Rate of Perceived Exertion and Cardiorespiratory Fitness in Older Adults with and without AD

By

Andrea Bevan

M.A., University of Colorado Colorado Springs, 2014

Submitted to the graduate degree program in Psychology and the Graduate Faculty of the University of Kansas in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Chair: Amber Watts, PhD

Member 2: Eric Vidoni, PhD

Member 3: Mike Vitevitch, PhD

Member 4: Sarah Kirk, PhD

Member 5: David Ekerdt, PhD

Date Defended: 6 June 2018

The dissertation committee for Andrea Bevan certifies that this is the approved version of the following dissertation:

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Chair: Amber Watts, PhD

Date Approved: 6 June 2018

Abstract

Exercise has many benefits for physical and cognitive health. However engagement in and adherence to exercise is challenging. There are many barriers to exercise in older adults including subjective exercise difficulty, or rate of perceived exertion (RPE) independent of objective cardiorespiratory fitness, measured by peak oxygen and carbon dioxide exchange (VO_2 peak). Subjective perception of exercise difficulty may especially be a barrier to exercise in individuals with Alzheimer's disease (AD). RPE is the most commonly used measure in exercise research, yet the relationship between RPE and objective fitness is not fully understood in older adults with and without AD. This relationship is important in understanding how to best support initiation, engagement, and maintenance of exercise in this population and is a first step in understanding appropriateness for use in this population. Multilevel modeling (MLM) statistical analyses were performed to explore the relationship between objective and subjective measures of fitness in older adults with and without AD during a multi-stage graded exercise test. Results indicate a negative relationship between objective fitness and subjective effort. Independent of cardiorespiratory fitness, older age, female gender, cognitive impairment, and use of heart medications each predicted greater self-reported effort (RPE) during exercise. Results are discussed in terms of social psychology phenomena and potential neuropsychological deficits leading to increased subjective feelings of effort. These findings establish the relationship between actual fitness level and perceived effort, highlight ways to support exercise behavior, and direct future exploration of barriers to exercise among older adults with and without AD.

Acknowledgments

I want to thank all of the academic and life mentors I have encountered throughout my journey returning for this academic pursuit. As a non-traditional student I was hesitant about my ability to not only succeed but to thrive on this path. With encouragement, patience, and a desire to teach, Drs. Robert Durham, Molly Maxfield, Amber Watts, Sarah Kirk, and Cyd Schnacke have helped me and allowed me to grow as a person and as a scientist-practitioner. Thank you cannot express the impact these amazing and kind people have had on my life. They have forever changed the trajectory of my life in ways I desire; to be a more knowledgeable, empowered, grounded, healed, and compassionate person.

I would like to acknowledge my esteemed dissertation committee, without whom this would not be possible. Each member's feedback improved and strengthened this project. A special thank you to Dr. Jeffery Hall and Daniel Reis, MA who were knowledgeable and patient enough to help me learn a new statistical method. Thank you to Eric Vidoni, PhD and Natasia Adams, MA for their help with data. Thank you all for helping usher this project to fruition.

To my friends, in and out of graduate school, and family who have supported me on this path, I thank you for your belief in me and support through various dark nights of the soul. A special thank you to Christina Khou, MA for traveling this path with me and offering sage advice when needed. The desire for this path may not be understood by all but I appreciate trusting this was my right path. I am humbled by all the love and support I have in my life and am so appreciative of countless people throughout this journey. It is only with the help and support of my mentors, support staff, friends, and family that I was able to achieve this milestone in my life. These individuals have helped me in tangible and intangible ways and I am forever grateful. My heartfelt thank you to you all.

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Chapter I: Introduction

Older adults are the most sedentary of all age groups (Caspersen, Pereira, & Curran, 2000; McAuley et al., 2009) and those with cognitive impairment are even more sedentary (Watts, Vidoni, Loskutova, Johnson, & Burns, 2013). This pattern of behavior leads to many deleterious health and cognitive effects (Mañas, Del Pozo-Cruz, Garcia-Garcia, Guadalupe-Grau, & Ara, 2017), which increases healthcare usage and familial caretaking burden (Gilhooly et al., 2016). It is estimated that at least one third of Alzheimer's Disease (AD) cases worldwide are attributable to seven modifiable risk factors, including physical inactivity (Stephen, Hongisto, Solomon, & Lönnroos, 2017). Therefore, addressing barriers to engagement in physical activity may prevent almost 300,000 cases of dementia per year, worldwide (Sallis et al., 2016).

Increasing exercise is a promising strategy to improve health and cognitive function in older adults with AD (Colcombe & Kramer, 2003; Maliszewska-Cyna, Lynch, Oore, Nagy, & Aubert, 2017). However, there are many barriers that prevent exercise in older adults who are experiencing age-related normal cognitive declines or neurodegenerative diseases that affect cognition. Barriers include health problems, pain, previous injury, belief that exercise is only a recreational pursuit, and the perception that sweating, labored breathing and muscle soreness are difficult negative outcomes (Schutzer & Graves, 2004). The present study will focus on barriers related to perceived difficulty of exercise in older adults with and without AD.

