



Physical activity and white matter hyperintensities: A systematic review of quantitative studies

Elisa R. Torres^{a,*}, Emily F. Strack^b, Claire E. Fernandez^b, Tyler A. Tumey^b, Mary E. Hitchcock^c

^a School of Nursing, 4123 Signe Skott Cooper Hall, 701 Highland Avenue, University of Wisconsin, Madison, WI 53705, USA

^b College of Letters and Science, 1305 Linden Drive, University of Wisconsin, Madison, WI 53706, USA

^c Department of Health Sciences Library, School of Medicine and Public Health, 2339 Health Sciences Learning Center, 750 Highland Avenue, Madison, WI 53705, USA

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ABSTRACT

Objective. White matter hyperintensities (WMH) are markers of brain white matter injury seen on magnetic resonance imaging. WMH increase with age and are associated with neuropsychiatric disorders. WMH progression can be slowed by controlling vascular risk factors in individuals with advanced disease. Since physical activity can decrease vascular risk factors, physical activity may slow the progression of WMH in individuals without advanced disease, thereby preventing neuropsychiatric disorders. The purpose of this systematic review was to examine the association between physical activity and WMH in individuals without advanced disease.

Methods. Articles published in English through March 18, 2014 were searched using PubMed, Web of Science, Cochrane Library and EBSCOhost.

Results. Six studies found that more physical activity was associated with less WMH, while 6 found no association. Physical activity is associated with less WMH in individuals without advanced disease when studies are longitudinal or take into consideration physical activity across the lifespan, have a younger sample of older adults, measure different types of physical activity beyond leisure or objectively measure fitness via VO₂ max, measure WMH manually or semi-automatically, and control for risk factors associated with WMH.

Conclusion. More physical activity was associated with less white matter hyperintensities in individuals without advanced disease.

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Introduction

White matter hyperintensities (WMH) are markers of brain white matter injury seen on magnetic resonance imaging (MRI). WMH increase with age (Decarli et al., 1995) and are associated with several disorders including late-onset depression (Herrmann, Le Masurier, and Ebmeier, 2008), cognitive decline, dementia, stroke, and increased risk for death (Debette et al., 2010). Reducing the risks for depression, cognitive decline, dementia and stroke is a major public health goal.

The progression of WMH can be slowed by controlling vascular risk factors. One study found that controlling blood pressure with medication slowed the progression of WMH in patients who had a stroke (Dufouil et al., 2005). Another study found vascular care composed of physical activity, diet, smoking cessation, and treatment of hypertension and dyslipidemia with medicine slowed the progression of WMH in patients with Alzheimer's disease (Richard, Gouw, Scheltens, and van Gool, 2010). In both studies, patients had advanced disease. From

a health promotion perspective, slowing the progression of WMH in individuals without advanced disease may delay or prevent disorders associated with WMH such as a stroke or Alzheimer's disease.

Physical activity is any body movement produced by skeletal muscles that results in energy expenditure (Caspersen et al., 1985). The total amount of physical activity is commonly measured, which takes into account intensity, frequency, duration (Shephard, 2003), as well as settings such as occupation, transportation, household and leisure (van Poppel et al., 2010). Since physical activity improves many vascular risk factors (Nelson et al., 2007), physical activity is a lifestyle factor that could slow the progression of WMH in individuals without advanced disease. Support for this hypothesis centers on the knowledge that vigorous intensity leisure physical activity prevents age-related white matter volume decline in healthy older adults (Colcombe et al., 2006). The purpose of this systematic review was to examine the literature for evidence that physical activity can slow the progression of WMH in individuals without advanced disease such as stroke or Alzheimer's disease.

Methods

We searched the literature published in English in PubMed, Web of Science, Cochrane Library, and EBSCOhost through March 18, 2014.

* Corresponding author. Fax: +1 608 263 5323.

