing and legs in shape of frog during the first period. During the second period the position of patients with AD was modified, it was addressed by changing the position of the legs (tied with a rope in the angle with Pelvis 90°) and in the last period of therapy, the position changed again with legs relying on pelvis approximately 90° and the knees in 70° on pillows as auxiliary; always patient lying supine in bed therapy.

c. Control intervention

Referring to the therapeutic intervention of control group patients it can be underlined that the same residential conventional exercises were pursued, such as: 30–40 min of physical exercise, proprioceptive, equilibrium stimulus, aerobic and walking.

In addition all outcome measures were captured at the beginning and in the end of intervention (after 24 weeks) from a blind estimator considering that the trial was drafted and implemented according to CONSORT guideline.

d. Statistical procedure

The statistical analysis was performed by using Statistical Package for Social Sciences – SPSS 21 Windows version, with the intention-to-treat the elaborations according to the last value forward method. In the first moment there were established the treatment variables. Thus a descriptive statistical analysis (frequency, mean, standard

Table 1 Complementary study variables.

Variable	Description	Category	Response
Gender	Important for the study analysis	Dichotomic	Male vs. female
Level of education	Important for the cognitive tests	Qualitative	Basic (B) vs. medium (M) vs. high (H)
Alzheimer phase	Important for the treatment	Qualitative	Mild (M) and moderate phase(MD)
Daily training	Social insertion	Dichotomic	Aerobic exercise, walking, arts/animations

deviation) was performed for clinical, neuropsychological, functional and psycho-behavioral variables at baseline and in the end of study, while quantitative variables were expressed as mean plus standard deviation. Additionally, two-tailed Student *t*-tests were performed for continuous variables and Chi-square tests for categorical ones in order to evaluate the homogeneity of 2 groups in baseline. Furthermore variables normality diagnosis has been realized through Kolmogorov–Smirnof-test for $n \square 50$. Nonetheless, the repeated measures of mixed model were used to determine the timing treatment effect (on behalf of pre-test T0 and post-test T1 outcomes) within-subjects and type of treatment between-subjects. And intuitively the main hypothesis of interest was the one of interaction group-by-time. In this regards, between-groups effect size was calculated by using Cohen's *d* coefficient where an effect size greater than 0.8 was considered large, around 0.5 moderate and less than 0.2 small. The statistical examinations were performed at 95% confidence level and correspondingly a *p*-value lower than 0.05 was considered statistically significant.

Results

Closely referring to December 2016–July 2017 period evaluations, 210 patients were assessed eligible for this study and the sample composed by 174 patients was randomized after the application of exclusions criteria; of whom 16 participants were absent at first visit, 17 declined to be followed up and 6 patients passed away (intention-to-treat analysis, Fig. 1). By this way, outcome measurements were completed on 135 participants. Correspondingly, the sample was composed of 34% male ($n = 46$) and 66% female ($n = 89$) gender around the age of 67–92 (average age = 80.76, SD = 5.32). Specifically, to the control group (CG) which consists in 38% male ($n = 17$) and 62% female ($n = 28$) aged 73–92 years (average age = 81.87, SD = 4.83) was assigned the usual rehabilitation treatment while to 90 participants of the experimental group was assigned the GPR treatment (Table 2).

Comparatively must be added that no adverse effects were detected during the application of GPR treatment and none of patients altered the medication plan during this study.

Primary outcomes: cognitive abilities

Time × group interaction factors in baseline adjusted mixed models resulted to be significant in the cognitive function measured over the MMSE [$F(1,132) = 3118.9$, $p = 0.000$, partial $\eta = 0.47$]. Meanwhile the post hoc analysis indicated that patients receiving GPR intervention experienced a significantly greater improvement in cognitively, comparing with those who received the control intervention at baseline and after the follow up [mean and 95% CI, GPR/G, 0.6 (0.9–0.3), $p = 0.003$; CG, 1.7 (1.3–2.1), $p = 0.008$]. Between groups effect sizes were higher during all periods ($d > 0.8$) (Table 3).

Secondary outcomes

The outcomes related to QoL-AD questionnaire were divided and analyzed in two sub-scales, between caregivers and patients. Respectively, Qol-AD/C showed a significant effect of time × group [$F(1,132) = 86.4$, $p = 0.000$, partial $\eta = 0.39$]. Then, the post hoc analysis showed that GPR group participants experienced a significant improvement regarding the quality of life reported by the caregivers after 24 weeks of follow-up ($p < 0.02$ in all cases) compared to the CG which mean score decreased through time (Table 3).

The same analysis was done with QoL-AD/P and was again referred a significant time × group interaction [$F(1,132) = 72.2$, $p = 0.000$, partial $\eta = 0.35$]. Even in this case, the post hoc analysis showed a significant improvement of the GPR group after the follow-up concerning QoL-AD questionnaire ($p < 0.03$ in all cases) compared with CG one which the mean score decreased through 24 weeks.

