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Exploring the Relationship between Physical Activity and Everyday Cognitive Function in Older Adults: Within- and Between- Person Variability

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Exploring the Relationship between Physical Activity and Everyday Cognitive Function in Older Adults: Within- and Between- Person Variability

by

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Abstract

Research suggests that physical activity may play a role in preserving cognitive function in older adulthood. However, the exact nature, direction, and magnitude of observed associations remain unclear. The current study utilized a microlongitudinal design to repeatedly assess cognitive function and physical activity across five days. Two studies examined relationships between physical activity, physical fitness, and cognitive function among community-dwelling older adults. The first study examined associations between baseline performance in a measure of everyday cognition and multiple measures of physical activity and physical fitness. Bivariate analyses revealed that objectively measured physical activity of moderate-to-vigorous intensity, repeated chair stand time and 6-minute walk distance were significantly associated with everyday cognition. After adjusting for covariates in a multiple regression model, physical activity was not significantly associated with everyday cognition. However, a composite physical fitness score created from 6-minute walk distance and repeated chair stand time was significantly associated with DECA, and the full model accounted for 38% of the variance in baseline DECA performance.

The second study investigated within- and between-person relationships between daily physical activity and cognitive function. Study participants wore an activity monitor and completed a battery of cognitive assessments for five days. Multilevel modeling analyses indicated that same-day total number of steps was significantly associated with better visual speed of processing but not everyday cognition, or inductive reasoning. Time spent in moderate-to-vigorous activity was not significantly associated with same-day cognitive performance in any domain. However, previous-day moderate-to-vigorous physical activity was significantly associated with better inductive reasoning and speed of processing the following day, after controlling for age, gender and physical fitness. Time spent in moderate-to-vigorous activity explained 16% of the within-person variability in speed of processing. Physical fitness and age did not explain significant variability in between-person cognitive function.

Results obtained in the present study varied according to how physical activity and cognition were operationalized and measured. Associations between physical activity and cognition were more evident with moderate-to-vigorous activity, as opposed to total activity, and an acute temporal relationship was suggested, with better cognitive performance following engagement in moderate-to-vigorous physical activity. Results also indicated that within-person fluctuations in domains of cognitive performance were positively associated with physical activity, and were more pronounced with cognitively complex tasks that were timed.

Chapter One:

Introduction

Cognitive function encompasses a group of mental processes characterized by knowing, thinking, learning, understanding and judging. Varying degrees of this ability to become aware of and process information are necessary to successfully navigate through all but the most basic of everyday activities. A substantial body of research indicates that cognitive abilities decline with advancing age, (e.g., Craik & Salthouse, 2000; 2004), and decline is more pronounced after age 60. Earlier onset and more severe decline increases the risk of functional impairment, dementia, and Alzheimer's disease (AD) with increasing age (Jacobs, et al., 1994).

Negative outcomes associated with cognitive decline result in an increased need for care for those affected, and subsequently greater demand for human and monetary resources (Haan & Wallace, 2004). Ranking behind only heart disease and cancer in most expensive medical conditions, the estimated 1997 cost of dementias in the United States was 100 billion dollars (Kirschstein, 2000). With approximately 20% of the U.S. population expected to be over the age of 65 by the year 2030, and adults over 85 representing the fastest growing segment of the population (Hobbs, 2008), the potential financial burden of AD and other dementias is significant. There has been growing interest in helping older adults maintain functional independence by preserving cognitive function for as long as possible. It has been suggested that if current interventions could delay the onset and progression of AD by only one year there would be 9.2 million fewer cases of the disease in 2050 (Brookmeyer, Johnson, Ziegler-Graham, & Arrighi, 2007), which would simultaneously lessen the collective public health burden and extend functional independence for millions of individuals.

Evidence suggests that physical activity may play a protective role in maintaining cognitive health among older adults, as measured by tests of neurophysiologic structure and function and traditional behavioral assessments of cognition (McAuley, Kramer, & Colcombe, 2004). Inverse relationships between cognitive decline and self-reported physical activity (e.g., Lindwall, Rennemark, & Berggren, 2008; Lytle, Bilt, Pandav, Dodge, & Ganguli, 2004; Middleton, Kirkland, & Rockwood, 2008; van Gelder, et al., 2004; Yaffe, Barnes, Nevitt, Lui, & Covinsky, 2001), as well as physical fitness (Wang, Larson, Bowen, & van Belle, 2005) among older adults have been demonstrated in multiple studies. Similar relationships have been observed between physical activity and risk of dementia, vascular dementia, and AD (Podewils, et al., 2005; Ravaglia, et al., 2008). Intervention trials have shown improved cognitive function in response to physical fitness training (Colcombe & Kramer, 2003), and the association between physical activity and cognition seems to be most apparent with more complex cognitive processes (Bixby, et al., 2007; Hillman, Kramer, Belopolsky, & Smith, 2006; Smiley-Oyen, Lowry, Francois, Kohut, & Ekkekakis, 2008). There have been few studies, however, which have examined the relationship between physical activity and the ability to perform cognitively complex real-world activities. The purpose of this project was to explore the relationship between daily physical activity, physical fitness, and cognitively complex everyday activities necessary to remain functionally independent, referred to as instrumental activities of daily living (IADL; Lawton & Brody, 1969).

Everyday cognitive function represents the functional domain of cognition associated with the ability to perform cognitively complex activities within real-world context. Also termed everyday cognitive competence (Willis, 1996), everyday task competence (Owsley, Sloane, McGwin Jr, & Ball, 2002; Willis, Jay, Diehl, & Marsiske, 1992), and everyday problem solving (Blanchard-Fields, Mienaltowski, & Seay, 2007; Diehl, Willis, & Schaie, 1995; Marsiske & Willis, 1995), everyday cognitive function may be particularly important in maintaining functional independence. Research suggests that multiple basic abilities, namely inductive reasoning, memory, knowledge, and speed of processing are related to everyday cognition (Allaire & Marsiske, 1999, 2002; Willis, et al., 1992). However, these abilities as assessed with traditional laboratory-based measures do not seem to fully explain everyday cognitive competence in instrumental domains such as medication use, finance, and nutrition/food preparation (Allaire & Marsiske, 1999), suggesting a uniquely measured component of older adult cognition with everyday cognitive functioning assessments (i.e. tasks performed within a naturalistic framework).

Measures of everyday cognition have better explained self-reported IADL function than traditional tests of basic abilities in older adults (Allaire & Marsiske, 2002). In addition, everyday cognitive task performance has longitudinally predicted mortality (Allaire & Willis, 2006; Weatherbee & Allaire, 2008) and clinically-rated cognitive impairment (Allaire & Willis, 2006) among older adults, even after controlling for basic cognitive abilities. Similarly, Allaire and colleagues (2008) found that although subjective ratings of IADL performance were uniform among participants with and without psychometrically defined MCI, those with MCI performed more poorly than those without on an everyday memory test battery. Moreover, poorer performance within the everyday domains of finance and medication was significantly associated with MCI, even after controlling for performance on two global cognitive screening tools. These results indicate that measures of everyday cognition may be better suited to assessing older adults' real-world IADL function and risk of adverse outcomes than measures of basic abilities, self-reports, or global screening measures of cognition. Thus, a better understanding of everyday cognition and factors that promote maintenance of everyday cognitive abilities are particularly important for older adults.

In addition to decrements in cognitive function with advancing age, greater intraindividual variability, or short-term within-person inconsistency in cognitive task performance has been noted (Bunce, MacDonald, & Hultsch, 2004; Hultsch, MacDonald, & Dixon, 2002; MacDonald, Hultsch, & Dixon, 2003; Miller & Odell, 2007; Nesselroade & Salthouse, 2004). While some research suggests that inconsistency is not a stable person-level trait among cognitively intact populations (Ram, Rabbitt, Stollery, & Nesselroade, 2005), cross-domain associations have been observed between physical functioning inconsistency and fluctuations in cognitive performance (Strauss, MacDonald, Hunter, Moll, & Hultsch, 2002). Moreover, patterns of within-person inconsistency across multiple domains have differentiated cognitively-healthy older adults from those with dementia (Strauss, et al., 2002) and predicted subsequent cognitive decline and more pronounced inconsistency (MacDonald, et al., 2003). Specifically, poorer overall performance in tests of physical function, greater intraindividual variability in performance on tests of physical function, and greater within-person inconsistency in cognitive performance measures across four testing sessions were noted among cognitively compromised individuals as opposed to those who were cognitively intact.

Relatively recent advances in methodological and analytical techniques have enabled simultaneous examination of both between- and within- person variability in cognition. Studies utilizing micro-longitudinal bursts (Nesselroade, 1991) or daily diary designs (Neupert, Stawski, & Almeida, 2008) and sophisticated statistical modeling techniques (Hertzog & Nesselroade, 2003; Nesselroade & Ram, 2004) have enabled the observation and subsequent study of between- and within-person patterns of age-related cognitive variability, as well as interrelationships between the two. To this author's knowledge, only one study to date has fully utilized these methodological advances to explore within- and between-person relationships between physical activity and cognitive function (Whitbourne, Neupert, & Lachman, 2008). After controlling for education, cognitive ability, gender, and health, daily self-reported physical activity was associated with fewer self-reported memory failures on the day of, as well as the day following physical activity participation. Furthermore, older adults realized greater benefit from physical activity participation than younger and middle-aged adults. This author is not aware of any such micro-longitudinal examinations utilizing objective measures of physical activity, physical fitness, and cognitive function.

The primary questions addressed by this study were: (1) What are the relationships between physical activity, physical fitness, and everyday cognition?; (2) How much variability in everyday cognition is accounted for by daily physical activity?; (3) How much variability in everyday cognition is accounted for by physical fitness?; and (4) Does physical fitness moderate the relationship between physical activity and within-person variability in everyday cognitive performance? In addition to the primary study objectives, several secondary questions were explored. The first was, “Are observed relationships different according to how physical activity and physical fitness are operationalized?” Secondly, “What are the relationships between physical activity, physical fitness and measures of complex basic cognitive abilities?” Study hypotheses were: (H1) Higher levels of physical activity would be associated with better scores on measures of everyday cognition; (H2) More physically active and fit older adults were expected to perform better on measures of everyday cognition; (H3) It was hypothesized that physical activity would explain a significant amount of within-person variability in cognitive function; (H4) Physical fitness was expected to account for a significant amount of between-persona variability in everyday cognition; (H5) A significant interaction between physical fitness, physical activity, and variability in cognitive performance was anticipated. Specifically, it was hypothesized that more physically fit older adults would experience less daily fluctuation in everyday cognitive function than less physically fit older adults, regardless of daily physical activity variability; (H6) Objective physical activity and physical fitness measures were expected to be more strongly related to cognitive function than subjective; and (H7) It was hypothesized that associations between physical activity and basic cognitive abilities would be similar to everyday cognition, though to a lesser degree.

Chapter Two:

Study One: The Association between Physical Activity, Physical Fitness, and Everyday Cognitive Function among Community-Dwelling Older Adults

Research suggests that physical activity and exercise may contribute to preserved cognitive function with advancing age (Angevaren, Aufdemkampe, Verhaar, Aleman, & Vanhees, 2008; Colcombe & Kramer, 2003; van Uffelen, Chin A Paw, Hopman-Rock, & van Mechelen, 2008). Although there is general agreement of a positive association between physical activity and cognition, diverging results across studies have not allowed clear inferences regarding the exact nature and direction of the relationships between physical activity, physical fitness, and cognitive health. Questions also remain about the efficacy and effectiveness of various modes of physical activity as a means to prevent age-related cognitive decline and/or promote plasticity and other potential mechanisms of action (Hertzog, Kramer, Wilson, & Lindenberger, 2009). The purpose of this study was to examine physical activity and physical fitness/function, both assessed with multiple subjective and objective measures, in relation to everyday cognition.

Among the complications in interpreting the existing evidence, and perhaps contributing to inconsistencies in the literature, is variability in the theoretical and methodological frameworks used to study the relationships between physical activity, fitness and cognition. For example, physical activity, exercise, and physical fitness are often used interchangeably in the literature. Though related, they represent different constructs. Caspersen and colleagues (1985) defined physical activity as “any bodily movement produced by skeletal muscles that results in energy expenditure” (p. 126). Physical fitness was defined by these authors as “a set of attributes that are either health- or skill-related” (p. 126). Exercise was noted as a specific subset of physical activity distinguished as planned, structured, repetitive, and purposeful (p. 126).

Intervention trials among older adults have provided evidence for a positive causal association between planned, structured physical activity and multiple domains of physical fitness, such as aerobic endurance (Keysor & Jette, 2001; Taylor, et al., 2004), strength, flexibility, agility, and balance (Keysor & Jette, 2001; Simons & Andel, 2006; Taylor, et al., 2004). In other words, physical fitness is the positive physiological adaptation to physical activity. Further, a dose-response relationship seems clear, with better physical fitness outcomes resulting from more vigorous and greater total physical activity (Paterson & Warburton, 2010).