E-mail addresses: ertorres@wisc.edu (E.R. Torres), estrack@wisc.edu (E.F. Strack), cfernandez2@wisc.edu (C.E. Fernandez), tumey@wisc.edu (T.A. Tumey), mhitchcock@library.wisc.edu (M.E. Hitchcock).

Inclusion criteria comprised cross-sectional, longitudinal and experimental studies of human subjects, and any measurement of physical activity or WMH. Since the focus of this study was on health promotion, exclusion criteria comprised studies focused solely on individuals with advance diseases associated with WMH, specifically depression, cognitive decline, dementia and stroke. Table 1 describes the keyword searches in each of the databases. Leukoaraiosis was included as a search term as it is a synonym for WMH. Leukoencephalopathy/leukoencephalopathies were included as search terms as they are broad term that applies to all brain white matter diseases. Two reviewers performed an independent screening of each study. Abstracts were reviewed, and full-text articles were inspected. We also examined the reference lists from full-text articles to seek additional sources.

Results

The process of inclusion of studies identified for review and analysis is shown in Fig. 1 (Liberati et al., 2009). Of the 256 non-duplicate articles found, we excluded 245 during a secondary screen. The most common reason for exclusion was that the study measured physical activity or WMH, but not both. We excluded other studies due to methodological issues, such as measuring white matter, but not WMH. Some studies measured mobility, gait, or cognitive exercises, but not physical activity. Since the purpose of this review was to determine the effects of physical activity on WMH, WMH had to be the dependent variable. Finally, we excluded studies in which the association between physical activity and WMH was undeterminable.

Studies included in the review (Fig. 1) represent data collected in six countries: the United States, the United Kingdom, Iceland, Finland, Austria, and Australia. Per Table 2, seven of the studies were cross-sectional (Ho et al., 2011; Rosano et al., 2010; Saczynski et al., 2008; Sen et al., 2012; Smith et al., 2009; Tseng et al., 2013; Zheng et al., 2012). Per Table 3, the five longitudinal studies (Carmelli et al., 1999; Gow et al., 2012; Podewils et al., 2007; Rovio et al., 2010; Willey et al., 2011) measured physical activity at baseline and WMH from three (Gow et al., 2012) to 25 years (Carmelli et al., 1999) later. All except one of the studies were community- or population-based (Tseng et al.,