The most commonly used measure for assessing subjective difficulty of exercise is a rating of perceived exertion (RPE). This numerical rating scale measures the perception of effort and strain during exercise. The use of RPE assumes that individuals are able to accurately perceive their own effort based on bodily sensations. This assumption may not be valid for individuals with cognitive impairment. It is important to understand the cognitive resources needed when assessing perceived difficulty of exercise gauging the appropriateness of this widely used measure and inform potential interventions for this population. Therefore, the first aim of the present study is to evaluate the degree to which the objective measure of cardiorespiratory fitness via exercise testing correlates with the most commonly used subjective measure. The second study aim is to examine the differences in the relationship between objective cardiorespiratory fitness and subjective ratings of exertion between individuals with and without mild AD.

Chapter II: Literature Review

Before we can understand how to support beneficial exercise habits in older adults with and without AD, the present study aims to highlight how the measures used to study cardiorespiratory fitness and RPE are critically important to understanding barriers to exercise. In particular, we are interested in the perception that exercise is difficult or unpleasant. Identifying the relationship between objective and subjective measures of physical effort is a first step in understanding appropriateness for use of these measures in older adults with and without cognitive impairment, and the common adaptations of these measures for appropriate use in this population.

Measurement of Fitness

Exercise testing in research on older adults typically includes both objective and subjective measures. The gold standard in objective measures of cardiorespiratory fitness is measured by maximal rate of oxygen consumption (VO_2 max) and respiratory exchange rate (RER), usually assessed during exertion on a treadmill test according to a protocol of increasing speed and incline. The most commonly used subjective measure is RPE during this treadmill test, simultaneous with the assessment of multiple measures of carbon dioxide and oxygen exchange, including VO_2 max and RER. Each measure compliments the other, as no one measure is all inclusive of cardiorespiratory fitness. The importance of RPE, this subjective feeling, cannot be overstated, as the lived experience and interpretation of the experience drives behavior, including whether or not an individual engages in exercise (Borg, 1982; Koltyn, 2005). Borg (1982) developed the first measure of RPE to investigate how subjective feelings inform objective findings. Borg understood that what people feel is what drives them to seek medical attention, and how people feel during exercise can drive them to engage in exercise or not.

A graded exercise test (GXT) on a treadmill or a cycle ergometer is typically used to obtain these measures. Physical stability and ambulation abilities are needed for the treadmill test; otherwise the cycle ergometer test can be used. During the GXT, measures of oxygen and carbon dioxide concentrations, (volume of oxygen: VO_2) are captured via a 2-way breathing mask every 15 seconds from the inhaled and exhaled air exchanged during exercise, and then a subsequent algorithm is applied to evaluate whether VO_2 max criteria are met (Hyde & Gengenbach, 2007). Speed and/or incline are increased at every two minute interval. Heart rate, blood pressure, and RPE are captured at the last 30 seconds of each graded interval (Modified Bruce Protocol; Hollenberg, Ngo, Turner, & Tager, 1998).

VO_2 max and VO_2 peak.

Maximal rate of oxygen consumption (VO_2 max) determined during a GXT reflects aerobic physical fitness and is an important determinant of endurance capacity (Hyde & Gengenbach, 2007; Taylor, Buskirk, & Henschel, 1995). VO_2 max is the one value that represents the individual's ability to consume, distribute, and utilize oxygen during physical exertion. That is, the inhalation of oxygen, the transportation of oxygen via the circulatory system, and the use of oxygen in motor muscle over time. VO_2 max is widely accepted as a single measure of cardiovascular and cardiorespiratory fitness and maximal aerobic power.

However, truly reaching VO_2 max and its meaning is fraught with controversy (Schaun, 2017). This measure was initially developed for the training of elite athletes and individuals in the military, however it is still useful and widely used for older adults, though modifications to this exchange rate threshold have been suggested (Huggett, Connelly, & Overend, 2005). A common practice when 2-way breathing methods are not available is to predict VO_2 max via an equation from several values such as resting heart rate, age, and a constant value including time, distance, and/or weight (e.g., Uth–Sørensen–Overgaard–Pedersen estimation, Rockport fitness walking test). When a percentage of the predicted maximum heart rate is achieved, it is also presumed the maximal rate of oxygen consumption (VO_2 max) has also been achieved. This estimation process may not be accurate in all populations though. Given the multiple ways objective fitness is measured, drawing clear conclusions across studies and across populations may be challenging. The current study is not using an estimation of fitness formula, but rather actual derived oxygen and carbon dioxide exchange rate via VO_2 peak.

Although VO_2 max varies by age, gender, fitness, and training experience, in general, the higher the VO_2 max, the better fitness a person is said to have. For example, the average untrained healthy male will have a VO_2 max of approximately 35-40 mL/(kg*min), which takes into account body weight, and an elite male athlete will have around 85mL/(kg*min). Whereas the average untrained healthy female will have a VO_2 max of approximately 27-31 mL/(kg*min) and an elite female athlete will have around 77 mL/(kg*min). The value of VO_2 max can improve with training and decrease with age, though even this is highly variable between individuals.