Measurement approaches to physical activity can be categorized into two general types, subjective and objective. Subjective measures of physical activity have differed greatly, ranging from two basic questions about frequency of light intensity and strenuous exercise in the past 12 months (Lindwall, et al., 2008), to more complex multiple-scale measures (Roth, Goode, Clay, & Ball, 2003). Although generally more costly and often labor and technology intensive than questionnaires, pedometers (Lautenschlager, et al., 2008) and accelerometers (Hawkins, et al., 2009), have been used to objectively measure physical activity in older adults. These instruments are able to overcome several weaknesses associated with subjective assessments, such as difficulty in capturing lower-intensity and unstructured ambulatory activity (Tudor-Locke & Myers, 2001). They also do not rely on recall, and therefore are not subject to inaccurate memory, bias, or nonrepresentative recall periods (Brach, Kriska, Glynn, & Newman, 2008). Limitations of pedometers are the inability to measure non-ambulatory activities or capture frequency, intensity, and mode of ambulatory activities. In addition, slow and abnormal gaits may adversely affect step count reliability (Brach, et al., 2008), as can central obesity (Tudor-Locke & Myers, 2001). Accelerometers have the ability to continuously collect and store data for relatively long periods of time and allow measurement of frequency, intensity, and duration of ambulatory activities. Like pedometers, however, most accelerometers do not capture upper-body or non-ambulatory movement (Murphy, 2009), provide no information on mode of activity (Brach, et al., 2008), and must be worn correctly during all waking hours to provide accurate assessments.

Measures used to assess physical fitness in relation to cognitive function fall into two general domains, physical function and cardiorespiratory fitness. Within the physical function domain, performance tests have included repeated chair stands to measure lower body strength and power (Atkinson, et al., 2010; Larson, et al., 2006; Taaffe, et al., 2008; Williamson, et al., 2009), short-distance timed walks for gait speed assessment (Atkinson, et al., 2010; Deary, Whalley, Batty, & Starr, 2006; Williamson, et al., 2009), and grip strength as a measure of functional upper body strength (Atkinson, et al., 2010; Deary, et al., 2006; Larson, et al., 2006; Oswald, Gunzelmann, Rupprecht, & Hagen, 2006; Taaffe, et al., 2008; Williamson, et al., 2009). Cardiorespiratory fitness has been assessed using standard graded exercise testing protocols (Barnes, Yaffe, Satariano, & Tager, 2003; Colcombe, et al., 2006; Hoffman, et al., 2008; Smiley-Oyen, et al., 2008), lung function testing (Deary, et al., 2006), and/or field tests, such as the 6-Minute Walk Test (Smiley-Oyen, et al.).

Complexity in performing and generalizing research related to physical activity, physical fitness, and cognition may also be attributed to the range, overlap, and variable definitions of specific cognitive domains assessed. Cognitive outcomes across studies have ranged from global screening tools (e.g., Atkinson, et al., 2010) to various domain-specific measures such as executive function, attention, processing speed and others (for review, see Angevaren, et al., 2008; Colcombe & Kramer, 2003; van Uffelen, et al., 2008). One domain that has not been commonly explored in relation to physical activity is everyday cognition. Also known as cognitive competence (Willis, 1996), everyday task competence (Owsley, et al., 2002; Willis, et al., 1992), and everyday problem solving (Blanchard-Fields, et al., 2007; Diehl, et al., 1995; Marsiske & Willis, 1995), everyday cognition refers to the ability to perform cognitively-complex activities in real-world context.

Everyday cognition has been operationalized and assessed in a number of ways by researchers, perhaps reflecting diverging theoretical perspectives on adult intelligence and cognitive aging (Berg, 2008). Many measurement tools draw on the instrumental activities of daily living (IADL), identified by Lawton and Brody (1969) as necessary to live independently. While some instruments ask for subjective ratings of IADL performance, objective measures typically include performing tasks or solving problems from one or more of the IADL functional domains of health care/medications, finance, food preparation (Allaire & Marsiske, 1999; Diehl, et al., 2005; Diehl, et al., 1995; Finucane, Mertz, Slovic, & Schmidt, 2005; Owsley, et al., 2002), shopping, telephone use (Owsley, et al., 2002), or driving (Willis, et al., 2006). Objective measures of everyday cognition have better explained self-reported IADL function than basic neuropsychological measures (Allaire & Marsiske, 2002). They have also predicted cognitive impairment (Allaire, et al., 2008) and mortality (Allaire, et al., 2008; Allaire & Willis, 2006), even after controlling for basic neuropsychological and global cognitive function scores (Allaire, et al., 2008; Allaire & Willis, 2006). Exploring the associations between physical activity, physical fitness and everyday cognition may be particularly significant in understanding how real-world cognitive function might be influenced by physical activity and if physical activity engagement contributes to prolonged functional independence among older adults.

In the current study, we examined multiple measures of physical activity and physical fitness in relation to everyday cognition. It was hypothesized that higher levels of physical activity would be related to better everyday cognition, and that this relationship would be stronger for moderate-to-vigorous activity. Better physical fitness was expected to be associated with better everyday cognitive function, and associations would be specific to the dimension of physical fitness measured. Finally, it was hypothesized that the associations would remain, even after controlling for demographic, health and basic cognitive ability variables.

Method

Participants

Participants were enrolled in a microlongitudinal research study that consisted of cognitive testing and physical activity monitoring. The study was limited to cognitively-intact community-dwelling older adults $\geq$ 60 years of age residing within an independent-living retirement community in Florida. All study visits took place at a central location within the residential community. A total of 60 participants were recruited for the study, with a mean age of 69.6.0 ± 6.6 years. The study sample included 62% females and 88% whites. Study exclusion criteria included signs of cognitive impairment as indicated by the Modified Mini Mental State exam global screening instrument (3MS; Teng & Chui, 1987), impaired near visual acuity with correction, and conditions likely to result in cognitive impairment (e.g., Alzheimer's disease, dementia, Parkinson's disease, traumatic brain injury, stroke, mini-stroke, transient ischemic attack, or other neurological disorder), terminal illness, active treatment for cancer, or current enrollment in any phase of a cardiac rehabilitation program. Participants were required to perform all physical fitness assessments without the use of ambulatory assistive devices. Physician consent to participate in physical fitness testing was required for individuals with medical conditions that were not exclusion criteria for the study, but increased the risk associated with physical fitness testing (e.g., diabetes, cardiovascular conditions, metabolic disease, arthritis, or orthopedic problems). The study was approved by the Institutional Review Board at the University of South Florida, and written informed consent was obtained from each study participant.

No participants were excluded based on the 3MS cognitive screening, visual acuity. Three participants were excluded during preliminary or baseline screening due to health conditions. Six participants withdrew from the study after preliminary eligibility screening due to seasonal relocation (n=4) or failure to obtain physician consent to complete physical fitness assessments (n=2). For the present cross-sectional analyses, we used data from 51 participants who completed baseline cognitive assessments, wore a physical activity monitor for the 5-day study duration, and completed subjective health and physical activity questionnaires on the final visit (n=51); 60% female, 89% white, and mean age 70.1 ± 7.0 years). Participants who completed the study were older than those who were excluded or withdrew from the study, (66.8 ± 2.7 years), $t(30.6) = 2.5$, $p<0.05$. There were no significant differences in gender, race or education between the two groups. See Table 2.1 for sample characteristics and descriptive results.

Table 2.1: Sample Characteristics

Demographic Characteristics	*Percent*	Physical Activity and Physical Fitness Measures	*Mean(SD)*	Cognitive Measures	*Mean(SD)*
Age		Total Steps (4 days)	21,386(12,814)	DSS	49.0(9.1)
Mean(SD)	70.1(7.0)				
		Moderate/Vigorous Activity		DECA	11.6(1.3)
Gender		total minutes (4 days)	75.8(88.1)		
Male	40				
Female	60	Subjective Physical Activity			
		weekly frequency - all	22.3(9.5)		
Race					
White	88.5	Subjective Physical Activity			
Non-white	11.5	weekly frequency - mod/vig	9.9(5.1)		
Education		6-Minute Walk Test (feet)	1,763(385)		
0-12 years	7.7				
13-16 years	30.8	Grip Strength (lbs)	65.9(24.2)		
17+ years	61.4				
		4-Meter Gait Speed (sec.)	3.42(0.51)		
General Health					
Mean(SD)	73.1(15.9)	Repeated Chair Stand (sec.)	11.8(3.16)		
3MS		Subjective Physical Function	87.0(13.2)		
Mean(SD)	95.2(4.1)				

* Due to missing data, sample range is 45-51.

Measures

Screening measures. Measures were administered in the following order to determine eligibility for participation.

Health status and medication use. Health status and medication use were evaluated using slightly modified versions of previously validated detailed medical history and medication questionnaires (Jobe, et al., 2001). The medical questionnaire, administered verbally, was modified to include all health exclusion criteria. The written medication questionnaire was modified to include over-the-counter, as well as prescription medications.

Mental status. The 3MS was used to screen for possible cognitive impairment or dementia. The 3MS is a 27 item questionnaire (19 Mini-Mental State Exam items plus eight additional questions), which assesses cognitive function across 15 domains. It includes orientation to time and place, attention, concentration, long and short term memory, language ability, and abstract thinking. A maximum possible score on the 3MS is 100; a score of 80 or less is indicative of cognitive impairment (Fitzpatrick, et al., 2007). Individuals with scores $\leq$ 80 were excluded.

Resting Heart Rate (HR) and Blood Pressure (BP). Resting HR was ascertained via a 30-second radial palpitation after five minutes of quiet sitting. BP was assessed manually using a standard sphygmomanometer and stethoscope immediately after resting heart rate at baseline. Two trials were performed with two minutes of sitting quietly between each trial. Participants were excluded from baseline physical fitness testing if resting HR $<$ 50 bpm or $>$ 110 bpm, or if systolic BP $\geq$ 140 or diastolic BP $\geq$ 90 on two trials. Participants excluded from baseline physical fitness testing due to clinically-significant, abnormal, resting HR or BP were referred to their primary care physicians for evaluation.

***Near visual acuit*y.** Near visual acuity was assessed using standard procedure with a visual acuity chart at a distance of 40 cm with participant's usual correction

(Good-Lite, 2011). Adequate near visual acuity, evidenced by a Snellen score of 20/50 or better was required to participate.

Acute contraindications to exercise. Individuals were excluded from baseline physical fitness testing, if on the day of baseline testing, he or she was experiencing chest pain, dizziness, lightheadedness, shortness of breath, blurred vision, skipped heart beats, racing pulse, or any musculoskeletal difficulties that would prevent rising from a chair without assistance, walking the approximate distance of a city block, or gripping a pair of pliers. No participants were excluded from baseline physical fitness testing due to acute contraindications to exercise.

Physical activity.

Objective physical activity. The ActiPed activity monitor (FitLinxx, Shelton, CT; Weyand, et al., 2001), shown in figure 2.1, was used to assess ambulatory activity during day-to-day life for five days. The shoe-mounted device contains an accelerometer that captures, calculates, and transmits step counts to an internet-based database. The ActiPed provides no feedback to participants, so as to not encourage 'performance behavior.' Step detection accuracy exceeding 90% at usual and maximal walking speeds has been found for older adults with unimpaired gait (Moy, Matthess, Stolzmann, Reilly, & Garshick, 2009). Based on prior research suggesting varying results as a function of physical activity intensity and total amount of physical activity (Lindwall, et al., 2008; Podewils, et al., 2005; van Gelder, et al., 2004), the following output data were the focus of the present study: (a) total number of steps (walking, running, other) during four complete days of activity monitoring following baseline testing, and (b) total minutes spent in moderate and vigorous activity across the four activity days. The ActiPed software calculates moderate activity time based on energy expenditure requirements of 3.5-7kcal/min or 3.0-6.0 METs. Vigorous activity was defined by an energy expenditure requirement of at least 7kcal/min or greater than 6.0 METs (Ainsworth, et al., 2011; Thompson, Gordon, & Pescatello, 2010, p. 32).

Subjective physical activity. Participants self-reported physical activity on the final testing day using the CHAMPS questionnaire, a reliable and valid instrument used in prior research (Stewart, et al., 2001). The CHAMPS activity questionnaire was developed to assess a typical week of activity in the past month for participants in a community exercise intervention trial. Items assess a variety of ambulatory activities, as well as non-ambulatory activities that could not be measured using the ActiPed. The following data were derived from the CHAMPS, per the published scoring protocol: (a) weekly frequency of all activities and (b) weekly frequency of moderate-intensity (or greater) activities. Adequate two-week test-retest reliability scores of 0.70 and 0.62 have been demonstrated for the CHAMPS moderate-intensity and all activity measures, respectively (Stewart, et al., 2001).

Figure 2.1: Actiped Activity Monitor

Physical fitness.