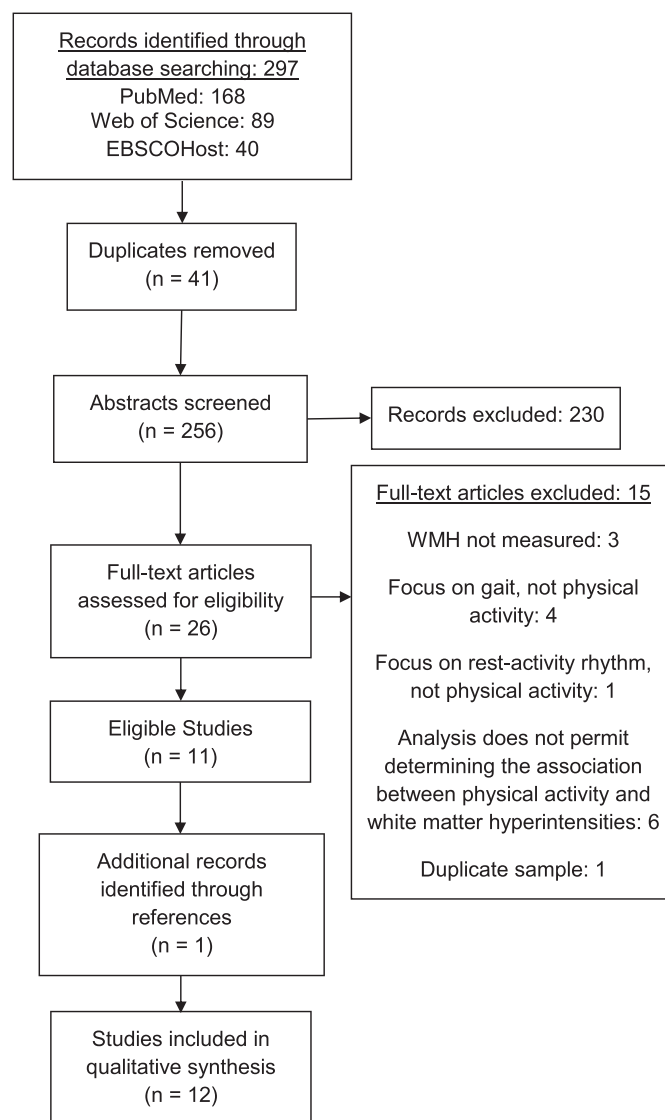


Fig. 1. Flow diagram of articles published in English through March 18, 2014.

Table 1
Keyword searches of articles published in English through March 18, 2014.

Databases	Search terms
PubMed	("Leukoencephalopathies"[Mesh] OR "Leukoaraiosis"[Mesh] OR (white matter hyperintensities[All Fields] OR white matter hyperintensity[All Fields]) OR "white matter lesion"[All Fields]) AND ("Motor Activity"[Mesh] OR "Exercise"[Mesh] OR "physical activity"[All Fields] OR ("exercise"[MeSH Terms] OR "exercise"[All Fields]))
Web of Science	TOPIC: (white matter hyperintensities OR white matter hyperintensity OR white matter lesions OR white matter lesion OR leukoaraiosis) AND TOPIC: (physical activity OR exercise)
Cochrane Library	("white matter hyperintensities" OR "white matter hyperintensity" OR "white matter lesions" OR "white matter lesion" OR "leukoaraiosis") AND ("physical activity" OR "exercise")
EBSCOhost:	(MH "Physical Activity") OR "physical activity" OR (MH "Exercise") OR (MH "Physical Fitness") OR (MH "Physical Performance") OR (MH "Physical Endurance") OR (MH "Exercise Test") OR (MH "Activity and Exercise Enhancement (Iowa NIC (Non-Cinahl))" OR (MH "Physical Activity (Omaha))" OR (MH "Physical Education, Adapted") OR (MH "Activity Therapy (Iowa NIC)")
CINAHL Plus	AND DE "White Matter" OR DE "Leukoaraiosis" OR DE "Leukoencephalopathy" OR white matter hyperintensit* OR "white matter lesion"
PsycInfo	
PsycARTICLES	
SocIndex	
Social Sciences	

2013). The non-community/population-based study was the only one designed to examine the association between physical activity and WMH (Tseng et al., 2013). All studies focused on older adults, excluded individuals with contraindications to MRI, and excluded those missing data on variables of interest. Five studies reported no other exclusion criteria (Carmelli et al., 1999; Gow et al., 2012; Podewils et al., 2007; Rovio et al., 2010; Saczynski et al., 2008). Four studies excluded adults with cognitive impairment or dementia (Ho et al., 2011; Sen et al., 2012; Tseng et al., 2013; Zheng et al., 2012), while another study accounted for adults with cognitive impairment or dementia in the analysis (Podewils et al., 2007). Three studies excluded adults with a history of neurological disorders (Tseng et al., 2013), such as stroke (Sen et al., 2012; Willey et al., 2011). The study originally designed to examine the association between physical activity and WMH excluded a number of potential confounders—that is smoking, recreational drug use, cardiovascular or cerebrovascular diseases, dementia, and major psychiatric and neurologic disorders (Tseng et al., 2013).

Six of the twelve articles showed a statistically significant association between physical activity and WMH, with more physical activity associated with less WMH (Gow et al., 2012; Podewils et al., 2007; Rovio et al., 2010; Saczynski et al., 2008; Sen et al., 2012; Tseng et al., 2013). One article found a statistically significant association in crude analyses,

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