THE CASE FOR MULTIPLE HEALTH BEHAVIOR CHANGE INTERVENTIONS IN MULTIPLE SCLEROSIS

BY

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THESIS

Submitted in partial fulfillment of the requirements
for the degree of Master of Science in Kinesiology
in the Graduate College of the
University of Illinois at Urbana-Champaign, 2016

Urbana, Illinois

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Abstract

Background: Multiple sclerosis (MS) is a chronic, non-traumatic disease of the central nervous system (CNS). There is a growing need for alternative approaches to managing healthcare in MS. Targeting multiple, co-occurring health risk factors represents a holistic approach for managing comorbidities and many of the neuroperformance consequences of MS.

Methods: Sixty-nine participants with MS completed self-report measures of smoking status, nutrition, alcohol use, physical activity levels, comorbidity and neuroperformance outcomes and sociodemographic and clinical characteristics. The data were analyzed using *t*-tests and chi-square analyses in SPSS Statistics 22.0.

Results: Of participants with two or more risk factors, 90.3% were not meeting dietary and physical activity guidelines. Total number of comorbidities (z=2.36, p=0.02), cardiovascular disease symptoms (z=2.63, p=0.01), T25FW speed (z=2.53, p=0.01), and 6MW distance (z=2.61, p=0.01) had significant differences in the cluster of co-occurring poor nutrition and insufficient levels of physical activity. There was a significant difference between those reporting two vs. one risk factor for number of comorbidities (z=2.41, p=0.02), cardiovascular disease symptoms (z=2.40 p=0.02), T25FW speed (z=2.39, p=0.02) and 6MW distance (z=2.68, p=0.01).

Conclusion: Our results suggest that a clustering of insufficient physical activity and poor nutrition was reported in 90.3% of participants with two or more risk factors. The presence of that cluster further appeared to be synergistically associated with comorbidity and neuroperformance markers. This research could inform future investigations of multiple health behavior change in persons with MS.

To Mom and Dad

ACKNOWLEDGMENTS

Many people in my life deserve recognition for their support during my time at the University of Illinois. None of where I am today would have been possible without you in my life, and I can't express how grateful I am to each and every one of you.

This project would not have been possible without my advisor and mentor, Dr. Robert Motl. You have profoundly shaped my learning experience since the day I began working as a research coordinator. Thank you for your unwavering support and pushing me to always try my hardest. I will carry many lessons from you throughout my career.

Thank you to Dr. Naiman Khan and Dr. Jennifer Barnes for their thoughtful guidance and valuable help with this project. Your time and efforts are so appreciated.

I would like to thank the entire past and present ENRL team, especially Ipek Ensari, Brynn Adamson, Rachel Klaren, Lizzie Hubbard, Dominique Kinnet-Hopkins, Yvonne Learmonth, Emmerson Sebastiao, and Sarah Sommers, for their constant support, loving encouragement, and plethora of coffee walks. You made coming to work every day awesome.

To my parents, I can't thank you enough for your unending support and always encouraging me to climb higher. George, you are the best roommate I've ever had the pleasure of living with, all your support, coffee, and laughs got me through the past two years. Vasile, you have been an unending source of support, encouragement, and love through all my endeavors and multiple life changing decisions. I absolutely cannot wait to begin our next adventure together.

Finally, I must express my very profound gratitude for the ENRL participants who shared their lives with me and so willingly gave of their time and effort. Thank you.

TABLE OF CONTENTS

CHAPTER 1

INTRODUCTION

Multiple sclerosis (MS) is a chronic, non-traumatic disease of the central nervous system (CNS). The disease course is variable, and approximately 85% of MS patients begin with a relapsing-remitting MS (RRMS) course in which recurrent, intermittent episodes of inflammatory-mediated demyelination of axons and destruction of myelin, myelin forming cells and axons of the brain and spinal cord occur (1). In later stages of the disease, additional neurodegenerative processes result in further, irreversible neuroaxonal loss (2). MS has an estimated prevalence of 400,000 adults in the United States and occurs in upwards of three times as many women as men (3) MS further is the leading the leading cause of neurological disability in young adults (4). Indeed, damage to the CNS accumulates overtime and results in a range and severity of symptoms including walking and cognitive disability, and symptomatic fatigue, depression, and anxiety (5) (6).

RRMS is primarily managed through disease modifying therapies (DMTs) that can decrease the number of lesions and the rates of relapse and disability progression (7). However, in the absence of relapse, DMTs are only modestly effective in slowing progression of disability, with only 52% reporting some improvement in mobility; it is estimated that by 15 years after diagnosis, approximately 40% of individuals with MS will need some form of walking assistance (8). There is further a high prevalence of comorbidities in persons with MS which has been associated with disease exacerbation, and cannot be treated solely through DMTs (9). The limited efficacy of DMTs on functional and neurologic disability, in addition to the complex health concerns of persons with MS, highlight the need for holistic approaches to managing health in MS.

Targeting multiple, co-occurring health risk factors represents a holistic approach for managing comorbidities and many of the neuroperformance consequences of MS. In the general population, smoking, poor diet, excess alcohol consumption, and insufficient levels of physical activity, collectively known as the SNAP risk factors, represent the leading causes of preventable morbidity and mortality (10). Recent studies have indicated that the majority of American adults reported two or more co-occurring health risk factors and only 3% of adults met all four behaviors goals of being a non-smoker, having a healthy weight, being physically active, and eating five or more fruits and vegetables a day (11). There is evidence of greater pharmaceutical and disability burden costs from co-occurring SNAP risk factors, as well as synergistic negative influences on health such as an increased risk of cancer, diabetes, obesity, cardiovascular disease, depression and anxiety, and an overall of health (12) (13) (14). Emerging research investigating multiple health behavior change interventions, has reported significant changes in multiple health behaviors such as smoking, physical activity, and improved diet that suggests intervening on multiple health risk factors is indeed effective (11). Indeed, intervening on co-occurring risk factors offers potentially optimized health benefits, health promotion opportunities, and reduced health care costs (11).

Targeting co-occurring SNAP risk factors in persons with MS represents a potentially novel approach to managing symptoms and disability, and to our knowledge has not yet been investigated. Research is needed to a) examine the prevalence of individual and co-occurring SNAP risk factors in MS and any SNAP risk factor clusters, b) identify any subpopulations of persons with MS that are predisposed to SNAP risk factor clusters; and c) examine the association of SNAP risk factor clusters with health and neuroperformance outcomes to inform the design and necessity of multiple health behavior change interventions in MS.

Therefore, this thesis involved two studies on SNAP risk factor in MS. The first study investigated the prevalence of individual and co-occurring SNAP risk factors in persons with MS to identify the existence of any SNAP risk factor clusters. The study further examined the clinical and sociodemographic associations between individual and co-occurring SNAP risk factor in order to identify any subpopulations of persons with MS who are more susceptible to co-occurring or clustering SNAP risk factors. The second study explored health and neuroperformance outcomes and their associations with co-occurring poor nutrition and insufficient levels of physical activity, the most commonly occurring risk factor cluster identified in the first study. Such an investigation could inform the design of future multiple health behavior change interventions in persons with MS.