During laboratory GXTs, meeting four criteria is required to accurately estimate VO_2 max (Foster et al., 1984; Howley, Bassett, & Welch, 1995): 1. The ratio of carbon dioxide expired to oxygen consumed (respiratory exchange rate (RER) must be greater than 1.15), 2. The participants must achieve plus or minus 10 beats per minute for the predicted maximum heart rate (± 10b/ min predicted MHR), which is adjusted for age (e.g., 220 – age; Tanaka, Monaham, & Seals, 2001), 3. There must be sustained oxygen intake with trivial increases despite work load increase of 150 millimeters per minute of oxygen intake (plateau of ≤ 150 ml/min VO_2), 4. The rate of perceived exertion must be self-reported greater than 17 indicating "very hard" (RPE > 17 (6-20 rating scale)). A valid measurement of VO_2 max has been achieved when at least three of the four criteria are met. If these maximum criteria are not met, an alternative is VO_2 peak, which is a useful and appropriate measure for older adults. VO_2 peak is merely the highest ratio of carbon dioxide and oxygen exchange, averaged every 15 seconds, at each interval of a GXT. Therefore, VO_2 peak, suggests a person has given maximal effort in an aerobic capacity test, but does not meet the criteria for VO_2 max related to endurance. It has been suggested that using VO_2 peak as opposed to VO_2 max offers a similar proxy for aerobic fitness without the undue strain on older adults (Huggett et al., 2005) and that VO_2 peak on a maximal-effort incremental exercise test is likely to be a valid measure of VO_2 max (Day, Rossiter, Coats, Skasick, & Whipp, 2003). Estimates that VO_2 max declines at a rate of 1% per year after the third decade of life (Astrand, 1960) and about 15% per decade between the ages of 50 and 75 years of age (Rogers, Hagberg, Martin, Ehsani, & Holloszy, 1990) support age-related assessment modifications from using VO_2 max for older adults and to instead use VO_2 peak.

RER.

The respiratory exchange rate (RER) is a measured ratio of inhaled oxygen and exhaled carbon dioxide. At rest, this ratio should be 1:1 if the heart and lung function are within normal limits. Some medications can affect this ratio such as medications that increase or decrease the output of the heart and lungs (e.g., beta agonists such as albuterol, beta blockers such as propranolol (Pearson, Bank, & Patrick, 1979; Van Baak, 1998; Wonish, 2002). Therefore, RER represents an objective measure of how the body takes in oxygen and the heart, lungs, and muscles use the oxygen by bringing it to the cells to make adenosine triphosphate (ATP), which is energy for the cells (Taylor et al., 1995). One by-product of this process is the need to expel carbon dioxide. When demand for increased oxygen occurs, such as with exercise, there is an increase in consumption and use of oxygen, and subsequent need to expel more carbon dioxide. Volitional exhaustion is when the participant stops the GXT due to their perceived threshold level of exhaustion, which may or may not match up to the objective measure of the RER threshold. It is therefore important for the exercise physiologist performing the exercise testing to both push and yield according to the specific participant and observed cues of exhaustion.

There is a limit to the consumption of oxygen even when the body demands increase. This threshold results in the body's need to expel more carbon dioxide, which moves the RER carbon dioxide to oxygen ratio at or above 1.15. This threshold is also called ventilatory threshold (VT) and indicates the person is crossing over into anaerobic processing or metabolism, which is different than cardiorespiratory fitness. Once this threshold is reached, it can be assumed the exercise test is valid for VO_2 peak, or VO_2 max if the three of four criteria are met. The common threshold of a valid GXT in the literature for older adults exceeds RER of 1.10, though no threshold for older adults is established (Wonisch et al., 2002;). Time to reach this threshold for older adults is typically 10-13 minutes (Modified Bruce Protocol; Hollenberg et al., 1998).

RPE.

RPE is a widely used subjective measure of physical strain or intensity and has been translated into many different languages. RPE is a numerical and verbal expression scale of how hard a person feels their body is working. There are two paradigms by which the cognitive function of RPE is investigated: production, which is active, and estimation, which is passive

(Eston & Parfitt, 2006). The production paradigm is when a person is asked to reproduce, from memory, an exercise experience or estimated intensity. The estimation paradigm is based on the interpretation of the current exercise experience where the person is asked to describe or estimate the perceived exertion at intervals dictated by the researcher. The production or estimation of RPE draws on an effort-matrix of perceptual/psychological, physiological, and performance/situational gestalt (Eston & Parfitt). That is, the interpretation of how effortful the physical activity is, the bodily sensations and feedback, and the actual performance of a specific physical activity all inform the expression of RPE. It is conceivable depending on when a cognitively healthy older adult's last exercise activity took place, that memory of that experience may be difficult to retrieve and match up with the current experience. The recall and retrieval of the exercise experience may even be more difficult for people with cognitive impairment. Verbal memory is one area that may impact the expression of RPE. The ability to accurately gauge exertion is important for safety (i.e., not reaching the point of overexertion), and for the motivation to engage in exercise to obtain the benefits it confers (i.e., reaching adequate degree of effort for physiological benefit). The assessment of RPE integrates information from various bodily sensations and processes (Hampson, Gibson, Lamert, & Noakes, 2001; Mihevic, 1981), yet exactly how these factors impact RPE is not fully understood. Notably however, there are assumptions made for the use of RPE in those with cognitive impairment that may not be valid compared to those who are cognitively intact. An often overlooked concept related to RPE is interoception. Interoception is the ability to consciously perceive internal bodily states that inform felt experiences (Vaitl, 1996). Though not examined in the current study, interoception is a concept worth noting as a possible factor in RPE and area for future studies.

