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Physical activity and depression in middle and older-aged adults with multiple sclerosis

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Abstract

Background—Depression is common among people with multiple sclerosis (MS), and research shows that individuals, including individuals with MS, who are more physically active report lower rates of depression. However, little is known about the relative importance of *level* of physical activity (e.g., moderate versus vigorous) in relationship to depression, or the role that age might play in this relationship among people with MS. The current study sought to (1) clarify the associations between moderate and vigorous physical activity and depression in a sample of individuals with MS, (2) determine the associations between age and physical activity, and (3) test for the potential moderating influence of age on the associations between physical activity and depression.

Objective/Hypothesis—Cross-sectional survey.

Methods—112 individuals with MS completed a survey assessing demographic variables, amount of moderate and vigorous physical activity, and depression.

Results—There was a gradual decrease in the amount of moderate and vigorous physical activity as age increased, but this decrease was not statistically significant. Moderate physical activity was significantly (negatively) associated with depression across all age cohorts. Time spent in vigorous physical activity was significantly (negatively) associated with depression among the middle-aged but not younger or older participants who are physically active.

Conclusions—The findings support a link between moderate physical activity and depression and, for middle-aged individuals, vigorous physical activity and depression in persons with MS. The findings indicate that research examining the impact of activity enhancing treatments on depression in individuals with MS is warranted.

Keywords

Multiple sclerosis; physical activity; depression

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Introduction

Depression is a common problem in individuals with disabilities [1, 2], including those with multiple sclerosis (MS) [3, 4]. One potential treatment for depression is promoting increased physical activity.

Studies show that people are physically active have lower rates of depression by about 30–45% in cross-sectional investigations and 15–25% in prospective studies [5]. Physical activity intervention trials have also demonstrated the efficacy of physical activity as a treatment for depression [6, 7]. For example, one early study of older individuals with major depression demonstrated that a three-day-per-week aerobic exercise training program was as effective as Zoloft for treating major depressive disorder after 16 weeks of treatment [8]. Another study investigated the dose of physical activity that is needed to promote decreased depression among a sample of young adults (ages 20–45 years) with mild to moderate depression [9]. Participants were randomized to one of four treatment conditions (3 days/week of low energy expenditure exercises, 3 days/week of high energy expenditure exercises, 5 days/week of low energy expenditure exercises, or 5 days/week of high energy expenditure exercises) or a control group (3 days/week of flexibility exercises). The investigators found that those participating in the high energy expenditure exercises (regardless of frequency) had significantly reduced depressive symptoms compared to the low energy expenditure or control conditions, with no differences between the latter groups. Recent systematic reviews of the body of research in this area conclude that exercise appears to be clinically effective, but also note that many of the studies suffer from significant methodological weaknesses. More methodologically sound studies are needed to provide accurate estimates of the true effects of exercise on depression [6, 7].

An important question concerns the extent to which the benefits of exercise on depression in otherwise healthy individuals generalize to individuals with disabilities, who have lower rates of physical activity [10] and might find typical exercise programs to be challenging because of physical limitations. For example, MS is an autoimmune disorder that causes damage to the myelin sheath that surrounds axons in the brain and spinal cord, often resulting in muscle weakness, fatigue, and imbalance. As a result, individuals with MS can have reduced mobility, which could contribute to an increased risk of secondary health conditions such as coronary heart disease [11]. Clinically, there is general agreement that exercise and activity can be helpful for individuals with MS [12, 13]. However, little is known about the association between physical activity and depression in MS populations.

Two recent cross-sectional studies suggest that physical inactivity is related to greater depressive symptom severity in individuals with MS [14, 15]. In the first of these, Stroud and Minahan administered a survey to 121 individuals with MS that included measures of physical activity, depressive symptoms, and quality of life. Based on their responses, participants were classified as “Exercisers” or “Non-exercisers.” Even though this study found that exercisers reported significantly better scores than Non-exercisers on all of the quality of life domains assessed, including depression [14], the findings have limited generalizability, because most people undertake some form of exercise. In a second study, Suh and colleagues [15] asked 96 individuals with MS to wear an accelerometer for 7 days (as an objective measure of physical activity) and complete the Hospital Anxiety and Depression scale. They found that objectively measured physical activity was significantly negatively associated with depression ($r = -0.25$). These two studies indicate that increasing physical activity may be as promising an approach to ameliorating depressive symptoms in persons with MS as it is in the general population. However, we were not able to identify any intervention studies that have utilized this approach.