Also the GDS outcomes ascertained a significant time × factor interaction [$F(1,132) = 110.1$, $p = 0.000$, partial $\eta = 0.45$] and the post hoc analysis showed a significant

Table 2 Baseline demographics for both groups.

	Characteristic	GPR group ($n = 90$)	Control group ($n = 45$)	*p*-Value
Demographics	Age (y), SD	80.21 (5.4)	81.9 (4.8)	0.089
	Female sex, *n* (%)	61 (67%)	28 (62%)	0.524
	Level Education M (%)	80 (88.9%)	27 (60%)	0.204
	Alzheimer PhaseMD (%)	54 (60%)	23 (51.1%)	0.089
Outcomes, SD	MMSE	21.2 (2.7)	19.4 (3.9)	0.003*
	Qol-AD/C	33.7 (4.8)	32.7 (7.8)	0.356
	Qol-AD/P	33.8 (5.2)	34.2 (6.3)	0.712
	GDS	5.3 (2.1)	8.4 (3.2)	0.000*
	BI	92.3 (9.4)	68.6 (21.7)	0.000*
	NPI	18.9 (4.5)	17.3 (6.3)	0.092
	TS	10.9 (1.5)	7.9 (3.3)	0.000*

Abbreviations: SD, standard deviation; Alzheimer Phase MD, moderate cognitive Alzheimer phase (2 levels analyzed: mild and moderate); Education Level M, medium level of education (3 levels in tot analyzed: high, medium, basic); Qol-AD/C, Quality of Life in Alzheimer's Disease/Caregivers report; Qol-AD/P, Quality of Life in Alzheimer's Disease/Patients report; GDS, Geriatric Depression Scale; MMSE, Mini Mental State Examination; NPI, Neuropsychiatric Inventory; BI, Barthel Index; TS, Tinetti Scale.

Table 3 Mean (SD) for outcome measures at all study visits for each group, mean (SD) difference within groups and mean (95% CI) difference between groups.

Outcome	Study sample				Difference within groups		Effect Size	Difference between groups
	Baseline/T0		24 weeks/T1		T1 minus T0		24 weeks	T1 minus T0
	GPR ($n=90$)	CG ($n=45$)	GPR ($n=90$)	CG ($n=45$)	GPR ($n=90$)	CG ($n=45$)	Cohen's d	GPR − CG
MMSE	21.2 (2.7)	19.4 (3.9)	21.9 (2.81)	17.7 (3.4)	0.66* (0.14)	1.71* (0.2)	1.3	2.6* (2.1, 3.09)
QoLAD/C	33.7 (4.8)	32.7 (7.8)	35.3 (5.3)	30.4 (7.1)	1.57* (0.25)	2.28* (0.35)	0.7	3.9* (3.1, 4.7)
QoLAD/P	33.8 (5.2)	34.2 (32.1)	35.5 (5.4)	32.1 (6.02)	1.63* (0.258)	2.13* (0.36)	0.6	3.7* (2.8, 4.6)
GDS	5.3 (2.1)	8.4 (3.2)	4.1 (2.1)	9.2 (2.4)	1.22* (0.15)	0.8* (0.22)	−2.2	2.8* (3.4, 2.3)
BI	92.3 (9.4)	68.6 (21.7)	93.6 (8.5)	65.3 (20.6)	1.33* (0.39)	3.33* (0.55)	1.8	6.8* (5.2, 8.4)
NPI	18.9 (4.5)	17.3 (6.3)	15.6 (3.9)	21.5 (6.3)	3.36* (0.24)	4.13* (0.35)	−1.1	7.2* (8.04, 6.4)
TS	10.9 (1.5)	7.9 (3.3)	11.9 (1.4)	7.51 (3.3)	0.96* (0.09)	0.44* (0.13)	1.7	1.7* (1.3, 2.1)

Abbreviations: GPR, Global Postural Reeducation Group; CG, control group; SD, standard deviation; T0, baseline time; T1, 24 weeks post intervention; MMSE, Mini Mental State Examination; Qol-AD/C, Quality of Life in Alzheimer Disease/Caregivers; Qol-AD/P, Quality of Life in Alzheimer Disease/Patients; GDS, Geriatric Depression Scale; BI, Barthel Index; NPI, Neuropsychiatric Inventory; TS, Tinetti Scale.

difference after 24 weeks of intervention ($p=0.000$ in all cases).

In the same line remained even BI outcomes, as time × group interaction demonstrated a significant improvement of the autonomy of participants [$F(1,132)=74.2$, $p=0.000$, partial $\eta=0.36$]. Its post hoc analysis showed a significant improvement of autonomy after 24 weeks of follow-up ($p=0.000$ in all cases).

Moreover NPI outcomes of time × group interaction showed a significant improvement of neuropsychological aspects [$F(1,132)=314.3$, $p=0.000$, partial $\eta=0.70$], where post hoc analysis revealed significant in all cases ($p=0.000$). Ultimately, the last TS outcomes as per time × group interaction demonstrated a significant improvement of equilibrium [$F(1,132)=83.9$, $p=0.000$, partial $\eta=0.38$] with significant post hoc analysis ($p=0.000$ in all cases). (Table 3).