Internal and external contributors to RPE.

During exercise testing, two commonly used RPE scales include values ranging from 6 to 20 (*very, very light* to *very, very hard*) or 0 to 10 (*nothing at all* to *very, very strong*; Borg, 1982). The original scale, using the 6 to 20 values, follows the general heart rate of a healthy young adult by multiplying by 10. For example, a perceived exertion of 12 would be expected to coincide with a heart rate of roughly 120 beats per minute. Borg then constructed a category (C) and ratio (R) scale (CR-10) with values from 1 to 10. These values are best suited to describe an overriding sensation arising either from a specific area of the body (e.g., muscle pain, ache or fatigue in the quadriceps) or from pulmonary responses (breathlessness and dyspnea, chest pain, and angina). Borg's RPE scale ranging from 6 to 20 is the relevant measure and a measure commonly used in research along with complimentary objective measures of strain such as heart rate, blood pressure, and oxygen consumption. In the reproduction paradigm, participants are asked to evaluate the level of exertion felt or reproduce a particular level of exertion based on feedback from the body and memory of past exercise experience, and match it to their level of fitness and endurance. If a person is unable to accurately integrate the body's feedback, over-exertion can occur leading to injury or putting the cardiovascular or respiratory systems in danger compared to the individual's level of fitness. Under-exertion compared to actual fitness level can also occur, acting as a barrier to the cognitive and health benefits of exercise. Many sources of internal, external, and interpretative feedback culminate for this one subjective rating of strain.

RPE is the integration of a combination of afferent bodily sensations, external environmental cues, and the interpretation of this information. Sources of afferent information such as bodily sensations to the brain that are thought to impact RPE include cardiopulmonary, peripheral, and metabolic factors. Cardiopulmonary factors include heart rate, oxygen uptake, respiratory rate, and ventilatory rate. Peripheral and metabolic factors include blood lactate level, blood and muscle pH, mechanical strain, muscle damage, core temperature, carbohydrate availability, and skin temperature (Hampson et al., 2001). Despite research into these areas as related to perceived exertion (Mihevic, 1981), the perception of whole body exertion during exercise and fatigue is not fully understood. External environmental cues can include ambient temperature, physical apparatus of testing (e.g., treadmill), or cognitive distraction from internal sensations. There have been mixed results in studies of cognitive distraction during RPE and exercise tasks in adults. For example, when pain and muscle fatigue come into focus (internal sensations), RPE goes up, however, when conscious distraction from pain and muscle fatigue occurs (external focus), RPE has also increased among adults (Lohse & Sherwood, 2011). Interestingly, in men, exercising to music was found to result in lower RPE compared to a sensory deprivation condition despite high or low exercise intensity (Nethery, 2002). Finally, a meta-analysis demonstrated caffeine reduces RPE compared to a placebo during exercise (Doherty & Smith, 2005). Thus, different demands on attention and cognitive load impact the interpretation of RPE during exercise. Older adults with and without cognitive impairment may be impacted differently in their ability to accurately report RPE given the multitasking involved with simultaneous processing of internal and external stimuli. While the relationship between RPE and objective or estimated HR has been explored (Shigematsu, Ueno, Nakagaichi, Nho, & Tanaka, 2004; Shono et al., 2000), the relationship between RPE and VO_2 peak, the actual exchange rate of oxygen (O_2) and carbon dioxide (CO_2), in older adults with and without cognitive impairment, is lacking.

Developmental trajectory of RPE.

There is evidence that RPE has a cognitive developmental trajectory across the life span (age 4 to adulthood) following Piaget's stages of cognitive development (Groslambert &

Manhon, 2006). In the sensorimotor stage (0 to 3 years), an individual is not able to rate perceptions. In the preoperational stage (4 to 7 years), perception progresses from peripheral sensory cues and expands to cardiorespiratory cues. In the concrete operational stage (8-12 years) there is evidence for some discrimination between 4 of 10 levels of exertion. Finally, in the formal operational stage (13 to 18 years), there is an understanding and accuracy of RPE using the Borg scale. During middle age through older adulthood, typical aging does not impair RPE, however, this perception can be interrupted by cognitive impairment or injury (Boutcher, 2000; Chodzko-Zazko & Moore, 1994). A complex set of influences on RPE with older age includes changes in cerebral blood flow and metabolic changes (Ances et al., 2010; Huettel, Singerman, & McCarthy, 2001).