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An important dimension of physical activity is intensity. For example, people can engage in regular moderate activities – activities that cause small increases in breathing or heart rate – throughout the week. Others might engage in more vigorous activities – activities that cause large increases in breathing or heart rate – when they are active. Moreover, it might be expected that more vigorous physical activity might be increasingly challenging as people age, given that physical activity is known to decline as people age in the general population [16] as well as in those with disabilities [10]. Yet, the extent to which physical activity changes as a function of age in persons with MS, and whether or not the associations between activity and depression vary as a function of age in the MS population, is unknown. This information is important for determining whether, and for whom, physical activity programs might be effective for individuals aging with MS.

The current study sought to (1) clarify the associations between moderate and vigorous physical activity and depression in a sample of individuals with MS, (2) determine the associations between age and physical activity, and (3) test for the potential moderating influence of age on the associations between physical activity and depression. Based on the research cited above, we hypothesized that both moderate and vigorous physical activity would be negatively associated with depression, and that we would see lower levels of physical activity among older versus younger patients. We did not have a specific hypothesis about the potential moderating effects of age on the associations between physical activity and depression, as this has not yet been examined in previous research.

Methods

Procedures

A survey that included the study measures was mailed to 176 individuals with MS who had completed a previous mail survey examining quality of life issues of people with MS [17], and expressed a willingness to participate in future survey studies. Inclusion criteria for study participation included (1) being 18 years of age or older and (2) having a diagnosis of MS that had been made by a medical professional. Of the 176 surveys mailed, 112 completed surveys were returned between October 2004 and August 2005, yielding a response rate of 64%. All of the study procedures were approved by the University of Washington Institutional Review Board. All of the participants signed an informed consent form and were paid $25 for participation. One other study has been published using data from the current survey [18], although the study questions addressed in the previous study are not related to those in the current analyses.

Measures

Demographic variables—All participants were asked to provide information about their current age, sex, education level, and employment status.

MS course and MS disease progression/severity—MS course was assessed by asking the participants to identify a pictorial graph that corresponded with their disease course over time [19]. The graphs included written descriptions of the four clinical courses of MS that were recognized at the time of the study: relapsing/remitting, secondary progressive, primary progressive, and progressive relapsing [20]. Evidence supports the validity of this strategy for classifying MS clinical course in survey research [19].

MS disease severity was assessed using the mobility subscale of the Self-Administered Expanded Disability Status Scale (SA-EDSS) [21]. This scale is commonly used to indicate MS severity in research [22–24]. The mobility scale contains three items that respondents use to indicate (1) the greatest distance that they can walk on an average day (rated on a 7-

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point Likert scale from 1 = “A few steps” to 7 = “More than 3 tenths of a mile without stopping to rest (a little further than 5 football field lengths)”); (2) the level of assistance they need for walking (rated on a 4-point Likert scale from 1 = “No help” to 4 = “A walker”); and (3) their use of a wheelchair for mobility (yes or no), and if yes, the extent to which they can sit up or bear weight on their legs (rated on a 4-point Likert scale from 1 = “On an average day, I cannot sit up in a chair” to 4 = “On an average day, I can bear weight on my legs (stand up and move) and get myself from one chair to another.” The Self-Administered Mobility items are combined into a scale score that ranges from 4 to 8, with lower scores indicating more independence in mobility (i.e., less disease progression). Research supports the validity of the SA-EDSS mobility item as a measure of MS disease progression through its significant associations with self-report ratings of problems with thinking, slurred speech, vision loss, pain, depression, fatigue (all positive associations), and engagement in paid work (negative association)[23]

Physical activity—Moderate and vigorous physical activity was assessed using items from the 2003 Centers for Disease Control and Prevention Behavioral Risk Factor Surveillance System (BRFSS) Survey Questionnaire [25]. Participants reported whether or not they engaged in at least 10 minutes of moderate activities (activities that cause small increases in breathing or heart rate) or vigorous activities (activities that cause large increases in breathing or heart rate) outside of work in a usual week, and if so, (1) how many days per week they do these activities and (2) on the days when they do these activities for at least 10 minutes at a time, the total time per day they spend doing these activities. In order to emphasize that we were interested in assessing physical activity outside of an employment setting, we revised the original BRFSS instructions by adding the following text:

> We are especially interested in how physically active you are during a typical week; excluding activity that is part of your employment or self-employment. For physical activity outside of work we distinguish two types: **vigorous** and **moderate**.

