

CLINICAL SCIENCE

Physical activity attenuates neuropsychiatric disturbances and caregiver burden in patients with dementia

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INTRODUCTION: A significant benefit from physical activity has recently been described in some patients who suffer from neurodegenerative diseases.

OBJECTIVE: To assess the effects of physical activity on neuropsychiatric disturbances in demented patients and on the mental burden of their caregivers.

METHODS: Assisted by a public geriatric psychiatry clinical unit, we studied 59 patients with dementia. Patients were divided into three groups according to their diagnosis and level of physical activity. Data were assessed through a semi-structured interview. Patients were evaluated with the Neuropsychiatric Inventory, the Mini-Sleep Questionnaire and the Baecke Questionnaire. The data were statistically analyzed using the Mann-Whitney U test and linear regression, with the level of significance set at 5%.

RESULTS: Patients with Alzheimer's or vascular dementia who engaged in physical activity had fewer neuropsychiatric symptoms than those who did not. When compared to the control group, the caregivers of patients with vascular dementia who engaged in physical activity had a reduced burden.

CONCLUSION: The regular practice of physical activity seems to contribute to a reduction in neuropsychiatric symptoms in dementia patients and to attenuate the burden of the caregivers of those patients.

KEYWORDS: Dementia; public health; exercise therapy; geriatric psychiatry; caregivers.

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INTRODUCTION

Dementia is an important public health problem, which is growing in both prevalence and complexity, particularly in developing countries. In Brazil, the prevalence of dementia has reached 7.1% for people over 65 years of age. Among these dementia patients, 54.1% were diagnosed with Alzheimer's disease, 9.3% with vascular dementia, and 14.4% with mixed dementia (Alzheimer's plus vascular).¹ Classical dementia is characterized by a persistent and progressive impairment of cognitive functions. This impairment leads to problems such as memory decay, aphasia, agnosia, apraxia, and executive dysfunction, all of which interfere with daily living. Dementia may impair the subject in different ways, but the most

common symptom pattern begins with a progressive difficulty in remembering new information. This difficulty occurs because of the disruption of cells in the areas of the brain involved in constructing new memories. Furthermore, dementia is associated with losses of judgment, orientation, and ability to understand and communicate effectively, and changes in personality and behavior.²⁻³

In addition to cognitive decline, neuropsychiatric phenomena, also called behavioral and psychological symptoms of dementia (BPSD) by the International Psychiatric Association Consensus Statement, frequently occur, with a prevalence of 10 to 73%.^{4,5} A Brazilian study has reported a BPSD prevalence of approximately 70% among patients with dementia, with apathy (56%), depression (48%) and sleep disorders (34%) being the most frequent secondary symptoms.^{6,7} Agitation, verbal or physical aggression, delusions, hallucinations and anxiety are also common in patients suffering dementia.⁷ BPSD significantly increase patient suffering, early institutionalization rates, caregiver burden, and mortality risk.^{8,9}

Several studies have reported that physical activity reduces neuropsychiatric symptoms and improves the functionality of patients with dementia, in addition to reducing caregiver burden. Apathy, depressive symptoms, sleep disturbances, agitation, emotional welfare, and functional capacity are the conditions most frequently reported to benefit from physical activity.¹⁰⁻¹¹ Regular physical activity, although it has been investigated less than cognitive performance, is considered an important non-pharmacological strategy for public health and symptom management for some neuropsychiatric disturbances.^{12,13}

After considering the established benefits of motor intervention for public health and taking into account previous Brazilian studies that have linked physical exercise with psychopathological features in the elderly, we hypothesized an association between regular physical activity and reduction of neuropsychiatric suffering in dementia.

Therefore, in the present study, we examined if physical activity could reduce neuropsychiatric suffering in a population of Brazilian patients with dementia, in addition to reducing the burden of their caregivers.

METHODS AND MATERIALS

Patients

We investigated 59 patients diagnosed with dementia as defined in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). In addition, we included the NINCDS-AIREN and NINCDS-ADRDA criteria¹⁴ for probable vascular dementia or Alzheimer's disease in patient evaluations. Mixed dementia was classified as Alzheimer's disease plus vascular dementia. To confirm the diagnosis of vascular dementia, we considered the following as risk factors for brain vascular pathology: uncontrolled hypertension, diabetes mellitus, hypercholesterolemia, obesity, smoking and a sedentary lifestyle. Evidence of hemiplegia or other neurological signs was also noted. Structural neuroimaging was used to confirm the existence of brain vascular lesions. The overall strategy of the present study involved simultaneous cross-sectional and retrospective procedures. We also assessed the subjects' caregivers to identify their burden during regular assistance of dementia patients.