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CHAPTER 2

INDIVIDUAL AND CO-OCCURRING SNAP RISK FACTORS: INVESTIGATION OF SMOKING, NUTRITION, ALCOHOL CONSUMPTION, AND PHYSICAL ACTIVITY IN PERSONS WITH MULTIPLE SCLEROSIS

Abstract

Background: Smoking, poor nutrition, excess alcohol consumption, and insufficient physical activity, underlie most preventable causes of morbidity in the general population and are possibly associated with comorbidities and health outcomes in MS. However, the frequency of co-occurrence of these risk factors among people with MS remains unclear.

Methods: Sixty-nine participants with MS completed self-report measures of smoking status, nutrition, alcohol use, physical activity levels and sociodemographic and clinical characteristics. The data were analyzed using *t*-tests and chi-square analyses in SPSS Statistics 22.0.

Results: Poor diet was the most common risk factor with 85.5% of the sample not meeting dietary guidelines. Of participants with two or more risk factors, 90.3% were not meeting dietary and physical activity guidelines. There were differential rates of meeting physical activity guidelines between men and women (χ^2= 7.5, p=0.01) such that 73% of women were not meeting physical activity guidelines, compared to 38% of men. There were further differential rates of the most commonly co-occurring risk factors, insufficient physical activity and poor nutrition by sex (χ^2=4.2, p=0.05), such that 65% of women reported the co-occurrence of insufficient physical activity and poor diet compared to 38% of men.

Conclusion: Our results indicate that: a) an overwhelming 85.5% of the sample was not meeting nutrition guidelines; (b) 90.3% of participants with two or more risk factors reported the co-occurrence of poor diet and insufficient levels of physical activity; and (c) physical activity levels and the total number of SNAP risk factors varied across sex.

Introduction

Multiple sclerosis (MS) is a chronic, immune-mediated disease of the central nervous system with a prevalence of 1 per 1000 persons in the United States (1). The disease presents with a range and severity of symptoms including loss of walking mobility, cognitive dysfunction, fatigue, and depression. There is additional evidence for the occurrence of comorbidities (e.g., hypertension, hyperlipidemia and chronic lung disease) among persons with MS, and co-morbidities seemingly result in diagnostic delays and disability progression (2). Smoking, poor nutrition, excess alcohol consumption, and insufficient physical activity, known as the "SNAP" risk factors, underlie most preventable causes of morbidity in the general population, and are possibly associated with comorbidities and health outcomes in MS (3). However, the frequency of co-occurrence of SNAP risk factors among people with MS remains unclear.

The four aforementioned and often co-occurring SNAP risk factors have been a consistent focus of health behavior research among adults from the general population (4) (5). One systematic review examined the patterns of co-occurring SNAP risk factors among adults from the general population in 56 studies that included two or more SNAP risk factors (3). Common patterns of risk factor co-occurrence included a 'healthy' group that reported no risk factors; this occurred in over 80% of the 56 studies. There was a group reporting all four risk factors and this occurred in 50% of the 56 studies. Roughly 45% of the studies reported poor diet co-occurring with low levels of physical activity. The presence of co-occurring SNAP risk factors was most common among men and those with lower levels of education, and further was prevalent among those with lower SES and younger age.

There has been some focus on SNAP risk factors among those with MS, but these often have been examined individually across separate research studies. These studies yield information about the individual SNAP risk factors, but not pattern of co-occurring SNAP risk

factors. For example, cross-sectional studies have reported that 13-40% of persons with MS screened positive for possible alcohol abuse or dependence (6) (7) (8). One study examined smoking rates in 350 persons with MS and reported that 15.2% of the sample were current smokers (9). Participants who were current smokers reported heavier smoking, consuming 20-30 cigarettes daily, and had been smoking 10 years or longer. Regarding nutritional behaviors, one cross-sectional analysis of persons with MS reported that less than half of participants (47.5%) engaged in healthy nutritional behaviors (10). Participants consumed less than recommended levels of carbohydrates, fiber, vitamin E, calcium and zinc, but greater amounts of saturated fat, protein, vitamins A and C, folic acid and iron. However, the authors did not conduct food-level analyses. One recent examination of physical activity rates in persons with MS reported that 58% of those with MS engaged in insufficient levels of physical activity (11).

We are aware of one study that has reported on multiple SNAP risk factors in the same sample of people with MS. That study included 8,983 persons with MS, and reported that 17.3% of participants self-identified as current smokers, 18.2% were at risk for alcohol abuse or dependence, and less than 25% reported regular participation in moderate or heavy leisure-time physical activity (12). Lower socioeconomic status correlated with a higher frequency of adverse health behaviors. Participants with lower education levels and income were more likely to smoke. Women, participants over 50 years, and those with lower levels of income had a lower risk of excess alcohol consumption. Lower levels of education and increasing disability were associated with less vigorous physical activity. That study did not include nutrition, and did not provide descriptive data on the patterns, distribution, and correlates of co-occurring SNAP risk factors.

To date, we are unaware of research that has formally examined the individual SNAP risk factors (e.g., smoking, poor nutrition, excess alcohol consumption, and insufficient levels of physical activity) and their co-occurrence in individuals with MS. The study of co-occurring health behaviors in a population provides a means of assessing groups whose lifestyles put them at greater risk for future illness and informing the design of tailored interventions (13). Consequently, there is increasing interest in studying the individual and co-occurrence of SNAP risk factors in persons with MS (12). Accordingly, this study examined (1) the occurrence of individual SNAP risk factors in persons with MS; (2) the prevalence and pattern of co-occurring SNAP risk factors; and (3) individual and co-occurring SNAP risk factors variation across sociodemographic and clinical characteristics. Such inquiry could inform future research targeting multiple health behaviors and holistic health interventions in MS.

Methods

Participants

Recruitment included advertising through the National MS Society Local Research page, our laboratory Facebook page, and contacting individuals in our laboratory database. The inclusion criteria were: (1) age 18-64 years; (2) relapse free in past 30 days; (3) ambulatory with or without assistance; and (4) not pregnant (pregnancy can affect health behaviors). Of the 92 individuals with MS who underwent screening, 8 were disqualified, 14 were qualified but declined to participate prior to testing due to scheduling issues, and 70 participants met inclusion criteria and were scheduled for testing. One participant declined to provide self-report information resulting in a final convenience sample of 69 persons with MS.

Measures and definitions of risk factors

Smoking status was assessed using the CDC Tobacco Use Questionnaire (14). Participants were asked “Have you smoked at least 100 cigarettes in your entire lifetime” and if

yes, “Do you now smoke cigarettes everyday, some days or not at all?”. Participants were then categorized as smokers if they currently smoked every day or some days, and non-smokers if they have never smoked 100 cigarettes or no longer did. Smoking was considered a risk factor.