In addition, we added the phrase “outside of work” in the questions asking whether or not participants engaged in at least 10 minutes of moderate or vigorous activities outside of work in a usual week for the same purpose.

Two dichotomous and two continuous physical activity level scores were computed from the participants’ responses to these items: (1) engaging or not engaging in *at least* 10 minutes of moderate physical activity in a usual week outside of work; (2) engaging or not engaging in *at least* 10 minutes of vigorous physical activity in a usual week outside of work; (3) overall number of minutes of moderate physical activity in a usual week outside of work (computed by multiplying the number of days participants stated they engaged in at least 10 minutes of moderate activity X the total number of minutes they usually spend engaging in these activities on the days when they do at least 10 minutes of moderate activity outside of work); and (4) overall number of minutes of vigorous physical activity in a usual week outside of work (computed by multiplying the number of days participants stated they engaged in at least 10 minutes of vigorous activity X the total number of minutes they usually spend engaging in these activities on the days when they do at least 10 minutes of vigorous activity outside of work).

Depression—Depression was assessed using the 9-item depression module from the Patient Health Questionnaire (PHQ-9) [26]. The PHQ-9 lists nine symptoms of depression, and respondents are asked to indicate the extent to which they experienced each of these over the past two weeks on 0 (not at all) to 3 (nearly every day) Likert scales. The PHQ-9 scale score can range from 0 to 27 (sum of scores of the nine items), with a higher score

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indicating a more pronounced severity or degree of depression. The PHQ-9 has a great deal of evidence supporting its reliability and validity as a measure of depression in medical patients [26,27].

Data Analyses

We first computed descriptive statistics (mean, standard deviations, minimum and maximum for age, frequencies and rates for categorical variables) for the demographic, MS-related, and study variables to describe the sample. We then compared the 112 participants who provided data for the current analyses to the 64 individuals who had participated in the previous survey, but did not elect to participate in the follow-up survey, using a t-test for age and chi-square analyses for the categorical variables (sex, race/ethnicity, and MS course). We then examined the distributions of the study variables, with a plan to normalize any variable(s) with a skewness greater than 1.0 prior to performing the planned parametric tests [28]. The PHQ-9 scale score, total minutes of moderate activities in the past week and total minutes of vigorous activity in the past week all had skewness greater than 1.0 (1.12, 1.97, and 2.76, respectively). Square root transformations reduced the skewness of the PHQ-9 scale score (to 0.04) and the minutes of moderate activity variable (to 0.17). However, a logarithmic transformation was required to correct the skew of the minutes of vigorous activity variable (to 0.70).

We examined the hypothesized associations between age and activity level by classifying participants into young adult (< 45 years old, n = 22), middle aged (45 – 64 years old, n = 76), and older aged (> 64 years old, n = 14) age cohorts, and compared rates of engaging in at least 10 minutes of moderate or physical activity between each cohort using chi-square analyses, and overall level of moderate and vigorous activity using Analysis of Variance (ANOVA). Pairwise comparisons between the age cohorts were planned if a significant main effect for age cohort emerged.

We also examined the association between physical activity and MS disease severity by computing zero-order Pearson correlation coefficients between minutes of moderate and vigorous physical activity and the Mobility scale score from the SA-EDSS. Next, to examine the direct associations between physical activity and depression, we (1) computed zero-order Pearson correlation coefficients between PHQ-9 scale scores and minutes spent engaging in moderate and vigorous activity in the past week and (2) used t-tests to compare the PHQ-9 scale scores between participants who did and did not engage in at least 10 minutes of moderate and physical activity in the past week.

