



Q/ Does physical exercise reduce dementia-associated agitation?

EVIDENCE-BASED ANSWER

A / NOT CONSISTENTLY. Physical exercise demonstrates inconsistent benefit for neuropsychiatric symptoms, including agitation, in patients with dementia (strength of recommendation: **B**,

inconsistent meta-analyses, 2 small randomized controlled trials [RCTs]). The care setting and the modality, frequency, and duration of exercise varied across trials; the impact of these factors is not known.

Evidence summary

Mixed results on exercise's effect on neuropsychiatric symptoms

A 2020 systematic review and meta-analysis of 18 RCTs investigated the effect of home-based physical activity on several markers of behavioral and psychological symptoms of dementia (BPSD). These symptoms were measured using the caregiver-completed neuropsychiatric inventory (NPI), which includes agitation. There was substantial heterogeneity between trials; however, 4 RCTs (472 patients) were included in a meta-analysis of the NPI. These RCTs were non-blinded, given the nature of the intervention.¹

Interventions to enhance physical activity ranged from 12 weeks to 2 years in duration, with 2 to 8 contacts from the study team per week. The type of physical activity varied and included cardiorespiratory endurance, balance training, resistance training, and activities of daily living training.¹

Exercise was associated with significantly fewer symptoms on the NPI, although the effect size was small (standard mean difference [SMD] = -0.37; 95% CI, -0.57 to -0.17). Heterogeneity in the interventions and assessments were limitations to this meta-analysis.¹

A 2015 systematic review and meta-analysis of 18 RCTs compared the effect of exercise interventions against a control group for the treatment of BPSD, utilizing 10 behavioral and 2 neurovegetative components of the NPI (each scored from 0 to 5) in patients

with dementia. Studies were included if they used ≥ 1 exercise intervention compared to a control or usual care group without additional exercise recommendations. Thirteen studies had a multicomponent training intervention (≥ 2 exercise types grouped together in the same training session), 2 used tai chi, 4 used walking, and 1 used dance and movement therapy. These RCTs were conducted in a variety of settings, including community-dwelling and long-term care facilities ($n = 6427$ patients).²

Exercise did not reduce global BPSD ($N = 4441$ patients), with a weighted mean difference (WMD) of -3.9 (95% CI, -9.0 to 1.2; $P = .13$). Exploratory analysis did not show improvement in aberrant motor behavior with exercise (WMD = -0.55; 95% CI, -1.10 to 0.001; $P = .05$). Limitations of this review included the small number of studies, heterogeneity of the population, and limitations in data accessibility.²

A 2017 hospital-based RCT evaluated the effects of a short-term exercise program on neuropsychiatric signs and symptoms in patients with dementia in 3 specialized dementia care wards ($N = 85$). Patients had a diagnosis of dementia, minimum length of stay of 1 week, no delirium, and the ability to perform the Timed Up and Go Test. The intervention group included a 2-week exercise program of four 20-minute exercise sessions per day on 3 days per week, involving strengthening or endurance exercises, in

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addition to treatment as usual. The control group included a 2-week period of social-stimulation programs consisting of table games for 120 minutes per week, in addition to treatment as usual.³

Of 85 patients randomized, 15 (18%) were lost to follow-up (14 of whom were discharged early from the hospital). Among the 70 patients included in the final analysis, the mean age was 80 years; 47% were female and 53% male; and the mean Mini-Mental Status Examination score was 18.3 (≤ 23 indicates dementia). In both groups, most patients had moderate dementia, moderate neuropsychiatric signs and symptoms, and a low level of psychotic symptoms. Patients in the intervention group had a higher adherence rate compared with those in the control group.³

The primary outcome was neuropsychiatric signs and symptoms as measured by the Alzheimer's Disease Cooperative Study–Clinical Global Impression of Change (ADCS-CGIC). Compared to the control group, the intervention group experienced greater improvement on the ADCS-CGIC dimensions of emotional agitation (SMD = -0.9 ; $P < .001$), lability (SMD = -1.1 ; $P < .001$), psychomotor agitation (SMD = -0.7 ; $P = .01$), and verbal aggression (SMD = -0.5 ; $P = .04$). However, there were no differences between groups in the physical aggression dimension. Trial limitations included potential impact of the drop-out rate and possible blinding issues, as nursing staff performing assessments could have seen to which group a patient was allocated.³

A 2016 factorial cluster RCT of 16 nursing homes (with at least 60% of the population having dementia) compared the use of person-centered care vs person-centered care plus at least 1 randomly assigned additional intervention (eg, antipsychotic medication use review, social interaction interventions, and exercise over a period of

9 months) ($n = 277$, with 193 analyzed per protocol). Exercise was implemented at 1 hour per week or at an increase of 20% above baseline and compared with a control group with no change in exercise.⁴

Exercise significantly improved neuropsychiatric symptoms. The baseline NPI score of 14.54 improved by -3.59 (95% CI, -7.08 to -0.09 ; $P < .05$). However, none of the study interventions significantly improved the agitation-specific scores. The primary limitation of this study was that antipsychotic prescribing was at the discretion of the provider and not according to a protocol. In addition, the authors noted that the trial was inadequately powered to correct for testing 3 primary outcomes.⁴

Editor's takeaway

Dementia and dementia with agitation are challenging conditions to treat. Disappointingly, physical exercise had inconsistent and generally minimal effect on agitation in dementia. Nevertheless, exercise had other positive effects. So, considering the benefits that exercise does provide, its low cost, and its limited adverse effects, exercise remains a small tool to address a big problem. **JFP**

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