Inadequate fruit and vegetable and whole grain consumption were used as an index of poor nutrition. Participants completed a three-day food record for two weekdays and one weekend day. Participants were instructed to record all foods and beverages consumed and a registered dietitian reviewed records with participants for improved accuracy. Inadequate fruit and vegetable consumption was defined as not meeting the fruit and vegetable guidelines outlined by the United States Department of Agriculture and MyPlate.gov (15). Recommendations are specific to age and sex. For example, women ages 31-50 should aim for a minimum of 2.5 cups of vegetables and 1.5 cups of fruit per day; men ages 31-50 should aim for a minimum of 3 cups of vegetables and 2 cups of fruit per day. Inadequate whole grain consumption was defined as not meeting the whole grain recommendation outlined by the USDA and MyPlate.gov e.g., half or more of all grains should be whole (16). Not meeting the guidelines for fruit and vegetables and whole grains was considered a risk factor. The Nutrition Data System for Research (NDSR; Nutrition Coordinating Center, Minneapolis, MN, USA) software was used to analyze dietary intake.

Excess alcohol consumption was further assessed using the 3-day food record. A score of ≥2 standard drinks per day for men, and ≥1 standard drinks per day for women exceeds health recommendations. Participants were categorized as meeting the guidelines or not; exceeding the guidelines was considered a risk factor (15). Physical activity levels were assessed using the Godin Leisure-Time Exercise Questionnaire (GLTEQ) (17). The GLTEQ includes 3 items that measure the frequency of mild, moderate, and strenuous physical activities that occur for at least

15 minutes during a person's leisure time. The frequency of vigorous and moderate activities were multiplied by 9 and 5 metabolic equivalents, respectively and then summed as a health contribution score (18). Participants accumulating 24 units or more were classified as active and meeting the guidelines, those accumulating 23 units or less were considered insufficiently active and not meeting the guidelines; not meeting the guidelines was considered a risk factor. This classification has been validated in healthy adults (19).

Procedures

This study was approved by a University Institutional Review Board, and participants provided written informed consent. Participants underwent a neurological evaluation by a Neurostatus-certified examiner for generation of an EDSS score, measurement of height and weight, and then completed self-report measures of smoking status, diet, alcohol use, physical activity levels and sociodemographic and clinical characteristics. Participants were remunerated for their time.

Statistical Analyses

Statistical analyses were performed in IBM SPSS Statistics for Windows (version 22; IBM SPSS Inc., Armonk, N.Y., USA). Characteristics of the sample are presented as frequencies and percentages, unless otherwise noted. We present the percent of participants reporting each individual SNAP risk factor for the sample. We then reported the percentage of the population with multiple SNAP risk factors (i.e., occurrence of SNAP risk factors summed per participant), and then the SNAP risk factor distribution (i.e., percent of the population not meeting guidelines across all possible patterns of SNAP risk factors). We compared the distribution of individual SNAP risk factors between sociodemographic and clinical factors using chi-square analysis. We report the median (IQR) of SNAP risk factors for significant sociodemographic and clinical factors. We further examined variation in the total number of risk factors (summed total of SNAP

risk factors) between clinical and demographic characteristics using non-parametric t-tests. The magnitude of differences based on Cliff's d was interpreted as small, medium, and large based on values of 0.1, 0.3, and 0.5, respectively (20). Exploratory analyses of the most commonly co-occurring risk factors were performed through chi-square analysis.

Results

Sociodemographic and Clinical Characteristics

Participants (N=69) were primarily female (69.6%), Caucasian (94.2%), and married (59.4%) (Table 1). Nearly half of participants were employed (49.3%), 85.5% had some college experience, and 68.1% had an annual household income greater than $40,000. The mean age, (mean (SD)), was 50.5 (8.9) years. The mean BMI (kg/m^2) was 28.7 (6.6). Participants primarily had RRMS (84.1%), mild to moderate disability (median EDSS score of 4.0 (2.0)), and a disease duration of 14.4 (10.5) years.

Occurrence of Individual SNAP Risk Factors

Poor diet was the most common SNAP risk factor with 85.5% of the sample not meeting dietary guidelines for fruit and vegetable (95.7%) consumption and whole grain consumption (87.0%) (Table 2). Insufficient physical activity was the second most prevalent SNAP risk factor such that 62.3% of the sample was not meeting physical activity guidelines for moderate-vigorous physical activity.

Co-occurring SNAP Risk Factors

As displayed in Table 3, 34.8% of the sample had one SNAP risk factor, whereas over half of participants (59.4%) had two or three co-occurring risk factors. Only 5.7% of participants had zero or four SNAP risk factors. Table 3 further presents all possible patterns of individual and co-occurring SNAP risk factors. The median number of SNAP risk factors reported was 2 (IQR = 1). Among participants with 1 or more SNAP risk factors, 70.8% were not meeting

dietary guidelines for fruit and vegetable and whole grain consumption. Of participants with 2 or more SNAP risk factors, 90.3% were not meeting dietary and physical activity guidelines. Smoking occurred only in participants who reported insufficient levels of physical activity and poor diet (e.g. 90% of participants reporting three or more SNAP risk factors).

Variation in Individual and Total Number of SNAP Risk Factors

Results of the chi-square analyses are reported in Table 4. Analyses of individual risk factors between sociodemographic and clinical characteristics revealed differential rates of meeting physical activity guidelines between men and women (χ^2= 7.5, p=0.01) such that 73% of women were not meeting physical activity guidelines, compared to 38% of men. Rates of meeting dietary guidelines varied by employment status such that 94% of employed individuals did not meet dietary guidelines, compared to 77% of unemployed individuals. Rates of meeting physical activity guidelines varied by BMI (χ^2= 4.9, p=0.05) such that 70% of overweight and obese individuals did not meet physical activity guidelines compared to 42% of individuals with a healthy weight. Smoking status was differential across household income (χ^2= 6.4, p=0.05), whereby 33% of individuals earning less than $40,000 per year were more likely to smoke compared to 8% of individuals earning more than $40,000 per year. Non-parametric *t*-test analyses assessing the variation of the total number of risk factors between sociodemographic and clinical characteristics revealed a significant difference between men and women (z=3.08, p=0.00), whereby women reported a higher total number of risk factors. No other sociodemographic or clinical characteristics were significantly different.

Exploratory chi-square analyses assessed the variation of the co-occurrence of insufficient physical activity and poor diet, the most common pair of co-occurring SNAP risk factors, revealed a differential relationship between sex (χ^2=4.2, p=0.05) such that 65% of

women reported the co-occurrence of insufficient physical activity and poor diet compared to 38% of men. The co-occurrence of physical activity and poor diet further varied across BMI (χ^2=4.1, p=0.05) whereby 65% of overweight and obese individuals reported the co-occurrence compared to 38% of individuals with a healthy weight.

Discussion

The present study involved a novel investigation of the individual and co-occurrence of SNAP risk factors and the variation across clinical and sociodemographic characteristics in a sample with MS. Overall, the results indicated that (a) an overwhelming 85.5% of the sample was not meeting nutrition guidelines independent of other SNAP risk factors; (b) 90.3% of participants with two or more risk factors reported the co-occurrence of poor diet and insufficient levels of physical activity; and (c) physical activity levels and the total number of SNAP risk factors varied across sex. These collectively suggest that persons with MS do indeed report the individual co-occurrence of SNAP risk factors; and that poor diet and insufficient levels of physical activity are the most commonly reported co-occurring SNAP risk factors in this population. This study further indicates that subpopulations of MS, specifically women, are more susceptible to the individual and co-occurrence of SNAP risk factors. Future research is needed to investigate the consequences of the individual and co-occurring SNAP risk factors and further, to reduce SNAP risk factors in MS through multiple health behavior change interventions.