Finally, we performed a hierarchical linear regression analysis to examine the associations between physical activity and depression while controlling for age and MS severity and test for possible Age X Activity interaction effects. The predictor variables were first centered in order to limit any potential problems with multicolinearity when testing for the planned interaction effects. In these analyses, the PHQ-9 scale score was the criterion variable. Age (centered) and the SA-EDSS Mobility scale score were entered as control variables in step 1. The two variables reflecting minutes of moderate and vigorous activity (both centered) were entered in step 2. Finally, interaction terms representing Age (centered) X Moderate Activity (centered) and Age (centered) X Vigorous Activity (centered) were both entered in the third step. Follow-up analyses were planned to help explain any significant interaction effects that emerged. We considered p-values < .05 to be significant and $p < .10$ was considered a trend.

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Results

Sample description

The sample consisted of 112 individuals with MS who had an average age of 52.59 years (SD = 10.78 years, Range = 25 to 82 years). Most participants (91, or 81%) were women. The most common MS course was relapsing-remitting (46%), followed by primary progressive (22%), and secondary progressive (32%). Almost all (97%) of the participants reported their race as white; two (2%) reported they were Native American, and one (0.9%) reported they were Hispanic. The demographic characteristics of the sample are presented in Table 1. The 112 individuals who provided data for the current analyses did not differ significantly from the 64 individuals who did not participate on any of the descriptive measures.

The average PHQ-9 scale score for the group as a whole was 6.41 (SD = 5.85) which represents a "mild" level of depressive symptoms [26,27]. About three-quarters of the sample (82, or 73%) reported that they engaged in 10 minutes or more of moderate physical activity at least once in the past week, and about a third (41, or 37%) reported they engaged in 10 minutes or more of vigorous activity in the past week. The average number of minutes per week of moderate and vigorous physical activity for the group as a whole was 48.66 (SD = 54.04 minutes) and 27.10 (SD = 50.76 minutes), respectively.

Physical activity as a function of age and MS severity

The results of the chi-square analyses and analyses of variance testing for differences between the three age cohorts in physical activity are presented in Table 2. As can be seen, there appears to be a gradual decrease in the frequency of engaging in moderate and vigorous activity as age increases. However, this decrease was not statistically significant for moderate physical activity, and showed only a non-significant ($p < .10$) trend for vigorous physical activity. In terms of minutes of physical activity (in the past week), there was a great deal of variability within and no significant differences between each age cohort, although the older cohort reported a substantial reduction in minutes of moderate physical activity, relative to the middle aged cohort. There was a non-significant ($p < .10$) trend for differences in the total minutes of vigorous physical activity between the age cohorts, with steady reductions in time spent engaging in vigorous physical activity from one age cohort to the next (see Table 2).

Minutes of moderate and vigorous physical activity were negatively and significantly moderately associated with the SA-EDSS Mobility scale scores (rs = −.39 and −.38, respectively; ps < .001).

Depression as a function of physical activity

Participants who reported that they engaged in at least 10 minutes of moderate activity in the past week reported significantly lower PHQ-9 scale scores (Mean = 5.51, SD = 5.54) than those who reported they did not engage in at least 10 minutes of moderate activity in the past week (Mean = 8.45, SD = 5.70, $t(109) = 2.43$, $p < .05$). However, the PHQ-9 scale scores in those who engaged in at least 10 minutes of vigorous activity and those who did not engage in at least 10 minutes of vigorous activity in the past week were virtually identical (Means = 6.44 and 6.39, SDs = 6.16 and 5.71, $t(110) = 0.04$, p = NS). Similarly, there was a statistically significant and moderate negative association between minutes of moderate exercise and depression ($r = −.25$, $p < .01$). However, the association between minutes of vigorous physical activity and depression was close to zero (and non-significant, $r = −.02$, p = NS).

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The results of the regression analyses predicting PHQ-9 scale scores from minutes of moderate and vigorous activity (and their interactions with age), controlling for both age and MS severity, are presented in Table 3. As can be seen, the control variables evidenced a non-significant trend ($p < .10$) to predict PHQ-9 scale scores, and the measure of MS severity (SA-EDSS Mobility scale score) was significantly and positively associated with depression. That is, individuals with higher levels of MS severity reported higher levels of depressive symptoms. Together, minutes of moderate and vigorous activity accounted for an additional statistically significant 6% of the variance in depressive symptoms, with virtually all of this being due to the effects of moderate activity.