Cardiorespiratory. Functional aerobic fitness was assessed with the 6-minute walk test (Butland, Pang, Gross, Woodcock, & Geddes, 1982), using a previously reported protocol (Lord & Menz, 2002). Validation of the test as a measure of healthy older adults' exercise capacity and endurance has been demonstrated through correlations with maximal oxygen consumption (Lipkin, Scriven, Crake, & Poole-Wilson, 1986). High one-week test-retest reliability has been shown (Harada, Chui, & Stewart, 1999). Participants were instructed to walk as many times around an indoor track as they were able to in six minutes. Total distance, rounded to the nearest 10-foot mark, was recorded by the test administrator.

Grip strength. Grip strength was assessed manually using a handgrip dynamometer. Grip strength has predicted disability, morbidity, increased medical complications, and mortality among older adults (Bohannon, 2008). Furthermore, it has been recommended as a stand-alone marker of frailty (Syddall, Cooper, Martin, Briggs, & Sayer, 2003). The degree to which individuals can maximally grip the dynamometer was measured using a digital Jamar hand dynamometer (Sammons Preston Inc., Bolingbrook, IL) in a seated position with wrist in neutral position and elbow flexed to 90 degrees. One practice trial was performed, followed by three test trials for each hand, where participants were encouraged to squeeze as hard as possible. The best single trial of the six was used to determine maximal grip strength in pounds.

Gait speed and functional lower body strength/power. Gait speed and functional lower body strength/power were assessed using previously established protocols (Guralnik, et al., 1994). Briefly, gait speed was measured during two 4-meter walks performed at the participants' usual pace. The faster of the two trials was recorded. Functional lower body strength and /power was assessed by repeatedly rising from a chair as quickly as possible up to five times. The time to complete all five stands (up to one minute) was recorded.

Subjective physical function. The Physical Functioning (PF) subscale of the SF-36 was used to subjectively assess physical function (Ware, Snow, Kosinski, & Gandek, 1993). Scores range from 0 to 100, with higher scores indicating better physical functioning.

Outcome measure.

Everyday cognition. The Daily Everyday Cognitive Assessment (DECA; Allaire, Neupert, & Weatherbee, 2010) was used to assess everyday cognition. The DECA was specifically designed for repeated measurements of the everyday cognitive domains of financial management, medication use, and nutrition/food preparation (Allaire, et al., 2010). Adapted from the previously validated Everyday Cognitive Battery (ECB; Allaire & Marsiske, 1999, 2002), it consists of eight different versions (to allow for a different test version each day, for up to 8 days), each containing two items for each of seven real-world stimuli (e.g. nutrition label), for a total of 14 items per test. Test-retest reliability of the DECA has not been published to date; however adequate to high Cronbach's alpha coefficients for each the four subtests of the ECB have been reported (ECB Inductive Reasoning Test, $\alpha = .88$; ECB Knowledge Test, $\alpha = .69$; ECB Declarative Memory Test, $\alpha = .81$; ECB Working Memory Test, $\alpha = .72$).

Covariate measures.

Demographic and health

Age, gender and highest education level attained were obtained at the initial visit. Health was assessed using the General Health (GH) subscale of the SF-36 (Ware, et al., 1993). Scores range from 0 to 100, with higher scores indicating better general health.

Basic cognitive ability. Speed of processing was assessed using the WAIS- Digit Symbol Substitution task (DSS; Wechsler, 1981). Performance of the DSS requires primarily taps perceptual speed of processing. Age-related declines in speed of processing are well documented (e.g., Bashore, Ridderinkhof, & van der Molen, 1997; Craik & Salthouse, 2000) and performance on speed of processing tests has predicted performance on tests of everyday cognition (Diehl, et al., 1995). The DSS contains 93 blank squares below squares that contain a number 1-9. Each number is paired with a different nonsense symbol in the key. Participants had 90 seconds to fill in as many blank squares with the symbol corresponding to the number in the square above it. The number correct in the allotted time (out of a maximum of 93) was recorded as the DSS score.

Procedure

Preliminary eligibility screening. After obtaining written informed consent, demographics, health status, mobility, medication information, and physician contact information (if required for physical fitness testing) were collected from each participant.

Baseline visit. At the baseline visit, additional measures to confirm eligibility were administered, including 3MS, resting HR and BP, near visual acuity, and acute contraindications to exercise. If eligible, cognitive assessments were followed by physical fitness tests. After testing, enrolled participants were introduced to the activity monitor.

They were instructed on placement, and to wear the device during all waking hours for the next four days.

Final visit. On the final day of testing, participants completed the SF-36 and CHAMPS questionnaires. Participants were instructed to continue wearing the activity monitor for the remainder of the day and return it to the testing location on a predetermined date at the end of the study period. Study procedures are summarized in figure 2.2.

Analyses

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 21 (IBM Corp., 2012). Bivariate correlations were performed to test for multi-collinearity. The physical activity variable and the physical fitness variable most strongly correlated with the DECA cognitive outcome variable were retained for further analyses. Multiple activity or fitness variables significantly correlated with DECA performance were assessed for multi-collinearity, and those correlated at a 0.60 level or higher were retained as a single variable by creating a composite. Next, multiple linear regression was used to test a model for predicting DECA performance from retained physical activity and fitness variables, while statistically controlling for age, gender, education, general health, and speed of processing. Independent and control variables were entered in four blocks. Model 1 included demographic and health covariates. Model 2 added DSS. Model 3 incorporated moderate-to-vigorous activity time. Finally, PFS was entered in the final model.

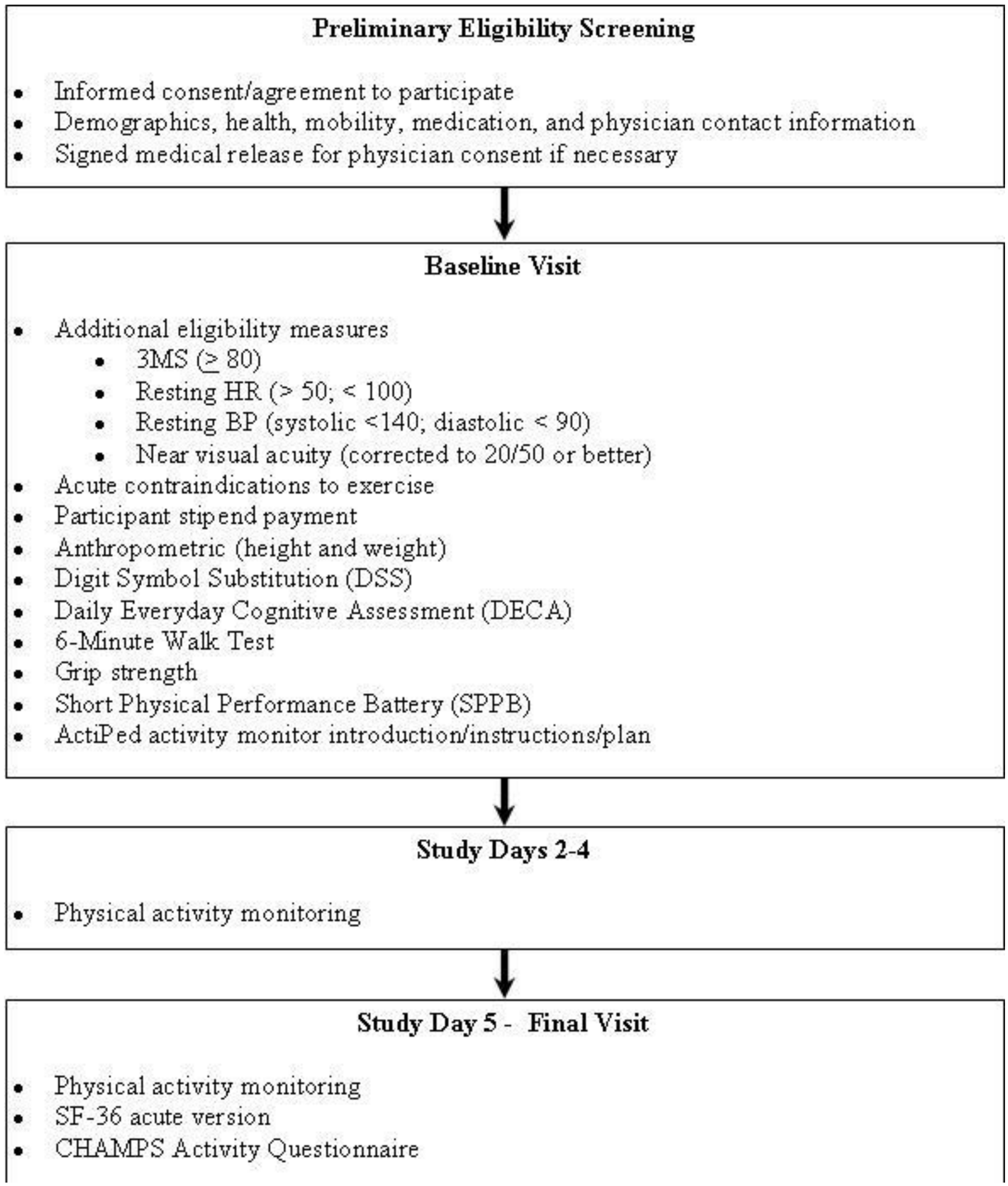

Figure 2.2: Study Flow Chart

Results

Of the 51 study participants, six were missing baseline physical fitness data due to lack of condition-specific physician consent or baseline blood pressure readings above inclusion criteria. Participants with complete and missing physical fitness data did not differ according to age, gender, education, race, subjective health or physical function, objective or subjective physical activity, or everyday cognition. Participants with missing physical fitness data had lower scores on the speed of processing task (35.2 $\pm$ 10.3) than those with complete data (43.9 $\pm$ 9.7), $t(49) = 2.07$, $p<0.05$. Objective physical activity data were missing from two participants due to technology problems while electronically registering their devices. The regression analysis was performed with missing data excluded pairwise, in order to allow all available data to be used.

Bivariate Correlations

Spearman and Pearson coefficients are summarized in Table 2.2. Performance on the DECA everyday cognitive function assessment was negatively associated with moderate and vigorous activity time ($p<0.05$), such that more time spent in moderate-to-vigorous activity was related to poorer cognitive function. DECA performance was correlated with lower times on the repeated chair stand ($p<0.05$) and distance walked in the 6-minute walk test ($p<0.05$), meaning that better cognitive performance was related to better performance on the repeated chair stand and 6-minute walk tests. Lower (faster) repeated chair stand times and distance walked during the 6-minute walk test were also moderately correlated with each other ($r=-0.60$, $p<0.001$). To reduce the number of variables retained for regression analyses and create a more parsimonious model, a physical fitness speed composite was created by taking the means of z-scores for each individual assessment. The basis for creating a speed composite was also theoretical, relating to Birren’s observation that generalized slowing occurs with advancing age (Birren, 1965). Of the four objective physical fitness assessments, the 6-minute walk test and repeated chair stand specifically included instructions to perform the tasks as quickly as possible, whereas the others did not. Based on bivariate correlation results, only moderate-to-vigorous activity time, physical fitness speed composite (PFS), age, gender, education, general health, and speed of processing (DSS) were retained for subsequent regression analyses.

Linear Regression Analyses

Multiple linear regression analysis was used to develop a model for predicting DECA performance from moderate-to-vigorous ambulatory activity time and PFS, controlling for age, gender, education, general health and speed of processing. Regression results are presented in Table 2.3.

Demographic and health variables did not account for a significant amount of variance in DECA scores in Model 1. Although the addition of speed of processing in Model 2 explained nearly 20% of the variance in DECA scores, it was no longer significant in Model 3 with the addition moderate-to-vigorous activity time. Adding PFS in the final model created a significantly more robust model to explain DECA performance and accounted for 38% of the variance in DECA scores. Specifically, DSS and PFS were significantly associated with better DECA performance. Physical fitness, but not physical activity, was positively associated with performance on the DECA everyday cognitive function task, even after controlling for basic cognitive ability.

Discussion

We examined the relationships between performance on a measure of everyday cognition within the IADL functional domains of medication use, financial management, and nutrition and food preparation, and subjective and objectively measured physical activity and physical fitness/function. At the bivariate level, no subjective measure of physical activity or physical fitness was related to everyday cognition. Only objectively measured physical activity of moderate-to-vigorous intensity, repeated chair stand time and 6-minute walk distance were significantly associated with DECA performance. More time spent in moderate-to-vigorous activity was associated with poorer everyday cognition. Similarly, Lindwall and colleagues (2008) found that several days a week of light intensity exercise was associated with better global cognition than strenuous or no exercise. These results were in contrast to more recent findings, in which positive dose-response relationships were reported between exercise intensity and neuropsychological assessments representing multiple cognitive domains (Brown, et al., 2012; Chang & Etnier, 2009). However, Chang and Etnier (2009) examined cognitive function in response to an acute bout of resistance exercise only, and Brown and others (2012) operationalized exercise intensity in terms the highest daily peak, and did not include time spent engaged in moderate-to-vigorous activity.