Poor diet was the most commonly reported SNAP risk factor with 85.5% of the sample not meeting dietary guidelines for fruit and vegetable and whole grain consumption. The nutritional habits of persons with MS have not been well studied, however, this study suggests that individuals with MS have comparable or worse nutritional habits than the general population (21). A recent CDC report estimated that only 13.1% of American healthy adults are meeting fruit recommendations and 8.9% are meeting vegetable recommendations (22). A diet rich in

fruit and vegetables may help reduce the risk of heart disease, certain types of cancer, obesity, and type 2 diabetes (16). According to recently published findings from the Whole Grains Council's 2015 Whole Grains Consumer Insights Survey, 63% of Americans report making half or more of their grains whole, which is associated with a decreased risk of heart disease, constipation, and enhanced weight management (23). Improved nutritional behaviors should be considered as a focus for effectively managing overall health and comorbidities in person with MS. Indeed, one study examining the correlates of nutritional behavior in persons with MS reported that nutritional self-efficacy (β=0.69, p< 0.001) was the strongest predictor of nutritional behaviors. These data support the development of future interventions to improve health behaviors in persons with MS.

More than half the sample (59.4%) reported two or more co-occurring SNAP risk factors. Importantly, 90.3% of those participants reported the co-occurrence of poor diet and insufficient levels of physical activity. Exploratory analyses further suggested variance of the co-occurrence of these two risk factors across sex and BMI. This co-occurrence is similar to the clustering of "energy balance behaviors of physical activity and diet" seen in the general population (4). Future investigations of co-occurring SNAP risk factors should specifically examine the co-occurrence and correlates and consequences of insufficient physical activity and poor diet to inform the design of multiple health behavior change interventions in MS. There is evidence that the two behaviors may predict one another, further suggesting that targeting the co-occurring risk factors in a multiple health behavior change intervention could be more effective than targeting the risk factors separately (24).

Smoking was reported by 15.9% of participants and excess alcohol consumption was reported by 10.1% of the sample. The two further did not co-occur (e.g. 0% of participants

reporting two or more co-occurring SNAP risk factors reported smoking and excess alcohol consumption together). This lack of a co-occurrence is different from examinations of co-occurring risk factors in the general population that have reported a clustering of 'addictive behaviors' such as smoking and excess alcohol consumption (4). It appears "addictive behaviors" are not nearly as prevalent in MS as the general population and furthers the case for the investigation of the co-occurrence of insufficient physical activity levels and poor diet as the most promising avenue for multiple health behavior change interventions in MS.

Both physical activity levels and the total number of SNAP risk factors varied across sex. Women reported a higher number of SNAP risk factors and were less physically active than men. Our finding is important as it identifies a subpopulation of persons with MS e.g. women, who are more susceptible to co-occurring SNAP risk factors. We further know that MS affects thrice as many women as men. This finding confirms the need for more investigations of the co-occurrence of SNAP risk factors, particularly among women with MS.

There are important limitations of the present study. The sample of persons with MS was relatively homogenous, consisting of primarily Caucasians and females. The sample included mostly participants with RRMS and was characterized by moderate disability. Therefore, our results may not be generalizable amongst those with other types of MS, more severe disability status and males. Our study further included self-report measures and these are subject to reporting biases. This exploratory study had a relatively small sample, and future research should examine SNAP risk factors in a larger, heterogeneous sample of persons with MS, particularly in those with higher disability levels and progressive forms of the disease.

The present study provides preliminary evidence of the individual and co-occurrence of SNAP risk factors in MS. Our evidence suggests that persons with MS are far from meeting

physical activity and diet guidelines for health benefits and that women are particularly susceptible. Such evidence supports additional examinations of the correlates of and interventions for individual and co-occurring SNAP risk factors, specifically diet and physical activity levels, in persons with MS.

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Tables

Table 1. Sociodemographic and Clinical Characteristics in the sample of persons with MS

Characteristic	MS (n=69)
Sex (% female)	69.6%
Age, years (mean (SD))	50.5 (8.9)
Race (% Caucasian)	94.2%
BMI (kg/m2) (mean (SD))	28.7 (6.6)
Marital Status (% married)	59.4%
Employed (% employed)	49.3%
Education (% some college)	85.5%
Annual Household Income (% over $40,000)	68.1%
EDSS, median (IQR)	4.0 (2.0)
Disease Course (% RRMS)	84.1%
Disease Duration, years	14.4 (10.5)

Note. BMI = Body-Mass Index.

Table 2. Occurrence of individual SNAP risk factors in the sample of persons with MS (n=69)

Behavior	Prevalence (%)
Smoking	15.9
Poor Diet	85.5
Excess Alcohol Consumption	10.1
Insufficient Physical Activity	62.3

Table 3. Prevalence and Patterns of Co-occurring SNAP risk factors

Number of Risk Factors	Risk Factor Prevalence (%)	Smoking	Poor Diet	Excess Alcohol Consumption	Insufficient Physical Activity	Pattern Prevalence (%)
0	4.3	No	No	No	No	100.0
1	34.8	Yes	No	No	No	0.0
1		No	Yes	No	No	70.8
1		No	No	Yes	No	12.5
1		No	No	No	Yes	16.7
2	44.9	Yes	Yes	No	No	3.2
2		Yes	No	Yes	No	0.0
2		Yes	No	No	Yes	0.0
2		No	Yes	Yes	No	6.5
2		No	Yes	No	Yes	90.3
2		No	No	Yes	Yes	0.0
3	14.5	No	Yes	Yes	Yes	10.0
3		Yes	No	Yes	Yes	0.0
3		Yes	Yes	No	Yes	90.0
3		Yes	Yes	Yes	No	0.0
4	1.4	Yes	Yes	Yes	Yes	100.0

Table 4. Variation in Individual SNAP Risk Factors by Clinical and Sociodemographic Factors

	Smoking ($\chi 2$)	**Poor Diet ($\chi 2$)**	**Excess Alcohol Consumption ($\chi 2$)**	**Insufficient Physical Activity ($\chi 2$)**
Sex	2.8	0.5	1.0	7.5**
Age	0.5	0.0	4.2	3.4
Race	0.3	0.7	1.0	0.3
BMI	0.9	0.0	2.6	4.9*
Marital Status	2.9	0.4	0.0	0.5
Employed	0.9	4.0*	1.5	0.4
Education	0.1	0.2	0.0	0.0
Annual Household Income	6.4*	2.6	1.1	0.7
Disability	0.9	0.5	4.1	0.4
Disease Course	1.3	0.3	0.0	0.3
Disease Duration	0.7	2.6	0.6	0.4

** Significant at the 0.01 level (2-tailed). * Significant at the 0.05 level (2-tailed). BMI = Body-Mass Index.

Table 5. Variation in Total Number of Co-occurring SNAP Risk Factors by Clinical and Sociodemographic Characteristics