Older Adults and RPE Studies

Studies of the relationship between increased age and RPE are lacking. The nature of variations among older adults related to fitness level, age-related heart rate, age-related oxygen uptake (Mitchell, Sproule, & Chapman, 1957), and affective and cognitive interpretations about exercise itself can make the relationship between age and RPE complex. RPE is a gestalt of physiological, psychological, and situational sensorium (Eston & Parfitt, 2006). Of the existing studies, few focus on the physiological and psychological aspects of RPE in older adults.

Heart rate and oxygen uptake are two physiological measures in which mixed results are seen for older adults and RPE. In adults, a reliable indicator of perceived exertion is heart rate, which increases linearly with increasing oxygen demand (Kollenbaum, 1990). In one study however, active older adults' heart rate did not correlate with RPE while snow skiing (Scheiber, Seifert, & Müller, 2011), but did during underwater treadmill GXTs in other studies (Nakanishi, Kimura, & Yokoo, 1999; Shono et al., 2000). During a cycle ergometer GXT, RPE was found to increase linearly along with HR and VO_2 among older adults (Shigematsu et al., 2004) and RPE and VO_2 were found to have a moderate to high correlation among healthy Chinese older adults (Chung, Zaho, Liu, & Quach, 2015). Thus, RPE was assumed to be an effective monitoring index of exercise intensity in middle-aged and older adults under certain exercise conditions. (Nakanishi et al; Shigematsu et al; Shono et al). Coronary artery disease (CAD) is a common health problem with increased age and affects physiological responses of the heart (Go et al., 2013). There is support for a relationship between CAD and the lack of reliability between heart rate and RPE. Kollenbaum found that physical overexertion occurred via lower rates of perceived exertion in those with CAD during exercise testing (Kollenbaum), even though minor exertion can induce a lack of oxygen to the heart. Together, these physiological findings suggest the variation in age-related physiological markers may be challenging to map onto a subjective measure of perceived exertion in older adults.

Psychological influences, such as self-efficacy and affect have been shown to influence RPE in older adults. Self-efficacy refers to the confidence people have in their own ability to achieve intended results or to succeed in a specific situation (Bandura, 1982). Affect refers to the entire topic of emotions, feelings, and moods together, all of which inform and are informed by cognitive processes (Fox, 2008). In one study, participants with high exercise self-efficacy were able to maintain a constant rate of increase in RPE with increased intensity during an exercise test before coming to volitional exhaustion and ending the exercise test. However, individuals with low exercise self-efficacy exhibited a slower rate of change in RPE with exercise intensity, with a gradual curve initially and a steeper increase at higher intensities (Hu, McAuley, Mottl, & Konopack, 2007). The perceived ability to exercise seemed to guide the experience of an incremental increase in bodily demand, where those who had low perceived ability to exercise also had lower ability to monitor the subtle changes in perceived effort (e.g., 7 to 13 on the Borg scale over one interval). Previous research has suggested cognitive processes are the primary motivation at lower intensities of exercise, such as past experiences, exercise goals, and personality; whereas bodily sensations are thought to dominate at higher intensities (e.g., 55-70% of maximum heart rate (MHR); Acevedo & Ekkekakis, 2006; Ekkekakis, 2003; Ekkekakis, Hall, & Petruzzello, 2005).

Exercise-related affect during self-paced or directed exercise among older adults was shown to have an affective pattern with three stages (Smith, Eston, Tempest, Norton, & Parfitt, 2015). The researchers demonstrated at the onset of exercise, baseline positive affect declined slightly, this decline stabilized around ventilator threshold (VT), 50-70% of VO_2 max, and finally negative affect was shown near the end of the exercise test, when the participant stated volitional exhaustion, ending the test. This suggests exercise is associated with a negative state or at least a decline in affect, indicating it is hard affectively to exercise for older adults. Specifically, this pattern of affect and perceived ability during exercise likely informs motivation and perceived strain to start and continue an exercise session. It stands to reason that reliance on cognitive processes, memory of past exercise experiences, as well as felt experiences in the body relating to RPE are aspects that may be negatively impacted in individuals with cognitive impairment.

Assumptions for RPE in individuals with cognitive impairment.

Given the cognitive demands of generating subjective ratings of exertion, using RPE to assess perceived exertion in individuals with cognitive impairment would seem to rely on assumptions that may be unwarranted. Decreases in cerebral blood flow and metabolic changes are seen in individuals with AD (Grady et al., 1998; Sase, Yamamoto, Kawashima, Tan, & Sawa, 2017; Wolters et al., 2017), which have been implicated in deficits in executive function, (McDade, et al., 2014), memory, attention, abstract reasoning, and language (Grady et al.), all of which may impact self-assessment and expression of perceived strain related to RPE.