A non-significant ($p < .10$) trend emerged with age having a moderating influence on the associations between physical activity and depression. This appears to be due to the trend for an Age X Vigorous Physical Activity interaction effect. We explored this trend by examining the zero-order correlations between minutes of vigorous activity and PHQ-9 scores separately for each age cohort. The association was weak and non-significant for the young and older aged cohorts (rs = .02 and −.05, ps = NS, respectively). However, among the middle aged cohort, minutes of vigorous activity was significantly and moderately negatively associated with depressive symptoms ($r = -.24$, $p < .05$).

Discussion

The findings indicate that both moderate and vigorous activity levels are lower for individuals with MS who are older, and that moderate physical activity was associated with lower levels of depression across all age cohorts. The data also suggest the possibility that more vigorous physical activity may be associated with less depressive symptoms in middle-aged individuals with MS. The results have important implications for designing studies that will examine the causal impact of physical activity on depression in persons with MS. The results also have important clinical implications regarding recommendations that clinicians might make for activity in persons aging with MS.

The findings only partially supported the hypothesis regarding the effects of age on physical activity. We did find a steady decrease in both moderate and vigorous physical activity from one age cohort to the next. Although the differences between the age cohorts in rates and minutes of physical activity were not statistically significant, they showed a non-significant trend for both the rate and minutes of vigorous activity. Whether or not the decreases observed are reliable will need to be determined by future research that will ideally include a larger sample that could provide more statistical power for detecting the effects of age.

If the age effect trends observed in this study are replicated, the findings provide both hope and potential areas of concern. On the positive side, the majority (57%) of older individuals with MS report that they are continuing to engage in at least some moderate physical activity. To the extent that this activity is linked to important health outcomes such as depression (and the findings in this study suggest that it is), improved physical function, and prevention of secondary health conditions, an increase in moderate physical activity could be an important treatment target for older patients with MS [29].

Of concern, however, was the finding that only half of the young adult sample reported at least some vigorous physical activities, and the great majority (88%) of the older age cohort reported that they did not engage in at least 10 minutes of vigorous physical activity in the past week. It might not be surprising that, like other aging populations, vigorous physical activity was found to decline in the current sample of people with MS. Moderate physical activities, such as walking, are the most popular physical activities to engage in, can be

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inexpensive, and are more gentle on the body as people age. Determining the best ways to bolster these types of activities with people aging with MS will be important.

In terms of the associations between physical activity and depression, we found that across all age groups, moderate but not vigorous physical activity was most important. The association between physical activity level and depression that we identified is consistent with previous research that has found significant associations between physical activity and depression in individuals with MS [14,15]. This suggests that the finding is reliable, despite the fact that different measures of activity level were used in each study. Our study is the first to our knowledge to distinguish moderate from vigorous activities, however. The fact that these two activity domains showed different associations to depression is an important finding that has substantial clinical implications if replicated; specifically, they suggest that there may be a need to encourage moderate, rather than vigorous, activity as means of reducing depression, especially among young and older adults. Two reviews of the literature regarding exercise in individuals with MS both conclude that: (1) most individuals with MS can tolerate exercise; (2) patients with MS should consult a rehabilitation expert before starting a new exercise regimen; (3) unless otherwise contraindicated, both resistance and endurance training should be included in the exercise regimen, as they can each result in different types of benefits; and (4) training frequency and intensity should be gradually increased until an end-point goal is reached [12, 13] . However, neither of these reviews discuss the relative importance of moderate versus vigorous exercise, nor do they address the important role of lifestyle activities and engaging in activities one finds pleasant or reinforcing. The current findings suggest that moderate levels of activity, which would be easier for many patients to engage in, might have more benefits than more vigorous forms of exercise in persons with MS. These activities could include various forms of physical activity (e.g., walking, swimming) or even active hobbies or other activities that are reinforcing for many people (e.g., gardening). An important next step is to test the impact of various forms of activity on exercise in a controlled clinical trial.