Characteristics	n (%)	Median (IQR)	Z statistic	*p*	Cliff's d
Sex					
Female	48	2 (1)	2.94	**0.00**	0.42
Male	21	1 (1)			
Age					
Under 50 years	25	2 (1)	0.38	0.70	0.05
50 years and older	44	2 (1)			
Race					
Caucasian	65	2 (1)	1.45	0.19	0.40
Other	4	2 (1)			
BMI					
Normal weight	21	1 (1)	1.60	0.11	0.23
Overweight or obese	48	2 (1)			
Marital Status					
Married	41	2 (1)	0.06	0.95	0.01
Not Married	28	2 (1)			
Employment Status					
Employed	34	2 (1)	0.38	0.70	0.05
Unemployed	35	2 (1)			
Education					
No college education	10	2 (2)	0.33	0.74	0.06
Some college education	59	2 (1)			
Annual Household Income					
<$40,000	22	2 (2)	1.65	0.10	0.02
>$40,000	47	2 (1)			
Disability					
No walking disability	34	2 (1)	0.68	0.49	0.09
Walking disability	35	2 (1)			
Disease Course					
RRMS	58	2 (1)	0.46	0.65	0.08
Progressive MS	11	2 (2)			
Disease Duration					
Less than 10 years	30	2 (0)	1.86	0.06	0.24
10 years or more	39	2 (1)			

BMI = Body-Mass Index.

CHAPTER 3
CO-OCCURRING POOR NUTRITION AND INSUFFICIENT LEVELS OF PHYSICAL ACTIVITY: CLUSTERING RISK FACTORS AND COMORBIDITY AND NEUROPERFORMANCE OUTCOMES IN MS

Abstract

Background: Research has documented the co-occurrence of poor diet and insufficient levels of physical activity in persons with MS. However, individual and co-occurring poor diet and insufficient physical activity as correlates of comorbidity and neuroperformance outcomes has not been studied in persons with MS.

Methods: Sixty-nine participants with MS completed self-report measures of nutrition, physical activity levels, comorbidity and neuroperformance outcomes, and sociodemographic and clinical characteristics. The data were analyzed using *t*-test analyses in SPSS Statistics 22.0.

Results: There was a significant difference in the number of comorbidities (z=3.31, p=0.00), T25FW speed (z=2.04, p=0.04), and 6MW distance (z=2.38, p=0.02) between physical activity levels, and between the number of cardiovascular disease symptoms and nutrition characteristics (z=2.35, p=0.02). Total number of comorbidities (z=2.36, p=0.02), cardiovascular disease symptoms (z=2.63, p=0.01), T25FW speed (z=2.53, p=0.01), and 6MW distance (z=2.61, p=0.01) had significant differences in the cluster of co-occurring poor nutrition and insufficient levels of physical activity. There was a significant difference between those reporting two vs. one risk factor for number of comorbidities (z=2.41, p=0.02), cardiovascular disease symptoms (z=2.40 p=0.02), T25FW speed (z=2.39, p=0.02), and 6MW distance (z=2.68, p=0.01).

Conclusion: Our results suggest that: (a) individually occurring poor diet and insufficient physical activity are associated with comorbidities and neuroperformance markers as is the cluster of co-occurring poor diet and insufficient physical activity; (b) the cluster of co-occurring poor diet and insufficient physical activity is synergistically associated with comorbidities and neuroperformance markers.

Introduction

MS is a chronic, immune-mediated disease of the central nervous system with an estimated prevalence of 1 per 1000 adults in the United States (1). The disease presents with a range of functional and symptomatic outcomes including loss of upper and lower body mobility and function, cognitive dysfunction, fatigue, loss of balance and coordination, and depression (2) (3). There is additional evidence for the occurrence of comorbidities, in particular hypertension, hyperlipidemia, and chronic lung disease among persons with MS that have been associated with diagnostic delays, disability progression, and decreased health related quality of life (4). In a recent report of emerging wellness trends conducted by the National MS Society, persons living with MS expressed interest in understanding and managing the consequences of the disease through diet and exercise (5). This calls for a focus on behaviors such as physical activity and diet that encourage healthy lifestyles, disease management, and reduced symptomology and impaired function in persons with MS.

Recent research has documented the co-occurrence of poor diet and insufficient levels of physical activity in persons with MS (6). An examination of smoking, poor nutrition, excess alcohol consumption, and insufficient physical activity levels in MS indicated that the most commonly reported risk factor was poor diet, with 85.5% of the sample not meeting fruit and vegetable and whole grain guidelines; 62.3% of the sample was not meeting physical activity guidelines (6). Of participants with two or more co-occurring risk factors, 90.3% reported the co-occurrence of poor diet and insufficient physical activity levels. This study confirmed findings from previous investigations of co-occurring risk factors in MS, but further presented novel evidence of a commonly occurring cluster of poor diet and insufficient physical activity (7).

Among the general population, the combination of multiple unhealthy behaviors synergistically impacts health outcomes (8) (9). Indeed, the co-occurrence of poor diet and insufficient levels of physical activity in the general population results in an increased risk of cancer, obesity, diabetes, and cardiovascular disease (CVD) (10). Several studies have examined physical activity and nutrition behaviors in MS individually; however, we are unaware of research examining the potentially synergistic effects of the two together.

It is likely that the co-occurrence of insufficient physical activity and poor diet is linked with comorbidities in MS, given the evidence suggesting physical activity and diet individually are associated with a variety of health conditions, most prominently cardiovascular disease (11). A recent study of comorbidities in MS reported that healthy diet ($B=-0.01$, $P<0.00$) and physical activity ($B=-0.15$,$p=0.05$) were associated with a decreased number of comorbidities (12), but did not specifically examine the association between co-occurring behaviors. It is further likely that the relationship of these combined risk factors extends beyond comorbidities and can influence neuroperformance markers (i.e., measures of how well a person performs on a physically or cognitively demanding task) (13). There is little research on nutritional behaviors and neuroperformance markers in MS; however, there is considerable evidence of associations of physical activity levels with comorbidities, and walking performance in MS (14).

To date, we are unaware of studies examining individual and co-occurring poor diet and insufficient physical activity behaviors as correlates of comorbidity and neuroperformance outcomes in MS. As such, this study examined individual and co-occurring poor diet and insufficient levels of physical activity and the relationship between comorbidity and neuroperformance outcomes in a sample of persons with MS. We predicted that poor diet and insufficient levels of physical activity would independently be associated with neuroperformance

outcomes and comorbidities, especially cardiovascular disease risk factors. We further hypothesized that the co-occurrence of poor diet and insufficient levels of physical activity would synergistically impact comorbidities and neuroperformance outcomes. Such inquiry could inform the necessity and development of future individual and multiple health behavior change interventions in MS.

Methods

Participants

Recruitment included advertising through the National MS Society Local Research page, our laboratory Facebook page, and contacting individuals in our laboratory database. The inclusion criteria were: (1) age 18-64 years; (2) relapse free in past 30 days; (3) ambulatory with or without assistance; and (4) not pregnant (pregnancy can affect health behaviors). Of the 92 individuals with MS who underwent screening, 8 were disqualified due to severe walking impairment that prohibited ambulation, 14 were qualified but dropped out prior to testing for scheduling reasons, and 70 participants met inclusion criteria and were scheduled for testing. One participant declined to provide self-report information resulting in a final convenience sample of 69 persons with MS.

