INPLASY

Physical activity interventions for the prevention and treatment of neurodegeneration and aging: A systematic review of randomized controlled trials

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INTRODUCTION

*R*eview question / Objective What utilities of physical activity interventions in the attenuation, prevention, and treatment of a broad spectrum of neurodegenerative processes, including: neuropsychological and neurocognitive function, limbic function, Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI) and Amnesic Mild Cognitive Impairment (aMCI), Parkinson's Disease (PD), and Multiple Sclerosis (MS) have been demonstrated by randomized controlled trials using: neuropsychological and neurocognitive testing batteries, neuroinflammatory biomarker analysis, neuroimaging biomarkers (structural magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion tensor imaging (DTI), positron emission tomography (PET))?

Condition being studied Several neurodegenerative diseases (e.g., Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI) and Amnesic Mild Cognitive Impairment (aMCI), Parkinson's Disease (PD), and Multiple Sclerosis (MS)) in addition to normal age-related neurodegeneration were studied in this review.

METHODS

Search strategy A systematic review of three relevant databases (PsycINFO, PubMed, Web of Science) was conducted. Database search terms were developed in collaboration with a Pennsylvania State University librarian, and databases were searched using the terms with Boolean logic operators "OR" and "AND". These terms included all variations of "(Mild Cognitive Impairment OR Alzheimer's Disease OR Parkinson's Disease OR Multiple Sclerosis OR Dementia OR Memory Impairment OR Healthy Aging) AND (Exercise Intervention OR Exercise Training OR Exercise Testing OR Metabolic Equivalent of Task) AND (Biomarker Analysis OR Amyloid OR Tau Protein OR Magnetic Resonance Imaging OR Functional Magnetic Resonance Imaging OR Diffusion Tensor Imaging OR Positron

Emission Tomography OR Disease Progression OR Functional Outcomes OR Quality of Life) AND (Randomized Controlled Trials)".

Participant or population This review included studies with human adult participants that were cognitively intact or that were diagnosed with selected neuropathologies (i.e., Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI) and Amnesic Mild Cognitive Impairment (aMCI), Parkinson's Disease (PD), and Multiple Sclerosis (MS)).

Intervention Physical activity interventions (i.e., aerobic exercise, resistance training, stretching exercise, multicomponent exercise, and vestibular exercise) were evaluated. Multicomponent interventions were defined as interventions utilizing more than one form of physical activity, such as an intervention that combines aerobic exercise and resistance training.

Comparator There was no comparative intervention used.

Study designs to be included Randomized controlled trials.

Eligibility criteria Inclusion criteria
- Language: Papers available in English
- Publication type: Peer-reviewed scholarly journal articles reporting primary research findings from randomized controlled trials
- Population/Age: Adult (greater than or equal to 18 years) human studies
- Physiological phenomenon of study: Alzheimer's Disease (AD), Mild Cognitive Impairment (MCI) and Amnesic Mild Cognitive Impairment (aMCI), Parkinson's Disease (PD), Multiple Sclerosis (MS), selective memory complaints/memory issues, or non-demented healthy aging
- Physical activity intervention: Includes a physical activity intervention program
- Imaging measure: Structural magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion tensor imaging (DTI), positron emission tomography (PET)
- Biomarkers: Cytokine, blood-biomarker, cerebrospinal fluid, or saliva analysis
- Behavioral measure: Includes behavioral, cognitive, neurocognitive, psychological, and/or neuropsychological assessment or battery
- Specificity of brain region analysis: Any, all brain region
- Outcomes: Any behavioral, cognitive, imaging, or exercise data which meets inclusion criteria

