Multiple Sclerosis and Related Disorders (2014) 3, 117–122

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/msard

Accelerometer measured physical activity and the integrity of the anterior visual pathway in multiple sclerosis

Brian M. Sandroff[a], Robert W. Motl[a,*], Jason P. Kam[b], John H. Pula[b]

[a]*Department of Kinesiology and Community Health, University of Illinois at Urbana-Champaign, Urbana, IL, USA*
[b]*Division of Neuro-ophthalmology, University of Illinois College of Medicine at Peoria and the Illinois Neurologic Institute, Peoria, IL, USA*

Received 25 March 2013; received in revised form 22 May 2013; accepted 27 June 2013

KEYWORDS
Optical coherence tomography;
Multiple sclerosis;
Accelerometers;
Physical activity;
Imaging;
Total macular volume

Abstract
Purpose: To examine the associations among objectively-measured physical activity with the optical coherence tomography (OCT) metrics of retinal nerve fiber layer (RNFL) thickness and total macular volume (TMV) in persons with multiple sclerosis (MS).
Methods: Eighty four participants with MS, without ocular disease or high myopia underwent a neurological examination for Expanded Disability Status Scale (EDSS) scoring, followed by OCT. Participants then wore an accelerometer during the waking hours of a 7-day period to objectively measure physical activity as steps/day.
Results: Mean RNFL thickness for the sample was 91.46 μm (SD=15.0), and mean TMV was 6.61 mm^3 (SD=0.5). The mean score from the accelerometer was 4287 steps/day (SD=2563). Steps/day was significantly associated with both RNFL thickness (*Wald* $\chi^2=46.48$, $p<0.001$) and TMV (*Wald* $\chi^2=1798.27$, $p<0.001$). After controlling for sex, MS subtype, disease duration, disability, and visual function, steps/day was significantly associated with TMV (*Wald* $\chi^2=58.93$, $p<0.001$), but not RNFL (*Wald* $\chi^2=0.001$, $p=0.973$).
Conclusions: Physical activity was associated with integrity of the anterior visual pathway, assessed by OCT, in persons with MS, and this association was independent of sex, MS subtype, disease duration, disability, and visual function. Researchers should consider examining the causal nature of the association between physical activity and markers of the visual system in MS.

1. Introduction

Multiple sclerosis (MS) is an immune-mediated disease that results in axonal damage and neuronal loss, particularly within the anterior visual pathways (i.e., retina, optic

*Correspondence to: University of Illinois at Urbana-Champaign, Department of Kinesiology and Community Health, 233 Freer Hall, 906 South Goodwin Ave., Urbana, IL 61801, USA.
Tel.: +1 217 265 0886; fax: +1 217 244 7322.
E-mail address: bsandro2@illinois.edu (B.M. Sandroff).

2211-0348/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.msard.2013.06.014

nerves, chiasm, and tracts) (Trapp et al., 1998; Frohman et al., 2008). This damage of the afferent visual pathway typically manifests as visual symptoms (Sakai et al., 2011; Pula and Reder, 2009). Physical activity, based on accelerometry metrics, has been associated with visual symptoms in persons with MS (Motl et al., 2008), glaucoma (Ramulu et al., 2012), and healthy adults (van Landingham et al., 2012). To date, we are unaware of research that has examined physical activity and integrity of the afferent visual pathways in MS or other populations.

We are interested in physical activity and the integrity of the afferent visual pathway, in part, because this behavior might be associated with neural health in persons with MS (Heesen et al., 2006) and buffer against visual dysfunction. To date, researchers have reported positive effects of physical activity on dendritic spine loss using the experimental autoimmune encephalitis (EAE) model of MS (Rossi et al., 2009) and positive associations between cardiorespiratory fitness, a surrogate of physical activity, and brain gray matter volume and white matter integrity in persons with MS (Prakash et al., 2010). If an association exists between physical activity and the integrity of the anterior visual pathway, this might support a biologically-based, behavioral approach for impacting visual symptoms in MS. This is important as visual functions are highly valued, but often compromised, in persons with MS (Heesen et al., 2008) and physical activity might ultimately represent an approach for maintaining the health of the visual system.