Measures

Definitions of risk factors

The definitions of poor diet and insufficient physical activity for this study have been described elsewhere (6). Participants completed a three-day food record for two weekdays and one weekend day that were reviewed by a registered dietitian with the participants. The guidelines for fruit and vegetable consumption recommend consuming between 1.5-3 cups of fruits and vegetables per day, depending on age and sex (15). Grain guidelines recommend making half of all grains whole (15). Not meeting the guidelines for both fruit and vegetable and

whole grain consumption was used as an index of poor nutrition and considered a risk factor. Physical activity levels were assessed using the Godin Leisure-Time Exercise Questionnaire (GLTEQ) which classifies the metabolic equivalents of physical activity as a health contribution score (16). Participants accumulating 23 units or less were considered insufficiently active and not meeting the guidelines; not meeting the guidelines was considered a risk factor.

Comorbidities

The occurrence of comorbidities was assessed through a questionnaire that includes comorbidities that are reported to be frequent in the general or MS populations and has been validated in MS (17). The questionnaire asks 'Has a doctor ever told you that you have …?' For each comorbidity, participants report the presence or absence of the condition, the year of diagnosis, and whether it is being treated currently. The total number of reported comorbidities was summed as a measure of the occurrence of comorbidities. Cardiovascular disease symptoms were further assessed through a Health History Questionnaire (18). Participants were asked to indicate symptoms they have experienced by marking "yes" or no' to symptoms such as "Pain or discomfort in the chest, neck, jaw, arms, or other areas that may be related to poor circulation." The total number of symptoms was summed as a measure of the occurrence of cardiovascular disease symptoms.

Neuroperformance outcomes

Lower extremity motor function was assessed through the Timed 25-Foot Walk (T25FW) and the Six Minute Walk (6MW). During the T25FW, participants were instructed to walk as quickly, but as safely as possible over a distance of 25 feet for two trials. The primary outcome of the T25FW trials was speed (i.e., feet/second). During the 6MW, participants were instructed to walk as far and as fast as possible in an accessible hallway for six minutes, according to

standardized instructions (19). A member of the research team followed 3-5 feet behind participants with a measuring wheel to quantify the distance walked, the primary outcome of the 6MW.

Procedures

This study was approved by a University Institutional Review Board, and participants provided written informed consent. Participants underwent a neurological evaluation by a Neurostatus-certified examiner for generation of an Expanded Disability Status Scale (EDSS) score, measurement of height and weight, and then completed self-report measures of diet, physical activity levels, comorbidities, cardiovascular disease symptoms, and sociodemographic and clinical characteristics. Participants further underwent assessments of neuroperformance outcomes. Procedures were conducted during a one-day visit to the laboratory. All participants were remunerated.

Statistical Analysis

All statistical analyses were performed in IBM SPSS Statistics for Windows (version 22; IBM SPSS Inc., Armonk, N.Y., USA). Descriptive statistics are listed in text and tables as frequencies and percentages, unless otherwise noted. We assessed the differences in number of comorbidities and neuroperformance outcomes in participants reporting individually occurring diet and physical activity risk factors vs those not reporting the risk factors using non-parametric *t*-tests. Analyses of the differences in number of comorbidities and neuroperformance outcomes between those reporting the cluster of poor diet and insufficient levels of physical activity and those not reporting the cluster were performed through non-parametric *t*-tests. Additional *t*-tests were performed to assess the difference in number of comorbidities and neuroperformance outcomes between those reporting only 1 risk factor vs those reporting 2 e.g., the cluster of poor diet and insufficient levels of physical activity. The magnitude of differences based on Cliff's d

was interpreted as small, medium, and large based on values of 0.1, 0.3, and 0.5, respectively (20).

Results

Sociodemographic and Clinical Characteristics

Sociodemographic and clinical characteristics are reported in Table 6. Participants were primarily female (69.6%), Caucasian (94.2%), and married (59.4%). Nearly half of participants were employed (49.3%), 85.5% had some college education, and 68.1% had an annual household income greater than $40,000. The mean age was 50.5 (SD=8.9) years. The mean BMI (kg/m^2) was 28.7 (SD=6.6). Participants primarily had relapsing-remitting multiple sclerosis (RRMS) (84.1%), mild to moderate disability (median EDSS score of 4.0 (SD=2.0)), and a disease duration of 14.4 (IQR=10.5) years.

Comorbidity, poor diet, and insufficient levels of physical activity

Results of differences in the number of comorbidities in participants reporting and not reporting individually occurring diet and physical activity risk factors are reported in Table 7. Analyses revealed a significant difference in the number of comorbidities between physical activity levels (z=3.31, p=0.00) whereby those not meeting physical activity guidelines reported a higher number of comorbidities than those meeting physical activity guidelines. There was a significant difference in the number of cardiovascular disease symptoms between poor diet (z=2.35, p=0.02), such that those who reported poor diet reported a higher number of cardiovascular disease symptoms.

Neuroperformance outcomes, poor diet, and insufficient levels of physical activity

Results of differences in neuroperformance outcomes in participants reporting and not reporting individually occurring diet and physical activity risk factors are reported in Table 8. There were significant differences in T25FW speed between physical activity levels (z=2.04,

p=0.04) such that those who reported insufficient levels of physical activity walked slower than those who reported meeting physical activity guidelines. Distance walked during the 6MW was further significantly different between physical activity levels (*z*=2.38, *p*=0.02) such that those who reported insufficient levels of physical activity walked significantly less than those meeting guidelines. However, there were no significant differences in T25FW (z=1.48, *p*=0.14) and 6MW (*z*=0.73, *p*=0.46) across diet risk category.

Comorbidity, neuroperformance outcomes, and the cluster of poor diet and insufficient levels of physical activity

The differences in number of comorbidities and neuroperformance outcomes between those reporting the cluster of poor diet and insufficient levels of physical activity and those not reporting the cluster are reported in Table 9. Total number of comorbidities (*z*=2.36, *p*=0.02), cardiovascular disease symptoms (*z*=2.63, *p*=0.01), speed during T25FW (*z*=2.53, *p*=0.01), and distance walked during the 6MW (*z*=2.61, *p*=0.01) had significant differences between those who reported co-occurring poor diet and insufficient levels of physical activity compared with those who did not report the co-occurring risk factors (i.e., those reporting only one or no risk factors). Those reporting the co-occurring cluster were more likely than those not reporting the cluster to have a higher number of comorbidities and cardiovascular disease symptoms, a slower speed on the T25FW, and walked a shorter distance on the 6MW. We repeated this analysis and confirmed a significant difference between those reporting two and those reporting only one risk factor; results are reported in Table 10. Those reporting two risk factors had a significantly higher number of comorbidities (*z*=2.41, *p*=0.02) and cardiovascular disease symptoms (*z*=2.40 *p*=0.02), walked slower on the T25FW (*z*=2.39, *p*=0.02) and less on the 6MW (*z*=2.68, *p*=0.01).