Although correlated at the bivariate level, when entered into the regression model, moderate-to-vigorous activity time did not predict DECA performance, with or without adjusting for covariates. DSS was a significant predictor of DECA performance; however, it did not explain a significant portion of the variance without PFS entered in the model that included moderate-to-vigorous physical activity. When PFS was added to the model, all variables accounted for 38% of the variance in DECA performance. These results are consistent with previous research indicating positive relationships between

Table 2.2: Results of Bivariate Correlations

	Gender	Education	General Health	Total Steps (4 days)	Moderate/ Vigorous Activity Time	All Physical Activity Frequency	Moderate/ Vigorous Physical Activity Frequency	6-Minute Walk Distance	Grip Strength	4-Meter Gait Speed	Repeated Chair Stand	Subjective Physical Function	DSS	DECA
Age	.274*	.026	.115	-.142	-.115	-.087	-.046	-.053	.081	.019	.153	-.135	-.243	-.040
Gender		.270*	-.109	-.021	.282	.042	.269	.240	.678**	-.139	-.201	-.001	-.447**	-.027
Education				.026	-.039	.206	.154	.096	.219	.115	.051	.155	.022	.063
General Health					.149	.024	.083	.506**	.130	-.212	-.215	.463**	.170	.097
Total Steps (4 days)					.419**	.168	.240	.565**	.140	-.384*	-.352*	.426**	.012	.096
Moderate/Vigorous Activity Time						.032	.119	.235	.353*	-.166	-.216	.120	-.207	-.301*
All Physical Activity Frequency							.720**	.105	.069	-.322*	-.038	.271	.040	.141
Moderate/Vigorous Physical Activity Frequency								.230	.309*	-.375*	-.071	.342*	-.059	.137
6-Minute Walk Distance									.495**	-.372*	-.603**	.461**	.073	.341*
Grip Strength										-.345*	-.227	.222	-.132	-.068
4-Meter Gait Speed											.589**	-.213	.191	-.034
Repeated Chair Stand												-.174	.171	-.354*
Subjective Physical Function													.228	.170
DSS														.377**
DECA														

* p<0.05. ** p<0.01. *** p<0.001

Table 2.3: Predictors of DECA Performance

	DECA performance							
	Model 1		Model 2		Model 3		Model 4	
Variable	*B*	95% CI	*B*	95% CI	*B*	95% CI	*B*	95% CI
Constant	13.3**	[4.31, 22.28]	9.31*	[0.27, 18.35]	9.89*	[0.58, 19.20]	6.57	[-1.90, 15.03]
Age	-.15	[-0.15, 0.06]	-.09	[-0.13, 0.07]	-.12	[-0.14, 0.07]	.11	[-0.07, 0.14]
Gender	-.02	[-1.60, 1.43]	.17	[-0.85, 2.28]	.21	[-0.79, 2.54]	.01	[-1.53, 1.59]
Education	.02	[-0.28, 0.32]	-.05	[-0.33, 0.25]	-.06	[-0.34, 0.24]	.002	[-0.26, 0.26]
General Health	.04	[-0.04, 0.05]	-.01	[-0.04, 0.04]	.03	[-0.04, 0.05]	-.19	[-0.07, 0.02]
DSS			.44*	[0.02, 0.16]	.42*	[0.01, 0.16]	.44**	[0.02, 0.15]
Moderate/Vigorous Activity Time					-.11	[-0.01, 0.01]	-.15	[-0.01, 0.004]
PFS							.55**	[0.50, 2.06]
R^2	0.03		0.17		0.18		0.38	
F	0.24		1.44		1.25		2.95	
ΔR^2			0.14		0.01		0.20	
ΔF			6.09*		0.41		11.03**	

* p<0.05. ** p<0.01. *** p<0.001

physical fitness and cognitive health among older adults (Atkinson, et al., 2010; Boyle, Buchman, Wilson, Leurgans, & Bennett, 2009; Fitzpatrick, et al., 2007; Wang, et al., 2005). For example, Fitzpatrick and colleagues (2007) examined associations between global cognitive function and normal and rapid pace walking in a large cohort of healthy elderly men and women. While normal pace walking was not associated with 3MS scores, participants in the slowest quartile of rapid pace walking speed were nearly twice as likely have a low, but not indicative of cognitive impairment, 3MS score (defined as 80-85, with a maximum of 100).

This study was unique in its use of a measure of everyday cognitive function. Much past research in this area has only used traditional neuropsychological tests of cognitive function. However, using tasks that are unfamiliar may not adequately account for the potential reallocation of cognitive resources among older adults that would allow compensation for age-related declines in selective cognitive domains when tasks are relevant and familiar (e.g., Blanchard-Fields, et al., 2007; Kliegel, Martin, McDaniel, & Phillips, 2007).

There have been few, if any, studies exploring associations between physical activity, physical fitness and everyday cognition. The present findings suggest that utilizing everyday cognition as an outcome has practical applicability in understanding how physical activity and fitness may contribute to older adults' ability to perform cognitively complex activities, beyond that which may be assessed by traditional neuropsychological measures.

While the current study was novel in its examination of objectively measured everyday cognition, and subjectively and objectively measured physical activity and physical fitness and function, several limitations must be noted. First, a single measure of everyday cognition was utilized. Ideally, multiple measures would be incorporated into a test battery. The present cross-sectional examination of physical activity and baseline physical fitness and everyday cognitive function provided no information as to the direction of observed relationships or long-term trajectories of function. Further, the relatively-short measurement periods (four days of objective physical activity monitoring and a subjective report of a typical week over the past month) may not have been representative of chronic activity patterns that produce physiological and/or neuropsychological adaptations. Finally, missing physical fitness data may have influenced results. Although participants with missing data did not significantly differ from the remaining sample by age, gender, education, race, subjective health or physical function, physical activity, or everyday cognition, they did not perform as well on the speed of processing task. In addition, to the resulting loss of statistical power, these missing data may indicate an unmeasured common factor among this group of participants that may have had some bearing on the findings.

It has been suggested that mechanisms associated with the physiological adaptations to physical activity, such as cardiorespiratory fitness, may also be responsible for neuropsychological adaptations (see, Marmeleira, 2012, for reveiw). Given the absence of strong bivariate associations between physical activity and fitness in the current study as would have been expected based on the dose-response nature of physical activity and fitness, the physical activity assessment methods may also not have been able to adequately detect relationships between physical activity and everyday cognitive function. It is also possible that the relatively small study sample did not provide enough statistical power to detect relationships between physical activity and everyday cognition. Additionally, this was a high-functioning, highly-educated, and relatively homogenous convenience sample. Results may not be generalizable to more diverse older adult populations.

There is an expanding body of evidence supporting the role of physical activity in promoting older adult cognitive health. However, not all studies, including the present examination, have shown strong associations. There also appear to be differential relationships depending on the dimensions represented by cognitive, physical activity, and fitness measures. Given the limited knowledge of cognitive mechanisms in general, it is possible that yet unknown or misunderstood factors have had primary or confounding influences. It is also unclear whether any potential associations between physical activity and traditional tests of cognition would transfer to cognitively-complex real-world tasks. Given these issues and knowledge gaps, several critical areas need to be addressed with future research. Of primary importance is establishing standardized operational definitions and measurement instruments to allow clearer interpretation of results across studies. Some of the current study limitations may be addressed in future research by utilizing objective physical activity measurement devices in combination with subjective reports done in daily dairy fashion to acquire more detailed activity information.

More randomized clinical trials are needed to investigate how cognition may be differentially affected by exercise subcomponents, namely intensity, frequency, duration, and mode of activity. Also, longitudinal studies that approach this area from a lifespan perspective and examine individual differences in intraindividual change will allow a better understanding of the effects of chronic physical activity on cognitive health, and/or the influence of cognitive health on physical activity participation. Although the ability to perform cognitively complex instrumental tasks is necessary to remain functionally independent (Lawton & Brody, 1969), the relationship between physical activity and cognitive function within naturally occurring contexts is a virtually untapped area of study. Given the practical relevance of everyday cognition, continuing to develop and validate measures of everyday cognition related to IADL function would provide researchers with the means to better explore the relationships between physical activity and IADL performance. Lastly, developing a deeper understanding of underlying mechanisms associated with physical activity, physical fitness and cognitive function would help address all of the above issues, and ultimately assist in developing physical activity recommendations to promote cognitive function, as well as physical function and general health.

Chapter Three:

Study Two: Exploring the Relationship between Daily Physical Activity and Cognitive Function in Older Adults: Within- and Between- Person Variability

Research indicates that cognitive abilities decline across multiple domains as we grow older (e.g., Craik & Salthouse, 2000; 2004), and decline is particularly evident after the age of 60. Earlier onset and more severe decline increases the risk of functional impairment, dementia, and Alzheimer's disease (AD) with advancing age (Jacobs, et al., 1994). Negative outcomes associated with cognitive decline result in an increased need for care for those affected, and consequently greater demand for human and monetary resources (Haan & Wallace, 2004). With approximately 20% of the U.S. population expected to be over the age of 65 by the year 2030, and adults over 85 representing the fastest growing segment of the population (Hobbs, 2008), the potential financial burden of cognitive decline and subsequent functional impairment is significant. Thus, there has been growing interest in helping older adults maintain cognitive fitness, and thereby health and functional independence, for as long as possible. Evidence suggests that physical activity may play a protective role in maintaining cognitive health among older adults, as measured by tests of neurophysiologic structure and function and traditional behavioral assessments of cognition (McAuley, et al., 2004). In 2009, the American College of Sports Medicine included cognitive outcomes in their Position Stand on Physical Activity and Exercise for Older Adults (Chodzko-Zajko, et al., 2009). This group concluded that the evidence from a combination of randomized controlled trials and/or observational studies was strong to overwhelming, but with some results that were inconsistent with the overall conclusion. Among other remaining questions, it is not yet clear what types and intensities of physical activity are related to cognitive function, what specific cognitive abilities that may differentially benefit from physical activity, and acute vs. chronic benefits. The purpose of this study was to examine the relationship between daily physical activity and day-to-day fluctuations in cognitive performance among older adults.

Inverse relationships between self-reported physical activity (e.g., Lindwall, et al., 2008; Lytle, et al., 2004; Middleton, et al., 2008; van Gelder, et al., 2004; Yaffe, et al., 2001), as well as physical fitness (Wang, et al., 2005) and general cognitive decline among older adults have been demonstrated in multiple studies. However, some studies have examined select components of physical activity, and reported varying results as a function of physical activity mode or intensity (Cassilhas, et al., 2007; Lachman, Neupert, Bertrand, & Jette, 2006; Lindwall, et al., 2008; Podewils, et al., 2005; van Gelder, et al., 2004). Intervention trials have provided support for a positive causal relationship between physical activity and improved cognition among older adults (see Colcombe & Kramer, 2003; van Uffelen, et al., 2008, for reviews). Short-term benefits of physical activity have been demonstrated both experimentally and through observation. For example, Kamijo and colleagues (2009) found that RT improved on simple and more cognitively complex flanker tasks as a result of moderate, but not light exercise. Similarly, Whitbourne, Neupert, and Lachman (2008) found that older adults had fewer memory failures on days of physical activity, as well as the following day.

The association between physical activity and cognition seems to be most apparent with more complex cognitive processes, such as executive function (Bixby, et al., 2007; Hillman, et al., 2006; Smiley-Oyen, et al., 2008), and those with a speed component (Colcombe & Kramer, 2003; Smiley-Oyen, et al., 2008). However, results across studies are not consistent, and the exact nature of the relationship between physical activity and cognition among older adults is still unclear (Bielak, 2010).

Though many domains and measures of cognitive function have been studied in relation to physical activity, one that has received little attention is everyday cognition. Everyday cognition refers to the ability to perform cognitively complex activities within real-world context. Research suggests that multiple basic abilities, namely inductive reasoning, memory, knowledge, and speed of processing are related to everyday cognition (Allaire & Marsiske, 1999, 2002; Willis, et al., 1992). However, these abilities as assessed with traditional laboratory-based measures do not seem to fully explain everyday cognitive competence in instrumental domains such as medication use, finance, and nutrition/food preparation (Allaire & Marsiske, 1999), suggesting a uniquely measured component of older adult cognition with everyday cognitive functioning assessments (i.e. tasks performed within a naturalistic framework). Measures of everyday cognition have also better explained self-reported IADL function than traditional tests of basic abilities in older adults (Allaire & Marsiske, 2002). These results indicate that measures of everyday cognition may be better suited to assessing the ability to perform real-world instrumental activities of daily living (IADL; Lawton & Brody, 1969) than measures of basic abilities, self-reports, or global screening measures of cognition. Thus, a better understanding of everyday cognition and factors that promote maintenance of everyday cognitive abilities are particularly important for older adults.