Study limitations

This study has a number of limitations that should be considered when interpreting the results. First, self-reported measures of physical activity were utilized and are known to overestimate physical activity levels. Future studies should determine whether the relationships we observed remain consistent when using objective measures of physical activity such as accelerometers. Another key limitation is that the sample size was relatively small, which likely limited our ability to detect effects that existed in the data. Thus, caution in interpreting differential importance of exercise to depression as a function of age is warranted. Future research is needed to determine if the moderating effects of age suggested by our findings represent a reliable result that would emerge in other samples

Another limitation to keep in mind is that these data were cross-sectional. As a result, it is not possible to draw causal conclusions regarding significant effects; we cannot conclude from these data, for example, that moderate levels of physical activity *caused* lower levels of depression, or that lower levels of depression *caused* an increase in moderate activity. Experimental research is needed to determine the extent to which systematic changes in moderate and vigorous activity impact depression and other health outcomes in persons with MS. The current findings indicate that such research is warranted.

In addition, all of the data were obtained via self-report. Some of the significant associations found could have been due to shared method variance. Future researchers should use more objective measures of activity (e.g., accelerometers as used by Suh and colleagues [15]) when possible. Another limitation is that the measures of depression and total minutes of moderate and vigorous activities in the past week were all positively skewed. It is possible

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that this may reflect floor effects and may have attenuated some of the correlations and limited our ability to determine the true associations among these variables. Finally, the items used to assess activity asked respondents to indicate their level of activity *outside of work*. Thus, it is possible that for some participants, the measure under-represented level of total moderate physical activity. This potential error in measurement could have attenuated the associations found. However, we still found significant associations between (moderate) activity and lower depression levels despite this.

Summary and conclusions

Despite the limitations of this study, the findings provide additional support for the importance of physical activity as being associated with depression in individuals with MS. The findings also raise the intriguing possibility that moderate physical activity may be more important to depression than vigorous physical activity. This is an important finding, as moderate activity would likely be less challenging than vigorous activity in individuals with MS who may find the regular performance of vigorous physical activity difficult. Research is needed to replicate the current findings in other samples of individuals with MS, and in particular to systematically examine the causal influences of both moderate and vigorous physical activity on depression and other important health outcomes in persons with MS [31,32]. Such research will provide clinicians with an important empirical foundation for making clear recommendations to their patients with MS.

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Table 1

Demographic characteristics of the study sample (N = 112)

Variable	Mean	SD
Age in years	52.59	10.78
	N	Percent
Sex		
Women	91	81%
Men	21	19%
Race/Ethnicity		
White	109	97%
Native American	2	3%
Hispanic	1	1%
MS course		
Relapsing-remitting	49	46%
Secondary progressive	34	32%
Primary progressive	23	22%
Unknown	6	

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Table 2

Physical activity as a function of age

	Age group			
Variable	**Young adult (n = 22)**	**Middle age (n = 76)**	**Older age (n = 14)**	**F or χ^2 (df)**
Engage in at least 10 minutes of moderate activity per week				
Yes	19 (86%)	55 (72%)	8 (57%)	3.81 (2)
No	3 (14%)	21 (28%)	6 (43%)	
Engage in at least 10 minutes of vigorous activity?				
Yes	11 (50%)	28 (37%)	2 (14%)	$4.71^{\dagger}$ (2)
No	11 (50%)	48 (63%)	12 (88%)	
Minutes of moderate activity, mean (SD)	44.32 (39.32)	53.36 (52.64)	30.00 (37.21)	1.20 (2)
Minutes of vigorous activity	45.23 (74.55)	25.46 (44.83)	7.50 (21.01)	$2.56^{\dagger}$ (2)

Note: Young adult = 18 – 44 years; Middle age = 45 – 64; Older age = 65 +

† $p < .10$

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Disabil Health J. Author manuscript; available in PMC 2013 October 01.

Table 3

Regression analyses predicting depression (PHQ-9) score from age, minutes of moderate and vigorous activity per week, and their interaction

Step and variable	R^2	ΔR^2	$F\Delta$	β	p
1: Control variables	.04	.04	2.51†		
Age				−.06	.549
MS severity (EDSS Mobility)				.23	.029
2: Minutes of activity/week	.10	.06	3.40*		
Moderate activity§				−.26	.012
Vigorous activity§				.03	.344
3: Interactions	.15	.04	2.70†		
Age X Moderate Activity§				.11	.279
Age X Vigorous Activity§				.17	.098

§Variable transformed to reduce skewness. Square root transformation was used for minutes of moderate activity and logarithmic transformation used for vigorous activity.