Discussion

The present study involved a novel investigation of individual and co-occurring poor diet and insufficient levels of physical activity and the relationship between comorbidity and neuroperformance outcomes in a sample of persons with MS. Our results suggest that (a) individually occurring poor diet and insufficient physical activity are associated with comorbidities and neuroperformance markers; (b) the cluster of co-occurring poor diet and insufficient physical activity is associated with comorbidities and neuroperformance markers; (c) the cluster of co-occurring poor diet and insufficient physical activity is synergistically associated with comorbidities and neuroperformance markers. Collectively, these results suggest that the cluster of co-occurring comorbidities and neuroperformance markers is highly prevalent in persons with MS and does indeed have significant associations with comorbidities and neuroperformance markers. This clustering of two co-occurring risk factors further appears to synergistically impact health outcomes, suggesting a need to target both behaviors concurrently, rather than one behavior individually. Future research should examine the design of multiple health behavior change interventions in MS.

This study confirmed our hypothesis that poor diet and insufficient levels of physical activity would independently be associated with neuroperformance outcomes and comorbidities, especially cardiovascular disease symptoms. Insufficient physical activity levels were associated with total number of comorbidities, while poor diet was not. Comorbidity is an area of increasing interest in persons with MS, however large gaps still exist in comorbidity research. To date, one other study has examined the relationship of health behaviors and comorbidity in MS (21). That study reported that alcohol dependence and smoking were associated with anxiety and depression. Ours is the first study to examine the correlates of diet and physical activity with

comorbidity in MS. Interestingly, poor diet was associated with total number of CVD symptoms while insufficient physical activity levels were not. Cardiovascular disease specifically, is highly prevalent in MS (22) (23). Previous investigations of physical activity and CVD reported significant associations between physical activity and the number of self-reported cardiovascular comorbidities, independent of disability status and other confounding variables (18). The small sample size of the present study may explain why this relationship was not observed here. Diet is strongly correlated with cardiovascular disease in the general population, consumption of fruits and vegetables and whole grains specifically are significantly associated with lower levels of CVD (24) (25) (26) (27). To our knowledge, this study presents preliminary evidence of an association of consumption of fruits and vegetables and whole grains and CVD in MS. Insufficient physical activity levels were associated with both reduced speed of the T25FW and shorter distance on the 6MW, while poor diet was not significantly associated with either function tests. This is not surprising given the substantial evidence of the association of physical activity and walking and mobility impairment in MS (28) (29) (30) (31).

We further hypothesized that the co-occurrence of poor diet and insufficient levels of physical activity would synergistically impact comorbidities and neuroperformance outcomes. Analyses of the differences in comorbidities and neuroperformance markers between those reporting the co-occurring cluster of poor diet and insufficient levels of physical activity revealed that those reporting the cluster had significantly more comorbidities and cardiovascular disease symptoms, and walked significantly slower on the T25FW and less on the 6MW. Importantly, when we assessed the difference in outcomes between those reporting one risk factor and those reporting the two co-occurring clusters, the differences remained significant. This association suggests a synergistic relationship between co-occurring insufficient levels of physical activity

and poor diet on comorbidities and neuroperformance markers in MS. Such an association necessitates future investigations of multiple health behavior change interventions in person with MS, as targeting multiple behaviors rather than one individual behavior may result in greater improvements in overall health and wellbeing.

The present study is not without limitations. The sample of persons with MS was relatively homogenous, consisting of primarily Caucasian females. The sample further included mostly participants with RRMS and was characterized by moderate disability. Therefore, our results may not be generalizable amongst other subpopulations of persons with MS such as men, individuals with progressive MS, or individuals with higher disability. Our study further included self-report measures and these are subject to reporting biases. Future research should examine the co-occurrence of these risk factors in a larger, heterogeneous sample of persons with MS.

The present study provides preliminary evidence of the associations of individual and co-occurring poor diet and insufficient physical activity in persons with MS. Our evidence suggests that this cluster of risk factors does indeed synergistically impact health outcomes. As such, future research should examine the design and implementation of multiple health behavior change interventions targeting co-occurring poor diet and insufficient physical activity levels in persons with MS.

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Tables

Table 6. Sociodemographic and Clinical Characteristics

Characteristic	MS (n=69)
Sex (% female)	69.6%
Age, years (mean (SD))	50.5 (8.9)
Race (% Caucasian)	94.2%
BMI (kg/m2) (mean (SD))	28.7 (6.6)
Marital Status (% married)	59.4%
Employed (% employed)	49.3%
Education (% some college)	85.5%
Annual Household Income (% over $40,000)	68.1%
EDSS, median (IQR)	4.0 (2.0)
Disease Course (% RRMS)	84.1%
Disease Duration, years	14.4 (10.5)

Note. BMI = Body Mass Index.

Table 7. Difference in Number of Comorbidities by Physical Activity and Nutrition Risk Factors

Characteristics	n	Median (IQR)	Z statistic	*p*	Cliff's d
COMORBIDITIES (#)					
Poor Nutrition					
Yes	59	2 (4)	1.18	0.24	0.23
No	10	3 (1)			
Insufficient Physical Activity					
Yes	43	3 (4)	3.31	**0.00**	0.47
No	26	2 (3)			
CVD SYMPTOMS (#)					
Poor Nutrition					
Yes	59	1 (3)	2.35	**0.02**	0.44
No	10	0 (0)			
Insufficient Physical Activity					
Yes	43	1 (3)	1.65	0.10	0.23
No	26	1 (1)			

Table 8. Difference in Neuroperformance Markers by Physical Activity and Nutrition Risk Factors

Characteristics	n	Median (IQR)	Z statistic	*p*	Cliff's d
T25FW (ft/s)					
Poor Nutrition					
Yes	59	4.8 (1.4)	1.48	0.14	0.12
No	10	5.8 (1.1)			
Insufficient Physical Activity					
Yes	43	4.7 (1.3)	2.04	**0.04**	0.30
No	26	5.4 (3.1)			
6MW (ft)					
Poor Nutrition					
Yes	59	1527.0 (760.0)	0.73	0.46	0.15
No	10	1637.0 (835.0)			
Insufficient Physical Activity					
Yes	43	1478.0 (316.0)	2.38	**0.02**	0.34
No	26	1768.0 (733.8)			

Table 9. Difference in Number of Comorbidities and Neuroperformance Outcomes by the 'Poor Diet and Insufficient Levels of Physical Activity' Cluster

Poor Diet and Insufficient Physical Activity Cluster	n	Median (IQR)	Z statistic	*p*	Cliff's d
Comorbidities (#)					
Yes	39	3 (4)	2.36	**0.02**	0.33
No	30	2.5 (3)			
Cardiovascular Disease Symptoms (#)					
Yes	39	1 (3)	2.63	**0.01**	0.35
No	30	0 (1)			
T25FW (ft/s)					
Yes	39	4.4 (3.3)	2.53	**0.01**	0.36
No	30	5.4 (2.4)			
6MW (ft)					
Yes	39	1430 (364)	2.61	**0.01**	0.37
No	30	1760 (326.8)			

Table 10. Difference in Number of Comorbidities and Neuroperformance Outcomes by Number of Reported Risk Factors