RPE assessment is based on a verbal, numerical, and facial expression chart that individuals must attend to and report on while exercising. Performing this task draws on memory of a previous exercise feeling, verbal anchors, sequencing skills, numerical ordering, and matching facial expressions to the assessment of a current experience every two minutes. Concurrent multitasking (Kieras, Meyer, Ballas, & Laubere, 2000; Salvucci, 2005), task switching (Altmann & Gray, 2008; Sohn & Anderson, 2001), and sequential multitasking (Altmann & Trafton, 2007) have all been studied in psychology, though not directly in the context of RPE or among individuals with AD. A stand-alone study evaluating the specific cognitive demands of producing RPE in those with AD is warranted. As such studies do not exist, the notion of competing cognitive resources involved in RPE is simply noted here. Use of the RPE scale demands cognitive resources related to these concepts, especially on how accurately an individual can perform various tasks at one time. Establishing whether RPE correlates with objective measures of physical exertion in older adults with and without AD is a necessary first step. Future studies should focus on parsing apart the specific or interrelated cognitive aspects of brain changes affected with normal and pathological aging related to RPE.

People in general as well as subgroups, such as older adults and those with AD, may have challenges accurately gauging one's own level of fitness due to compromised memory and sensing bodily sensations from a previous exercise reference point. For example, in those with AD, it might not be possible to accurately recall how long previous exercise sessions lasted or recognize limits of increased respiration or heart rate. Conversely, needing to recall that labored breathing and some fatigue is part of how exertion feels may not be accessible to individuals with cognitive impairment. It is with this in mind that the current study will first establish the relationship between objective and subjective measures of fitness as a first step and explore whether performance on a story recall test first among cognitively healthy older adults and separately on those with impairment, moderates this relationship.

Attention to environmental stimuli, and numerical and verbal anchors is needed to inform bodily feedback loops of perception of exertion. For example, if the ambient temperature outside necessitates a decrease in exertion, accurately assessing this feedback may be impaired causing dysregulation in body temperature, energy stores, and dehydration. Uneven or precarious terrain during physical activity may go unnoticed or conversely perseverated on. A study of community dwelling older adults found that gait speed was slower when participants engaged in dual cognitive tasks while walking (Smith, Cusack, & Blake, 2016). Though not yet studied, the cognitive demand of attending to environmental stimuli, verbal and numerical cues, and matching them to bodily sensations seems likely to create high cognitive load in older adults with AD, which may contribute to increased RPE.

Accurately interpreting cues from the internal and external environment are likely compromised in those with AD. Indeed, there is some evidence suggesting that heart rate and RPE do not correlate as strongly in those with brain damage and in those with AD, but demonstrate more variability between the two measures (Dawes et al., 2005; Yu & Bill, 2010) compared to cognitively intact individuals. People with AD may not be able to make necessary adjustments, unlike people who are cognitively intact. Impaired judgment due to semantic impairment, awareness, insight, and communication difficulties, (Burgio, Allen-Burge, Stevens, Davis, & Marson, 2000; Jacus et al., 2014; Mârdh, Nägga, & Samueisson, 2013) likely impact exercise behavior and the ability to subjectively rate the experience. Due to a lack of studies regarding the relationship of RPE and cognitive impairment, it is hard to draw clear conclusions. However, highlighting affected areas of the brain in those with cognitive impairment may help the field understand how this regulatory process may be compromised.

Pilot Research

Based on a small sample (*N*= 93) from The University of Kansas Alzheimer's Disease Center Registry (KU-ADC), we found that individuals with AD reported higher RPE than healthy older adults despite similar VO_2 max when the GXT is collapsed into one fitness measure. Aim 1 of the present study was to determine the relationship between an objective measure of exertion (VO_2 peak) and perceived exertion (RPE) during a GXT. This aim was evaluated for comparison among participants who did and did not reach maximum aerobic capacity during the exercise test (RER ≥ 1.11). Aim 2 was to determine whether AD status moderates this relationship. Aim 3 was exploratory. Among only cognitively healthy participants we evaluated whether verbal memory moderated the relationship between objective and subjective measures of fitness. Based on preliminary evidence suggesting delayed verbal memory in people with MCI predicted progression into AD (Park, Park, Sohn, Kim, & Park, 2016: Woolf, 2016), we evaluated whether verbal memory moderated the relationship between objective and subjective measure of fitness in those with cognitive impairment.

Chapter III: Methods

Method

Sample Recruitment

The sample was drawn for secondary analyses from The University of Kansas Alzheimer's Disease Center Registry (KU-ADC), a sample of convenience, which is a large registry of well-characterized AD patients and older adult controls without cognitive impairment who have previously undergone a full physical exam, neurological testing, and a review of medical history before being recruited into any studies. All testing was performed at the KU-ADC in Fairway, Kansas. Data are combined from three studies though all have the same exercise testing protocol through the KU-ADC. Participants with consent and GXT data include Trial of Exercise on Aging and Memory (TEAM; n = 95) for those without AD, and the Alzheimer's Disease Exercise Program Trial (ADEPT; n = 67) for those with AD. Participants were enrolled in a 26-week supervised exercise intervention study with baseline, 6-month, and 12-month data collection time points among older adults with and without probable AD respectively in which memory, executive function, and depressive symptoms were assessed. Only baseline data were used for the current study. Data from ACCEL (nonAD n = 46; AD n = 29) include older adult participants with and without mild AD who wore accelerometers to capture daily activity patterns. Participants in both studies engaged in a treadmill GXT using the Modified Bruce Protocol (Hollenberg et al., 1998) providing objective (VO_2 max, VO_2 peak, heart rate) and subjective (RPE) measures.