In addition to decrements in cognitive function with advancing age, greater intraindividual variability, or short-term within-person inconsistency in cognitive task performance has been noted (Bunce, et al., 2004; Hultsch, et al., 2002; MacDonald, et al., 2003; Miller & Odell, 2007; Nesselroade & Salthouse, 2004). A portion of intraindividual variability across repeated trials or measurement occasions can be attributed to factors such as measurement error, practice effects, cyclic variations, or adaptability to environmental disturbances (Lindenberger & von Oertzen, 2006). However, evidence suggests that these factors account for only a portion of within-person inconsistency, and remaining intraindividual variability represents meaningful processing fluctuations (Nesselroade & Salthouse, 2004). From a theoretical point of view, the ability to identify, quantify, and detect patterns of within-person variability facilitates the disentanglement of sources of variance in age-related processes (Nesselroade & Ram, 2004), leading to better integration, refinement, (Nesselroade & Salthouse, 2004), and testing (Anstey, 2004) of theories. In addition, more accurate partitioning of variance and refined theoretical frameworks create opportunities to elucidate mechanisms of aging processes (Neupert, et al., 2008). On a practical level, the ability to model individual positive or negative trajectories based on person-level characteristics, including variability in function or performance, may be of benefit in identifying factors, such as physical activity, that promote successful aging (Rowe & Kahn, 1987, 1997).

Relatively recent advances in methodological and analytical techniques have enabled simultaneous examination of both between- and within- person variability in cognition. Specifically, studies utilizing micro-longitudinal bursts (Nesselroade, 1991) or daily diary designs (Neupert, et al., 2008) and sophisticated statistical modeling techniques (Hertzog & Nesselroade, 2003; Nesselroade & Ram, 2004) have enabled the study of between- and within-person patterns of age-related cognitive variability, as well as interrelationships between the two. To our knowledge, only one published study to date has fully utilized these methodological advances to explore within- and between-person relationships between physical activity and cognitive function (Whitbourne, et al., 2008). In this study, daily self-reported physical activity was associated with fewer self-reported memory failures on the day of, as well as the day following physical activity participation, after controlling for education, cognitive ability, gender, and health. Furthermore, older adults realized greater benefit from physical activity participation than younger and middle-aged adults.

The present study extends the current literature by utilizing a daily diary design with objective measures of physical activity and multiple measures of cognitive function, including everyday cognition. Both total physical activity and moderate-to-vigorous activity were examined. Additionally, multilevel modeling techniques allowed examination of within- and between-person relationships between daily physical activity and cognitive function. Finally, temporal relationships were explored by examining physical activity the day of and the day prior to cognitive assessments. The specific aims of this study were: (1) Examine the relationship between total daily steps and cognitive function. It was hypothesized that performance on cognitive measures would be positively related to total number of daily steps. (2) Examine the relationship between time spent in moderate-to-vigorous intensity physical activity and cognitive function. Similar to total physical activity, a positive relationship was anticipated between cognitive function and time engaged in moderate-to-vigorous intensity physical activity.

(3) Examine the relationship between physical fitness and cognition. More physically fit older adults were expected to perform better on measures of cognition, and experience less daily variability in cognitive function.

Method

Participants

Participants were enrolled in a microlongitudinal research study that consisted of five days of repeated cognitive testing and physical activity monitoring. Participants included cognitively-intact community-dwelling older adults $\geq$ 60 years of age residing within an independent-living retirement community in Florida. All study visits took place at a central location within the residential community. Study exclusion criteria included signs of cognitive impairment, impaired near visual acuity with correction, and conditions likely to result in cognitive impairment (e.g., Alzheimer's disease, dementia, Parkinson's disease, traumatic brain injury, stroke, mini-stroke, transient ischemic attack, or other neurological disorder), terminal illness, active treatment for cancer, or current enrollment in any phase of a cardiac rehabilitation program. Participants were required to perform all physical fitness assessments without the use of ambulatory assistive devices. Physician consent to participate in physical fitness testing was required for individuals with medical conditions that were not exclusion criteria for the study, but that may have increased the risk associated with physical fitness testing (e.g., diabetes, cardiovascular conditions, metabolic disease, arthritis, or orthopedic problems). No participants were excluded based on cognitive status or visual acuity. Three participants were excluded during preliminary or baseline screening due to health conditions. Six participants withdrew from the study after preliminary eligibility screening due to seasonal relocation (n=4) or failure to obtain physician consent to complete physical fitness assessments (n=2). For the present analyses, we used data from 51 participants who completed baseline cognitive assessments and wore the physical activity monitor for the 5-day study duration (n = 51; 60% female, 89% white, and mean age 70.1 $\pm$ 7.0 years). Participants who completed the study were younger (66.8 $\pm$ 2.7 years) than those who were excluded or withdrew from the study (70.1 $\pm$ 7.0 years), $t(30.6) = 2.5$, $p<0.05$.. There were no significant differences in gender, race, or education between the two groups. See Table 3.1 for sample characteristics and descriptive analyses. The study was approved by the Institutional Review Board at the University of South Florida, and written informed consent was obtained from each study participant.

Measures

Screening measures. The following measures were used to determine eligibility for participation.

Health status and medication use. Health status and medication use were evaluated using modified versions of previously validated medical history and medication questionnaires (Jobe, et al., 2001). The medical questionnaire was modified to include all health exclusion criteria. The written medication questionnaire included all over-the-counter, and prescription medications.

Mental status. The Modified Mini Mental State exam (3MS; Teng & Chui, 1987) was used to screen for possible cognitive impairment or dementia. The 3MS is a 27 item questionnaire (19 Mini-Mental State Exam items plus eight additional questions), which assesses cognitive function across 15 domains. It includes orientation to time and place, attention, concentration, long and short term memory, language ability, and abstract thinking. A maximum possible score on the 3MS is 100; a score of 80 or less is indicative of cognitive impairment (Fitzpatrick, et al., 2007). Individuals with scores ≤ 80 were excluded.

Table 3.1: Sample Characteristics*

Variable	Mean	SD	Minimum	Maximum
Age	70.1	7.0	60	90
Female (%)	60		--	--
White (%)	88.5		--	--
Education (%)			--	--
0-12 years	7.7		--	--
13-16 years	30.8		--	--
17+ years	61.4		--	--
3MS	95.2	4.1	81	100
Physical Fitness**	-0.01	0.88	-2.0	1.7
Total Daily Steps	4,834	2,911	124	22,632
Moderate/Vigorous Activity (minutes)	18	19	147	0
DECA	11.6	1.3	5	14
LS	10.5	4.1	1	24
DSS	49.0	9.1	19	77

* Due to missing data, sample range is 45-51.
** Physical Fitness is a composite z score created from 6-minute walk test and repeated chair stand assessment.

Resting heart rate (HR) and blood pressure (BP). Resting HR and BP were assessed at baseline. Participants were excluded from baseline physical fitness testing if resting HR < 50 bpm or > 110 bpm, or if systolic BP ≥ 140 or diastolic BP ≥ 90 on two trials. Participants excluded from baseline physical fitness testing due to clinically-significant, abnormal, resting heart rates or blood pressures were referred to their primary care physicians for evaluation.

Near visual acuity. Near visual acuity was assessed using standard procedure with a visual acuity chart at a distance of 40 cm with participant's usual correction (Good-Lite, 2011). Adequate near visual acuity, evidenced by a Snellen score of 20/50 or better, was required to participate.

Acute contraindications to exercise. Individuals were excluded from baseline physical fitness testing, if on the day of baseline testing, he or she was experiencing chest pain, dizziness, lightheadedness, shortness of breath, blurred vision, skipped heart beats, racing pulse, or any musculoskeletal difficulties that would prevent rising from a chair without assistance, walking the approximate distance of a city block, or gripping a pair of pliers. No participants were excluded from physical fitness testing on the basis of acute contraindications to exercise.

Physical activity.

The ActiPed activity monitor (FitLinxx, Shelton, CT; Weyand, et al., 2001) was used to assess ambulatory activity during day-to-day life for five days. The shoe-mounted device contains accelerometer technology that captures, calculates, and transmits step counts to an internet-based database. The ActiPed provides no feedback to participants, so as to not encourage "performance behavior." Step detection accuracy exceeding 90% at usual and maximal walking speeds has been found for older adults with unimpaired gait (Moy, et al., 2009). Based on prior research suggesting varying results as a function of physical activity intensity and total amount of physical activity (Lindwall, et al., 2008;

Podewils, et al., 2005; van Gelder, et al., 2004), the following output data were the focus of the present study: (a) total number of steps (walking, running, other) during four complete days of activity monitoring following baseline testing, and (b) total minutes spent in moderate and vigorous activity across the four activity days. The ActiPed software calculates moderate activity time based on energy expenditure requirements of 3.5-7kcal/min or 3.0-6.0 METs. Vigorous activity was defined by an energy expenditure requirement of at least 7kcal/min or greater than 6.0 METs (Ainsworth, et al., 2011; Thompson, et al., 2010).

Outcome measures.

Everyday cognition. The Daily Everyday Cognitive Assessment (DECA; Allaire, et al., 2010) was specifically designed for repeated measurements of the everyday cognitive domains of financial management, medication use, and nutrition/food preparation Adapted from the previously validated Everyday Cognitive Battery (ECB; Allaire & Marsiske, 1999, 2002), it consists of eight different versions (to allow for a different test version each day, for up to 8 days), each containing two items for each of seven real-world stimuli (e.g. nutrition label), for a total of 14 items per test. Five of these versions were used in the present study. Test-retest reliability of the DECA has not been published to date; however adequate to high Cronbach's alpha coefficients for each the four subtests of the ECB have been reported (ECB Inductive Reasoning Test, $\alpha = .88$; ECB Knowledge Test, $\alpha = .69$; ECB Declarative Memory Test, $\alpha = .81$; ECB Working Memory Test, $\alpha = .72$).

Inductive reasoning. The Letter Series task (LS; Thurstone, 1962) was administered to evaluate inductive reasoning, or the ability to deduce general patterns from detailed information. Inductive reasoning ability has been associated with better everyday cognition among older adults (Allaire & Marsiske, 1999). Physical activity has been shown to moderate the relationship between aging and declines in inductive reasoning abilities (Perrot, Gagnon, & Bertsch, 2009). The LS task demands recognition of patterns in 30 reasoning problems that lack semantic content. Participants have four minutes to answer as many problems as possible. The number correct was marked as the LS score. Five distinct versions of the LS and DECA tasks were used to allow for repeated measures across five days, while reducing practice effects associated with repeated testing. All participants were administered the same five versions of these tasks; however the versions were arranged in different sequences to control for order effects and sequence assignments were counterbalanced across participants.

Speed of processing. The WAIS-R Digit Symbol Substitution task (DSS; Wechsler, 1981) was used to assess processing speed. Performance of the DSS requires several cognitive abilities including perceptual speed of processing. Age-related declines in speed of processing are well documented (e.g., Bashore, et al., 1997; Craik & Salthouse, 2000) and performance on speed of processing tests has predicted performance on tests of everyday cognition (Diehl, et al., 1995). In addition, positive associations have been observed between physical activity and speed of processing (Colcombe & Kramer, 2003). The DSS contains 93 blank squares below squares that contain a number from one to nine. Each number is paired with a different nonsense symbol in the key. Participants had 90 seconds to fill in as many blank squares with the symbol corresponding to the number in the square above it. The number correct in the allotted time (out of a maximum of 93) was recorded as the DSS score.

Covariate measures.

Physical fitness. A physical fitness speed composite was created by taking the means of z-scores for each of the following assessments.

Cardiorespiratory. Functional aerobic fitness was assessed with the 6-minute walk test (Butland, et al., 1982), using a previously reported protocol (Lord & Menz, 2002). Validation of the test as a measure of healthy older adult exercise capacity and endurance has been demonstrated through correlations with maximal oxygen consumption (Lipkin, Scriven, Crake, & Poole-Wilson, 1986). High one-week test-retest reliability has been shown (Harada, et al., 1999). Participants were instructed to walk as many times around an indoor track as they were able to in six minutes. Total distance, rounded to the nearest 10-foot mark, was recorded by the test administrator.

Functional lower body strength/power. Functional lower body strength and power was assessed using a previously established protocol (Guralnik, et al., 1994). Participants were asked to repeatedly rise from a chair as quickly as possible up to five times. The time to complete all five stands (up to one minute) was recorded.

Demographic. Age and gender information were obtained at the initial visit.

Procedure

Preliminary eligibility screening. After obtaining written informed consent, demographics, health, mobility, medication information, and physician contact information (if required for physical fitness testing) were collected from each participant.