Number of reported risk factors	n	Median (IQR)	Z statistic	*p*	Cliff's d
Comorbidities					
1	24	1.5 (3)	2.41	**0.02**	0.36
2	39	3 (4)			
Cardiovascular Disease Symptoms					
1	24	0 (1)	2.40	**0.02**	0.35
2	39	1 (3)			
T25FW					
1	24	5.4 (1.98)	2.39	**0.02**	0.36
2	39	4.4 (3.4)			
6MW					
1	24	1760.5 (237.0)	2.68	**0.01**	0.40
2	39	1430.0 (761.0)			

CHAPTER 4

OVERALL DISCUSSION

DMTS have limited efficacy in addressing disability progression and symptoms in MS (1) (2). Persons with MS further often have two or more comorbidities and a high frequency of adverse health behaviors, resulting in complex health care needs (3) (4). As such, there is a growing need for alternative, holistic, approaches to managing this chronic and incurable disease. Smoking, poor nutrition, excess alcohol consumption, and insufficient levels of physical activity, collectively known as the SNAP risk factors, are the leading modifiable causes of morbidity and mortality in the general population and have synergistic outcomes on health when they cluster, or co-occur (5) (6) (7) (8). Intervening on multiple co-occurring SNAP risk factors rather than individual risk factors (e.g., inventions designed to increase physical activity or improve nutrition habits) represents a potentially novel approach to managing symptoms and disability in MS with optimized health benefits.

Prior to the design of such interventions, important research is needed to inform the necessity and design of such interventions. This thesis involved two studies that addressed SNAP risk factors in MS. The first study investigated the individual and co-occurrence of SNAP risk factors and the variation across clinical and sociodemographic characteristics in a sample of persons with MS. The results from this study suggested that a) an overwhelming 85.5% of the sample was not meeting nutrition guidelines independent of other SNAP risk factors; (b) 90.3% of participants with two or more risk factors reported the co-occurrence of poor diet and insufficient levels of physical activity; and (c) physical activity levels and the total number of SNAP risk factors varied across sex. These collectively suggest that persons with MS do indeed report the individual co-occurrence of SNAP risk factors; and that poor diet and insufficient

levels of physical activity are the most commonly reported co-occurring SNAP risk factors in this population. This study further indicates that subpopulations of MS, specifically women, are more susceptible to the individual and co-occurrence of SNAP risk factors.

The second study examined health and neuroperformance outcomes associations with co-occurring poor nutrition and insufficient levels of physical activity, the most commonly occurring risk factor cluster identified in the first study. The results indicated that (a) individually occurring poor diet and insufficient physical activity are associated with comorbidities and neuroperformance markers; (b) the cluster of co-occurring poor diet and insufficient physical activity is associated with comorbidities and neuroperformance markers; (c) the cluster of co-occurring poor diet and insufficient physical activity is synergistically associated with comorbidities and neuroperformance markers. These results suggest that the cluster of co-occurring comorbidities and neuroperformance markers is highly prevalent in persons with MS and does indeed have significant associations with comorbidities and neuroperformance markers. Importantly, this clustering of two co-occurring risk factors further appears to synergistically impact health outcomes, suggesting a need to target both behaviors concurrently, rather than one behavior individually.

To date, one multiple health behavior change intervention has been designed for persons with MS. A randomized clinical trial of 113 women with physician confirmed MS were enrolled in either a 2-phase intervention program that included lifestyle-change classes for 8 weeks, followed by telephone check-ins for 3 months, or a control group (9). The intervention was based on a conceptual model integrating concepts from the health belief model, the Pender model of health promotion, and self-efficacy theory and informed by previous cross-sectional investigations. Topics for intervention sessions included maximizing health when living with a

chronic disabling condition, exercising and engaging in physical activity, eating healthy, and managing stress. The researchers reported a statistically significant group by time effect for self-efficacy for health behaviors, health-promoting behaviors, and the mental health and pain subscales of the Short Form Health Survey (SF-36). The primary strength of this study was its large sample size, use of a randomized clinical design and integration of theory in the intervention program. However, additional research employing theory based interventions is needed to explore modifying multiple health risk factors in MS, particularly co-occurring poor nutrition and insufficient levels of physical activity and to evaluate resulting changes in comorbidity and neuroperformance markers.

The present studies provide novel information on the prevalence and associations of the co-occurrence of insufficient physical activity and poor nutrition in a sample of persons with MS. Nevertheless, the generalizability of such conclusions is mainly limited to ambulatory, Caucasian, community-residing women with MS who have a relapsing-remitting disease course. The nature of these data is further cross sectional and therefore cannot be interpreted as casual and is limited by a small sample size. Future research should include larger samples as well as the inclusion of longitudinal data to determine the possible impact of changes in physical activity and nutrition habits on comorbidity and neuroperformance outcomes over time.

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CHAPTER 5

CONCLUSION

In conclusion, the present studies provide a novel evaluation of the prevalence and associations of individual and co-occurring SNAP risk factors and associations with comorbidity and neuroperformance outcomes in a sample of persons with MS. This research provides evidence of a clustering of insufficient physical activity and poor nutrition in persons with MS that is synergistically associated with comorbidity and neuroperformance markers. This research highlights the importance of focusing on multiple health behavior change rather than individual behaviors. Future research that focuses on co-occurring risk factors will expand subsequent efforts to provide an alternative and holistic approach to managing MS.

APPENDIX A
IRB APPROVAL LETTER

UNIVERSITY OF ILLINOIS
AT URBANA-CHAMPAIGN

Office of the Vice Chancellor for Research
Institutional Review Board
528 East Green Street
Suite 203
Champaign, IL 61820

March 19, 2014

Robert Motl
Kinesiology & Community Health
350 Freer Hall
906 S Goodwin Ave
M/C 052

RE: *Dietary sodium smoking and physical inactivity in multiple sclerosis: The multiple risk-factors in MS study*
IRB Protocol Number: 14526

Dear Dr. Motl:

Your response to required modifications for the project entitled *Dietary sodium smoking and physical inactivity in multiple sclerosis: The multiple risk-factors in MS study* has satisfactorily addressed the concerns of the University of Illinois at Urbana-Champaign Institutional Review Board (IRB) and you are now free to proceed with the human subjects protocol. The UIUC IRB approved the protocol as described in your IRB-1 application with stipulated changes, as part of their monthly review. Certification of approval is available upon request. The expiration date for this protocol, UIUC number 14526, is . The risk designation applied to your project is *no more than minimal risk.*

Copies of the attached date-stamped consent form(s) must be used in obtaining informed consent. If there is a need to revise or alter the consent form(s), please submit the revised form(s) for IRB review, approval, and date-stamping prior to use.

Under applicable regulations, no changes to procedures involving human subjects may be made without prior IRB review and approval. The regulations also require that you promptly notify the IRB of any problems involving human subjects, including unanticipated side effects, adverse reactions, and any injuries or complications that arise during the project.

If you have any questions about the IRB process, or if you need assistance at any time, please feel free to contact me or the IRB Office, or visit our Web site at http://www.irb.illinois.edu.

Sincerely,

Anita Balgopal, PhD
Director, Institutional Review Board

Attachment(s)

c: Kenneth Wilund
Jennifer Barnes
Elizabeth Hubbard
Julia Balto
Ipek Ensari

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