Participants. Participants (N = 237; AD = 96; nonAD = 141) with a mean age of (M_{age} = 72.16, SD = 6.87) attended a baseline clinical and exercise evaluation (see Table 1 for descriptives and group differences). For the present study, we included participants with no cognitive impairment, mild cognitive impairment, or dementia with etiology diagnosis of probable AD based on clinical and cognitive test results using standard criteria (Albert et al., 2011; McKhann et al., 1984): Clinical Dementia Rating (CDR) of 0.5, or 1 (very mild to mild dementia); (Morris, 1993), at least 55 years of age, community dwelling, adequate visual and auditory ability to perform cognitive testing, stable medication dose, and ability to participate in scheduled exercise evaluation. The sample was almost all White; therefore ethnicity was not included as a variable because it would not meaningfully account for any variance in the models.

Exclusion criteria included clinically significant psychiatric disorder, systemic illness or infection likely to affect safety, clinically-evident stroke, or significant musculoskeletal symptoms that prohibit exercise testing. The KU-ADC registry excludes individuals with active

(< 2 years) ischemic heart disease (myocardial infarction or symptoms of coronary artery disease) or uncontrolled diabetes mellitus.

Measures

Body mass index. Whole body mass was determined using a digital scale accurate to ±0.1kg (Seca Platform Scale, Seca Corp., Columbia, MD), and height (in cm) was measured by stadiometer with shoes off, from which body mass index (BMI; weight (kg)/height (m^2)) was then calculated.

Treadmill test. Cardiorespiratory capacity (VO_2 peak) was measured by a graded treadmill exercise test (GXT) using a modified Bruce protocol (Hollenberg et al., 1998) designed for older adults, in which participants began walking at a pace of 1.7 miles per hour at 0% incline, and the grade and/or speed was increased at each subsequent 2-minute interval. Participants were attached to a 12-lead electrocardiograph (ECG) to continuously monitor heart rate rhythm. A 2-way, on-rebreathing valve, headgear, mouthpiece, and nose clip were worn and blood pressure and RPE were acquired during the last 30 seconds of each stage. Expired gases were collected continuously and oxygen uptake and carbon dioxide production were averaged at 15-second intervals. (TrueOne 2400, Parvomedics, Sandy, UT). This standard protocol was followed for all studies being combined in the present analyses. VO_2 peak is used as a proxy for fitness within the stages of the GXT instead of VO_2 max due to the appropriateness for older adults and potential loss of information with this one value when collapsing across the exercise test. The studies were active with data collection between the years of 2010 to 2014 (Vidoni et al., 2015; Watts et al., 2013).

Individuals were instructed to abstain from consuming food and caffeine beginning 3 hours before their scheduled test. Calibration procedures were performed on the metabolic cart before each test according to manufacturer’s specifications. An exercise physiologist familiarized each participant with the exercise equipment and testing protocol and explained the Borg Rating of Perceived Exertion (RPE) Scale. The exercise test was terminated if the participant reached volitional exhaustion by expressing the need to stop on the Borg scale (i.e., > 17). One of two scenarios occurred if this happened: 1) if the participant did exceed RER of 1.10, they were asked to come back for additional exercise testing or 2) if the participant exceeded an RER of 1.10, meaning absolute test termination criteria according to ACSM guidelines (ACSM, 2010), then participants were included in the study.

Cognitive measures – Immediate and Delayed Recall. The Craft Story 21 Recall (immediate and delayed; Craft et al., 1996) or Logical Memory I and II (immediate and delayed recall; WMS- third edition, Wechsler, 1997) were administered as part of a larger battery of cognitive tests. Instructions include that a story will be read aloud, to listen carefully, and try to remember as much as possible. After the immediate recall occurs, participants are told they will be asked to recall the story again later (delayed recall). Verbatim words are scored with a point and summed separately for both time points. Equivalent scores for both tasks were normed and validated by the Alzheimer's Disease Centers (ADC) in 2015 opting for a newer non-proprietary version of the test battery and allowing for comparison of both tasks together (Monsell et al., 2017; Kolen & Brennan, 1995). All immediate and delayed recall scores regardless of test were adjusted accordingly for a single score for comparison. Among those who are cognitively normal determined by a CDR score of 0, "very mild dementia" determined by a CDR score of 0.5, and "mild dementia" determined by a CDR of 1 we will explore whether immediate and delayed story recall scores moderate the relationship between VO_2 peak and RPE scores.