Baseline visit. At the baseline visit, additional measures to confirm eligibility were administered, including global cognitive screening, resting HR and BP, near visual acuity, and acute contraindications to exercise. If eligible, screening measures were followed by cognitive assessments. Cognitive testing instructions were provided in writing, as they were presented in subsequent visits when participants self-administered the assessments. The tester answered any questions and observed each participant successfully self-administer cognitive assessments during the baseline testing visit to ensure proper performance on subsequent days. Physical fitness testing was performed after cognitive assessments were complete. After testing, enrolled participants were introduced to the activity monitor. They were instructed on placement, and to wear the device during all waking hours for the next four days, or until cognitive testing visits were completed. The tester observed successful placement by each participant and then registered the devices as required to activate and wirelessly collect activity data in the database. The tester assisted participants in creating a plan for remembering to wear the monitor and time/location of return. At the conclusion of the baseline visit, the next four assessment visits were scheduled for eligible participants. Participants were given a $10 gift card regardless of enrollment status.

Testing days 2-5. Cognitive assessments were self-administered in daily diary fashion at a centrally located activity center within the community. Participants picked up and returned completed testing packets at this location, and the day and time of packet pick up/completion was noted on the outside of the packet by a community staff member. The tester contacted participants on the day 2 to check for activity monitor adherence and troubleshoot adherence or testing difficulties if necessary. The tester remained blinded to activity totals until after data collection was complete for each participant to reduce the possibility of tester bias.

Data Analysis

Multi-level modeling analyses were conducted using SAS software, Version 9.3, Proc Mixed. Utilizing multi-level modeling techniques allowed for the simultaneous examination of associations between repeated measures of cognitive performance and physical activity, as well as the relationships between cognitive performance and person-level characteristics that do not change over time. At Level 1, each person's daily physical activity was the within-person predictor of cognition. At Level 2, daily physical activity became the outcome, with person-level covariates included as between-person predictor variables. Conditional means models were run for each of the cognitive outcomes to test: 1) whether there were relationships between daily physical activity and cognitive performance, 2) how much within-person variance in the cognitive measures was accounted for by physical activity, and 3) how much between-person variance in cognitive outcomes were accounted for by age, gender, and physical fitness. Separate models were run to assess the relationships between each of the three cognitive outcomes and each of the two physical activity variables on the same day, as well as physical activity on the previous day (lagged effects), for a total of 12 models. The structure of the tested models is illustrated below:

$$\text{Level 1: Cognition}_{it} = \beta_{0it} + \beta_{1it}\,(\text{Physical Activity}) + r_{it}$$

$$\text{Level 2: } \beta_{0i} = \gamma_{00} + \gamma_{01}\,(\text{Age}) + \gamma_{02}\,(\text{Gender}) + \gamma_{03}\,(\text{Physical Fitness}) + u_{0i}$$

$$\beta_{1i} = \gamma_{10}$$

In Level 1, the intercept, $\beta_{0it,}$ represents the expected cognitive score for person *i*. The slope, β_{1it}, is the expected change in cognitive performance that is associated with physical activity. The error term, r_{it}, denotes how much individual *i* fluctuates in cognitive performance. The individual intercepts (β_{0i}) and slopes (β_{1i}) become the outcome variables in the Level 2 equations, where the average cognitive performance for the sample when there is no physical activity is represented by $\gamma_{00,}$ and the average change in cognition associated with physical activity is γ_{10}. Also in Level 2, age (γ_{01}), gender (γ_{02}), and physical fitness (γ_{03}) were included as between-person person predictors of cognitive performance. The between-person covariates (age and physical fitness) were centered around their grand mean, meaning that the sample average cognition (γ_{00}) corresponds to cognitive performance when covariates were at their mean and there was no physical activity. The degree to which people vary from the sample cognitive score is represented by u_{0i}.

In order to determine mean scores and partition variance between- and within-people for each of the physical activity and cognitive variables, fully unconditional models (also referred to as null or empty models) were performed prior to testing conditional models that included predictor variables. Variance was partitioned by calculating the ratio of between- to within-person variability, or intraclass correlation coefficients (ICC = $\tau_{00/}$ (τ_{00+} σ^2)). All subsequent models were compared to the fully unconditional models (uc) to determine whether or not more variance at Level 1 or Level 2 was explained by the inclusion of predictors in conditional models (c). The equation used to compute additional variance explained between-people (R^2 between) was (τ_{00uc} - τ_{00c})/ $\tau_{00uc.}$ The amount of within-person variance explained by Level 1 (within-person) variables (R^2 within) was calculated using the equation (σ^2_{uc} - σ^2_{c})/ $\sigma^2_{uc.}$

Results

Of the 51 study participants, six were missing baseline physical fitness data due to lack of condition-specific physician consent or baseline blood pressure readings above inclusion criteria. Participants with missing and complete physical fitness data did not differ by age, gender, physical activity, or everyday cognitive task performance. Participants with missing physical fitness data had lower mean scores on the tasks of inductive reasoning (5.9 $\pm$ 1.8) and speed of processing (41.1 $\pm$ 8.2) than those with complete data (inductive reasoning; 11.0 $\pm$ 4.0), $t(48) = 2.8$, $p<0.01$; (speed of processing; 49.8 $\pm$ 8.8), $t(49) = 2.3$, $p<0.05$. Objective physical activity data were missing from two participants due to technology problems while electronically registering their devices.

Sample means for each of the dependent and independent variables are presented in Table 3.1. Results of the null models revealed that between-person differences accounted for 41% of the variability in total number of daily steps (τ_{00} = 5,532,501, z = 4.08, $p < 0.001$), while within-person fluctuations accounted for 59% of the daily step variability (σ^2 = 7,870,915, z = 11.77, $p < 0.001$). Between-person differences in number of minutes of moderate-to-vigorous activity accounted for 48% of the total daily variability (τ_{00} = 239.62, z = 4.26, $p < 0.001$, and the remaining 52% of the variance was within-people (σ^2 = 257.55, z = 11.78, $p < 0.001$). There was also significant between- and within-person variability for all three cognitive outcomes. Between-person differences explained 35% of the DECA variability (τ_{00} = 1.27, z = 3.57, $p < 0.001$), 34% of the LS variability (τ_{00} = 15.36, z = 4.48, $p < 0.001$), and 60% of variance in DSS (τ_{00} = 70.26, z = 4.26, $p < 0.001$). Within-person fluctuations accounted for the remaining 65%

of the variance in DECA ($\sigma^2 = 2.33$, $z = 9.91$, $p < 0.0001$), 66% of the LS variability ($\sigma^2 = 7.80$, $z = 9.92$, $p < 0.001$), and 40% of the variability in DSS ($\sigma^2 = 46.56$, $z = 9.16$, $p < 0.001$). The significant variance at both levels for each cognitive outcome provided justification to test subsequent models with the addition of predictors in order to explain this variance.

Relationships between Total Number of Daily Steps and Cognition

Results for DECA are presented in Table 3.2, LS in Table 3.3, and DSS in Table 3.4. Age, gender, physical fitness, and the total number of daily steps the same day or the day prior to testing were not associated with better DECA or LS performance. However, female gender and same-day total steps were related to better DSS scores. The inclusion of age, gender, and physical fitness explained 15% of the between-person variance in DSS, and total daily steps accounted for 7% of the within-person variance in DSS scores. When the model using lagged total number of daily steps was tested (total number of steps the day prior to cognitive assessments), no significant associations within- or between-people were observed for any cognitive outcome.

Relationships between Time Spent in Moderate-to-Vigorous Activity and Cognition

Minutes of same-day moderate-to-vigorous activity were not associated with associated with better performance on any cognitive task. The only significant relationship was between female gender and better performance on DSS. However, when the models were tested using lagged moderate-to-vigorous activity time, minutes of moderate-to-vigorous activity was a significant predictor of better performance on LS and DSS tasks the following day. Although this relationship did not account for any additional within-person variance in LS scores than the fully unconditional model, minutes of moderate vigorous activity the previous day explained 16% of the within-person variance in DSS. Female gender was again related to better DSS performance, and person-level covariates accounted for 13% of the between-person differences in DSS.

It should be noted that subsequent models were tested to allow the physical activity slopes (rates of change) to vary across people. However, results of these models indicated that slopes did not vary significantly between people for DECA or DSS, and the models did not converge for LS. It was concluded that allowing the slopes to vary did not better explain the data; that is, there seems to be no difference in the patterns of change associated with the relationships observed between physical activity and cognition.

Discussion and Conclusions

The primary aim of this paper was to examine within- and between person relationships between daily physical activity and cognitive function, as well as the association between physical fitness and cognitive function. Physical fitness was not significantly related to performance on any of the cognitive measures. While not all expectations were met, the results support past research and contribute new information to the existing literature. First, we found that while total number of daily steps was related only to same-day performance on DSS, there were several significant relationships when moderate-to-vigorous intensity activity was examined. In addition, a temporal relationship was suggested, evidenced by previous-day moderate-to-vigorous activity predicting better performance on LS and DECA tasks than same-day activity. Gender was a between-person predictor of DSS scores in three of the four models tested. Specifically, females performed better than males. Although this outcome was not

Table 3.2: Multilevel Modeling Estimates and Standard Errors Predicting DECA Performance

Fixed Effects	Total Steps		Previous Day Total Steps		Moderate to Vigorous Activity		Previous Day Moderate to Vigorous Activity	
	B	SE	*B*	SE	*B*	SE	*B*	SE
Intercept (β_0)								
DECA Performance (γ_{00})	11.65***	0.31	11.75***	0.32	11.78***	0.27	11.68***	0.26
Age (γ_{01})	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Gender (γ_{02})	-0.28	0.44	-0.23	0.46	-0.24	0.44	-0.37	0.45
Physical Fitness (γ_{03})	-0.42	0.26	-0.30	0.27	-0.47	0.25	-0.43	0.25
Physical Activity Slope (β_1)								
Intercept (γ_{10})	0.0000	0.0000	0.000	0.000	-0.0038	0.0060	0.009	0.005

Note: n=44 participants, 214 occasions

* $p<0.05$. ** $p<0.01$. *** $p<0.001$

Table 3.3: Multilevel Modeling Estimates and Standard Errors Predicting Letter Series Performance

Fixed Effects	Total Steps		Previous Day Total Steps		Moderate to Vigorous Activity		Previous Day Moderate to Vigorous Activity	
	B	SE	*B*	SE	*B*	SE	*B*	SE
Intercept (β_0)								
Letter Series Performance (γ_{00})	10.44***	0.89	11.77***	0.88	10.97***	0.83	10.89***	0.80
Age (γ_{01})	0.02	0.10	-0.02	0.10	0.02	0.10	0.02	0.10
Gender (γ_{02})	-0.08	1.39	-0.58	1.37	-0.18	1.39	-0.24	1.36
Physical Fitness (γ_{03})	0.76	0.80	-0.12	0.79	0.12	0.80	0.10	0.78
Physical Activity Slope (β_1)								
Intercept (γ_{10})	0.0001	0.0001	0.000	0.000	0.012	0.012	0.025*	0.010

Note: n=44 participants, 214 occasions

* $p<0.05$. ** $p<0.01$. *** $p<0.001$

Table 3.4: Multilevel Modeling Estimates and Standard Errors Predicting Digit Symbol Substitution Performance

Fixed Effects	Total Steps		Previous Day Total Steps		Moderate to Vigorous Activity		Previous Day Moderate to Vigorous Activity	
	B	SE	*B*	SE	*B*	SE	*B*	SE
Intercept (β_0)								
Digit Symbol Substitution Performance (γ_{00})	50.26***	1.82	52.33***	1.79	51.53***	1.64	51.40***	1.62
Age (γ_{01})	0.24	0.20	0.21	0.20	0.23	0.20	0.20	0.20
Gender (γ_{02})	-5.67*	2.74	-5.02	2.76	-6.04*	2.72	-6.60*	2.75
Physical Fitness (γ_{03})	-1.22	1.60	-2.01	1.59	-1.48	1.56	-1.57	1.57
Physical Activity Slope (β_1)								
Intercept (γ_{10})	0.0004*	0.0002	0.000	0.000	0.052	0.029	0.114***	0.024

Note: n=44 participants, 187 occasions

* p<0.05. ** p<0.01. *** p<0.001

hypothesized in the current study, previous research indicates that females perform better than males on processing speed tasks that involve digits or alphabet symbols (see, Roivainen, 2011, for review).

Physical Activity and Everyday Cognition

The present results suggest that physical activity, regardless of intensity level, is not associated with everyday cognition, as measured with the DECA instrument. While this measure incorporates multiple components of higher level cognitive functioning that are believed to benefit from physical activity (Allaire & Marsiske, 1999), there are several possible explanations for the lack of any observed relationship. First, this sample was highly educated, and all living independently. Although there was significant between- and within- person variability, the mean DECA scores from this high-functioning group were relatively high, and may have resulted in ceiling effects. Secondly, evidence suggests that cognitively complex activities with a speed component may selectively benefit from physical activity (Colcombe & Kramer, 2003; Smiley-Oyen, et al., 2008). While the DECA does contain cognitively-complex real-world types of problems, there are no imposed time constraints in solving the problems, and thus no direct measurement of processing speed.