The patients were referred from the geriatric psychiatry outpatient clinic of a Brazilian public medical school. A trained clinical diagnosis team carefully evaluated all patients. The final diagnoses of dementia were established by a university neuropsychiatric service geriatric psychiatrist with long-term experience with Alzheimer's and vascular dementia. Patients diagnosed with other neuropsychiatric conditions, such as depression, and lacking an established diagnosis of dementia were excluded.

Procedures

Initially, the patients were classified into Alzheimer's (39.0%), mixed (28.8%) or vascular dementia (32.2%). All patients were rated according to the Clinical Dementia Rating (CDR) scale:¹⁵ 0 = cognitive normality, 0.5 = questionable dementia, 1 = mild dementia, 2 = moderate dementia, and 3 = severe dementia. The CDR scale was validated for the detection and staging of dementia in Brazilian patients by Chaves et al.¹⁶ Next, the patients were distributed into two groups based on their level of physical activity in the

preceding six months: a) patients who had a higher level of physical activity and b) patients with a lower level of physical activity. Caregivers were classified in accordance with the diagnosis of their respective patients. Participants who suffered from major depression, bipolar disorder, schizophrenia, or other neuropsychiatric conditions were excluded.

The data were assessed by the following steps. First, a semi-structured interview was used to collect both demographic and clinical information. Second, patient cognitive functions were assessed by the Cognitive Section of the Cambridge Examination for Mental Disorders of the Elderly (CAMCOG),¹⁷ adapted to the Brazilian population and with a distinct cutoff points based on level of schooling. Bottino et al.¹⁸ adapted and translated the CAMCOG for use in the Brazilian community and recommended scores of 60 and 80 as cutoffs to identify normal/non-normal cognitive functions for low and high formal education, respectively. Third, distinct neuropsychiatric symptoms suffered by the patients in the preceding three weeks were evaluated using the Neuropsychiatric Inventory (NPI).¹⁹ The NPI evaluates several symptoms presented by the subjects, including the following: delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, elation/euphoria, apathy, disinhibition, irritability, aberrant motor behavior, sleep disturbances, and appetite changes. The patient caregiver's burden was also assessed with the NPI, with higher scores indicating greater patient dementia severity. The reliability of the Brazilian Portuguese version of the NPI has been reported by Camozzato et al.²⁰ Following the NPI, we used the Mini-Sleep Questionnaire (MSQ) to gather data on patient sleep in the preceding two weeks.²¹ The MSQ was adapted for the Brazilian community by Aloe and Tavares,²² and according to these authors, patients with scores from 10 to 24 are classified as getting good sleep, those with scores from 25 to 27 are classified as mildly sleep impaired, those with scores from 28 to 30 are moderately sleep impaired, and those with scores more than 30 are classified as severely sleep impaired. Following the sleep assessment, the patient physical activity profiles were evaluated by means of the Modified Baecke Questionnaire for the Elderly (MBQE),²³ an adapted version of the original Baecke questionnaire. The modified questionnaire was designed to measure habitual physical activity specifically in the elderly by assessing three physical activity domains (household, sports and leisure activities). It has good validity, and it was evaluated by both a physical activity diary and a pedometer as reference criteria, with resultant correlations of 0.78 and 0.72, respectively. MBQE reproducibility has also been shown to be good, with a correlation of 0.89 between the test and retest.²³ In Brazil,²⁴ a study carried out only in older women indicated a 60% agreement between the classifications of more and less physically active women based on both pedometer and evaluation of physical activity diaries. For that study, the test-retest reproducibility was 0.83. In Portugal,²⁵ a validity study in older men and women demonstrated a correlation of 0.70 between the MBQE and accelerometer scores.

In addition to the MBQE, diary, and pedometer, the authors directly interviewed caregivers and family members to determine the physical activity of the patients, particularly for patients suffering from moderate or moderately severe dementia. For the interviewed evaluations, patients from the three dementia groups were divided into

lower and higher levels of physical activity based on established scores for this purpose. Physical activity was considered systematized when regular exercise was performed at least twice a week for 30 minutes or more and for at least six months.

Statistical analysis

We used SPSS software for statistical analyses. The data were first analyzed using descriptive statistics (median and confidence interval). Using the Kruskal-Wallis and Mann-Whitney *U* tests, we verified group homogeneity and group associations. To test the effects of the independent (predictor) variables on a single dependent (criterion) variable, we applied a stepwise linear regression. A two-tailed 5% significance level was adopted for these analyses ($p < 0.05$). We chose to use non-parametric statistics because the data presented a non-normal curve.

