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Physical activity and information processing speed in persons with multiple sclerosis: A prospective study

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ABSTRACT

Objective: There is increasing recognition of the possible association between physical activity and information processing speed (IPS) in multiple sclerosis (MS), but this is based on a limited number of cross-sectional studies with small samples. There further are unresolved methodological issues such as the appropriate mode (i.e., written or oral administration) and measure (e.g., Symbol Digit Modalities Test (SDMT) & the Paced Auditory Serial Addition Test (PASAT)) of cognitive assessment. This prospective study further examined methodological issues influencing the association between physical activity and IPS in 82 persons with MS.

Methods: Participants wore an accelerometer during the waking hours over 7 days for measuring physical activity as steps/day and six-months later completed two versions of the SDMT and the PASAT.

Results: Steps/day was significantly, moderately, and similarly associated with oral ($r_s = .45$, $p < .01$) and written ($r_s = .51$, $p < .01$) SDMT performance, but weakly associated with scores on the PASAT ($r_s = .23$, $p = .02$). After controlling for age and disability status as covariates of IPS, the associations among steps/day and oral ($pr_s = .25$, $p = .02$) and written ($pr_s = .29$, $p = .01$) SDMT performance were attenuated, but statistically significant, whereas after controlling for age and disability status, the association between steps/day and PASAT performance was not statistically significant ($pr_s = .12$, $p = .34$).

Conclusions: These results support inclusion of either oral or written administrations of the SDMT, rather than the PASAT, as measures of IPS in future physical activity interventions.

1. Introduction

Multiple sclerosis (MS) is a neurological disease characterized by inflammation, demyelination, and atrophy (Trapp & Nave, 2008; Vollmer, 2007) within the central nervous system (CNS). This CNS damage often manifests as cognitive impairment (Benedict et al., 2006), particularly deficits in information processing speed (IPS) (Bobholz & Rao, 2003). IPS is defined as the speed with which a variety of cognitive processes are able to be executed efficiently by the CNS (Salthouse, 1996). Importantly, impaired IPS has been associated with unemployment, social isolation, loss of driving ability, and compromised quality of life in persons with MS (Benedict et al., 2005). There are no approved pharmacological treatments for this cognitive impairment in MS (Benedict & Zivadinov, 2011), and there is conflicting evidence regarding the effectiveness of cognitive rehabilitation (e.g., remediation of learning and memory) for improving IPS (e.g., Amato, Portaccio, & Zipoli, 2006; O'Brien, Chiaravalloti, Goverover, & DeLuca, 2008; Parisi et al., 2012).

Physical activity may be a behavioral approach for preventing or even treating cognitive impairment in MS (Motl, Sandroff, & Benedict, 2011). This is based on the gerontology literature (Ratey & Loehr, 2011) and a limited number of cross-sectional studies primarily focusing on physical fitness in persons with MS. For example, one study reported a positive association between aerobic fitness and measures of IPS in 21 persons with relapsing-remitting MS (Prakash, Snook, Motl, & Kramer, 2010). Another study reported associations among multiple domains of fitness (i.e., aerobic fitness, balance, and muscular strength) and IPS in 31 persons with MS (Sandroff & Motl, 2012). Importantly, physical fitness is a largely genetic characteristic of a person that reflects aerobic capacity, muscle strength, and balance, whereas physical activity is a modifiable behavior (Bouchard, Shephard, & Stephens, 1994). To our knowledge, there is only one published study directly

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examining physical activity and IPS in persons with MS. That study reported an association between physical activity, based on steps/day from an accelerometer, and IPS, based on a composite measure, consisting of scores from the Paced Auditory Serial Addition Test (PASAT) and Symbol Digit Modalities Test (SDMT) ($r = .39$) in 33 persons with MS, after controlling for age, sex, and education (Motl, Gappmaier, Nelson, & Benedict, 2011). However, there are several concerns with that study that limit our understanding of the association between physical activity and IPS in MS. Such concerns include the cross-sectional study design, relatively small sample size, and lack of control for disability status as a potential confounder of the association between physical activity and the composite measures of IPS. That study further did not provide an indication of the association between physical activity and measures of IPS separately, and using a composite measure of IPS might not accurately reflect the true association of IPS with physical activity in persons with MS. The SDMT is often considered as a measure of IPS and selective attention in the visual modality, whereas the PASAT is often considered an auditory measure of IPS along with working memory and selective attention (Drake et al., 2010). In other words, although both the SDMT and PASAT are considered tests of IPS, the tests do not only measure IPS. The SDMT generally has more strongly correlated with brain imaging metrics and is thought to be more sensitive to cognitive impairment in persons with MS relative to the PASAT, which can be susceptible to frustration—potentially confounding cognitive performance (Benedict et al., 2002).