Physical Activity and Inductive Reasoning

More minutes of moderate-to-vigorous activity on one day was associated with better inductive reasoning on the following day. These results support prior research indicating a relationship between physical activity and higher-order cognitive function with a speed component (it was a timed task), as well as a selective benefit with higher intensity exercise. It also suggests relationship directionality, as associations were only observed when examining lagged moderate-to-vigorous activity.

Physical Activity and Speed of Processing

The most notable relationships were observed between physical activity and speed of processing. Better performance on the DSS was associated with total number of daily steps and time spent in moderate-to-vigorous activity on the same day, as well as time spent in moderate-to-vigorous activity on the previous day. Same-day moderate-to-vigorous activity accounted for only 5% of within-person variability, but time spent in moderate-to-vigorous activity the previous day accounted for 17% of within-person fluctuations in speed of processing.

These results support existing evidence suggesting a distinct benefit of physical activity to speeded tasks with a degree of cognitive complexity. Findings are also consistent with previous research suggesting that better cognitive function is more strongly related to physical activity intensity than total physical activity (Cassilhas, et al., 2007; Lachman, et al., 2006; van Gelder, et al., 2004). For example, Van Gelder and colleagues (2004) found that study participants in the lowest quartile of baseline activity intensity had significantly more cognitive decline over ten years, compared to those in all other quartiles, while baseline activity duration was not predictive of decline. Similarly, higher levels of resistance have been associated with better performance on cognitive measures than lower levels of resistance following resistance training interventions (Cassilhas, et al., 2007; Lachman, et al., 2006).

The current study findings may be partially attributed to study design, and possibly indicative of enhanced practice effects, particularly in relation to DSS performance. The DECA and LS cognitive outcome measures had unique versions of the same task for each testing day in order to control for practice effects. In contrast, there was only one version of the DSS instrument, and as a result, all study participants repeated the same assessment on each testing day. Although greater within-person processing fluctuations are generally recognized as problematic in that they may signify a lack of cognitive processing robustness (Li, Lindenberger, & Sikström, 2001) or impending decline (MacDonald, et al., 2003), intraindividual variability may also indicate positive adaptations (Allaire & Marsiske, 2005; Miller & Odell, 2007). To the extent that practice effects can represent an adaptive form of within-person variability, it is possible that positive adaptation to the DSS task was associated with physical activity engagement, especially time spent in moderate-to-vigorous physical activity. Further, time spent in moderate-to-vigorous activity may have enhanced practice effects, as suggested by differences in within-person variability in DSS accounted for by same-day activity (5%) and previous-day activity (17%).

In addition to limitations already noted, several other factors may have influenced the study findings. First, when measuring same-day physical activity, we could not control for how much physical activity occurred before vs. after cognitive testing. It is plausible that significant amounts of daily physical activity occurred after daily cognitive testing, thus masking true same-day effects of physical activity. However, this would still support the existence of a temporal relationship between physical activity and better cognition. In addition, activity monitors only capture ambulatory physical activity, and may neglect significant amounts of non-ambulatory physical activity. Physical fitness data were missing from six participants. Participants with missing fitness data were not statistically different from those without missing data with regards to age, gender, education, race, physical activity or everyday cognitive function. However, they had lower mean scores on the speed of processing and inductive reasoning tasks, suggesting that inferences regarding the relationship between physical fitness and cognitive function from the present analyses must be made with caution. Finally, as mentioned previously, this was a self-selected group of high-functioning and well-educated older adults residing in an independent-living community. Findings may not be generalizable to the general older adult population.

Present findings suggest that activity intensity, but not necessarily total activity, may be associated with better cognitive function and/or enhanced practice effects among older adults. There also may be acute benefits realized from moderate-to-vigorous intensity physical activity engagement. This relationship appears to be selective for cognitively complex tasks involving a speed component and/or repeated tasks. Further investigation is necessary to determine if there may be a relationship between physical activity and everyday cognitive tasks that involve a speed component. In addition, a better understanding of how physical activity may influence positive adaptations or enhanced learning among older adults would be beneficial. Both have potential implications in maintaining real-world function and the ability to live independently for as long as possible.

Chapter Four:

Discussion and Conclusion

Study Results

The specific aims of this study were to: (1) Examine the relationships between physical activity, physical fitness, and everyday cognition, (2) Explore the amount of within- and between-person variability in everyday cognition that is accounted for by daily physical activity, and, (3) Investigate physical fitness as a potential moderator in the relationship between daily physical activity everyday cognitive function. Within the primary aims was a subset of secondary questions that were also examined. Namely, (1) Whether observed relationships were different according to how physical activity and physical fitness were operationalized, and (2) Were the relationships between physical activity, physical fitness and complex basic cognitive abilities similar to those observed with everyday cognition.

The first set of analyses in paper one addressed the relationships between baseline performance in a measure of everyday cognition (DECA) and multiple measures of physical activity and physical fitness (specific aim 1, secondary question 1). At the bivariate level, subjectively assessed physical activity and physical fitness were not related to everyday cognition. Only objectively measured physical activity of moderate-to-vigorous intensity, repeated chair stand time and 6-minute walk distance were significantly associated with DECA performance. Specifically, more time spent in moderate-to-vigorous activity was correlated with poorer everyday cognition. When entered into a regression model with covariates, moderate to vigorous activity time was not significantly associated with everyday cognition, and the model was not significant However, when the physical fitness speed composite was included, this model accounted for 38% of the variance in baseline everyday cognitive performance, even controlling for visual speed of processing. These results suggested positive relationships between everyday cognition and physical fitness, particularly objective measures that incorporate a speed and/or lower body muscular power component. Further, these associations appeared to be independent of basic cognitive function in the speed of processing domain.

The remaining study questions were the focus of paper two. Similar to regression results reported in paper one, there was no relationship found between daily physical activity and everyday cognition. Time spent in moderate-to-vigorous physical activity, but not total daily steps, was related to better performance on tasks of inductive reasoning and visual speed of processing the following day. Although within-person fluctuations in daily moderate-to-vigorous physical activity were positively associated with inductive reasoning and speed of processing, physical fitness did not explain any of the between-person variance, and did not modify the within-person relationships between physical activity and cognitive function. The only covariate that accounted for a significant portion of between-person differences was gender. Consistent with previously reported results indicating a female advantage in processing speed tasks with digits or alphabet characters (Roivainen, 2011), females performed better on the Digit Symbol Substitution speed of processing task. An unexpected but interesting finding was the strength of the within-person relationship between physical activity and speed of processing. Although not compared directly, physical activity accounted for a larger percentage of within-person speed of processing fluctuations than inductive reasoning variability, in their respective models. This may be due to selective associations with specific cognitive abilities, particularly those with more complexity and a speeded component. However, it might also reflect methodological differences in the assessment administration. The task of inductive reasoning had multiple versions that limited practice effects by allowing administration of different version on each testing day. However, the same speed of processing task was administered at all visits, likely resulting in greater practice effects.

Objectively-measured ambulatory physical activity was not associated with everyday cognition in either study after controlling for covariates. Daily time spent engaged in moderate-to-vigorous ambulatory activity, but not total daily steps, was associated with better inductive reasoning and visual speed of processing. Further, temporal directions were suggested by examining lagged physical activity. Positive associations were found for previous day physical activity, but not same-day physical activity, suggesting an acute relationship between moderate-to-vigorous physical activity and better cognitive function.

Potential Mechanisms

Mechanisms of cognition, age-related cognitive decline and dementia, in general, are complex and not fully understood. Understanding the relationships between physical activity, physical fitness, and cognitive function and the corresponding mechanisms of action, therefore, have been limited by the still-evolving body of literature. Based on existing research, however, multiple mechanisms of action have been proposed. Obesity, hypertension, cardiovascular disease, type 2 diabetes mellitus, and metabolic syndrome have been associated with poor cognitive outcomes in later life (Craft, et al., 2012; Haan & Wallace, 2004; Nash & Fillit, 2006). Physical activity reduces the risk for these conditions (CDC, 1996). One plausible mechanistic explanation for the positive relationship between physical activity and older adult cognitive health is through the reduction of these risk factors.

Inflammation appears to have a role in age-related cognitive decline. Cognitive impairment in older adulthood has been prospectively associated with increased levels of inflammatory markers, interleukin-6 and C-reactive protein (Yaffe, et al., 2003). Further, animal model studies suggest that pro-inflammatory mediators such as interleukin-1that interfere with long-term memory may be released in the brain in response to trauma in older adults. This has been supported by human subject observations whereby delirium and subsequent dementia are often initiated by acute infections, surgery or drug interactions. (Craft, et al., 2012). Lower levels of multiple inflammatory markers have been measured in more physically active older adults (Geffken, et al., 2001). In rat models, exercise has resulted in improved cognition and increases in what appear to be protective neuroinflammatory factors in healthy rats (Parachikova, Nichol, & Cotman, 2008), as well as reversed age-related cognitive changes following infection and injury. Physical activity may influence cognition through the alteration of inflammatory factors associated with cognitive decline.

According to Harman's free radical theory of aging (1956), reactive oxygen species produced as a by-product in normal cellular metabolism, and the corresponding oxidative stress, are key components in the nearly universal decline seen in all aging biological systems. Further, it is hypothesized that increased oxidative stress can promote premature aging and age-related systemic deterioration. Cui, Hofer, Rani, Leeuwenburgh & Foster (2009) examined the effects of exercise on oxidative stress in the brains of rats. Though aging was generally associated with increased cerebellar lipid peroxidation, rats who engaged in lifelong wheel running had reduced DNA, RNA and lipid oxidation. Moderate exercise initiated later in life resulted in lower levels of lipid oxidation, but no difference in DNA or RNA oxidation. An inverse relationship was demonstrated between lipid oxidation and grip strength, which was used to measure cerebellar control of motor strength in the rodents. Additionally, task acquisition and memory retention has been positively related to exercise and vitamin E supplementation through enhancement of the cholinergic neurotransmitter system in the cerebral cortex of aging rodents (Jolitha, Subramanyam, & Devi, 2009). The observed improvement in neurotransmitter function was hypothesized to be a result of reductions in oxidative damage to the cholinergic system. These results suggest physical activity may result in decreased levels of oxidative damage in the brain, thereby directly and indirectly promoting the preservation of cognitive health later in life.

Another potential mechanism of action is enhanced neuronal function and brain plasticity, activated by physical activity. Exercise has been associated with formation of new neurons (neurogenesis), new synapses (synaptogenesis), new vascular structure formation (angiogenesis), increased strength of dendritic spines, increased levels of vascular growth factors, neurotransmitters and neurotrophic growth factors in animal models (van Praag, 2009). Though most research in this area has been performed in animal models, MRI technology was used to measure cerebral blood volume (CBV) in exercising humans after CBV was confirmed as a correlate of neurogenesis in rodents (Pereira, et al., 2007). Exercise resulted in increased human hippocampal CBV, which was in turn, positively correlated with better cognitive function.

In a recent review, Hötting and Röder (in press) summarized evidence from human studies. In addition to enhanced mitochondrial energy production in neuronal tissue and better oxygen and nutrient supply as a result of increased cerebral blood flow associated with aerobic exercise, a number of possible mechanisms have been investigated. Among them, functional imaging studies have suggested that cognitive benefit may be attributed to increased grey matter in the hippocampus and frontal regions of the brain, more efficient activation and deactivation of task-relevant areas in the brain, and increased functional connectivity between different areas in the brain.

Brain-derived neurotrophic factor (BDNF) appears to play a key role in aging brain plasticity. Though aging is associated with decreased levels of BDNF, and decreased levels of BDNF are related to cognitive decline and dementias, it has been shown to increase as a result of exercise in rat models (Cotman & Berchtold, 2002). Conversely, better cardio-respiratory fitness and long-term self-reported activity levels have been associated with lower resting levels of serum BDNF in humans (Currie, Ramsbottom, Ludlow, Nevill, & Gilder, 2009). Several explanations for these results were suggested, including the possibility that exercise results in a more efficient uptake of serum BDNF into the central nervous system, thereby promoting cognitive health. Alternatively, because it is unknown whether BDNF is able to cross the blood-brain barrier, it is unclear whether serum BDNF measurements from peripheral neurons are indicative of central BDNF levels.

Finally, there may be interrelated biological and psychosocial mechanisms at play which influence the relationship between physical activity and cognition. For example, though hippocampal progenitor cells proliferate in response to exercise in rats, social isolation has been shown to prevent this response (Leasure & Decker, 2009). Similarly, behavioral indicators of cognitive function did not improve following a 4-month exercise intervention in depressed middle-aged and older adults (Hoffman, et al., 2008). Potential social and psychological mechanisms were also investigated by Vance, Wadley, Ball, Roenker and Rizzo (2005). Using structural equation modeling for analyses, better cognition, as measured by tests across multiple domains, appeared to be directly influenced by higher levels of physical activity and fewer depressive symptoms. In addition, physical activity was directly related to larger social networks, which in turn led to better cognition through fewer depressive symptoms. These results suggest that complex relationships between multiple factors at the biological, psychological and sociological levels underlie the diverging associations observed in various studies.