Exclusion criteria

- Language: Papers in non-English
- Publication type: Secondary reporting of research, research reviews, magazine articles, abstracts
- Population: Non-human, animal, or theoretical models
- Age: Youth (less than 18 years)
- Physiological phenomenon of study: All other neurological disorders, cardiovascular disorders, metabolic disorders
- Physical activity intervention: No presence of physical activity measurement or intervention
- Imaging measure: No presence of structural magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion tensor imaging (DTI), positron emission tomography (PET), cytokine, blood biomarker, cerebrospinal fluid, or saliva analysis
- Biomarkers: No presence of structural magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion tensor imaging (DTI), positron emission tomography (PET), cytokine, blood biomarker, cerebrospinal fluid or saliva analysis
- Behavioral measure: Does not include any behavioral, cognitive, neurocognitive, psychological, or neuropsychological measure
- Specificity of brain region analysis: Spinal cord, peripheral nervous system, facial nerves
- Outcomes: Any behavioral, cognitive, imaging, or exercise data which do not meet inclusion criteria.

Information sources A systematic review of three relevant databases (PsycINFO, PubMed, Web of Science) was conducted.

Main outcome(s) The effectiveness of the physical activity interventions were evaluated by comparing baseline testing with post-intervention testing. These testing measures included neuropsychological and neurocognitive testing batteries, neuroinflammatory biomarker analysis, neuroimaging biomarkers (structural magnetic resonance imaging (MRI), functional MRI (fMRI), diffusion tensor imaging (DTI), positron emission tomography (PET)).

Quality assessment / Risk of bias analysis The Jadad scale for reporting randomized controlled trials was utilized to evaluate the risk of bias in and the quality of results from the studies included in the present analysis. The Jadad scale is a widely used valid measure of internal validity for randomized controlled trials that evaluates randomization, double-blinding, and a description of dropouts on a zero to five scale. Scores of zero to two indicate low quality results, and scores of three to five indicate high quality results. Within the randomization domain, one point is allocated for mentioning randomization; an additional point is

allocated for appropriate randomization methods, and a point is subtracted for inappropriate methods. Similarly, in the double-blinding category, one point is allocated for mentioning a double-blinding procedure; an additional point is allocated for appropriate procedures, and a point is subtracted for inappropriate procedures.

Strategy of data synthesis Systematic coding of relevant data fields was recorded and summarized by the authors to compare key findings between included articles. Regarding the biomarker, neuroimaging, and cognitive outcomes in terms of their effects on overall brain health, changes were either plainly stated or inferred from the data for each article. In terms of overall brain health, outcomes were evaluated as reversed neurodegenerative symptoms (improvements: pre-intervention overall brain health post-intervention overall brain health). Examples of how these outcomes were evaluated are as follows: For structural neuroimaging outcomes (e.g., MRI, DTI), improvements would be associated with reversed cortical atrophy, maintenance would be associated with no further cortical atrophy compared to pre-intervention, and degeneration would be associated with continued cortical atrophy; For PET neuroimaging, improvements would be associated with reductions in amyloid plaque accumulation or neurofibrillary tangles, maintenance would be associated with no further accumulation compared to pre-intervention, and degeneration would be associated with continued accumulation; For fMRI neuroimaging, improvements, maintenance/no changes, or degeneration that were not plainly stated were inferred from the consensus among the literature, and if no consensus was reached among the literature, these findings were omitted; For biomarker outcomes, improvements would be associated with reduced inflammatory proteins or upregulated neuroplasticity factors such as BDNF, maintenance would be associated with no changes from pre- to post-intervention, and degeneration would be associated with upregulated inflammatory proteins or reduced neuroplasticity factors. Data was also extracted for non-intervention controls from studies on neurodegenerative populations.

Subgroup analysis Comparisons were made between physical activity intervention types at the level of the whole sample and at the level of neurodegeneration type. Additionally, comparisons were made between neurodegeneration types to investigate the effectiveness of physical activity interventions as a whole without specifying the type of intervention.

Sensitivity analysis No statistical analyses were performed as part of this review. This review was intended to be an exploratory analysis of the differential effects of physical activity on various neurodegeneration types.

Country(ies) involved United States.

Keywords physical activity; exercise; neurodegeneration; aging; imaging; cognition; biomarkers.

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