Discussion

The efficacy of GPR method in patients with AD in this research has been evaluated during 24 weeks time period considering that sessions were held 2 times a week. In this merit, the analysis performed evidences an improvement in all the variables studied (cognition, mood, behavioral disorders, functional status, balance and quality of life) by highlighting the novelty in the ground.

Because unlike other physical therapies with a competitive orientation, which mainly seek the development of strength, endurance and extreme dexterity, the GPR trains the subject to be focused on the sensations that come from his body during a movement or while taking a posture.[22,23]

In addition it can be affirmed that GPR results useful concerning the proprioception improvement by emphasizing also the improvement of quality of movement unlike other rehabilitative therapies (e.g. pilates, chinotherapy etc.).[24] Indeed it uses the breath as a tool to change not only posture, but even the affective state. All this can contribute in order to have significant benefits in different areas (motoric, proprioceptive, respiratory and cognitive-affective ones).[25] Notwithstanding, this therapy requires a personalized therapeutic approach adapted to the specific needs of each patient by promoting greater effectiveness.

Marques et al., and Teodori et al., argue that in patients suffering pain during postural changes, GPR has proven to be effective even in postural and symptomatic improvements, but beyond the latter these evidences cannot significantly demonstrate the results.[25,26] Meanwhile according to Vanti et al., and Cunha et al., is proposed that GPR therapeutic sessions may be applied to conservative treatments of muscular-skeletal, rheumatic or cognitive diseases at the initial or chronic stage.[27,28]

Under the above mentioned circumstances worth to be underlined that the tolerance was very good and matching results are valuable because they provide useful data for developing controlled studies with this therapy. Moreover, considering that this is a pioneering study, it suggests that regardless of age GPR is a useful technique in treating patients with AD.

Referring to the research results, it is noted that control group (CG) presents lower cognitive levels compared to the GPR one (MMSE 19.4 vs. 21.2). Also the level of education in the CG group is lower compared to GPR (Education Level M 60% vs. 88.9%, Table 2).

Specifically, the developed statistical evidences of QoLAD/C vs. QoLAD/P caught the attention by demonstrating that QoLAD referred by caregivers was more effective than QoLAD referred by patients. Basically this is what we wanted to enable through the research undertaken, meaning comparing interpretations from two different groups on the same questionnaire.

But it should be mentioned that QoLAD/C results retrieved even were more efficient after 24 weeks compared to those of QoLAD/P (see Table 3), in RCT, they can be interpreted as study limits by admitting in any case that the test between subjects scores adjusted at baseline, does not affect the final results.

In this light it must be added that the results obtained from this study represent a stimulus for further research in this interesting and conservative treatment area. In

particular, it would be interesting to investigate the effectiveness of GPR in the pathologies covered by this study with the aid of additional randomized controlled trials as well as to expand the research into other neurological, rheumatic, prophylactic, musculoskeletal or other psychological, painful spine and limb disorders, by also comparing the results of this technique with those of other physio-chinesitherapy procedures.

Limits

The potential bias of the study is represented from the fact that randomization does not allow the sample homogenization; GPR group presented since at baseline the highest level of MMSE, BI, QoL/AD. Anyway after the adjustment of between-groups statistical analysis baseline scores is observed that the between groups inequality did not affect the study results.

From the other hand Tinetti Scale was not fully applied since only its balance assessment sub-scale fulfills the purpose of this study.

Another limit of the study is the geographic location of the elderly centers by recognizing some of them did not meet the criteria concerning the sample recruitment. Meaning that, a good part of the patients lacked differential diagnosis of Alzheimer's Disease and properly for this reason the study was spread in 3 different cities like Tirana (Albania), Murcia and Malaga (Spain).

The assignment of patient recruitment sites was not random, but closely related to professionals' expertise in postural therapy and obviously there where the access was permissible.

It should also be taken into consideration that postural technique requires individual sessions and special treatment rooms; they averagely last from 30 to 40 min in the elderly with a repetition frequency of 2 times per week in order to avoid the imbalance, headaches and especially the latter in cases of postural sessions extension.

In studies where therapies are applied in short-sessions there is much to be discussed as well as why 30–40 min of postural treatment sessions in some patients who practiced for the first time treatment were not very comfortable especially in cases when anxiety or depression symptoms were present. In this context the treatment duration was one of the reasons related to therapy abandoning by consideration also the effect of patient concentration and age as a disadvantage.

Conclusion

This study confirms the validity of a postural technique approach such as that of controlled and supervised GPR as well as the indication of an active lifestyle for subjects with mild and moderate AD but does not prove that this therapy is effective; throughout it can demonstrated feasibility and promise, but larger randomized controlled trials are needed to provide proof that GPR therapy is effective (and safe).

However, the idea of this study is that GPR acting broadly on the physical and psychological well-being of the elderly person with AD, can improve many metabolic and physiological aspects of the human body, thus allowing it to have a ''better aging'' process.

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Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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