Ethical Aspects

The Research Ethics Committee of the State University of São Paulo approved this study. A family member or a legal representative of the patient signed a free and informed consent form, according to the standards established by resolution 196/96 of the Brazilian National Health Council for research involving human beings.

RESULTS

We examined 59 patients with dementia (mean age: 76 years; mean schooling: 3 years - third grade completed) and their respective caregivers (mean age: 51 years; mean schooling: 1 year - first grade completed). Most caregivers were females (64.4%) and fell into three major categories: daughters or sons (64%), husbands or wives (22%) and other family members or professional caregivers (14%). Hypertension, diabetes mellitus, hypercholesterolemia, and obesity were the most common clinical comorbidities among patients with vascular or mixed dementia. Patients being pharmacologically treated for dementia took cholinesterase inhibitors (rivastigmine, donepezil and galantamine) and memantine. Patients who presented with agitation or aggression related to impulsivity or psychotic symptoms were treated with benzodiazepines or antipsychotics, when appropriate, for the necessary period. Patients with depression disorders used antidepressants.

Anticonvulsants, such as valproic acid, were recommended for controlling impulsivity.

Table 1 shows the patient demographic and clinical data for each kind of dementia and the demographic information of the caregivers.

In general, the patients exhibited a relatively low level of physical activity; most of them did not practice regular or systematized physical exercises (64% of the patients with Alzheimer's disease, 78% of the subjects with vascular dementia and 80% of the mixed dementia patients were sedentary). In general, the Alzheimer's disease patient group demonstrated more activity than the vascular or mixed dementia patient groups.

The frequency and intensity of neuropsychiatric symptoms varied by the type of dementia. Patients with Alzheimer's disease mainly presented apathy, aberrant motor behavior, irritability and delusions. Among patients with vascular dementia, irritability, anxiety and agitation were the most common symptoms. Those with mixed dementia most frequently presented with anxiety, agitation and depressive symptoms.

Patients suffering from Alzheimer's disease demonstrated a significant inverse correlation between level of physical activity and neuropsychiatric symptoms. Patients with a higher level of physical activity presented with fewer neuropsychiatric disturbances in comparison to those with lower levels of physical activity (NPI: 36.0 versus 28.5; Mann Whitney *U* test = 23; $p < 0.01$). In addition, in patients with vascular dementia, a higher level of physical activity led to presentation of fewer sleep disorders when compared to those with lower levels of physical activity (MSQ: 55.0 versus 31.0; Mann Whitney *U* test = 5.5; $p < 0.05$). Interestingly, a linear regression indicated that patients with vascular dementia presented better sleep quality when their caregivers also performed regular physical activity. We did not observe any reduction in neuropsychiatric symptoms associated with physical activity in patients who presented with mixed dementia. Tables 1 and 2 summarize these data.

DISCUSSION

The data suggest that an active lifestyle is an important public health factor in reducing neuropsychiatric symptoms, especially in patients with Alzheimer's dementia. In line with our hypothesis, we found distinct benefits from physical activity. Physically active patients with Alzheimer's disease

Table 1 - Clinical and demographic characteristics (medians and confidence intervals) of patients with Alzheimer's, vascular and mixed dementia, separated into higher and lower levels of physical activity.

Variables	Alzheimer's dementia		Vascular dementia		Mixed dementia	
	Lower PA Level	Higher PA Level	Lower PA Level	Higher PA Level	Lower PA Level	Higher PA Level
Age (years)	76.0 (57-91)	77.5 (67-86)	76.0 (52-83)	52.0 (50-68)	72.0 (70-84)	75 (58-89)
Schooling (years)	4.0 (0-15)	1.0 (0-11)	2.0 (0-3)*	4.0 (4-9)*	1.0 (0-4)	3.0 (0-4)
CDR	2.5 (1-3)	2.5 (1-3)	3.0 (1-3)	2.0 (1-3)	3.0 (1-3)	3.0 (1-3)
CAMCOG	36.0 (0-100)	37.5 (0-83)	17.0 (0-73)	35.0 (0-16)	43.5 (0-79)	28 (26-86)
Duration of dementia (years)	5.0 (1-10)	5.5 (1-15)	3.0 (1-28)	2.0 (1-8)	9.5 (2-28)	11.0 (10-18)
MBQE	0.5 (0.1-0.6)*	3.0 (1.0-7.4)*	1.0 (0.3-1.4)*	5.0 (1.9-6.3)*	0.5 (0.3-0.9)*	1.5 (1.2-2.0)*
NPI-patient	36.0 (0-102)*	28.5 (0-67)*	49.0 (0-98)	44.0 (20-72)	35.0 (0-60)	36.0 (2-74)
NPI-caregiver	17.0 (0-45)	14.0 (0-30)	18.0 (0-41)	20.0 (16-24)	15.0 (6-24)	17.0 (0-31)
MSQ	32.0 (17-55)	18.0 (8-31)	55.0 (47-58)*	31.0 (16-36)*	10.0 (5-36)	25.0 (5-52)