Implications

Real-World Cognitive Function.

Multiple basic abilities, including inductive reasoning, memory, knowledge, and speed of processing, have been associated with everyday cognitive tasks that are instrumental in nature (e.g., Allaire & Marsiske, 1999, 2002; Willis, et al., 1992). Data indicate that age-related decline in speed of processing (Patterson, Weatherbee, & Allaire, 2010) or multiple basic abilities (Diehl, et al.; Finucane, et al., 2005) explain age-related decrements in everyday cognition. Several studies have shown a relationship between speed of processing and tests of everyday cognition (Owsley, et al., 2002;

Patterson, et al., 2010). Patterson and colleagues (2010) found that processing speed was differentially related to overall multi-domain function and performance in the domain of finance. Faster processing speeds were associated with worse performance overall, but better performance in the financial domain. Further, although age was a significant predictor of overall performance, speed mediated this relationship. The two variables shared about 16% of the variance in overall task performance, but 15% was unique to processing speed. Also of note is that the Owsley et al. (2002) measure was scored by task accuracy and completion times. While most of the study sample committed few or no errors, there was wide variability in the time required to complete each task.

Results suggest that time-relevant and/or everyday tasks in the finance domain may rely more on processing speed than reasoning or memory, especially when tasks are relatively simple and familiar. No relationship was found between physical activity and everyday cognition in the current study; however the DECA lacked time-relevant tasks and did not selectively measure performance in the financial domain of everyday cognition. The strong relationship found between moderate-to-vigorous activity and a speed of processing suggests that a time-relevant measure of everyday cognitive function or selective analysis of financial problems may have revealed different results. An alternate or additional explanation for the amount of within-person variability explained by physical activity on the speed of processing task is that physical activity was associated with enhanced practice effects when repeating the same task over consecutive visits. Although this was not one of the research questions addressed in the current study, this may be an area of future inquiry with potential real-world implications. Considering practice effects as a positive type of fluctuation or adaptation, factors such as physical activity that may enhance these effects could be beneficial for older adults when learning a novel skill that will be repeated in day-to-day life.

The dual-process scheme of cognitive function (Baltes, Dittmann-Kohli, & Dixon, 1984; Dixon & Baltes, 1986) suggests that studying basic abilities and the application of these abilities in real-world settings as separate but interrelated components of adult cognition may lead to a better understanding of if and how gains, maintenance, and losses in one or both areas may interact to enhance or impair older adults' everyday cognitive function. It seems that the greatest strengths afforded by existing research are, (a) the expanding body of data that support relationships between physical activity and cognitive outcomes among older adults; (b) empirical evidence supporting associations between basic abilities and measures of everyday cognition; and (c) the documented relationships between measures of everyday cognition and functional and clinical outcomes. The practical significance of the present results lies in the potential for physical activity and/or fitness to indirectly influence everyday cognitive function by mediating or modifying one or more basic abilities such as speed of processing or inductive reasoning, or through a direct relationship with everyday cognition. Everyday cognition has been associated with better self-reported IADL function (Allaire & Marsiske, 2002) and quality of life (Gilhooly, et al., 2007), and shown to predict clinical outcomes such as mortality (Allaire & Willis, 2006; Weatherbee & Allaire, 2008), clinical dementia ratings (Allaire & Willis, 2006), and mild cognitive impairment (Allaire, et al., 2008). Understanding factors that may modify individuals' short- and long-term trajectories of cognitive function could have important implications. In addition to personal and clinical applicability, this information could potentially guide policy decisions, and inform research design.

Research Design and Interpretation.

Taken together, findings from studies one and two indicate that not all physical activity and physical fitness measures will reveal the same results. The way each construct is operationalized appears to be an important consideration. It is still unclear what measures of physical fitness are the most appropriate to use when studying the relationship between physical and cognitive fitness. Based on the results from paper one, it appears that including objective measures involving a speed and/or lower body power component would be warranted. Although objectively measured physical activity appeared to better detect relationships between activity and cognitive function, most accelerometers do not measure non-ambulatory activity. Utilizing a combination of objective accelerometer data and daily diary self-report physical activity may better assess total physical activity than either one separately. At the present time, this author is not aware of any such protocols that have been successfully tested. Given the differential effects observed with total and moderate-to-vigorous intensity activity, further study of the relationship between activity intensity and cognitive outcomes is important. Based on the current results, a modest amount of time spent engaging in higher-intensity activity may have significant effects on cognitive function.

Similar to physical activity and fitness, findings may be divergent according to the cognitive domain measured, as demonstrated by varying results with each outcome measure in the present investigations. This may be due to selective associations between cognitive abilities and physical activity, measurement method, or study design. Ideally, the measurement selection process should be guided by theory and past research, include instruments that indicate real-world function/ability transfer, and incorporate direct indices of brain function such as imaging or neuroelectric measures when possible.

Limitations

Several limitations may have influenced these results. First, the study sample was relatively small, and physical fitness data were missing for six participants due to inability to obtain physician consent for physical fitness testing or blood pressure readings above the inclusion criteria. Participants with missing physical fitness data did not differ from the rest of the sample with regards to age, gender, education, race, subjective health or physical function, physical activity engagement, or everyday cognitive function. They did, however, differ on baseline and mean speed of processing and inductive reasoning task scores. In addition to potentially limiting the statistical power and the ability to detect between-person differences in cognition that were attributable to physical fitness, differences may indicate that data are not missing completely at random. Consequently, inferences derived from statistical analyses should be interpreted with caution. Also, the study population was a well educated, high functioning, and relatively homogeneous group, and current findings may not be generalizable to other populations.

The scores on the measure of everyday cognitive function were high relative to the total possible score. It is possible that ceiling effects among the study participants influenced the lack of relationships observed in this domain. Further, this task was not timed, and as a result did not adequately assess the component of speed of processing that may be selectively associated with physical activity.

Regarding physical activity assessments, relatively short measurement periods (four days of objective physical activity monitoring and a subjective report of a typical week over the past month) may not have been representative of chronic activity patterns that produce physiological and/or neuropsychological adaptations. Additionally, the accelerometers were only able to capture ambulatory physical activity. Thus, considerable amounts of non-ambulatory physical activity participation may not have been detected and were inadvertently omitted from analyses. When considering same-day physical analyses in paper two, it was unclear how much physical activity occurred before vs. after cognitive testing. It is possible that significant amounts of daily physical activity occurred after daily cognitive testing, and did not reveal true same-day effects of physical activity. However, this would still support the existence of a temporal relationship between physical activity and cognitive function.

Lessons Learned

Physical Fitness Measurement.

Early in the project planning process, it became clear that there were no standardized measures or batteries of tests that were consistently utilized across studies of physical fitness and cognition. Further, several of the more commonly used measures and batteries of functional physical fitness had been studied in frail elderly or disease populations, not the active and healthy older adults that were being recruited for the present study. As a result of having little guidance in the literature, the decision was made to include multiple measures in the study protocol. Each would be examined at the bivariate level to make decisions regarding how proceed with multivariate analyses. In retrospect, this has led to several conclusions. First, the SPPB, though a widely used physical assessment battery, is not an ideal choice for older more physically fit older adults. Ceiling effects are encountered in this population if testing and scoring protocols are followed as published. In the present analyses, all testing protocols were followed, but raw data were used instead of transformed scores for the repeated chair stand and usual gait speed assessments. This allowed examination of performance variability among this high-functioning group, whereas the majority of the sample would have achieved the maximum score if the scoring protocol had been followed. However, this was not possible in the balance testing portion of the battery because each of the subtests is concluded at the end of ten seconds. When participants have maintained balance for ten seconds, they have achieved the maximum score possible for each stand.

The second observation is regarding the measurement of grip strength. There are a number of protocols used in various studies, if the protocol is reported at all. There are variations in posture, grip and arm positions, time between trials, numbers of trials, and scoring procedures (best single trial vs. average and single hand vs. two-hand). In the current analyses, the best score from six trials (three test trials for each hand) was utilized in order to encourage participants to get the highest score possible, as suggested in the Southampton protocol (Roberts, et al., 2011).

The final conclusion is that much more work needs to be done to determine appropriate functional physical fitness assessment methods for the growing population of active and healthy older adults, for whom tests have not been developed and validated. While they are more physically able than frail elders, age-related bio- and neurophysiologic changes differentiate them from younger populations.

Study Fidelity.

There was concern about study fidelity, particularly with regards to participants self-administering daily cognitive assessments and adhering to ActiPed activity monitor instructions. Multiple mechanisms were established to ensure continuous activity monitoring during all waking hours, from observation of correct placement at the baseline appointment to daily email, text or phone reminders. Overall, feedback from participants indicated that the daily reminders were not necessary for activity monitor adherence, as had been anticipated.

Similar safeguards were utilized to ensure cognitive assessments were self-administered correctly and consistently, including observation of assessment administration, written instructions provided for each day of testing, reminder cards with test visit appointments, and use of the same testing environment for all visits. These seemed to be effective means of supporting fidelity and will be considered for use in future studies. In addition, participants were provided with a daily log, on which they were instructed to note any difficulties they experienced with testing and/or activity monitor adherence. Participants were very forthcoming with information about not only any difficulties they had experienced, but also factors that they thought may have affected the study results. In retrospect, this may have been a missed opportunity to obtain more qualitative information about daily exercise or other relevant habits. Given that most activity monitors capture only ambulatory physical activity, utilizing a daily dairy to obtain reports of all physical activity throughout the day (including modes, perceived intensity, duration, etc.) in conjunction with objectively-measured data, may give more complete information about total daily physical activity.

Resource Considerations.

Aside from funding provided by the University of South Florida, School of Aging Studies to purchase the ActiPed activity monitors and several pieces of physical assessment equipment, financial and human resources for this dissertation project were limited. This was in part due to lack of grant funding, as well as the remote location of the study site. Nearly all of the recruitment, testing, administrative tasks, and study management duties were performed by the Principle Investigator, which resulted in slower progress than could have been realized based on participant response. As testing progressed, multiple study participants indicated a willingness to assist with the project in ways other than as a study subject. As taught in the study of gerontology, older adults have great capacity for, and find satisfaction in, engaging in meaningful vocational activities. Many of the study volunteers had prior experience collecting their own thesis or dissertation data, and with training, most likely could have provided instrumental assistance with participant recruitment, testing, and/or project management. One of the most important lessons learned in this project is to consider these largely untapped resources in the planning phase of research projects involving older adults. Even in funded studies, older adult volunteer (or paid) personnel may offer benefits such as peer connections to facilitate participant recruitment and retention. At the same time, these volunteers would have the opportunity to contribute to society in a way that is both personally meaningful and intellectually challenging.

Future Research Interests

I strongly believe that physical fitness measurement is a key issue in the field, not just in establishing standardized measures, but also in determining how to measure functional fitness in a growing population of young older adults that are less frail and more active than previous study populations. In order to assess differences in physical function as outcomes, as well as other outcomes associated with fitness differences, measurement techniques must be able to elucidate differences. Equipment with advanced technology may be able to assist in this way, but it is also important to develop assessments that can be administered relatively quickly and inexpensively outside of lab environments. The SPPB is such a battery of tests; however, current testing and scoring protocols seem to be inappropriate for high-functioning individuals, as evidenced by the inability to estimate variance when using the established testing and scoring protocols in the current study population.

My second area of research interest is in physical and cognitive outcomes associated with resistance training. I believe we have not realized the full potential of strength training due to limited knowledge about specific dosages and protocols to produce optimal physiologic adaptations (Liu & Latham, 2009). I am specifically interested in power or high-velocity training. Recent research has found a connection between high-velocity training and better physical function outcomes than traditional resistance training protocols (e.g., Leszczak, Olson, Stafford, & Brezzo, 2013; Marsh, Miller, Rejeski, Hutton, & Kritchevsky, 2009). As with resistance training in general, it is unclear what intensities, modes, frequencies, and volumes are the most effective. Also of interest is whether there may be similar or shared underlying mechanisms between muscular power training and cognitive speed of processing training. Both have resulted in improved functional outcomes as a result of interventions (Ball, Edwards, & Ross, 2007; Edwards, et al., 2005; Leszczak, et al., 2013; Reid & Fielding, 2012). Both involve performing work over time (power) and are believed to improve function via neural pathways (Henwood & Taaffe, 2005; Takeuchi, et al., 2011).

Lastly, knowing that protocols are only as effective as adherence to them, I am interested in how manipulations of mode, intensity, velocity, and duration may influence program adherence in older women. Older adults generally have low participation rates in resistance training, despite the potential functional and health benefits. For example, in a large cohort of older adults enrolled in the Health, Aging, and Body Composition Study, 40% of the study population reported engaging in walking for exercise, but only 5% participated in resistance training (Peterson, et al., 2009). I would like to examine the effects of various protocol delivery mechanisms on self-efficacy, short-term participation, and long-term adherence rates in resistance training programs among older adults, and women in particular, due to their increased risk for frailty associated with advancing age.

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