Another important concern regarding the relationship between physical activity and IPS in persons with MS includes variation and uncertainty in modes of assessing IPS based on oral and written administrations of neuropsychological tests. For example, researchers have administered either the oral or written version of the Symbol Digit Modalities Test (SDMT) (Smith, 1982) in studies of physical activity and IPS (e.g., Baker et al., 2010; Boyle, Buchman, Wilson, Bienias, & Bennett, 2007; Motl, Gappmaier, et al., 2011; O'Dwyer, Burton, Pachana, & Brown, 2007). The SDMT has been included as a test of IPS in several well-established MS-specific neuropsychological batteries (e.g., Rao's Brief Repeatable Battery and the MACFIMS), proposed as a replacement for the PASAT in the Multiple Sclerosis Functional Composite (MSFC) (Drake et al., 2010), and recently recommended as the sole test of IPS for the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) (Langdon et al., 2012). Importantly, only the oral administration of the SDMT (Rao, Leo, Haughton, St. Aubin-Faubert, & Bernardin, 1989) has been considered valid in persons with MS (Drake et al., 2010), and performance on the written version might be confounded by upper extremity motor impairment (Benedict et al., 2002). This confound might upwardly bias the association between physical activity and IPS such that upper extremity motor impairment could have a combined influence on physical activity and IPS assessment.

Based on the aforementioned concerns with previous research, the current study adopted a prospective research design, controlled for possible confounders of age, sex, education and disability, and examined the association between physical activity and oral and written assessments of IPS, separately, using neuropsychological testing in a relatively large sample of persons with MS. The primary advantage of a prospective research design is the ability to establish a temporal sequence in the associations between physical activity and IPS, whereas a cross-sectional design is limited by the simultaneous collection of physical activity and IPS data and therefore cannot establish a temporal sequence between variables. Prospective designs further reduce the likelihood that factors affecting physical activity at one time point bias cognitive performance, measured at a later time point (Hennekens & Buring, 1987).

2. Methods

2.1. Participants

The data included in this paper were added as exploratory outcomes within the six-month baseline testing period of an ongoing behavioral intervention for increasing physical activity and its influence on symptomatic and mobility outcomes in physically inactive persons with MS. Participants were contacted (a) by mail through a flyer that was distributed amongst patients in North American Research Committee on Multiple Sclerosis (NARCOMS) registry; or (b) by e-mail through a flyer that was distributed amongst participants in a database from previous studies conducted in our laboratory over the past five years. There were 511 participants who initially expressed interest and who were contacted via phone by the project coordinator. After explaining the study protocol, the project coordinator undertook screening for inclusion with 230 individuals who remained interested. The inclusion criteria involved (a) having a definite diagnosis of MS (in order to be included in previous studies, participants provided a physician's verification of MS diagnosis); (b) being relapse-free for the past 30 days; (c) being able to walk with or without an assistive device (i.e., cane, crutch, or walker); (d) being between 18 and 64 years of age; (e) being willing and able to travel to our laboratory to complete the cognitive assessments and wear an accelerometer; (f) participating in less than 3 days per week of physical activity behavior on average (this was included based on the primary aim of the intervention for increasing physical activity behavior in inactive persons with MS); (g) having a low risk for contraindications of physical activity based on no more than a single "yes" response on the Physical Activity Readiness Questionnaire (PAR-Q) (Thomas, Reading, & Shephard, 1992); (h) being able to provide a physician's approval for participation in the study. Of the 230 persons who were screened, 106 did not meet inclusion criteria, with the primary reasons being too physically active ($n = 57$) and unwillingness to travel to our laboratory ($n = 23$); 39 additional persons did not provide physician's approval; and 3 canceled the testing session due to scheduling conflicts. This resulted in a final sample of 82 persons with MS who were enrolled in this study.

2.2. Primary measures

Physical activity was objectively measured as steps/day using ActiGraph (Health One Technology, Fort Walton Beach, FL) model GT3X accelerometers. We chose to use steps/day as an objective measure of physical activity consistent with previous research on physical activity and IPS in MS. Steps/day is a simple and easily interpretable metric that can be monitored by participants in behavioral interventions as a means of setting and achieving physical activity-related goals (Dlugonski et al., 2013). The model GT3X accelerometer is small (3.8 × 3.7 × 1.8 cm), light weight (27 g), and contains a solid state, digital accelerometer that generates an electrical signal proportional to the force acting on it. The signal is digitized by a 12-bit, analog-to-digital converter at a rate of 30 Hz and integrated over a pre-programmed epoch interval; the epoch was 1 min in this study. The integrated value is stored in memory as step counts per minute and the integrator is reset. The data were retrieved from the accelerometer via a direct USB 2.0 connection with a personal computer and then imported into ActiLife 5 for validity check (i.e., ≥10 h wear time without periods exceeding 60 min of continuous zeros per day) and processing of steps/day. The average of steps/day across each of the 7 possible valid days was the main outcome from the accelerometer. This outcome has been validated in persons with MS (Busse, Pearson, Van Deursen, & Wiles, 2004; Motl, Snook, & Agiovlasitas, 2011)