Legends: PA: Physical activity; CDR: Clinical Dementia Rating; CAMCOG: The Cambridge Examination for Mental Disorders of the Elderly (Cognitive Section); MBQE: Modified Baecke Questionnaire for the Elderly; NPI: Neuropsychiatric Inventory; MSQ: Mini-Sleep Questionnaire.

*Significant difference between LA and HA ($p < 0.05$).

Table 2 - Stepwise linear regression analysis according to the correlation of level of physical with dependent and independent variables.

	Dependent variables	Independent variables	R
Alzheimer's dementia	CAMCOG	CDR and age	0.81
	NPI-patient	NPI-caregiver	0.95
Vascular dementia	MSQ	Physical activity	0.60
Mixed dementia	NPI-caregiver	WC	WC

Legends: WC: Without correlation.

presented with fewer neuropsychiatric disturbances. In addition, the caregivers of those patients exhibited a reduced burden. Patients with vascular dementia and an active lifestyle had a notable improvement in sleep quality.

In the present study, the rates of Alzheimer's disease (AD) (39%), vascular dementia (32.2%) and mixed dementia (28.8%) were different from the prevalence observed by Herrera et al.¹ In this context, these authors observed a prevalence of AD (55.1%) higher than what was observed in our study and rates of vascular dementia (9.3%) and mixed dementia (14.4%) lower than those seen our study population. Whereas these authors investigated the prevalence of dementia in a Brazilian community population, our study was conducted in a neuropsychiatric clinic at a teaching hospital, which receives patients with moderate or severe behavior disturbances, which are frequently associated with vascular brain lesions.

Psychopathological symptoms are commonly observed in dementia and frequently evaluated by the NPI.^{19,20} These disturbances aggravate the disability of patients, reduce their quality of life, and increase the burden of their caregivers.^{26,27} These aspects are in agreement with a recent descriptive review by Cummings et al.,²⁸ who confirmed that neuropsychiatric disturbances negatively affect quality of life for both demented patients and their caregivers. In addition, neuropsychiatric disturbances, especially psychotic symptoms, predict a more rapid rate of cognitive decline. Furthermore, these symptoms, in addition to aggression, have been identified as strong predictors of institutionalization. They also have been associated with an increased risk of mortality.²⁹

In the present study, we did not classify the patients into different groups according to their CDR scores. Because of this, it was impossible to control the influence of dementia severity on NPI scores. However, the median CDR score of the groups varied from 2.0 (1 to 3) to 3.0 (1 to 3), which indicated a moderately severe level of dementia, and the general NPI scores from patients and caregivers were compared to patients without dementia as well as their caregiver, which suggested that they were influenced by dementia severity. Several investigations have demonstrated that dementia severity has a strong negative impact on patient caregiver burden and neuropsychiatric symptoms among the demented.^{8,11,28}

Non-pharmacological interventions can contribute to minimizing the suffering of patients and caregivers. Several kinds of stimulation-oriented interventions, among them physical activity-based procedures, have a favorable impact on neuropsychiatric symptoms, mainly when interventions are combined with psychopharmacological treatments. In the present study, walking was the most

frequently reported physical activity. Few patients from our sample participated regularly in a systematized program of physical activity. It is likely that a generally sedentary lifestyle and trouble understanding the reasons for physical activity have contributed to the low rates of physical activity observed in these patients.

Some studies have used the MBQE to measure the level of physical activity in dementia. Christofolletti et al.¹² found a higher MBQE score in patients with Alzheimer's dementia than that observed in the present study. The type, intensity and duration of physical exercises have been commonly considered in physical activity programs for patients with dementia. Woodhead et al.³⁰ implemented a three-month aerobic activity program for such patients and observed an reduction in depressive symptoms and apathy. A 12-month randomized, controlled clinical trial by Rolland et al.³¹ evaluated the effects of an anaerobic activity-based program (which included strength, balance and flexibility training) on nursing home patients with Alzheimer's disease. The researchers reported an improvement in daily living activities and functional capacity and a reduction in neuropsychiatric symptoms.