The possible association between physical activity and integrity of the anterior visual pathway could be examined using accelerometers and optical coherence tomography (OCT). Accelerometers provide an objective measure of physical activity undertaken in one's normal environment and routine, and the metric of steps/day has been validated in persons with MS (Gosney et al., 2007; Sandroff et al., 2012). OCT provides a non-invasive approach for measuring axonal and neuronal integrity within the anterior visual pathway based on the property of light scattering (Frohman et al., 2006). OCT analyzes the average retinal nerve fiber layer (RNFL) thickness (based on micron-thickness of a 3.4 mm area of the inner-most ganglion cell axon layer of the retina) and the total macular volume (TMV; based on the peri-foveal area including the temporal region of the optic disc). The RNFL predominantly consists of ganglion cell axons (as opposed to cell bodies or photoreceptors), and by extension RNFL thickness can be primarily considered a metric of axonal integrity. The TMV consists of the entire cross-section of retinal tissue, including ganglion cell bodies, and, although axons are present, TMV may represent more overall neuronal integrity in persons with MS (Frohman et al., 2006; Gordon-Lipkin et al., 2007; Burkholder et al., 2009; Saidha et al., 2011; Sepulcre et al., 2007). Importantly, both RNFL thickness and TMV have been associated with MRI metrics of brain atrophy and lesion burden (e.g., Grazioli et al., 2008; Young et al., 2013).

This cross-sectional study examined the associations among objectively-measured physical activity, RNFL thickness, and TMV in persons with MS. We hypothesized that there would be positive associations between physical activity, RNFL thickness, and TMV, even after controlling for covariates of sex, MS subtype, disease duration, disability status, and visual function. This investigation is important considering both the evidence of an association between physical activity and visual symptoms and importance of visual functions for MS patients, and represents a first step in providing evidence for physical activity and neuronal health based on the integrity of the anterior visual pathway, prior to investing substantial time and resources into a randomized controlled trial.

2. Material and methods

2.1. Participants

This study was advertised as a study of OCT and mobility metrics for persons with MS conducted between the middle of September, 2010 through the end of December, 2010. Patients with MS were recruited who resided within an approximately 90-min drive of a Midwestern neurology practice. The inclusion criteria for participants involved (a) having a clinically definite diagnosis of MS and (b) being ambulatory either with or without use of an assistive device (i.e., unassisted, cane/crutch/walker use, but not confined to wheelchair). Exclusion criteria for each individual eye included (a) ocular disease (current or prior history of optic neuritis, glaucoma, macular degeneration, etc., assessed by a neuro-ophthalmologist) or (b) high myopia (minus 7.5 or higher). Although excluding individuals with optic neuritis restricted our sample size, we were interested in the possible differential associations of RNFL thickness and TMV, respectively, with physical activity, and previous research has indicated that RNFL thickness and TMV are less strongly correlated in individuals without a history of optic neuritis (Burkholder et al., 2009). We contacted 190 persons with MS, screened and scheduled 125 (65 were uninterested in the study after hearing a description from the project coordinator via telephone conversation and were not screened), and enrolled 96 persons with MS. Of the 125, 29 persons canceled the testing appointment and were not available to reschedule, and of the 96, 12 individuals were excluded from data analyses based on ocular history or pathology of the optic nerve, macular or retina based on a neuro-ophthalmologic examination prior to data collection. This resulted in a final sample of 84 persons with MS.

2.2. Primary measurements

2.2.1. Optical coherence tomography

All participants underwent time-domain OCT examination (Zeiss Stratus OCT 3, Carl Zeiss Meditec, Dublin, CA) performed by a neuro-ophthalmologist. When necessary, 1% phenylephrine intraocular mydriatic drops were instilled prior to scanning. Throughout scanning, the patient fixated on an internal target provided by the equipment. Each subject eye underwent sequential FAST RNFL circle scan and FAST macular scan protocols. If a scan had poor image quality, defined as improper disc centering, poor reference image acquisition, or a signal strength score of less than 7, it was repeated until we obtained an adequate scan. Average RNFL thickness was determined as the distance between the first reflection from the vitreo-retinal interface and the anterior boundary of the second reflective layer, corresponding to Bruch's Membrane, and TMV was recorded as an overall macular volume which did not contain