Depending on their functional capacity, patients with dementia require increasing levels of supervision and personal care. In such situations, caregivers experience high levels of stress and negative impacts on their health, such as depression. More than 40% of family members of people with Alzheimer's and other dementias present with emotional stress, and one third of family members of patients with Alzheimer's disease exhibit symptoms of depression.³²

In agreement with the results of previous studies, the present study found that patients with Alzheimer's dementia, who were more active when compared to those with other types of dementia, demonstrated a lower frequency and intensity of neuropsychiatric symptoms, especially sleep disturbances.^{12,30-33} Although patients with vascular dementia demonstrated difficulty walking, they still presented a relatively improved physical performance through improved sleep quality. For mixed dementia patients, higher activity levels did not offer significant symptom improvement compared to lower physical activity levels. However, patients who were more active presented fewer neuropsychiatric disturbances. The specific features of mixed dementia and the peculiarities of clinical severity could partially explain the small effects of physical intervention in reducing neuropsychiatric symptoms in these patients. The relatively small sample size could also have generated random statistical variation. The study analysis may be not sufficiently sensitive to detect differences in mixed dementia cases.

It is plausible that physical activity has distinct effects depending on the type of dementia. Accordingly, proportionally few patients with vascular and mixed dementia (only three patients in each group) were engaged in regular physical activity. This fact could be explained in part by the presence of common hemiplegia or other motor disturbances as a consequence of vascular dementia that could represent an important impediment for walking or other physical activities. However, the patients with vascular dementia, who regularly participated in some physical activity, still presented with improved sleep. Regular physical activity has been shown to improve sleeping architecture by increasing sleep depth and duration.³⁴ Physical exercise also produces a favorable impact on sleep

quality.³⁵ In addition, improved sleep enhances recuperation in active patients more than in inactive patients.³⁶

In the present study, when caregivers performed physical activities, particularly regular aerobic exercises, the patients under their care presented significantly fewer sleep disorders. Neil and Bowie¹¹ have previously observed that improved physical and emotional conditions of caregivers contribute to patient welfare and quality of life. Our results also agree with another study that showed that structured activities, especially walking, resulted in a reduction in aggressive behavior in the elderly, particularly those who were demented.³⁷

The regular practice of physical activity likely improves brain blood flow and oxygenation, contributing to an overall improvement in neuronal activity, and consequently, in the mental condition.³⁸ In addition, according to a systematic review by Cooper et al.,³³ activities that promote the stimulation of the skeletal muscle structures improve the relationship between patient and caregiver.

The benefits of motor intervention could at least partially be explained by the neuroprotective effects and neuroplasticity promoted by physical exercise. Previous studies have reported the positive effects of exercise on brain neuroplasticity, neuroprotection, and neurogenesis mediated by neurotrophins or other components such as brain-derived neurotrophic factor, vascular endothelial growth factor, and insulin-like growth factor, with overall favorable impacts on functional neuroimaging.³⁹⁻⁴¹ Though our results indicated that regular physical activity could ameliorate behavior disorders related to dementia, the benefits for cognitive functions are still controversial. In this context, in a systematic review, Eggermont et al.⁴² reported that exercise may not be beneficial for the cognitive functioning of all people with dementia if cardiovascular risk factors are present. On the other hand, Lange-Asschenfeldt and Kojda⁴⁰ agreed that regular exercise may counteract AD pathophysiology by increasing neuroplasticity and cognitive reserve, both of which are associated with brain vascular improvement.

This study has some limitations. The cross-sectional design, in combination with the retrospectively collected data, did not allow us to draw conclusions regarding causality. Because of this, it is impossible to confirm whether the improvement in neuropsychiatric disorders was supported by physical activity. Also, we did not verify if patients with high neuropsychiatric scores on the NPI, measured during the four weeks before their study interviews, did practice a lower level of physical activity before this period. In addition, it is possible that patients with severe dementia performed less physical activity independently of their dementia subtype and/or intensity of neuropsychiatric symptoms.

CONCLUSION

In conclusion, despite physical activity not being a regular practice for the greatest number of patients with dementia, some benefits were still found among those who had higher levels of activity. Because of the cross-sectional nature of our data, it is not advisable to make causative conclusions concerning physical activity and its effects. However, it is possible to consider that higher levels of physical activity, such as walking or other aerobic exercises, were related to the decrease in neuropsychiatric symptoms of patients with

Alzheimer's dementia and the accompanying attenuation of the burden of their caregivers. In patients with vascular dementia, higher levels of physical activity notably improved sleep quality.

Formulating strategies to improve adherence to a regular program of physical activity that will aid in reducing neuropsychiatric disturbances in patients continues to present a challenge for both public health professionals and caregivers.

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