Chapter IV: Data Analytic Strategy and Results

Data Analytic Strategy

Analyses were performed with a total of 237 participants initially including those on heart medication and no limit for RER. Analyses were then performed only on participants who reached RER ≥ 1.11, indicating a valid GXT test, totaling 167. Finally, analyses were again performed only on participants who reached RER ≥ 1.11 and were not on heart medication likely to interfere with relevant heart rate and VO_2 peak measures, totaling 124 (AD *n* = 62; nonAD *n* = 62). See *Figure 1* for sample flow.

Multilevel modeling (MLM) techniques were used to establish the relationship between the objective measure VO_2 peak, and the subjective (RPE) measures for each person at each stage during the 10-stage GXT. Calculating statistical power for MLM is a burgeoning topic without standard guidelines. However, it is generally accepted that with over 50 participants as a sample size, sufficient power can be assumed (Hox, 2010). MLM is appropriate for these data due to the non-independence of measures at each stage. Measures of VO_2 peak and RPE are nested within people at each stage of the 10 stages for the GXT. Visual inspection of Q-Q plots were used to determine normality of data. Random effects for the intercept and slope of VO_2 peak were tested for model fit using restricted estimated maximum likelihood (REML; Bolker et al., 2009; Pinheiro & Bates, 2000), guarding against type I error. Fixed factors such as age, gender, heart medication use, and CDR were tested for model fit using maximum likelihood (ML). R^2 was calculated with REML in a stepwise process to protect against overestimation of variance accounted for. Both a marginal R^2 and conditional version of R^2 are reported. The marginal R^2 denotes the variance explained in RPE by only fixed effects and the conditional R^2 denotes the entire model, including fixed and random effects (Nakagawa & Schielzeth, 2013). R^2

can increase or decrease in the conditional model, which is a common problem encountered when applying R^2 calculations to a model with random intercepts and random slopes, though reporting of both are still encouraged (Nakagawa & Schielzeth).

Level-1 variables are objective (VO_2 peak) and subjective (RPE) measures of fitness nested within people. VO_2 peak, a continuous variable, was mean centered for interpretation, thus residuals will vary around the mean. One *level-2* variable is the trichotomous AD status of CDR (0, 0.5, and 1), which will not vary within the nested data at level-1. The other *level-2* variable is immediate and delayed story recall scores. Both of these level-2 variables were tested separately as moderators. Age, gender, and heart medication use were included in the model as *level-2* variables. Race and education were not included in the analyses due to lack of variation in the sample to account for model fit. It is the moderating AD status *level-2* term that determines the presence of an interaction effect. Memory was examined as an exploratory *level-2* term based on limited findings regarding the progression of cognitive impairment (Park et al., 2017; Woolf et al., 2016) to evaluate if the relationship between objective and subjective fitness measures depended on memory differently across the cognitive subsamples. Statistical significance of fixed and random effects were determined by deviance of residuals using chi-square-versus-degrees-of-freedom analyses to test model differences. Descriptive statistics and group differences for all variables of interest were calculated (refer to Table 1). Differences in demographic and key variables between individuals with and without AD were estimated using t-test and chi-square analyses.

The independent variables were entered in the following order in stepwise models: VO_2 peak, age, gender, cognitive status (nonAD or AD = 0.5, AD = 1), on medication (yes/no), then the appropriate interaction term (VO_2 peak x Cognitive Status, VO_2 peak x Immediate Story Recall, or VO_2 peak x Delayed Story Recall). $\hat{\gamma}_{00}$ represents random intercepts or starting point for the individuals on VO_2 peak, $\hat{\gamma}_{10}$ represents the random estimate of slope or steepness of change for individuals on VO_2 peak, and $\widehat{\sigma}^2$ represents variance due to random differences. The first subscript denotes *level 1* random effects within participants ($_i$) and the second subscript denotes *level 2* fixed effects between participants ($_j$). The hierarchical regression equations are below:

Aim 1. The hierarchical regression equation for the relationship between objective and subjective fitness measures is below:

RPE = $\hat{\gamma}_{00}$ (random estimate for VO_2 peak intercept for individuals) + $\hat{\gamma}_{10}$ (random estimate for slope VO_2 peak) + $\hat{\gamma}_{01}$ (Age) + $\hat{\gamma}_{02}$ (Gender) + $\hat{\gamma}_{03}$ (On Medication) + $\widehat{\sigma}^2$ (random differences)

Aim 2. The hierarchical regression equation with the interaction terms is below:

RPE = $\hat{\gamma}_{00}$ (random estimate for VO_2 peak intercept for individuals) + $\hat{\gamma}_{10}$ (random estimate for slope VO_2 peak) + $\hat{\gamma}_{01}$ (Age) + $\hat{\gamma}_{02}$ (Gender) + $\hat{\gamma}_{03}$ (CDR = 0.5) + $\hat{\gamma}_{04}$ (CDR = 1) + $\hat{\gamma}_{05}$ (On Medication) + $\hat{\gamma}_{11}$ (VO_2 peak*CDR = 0.5) + $\hat{\gamma}_{12}$ (VO_2 peak*CDR = 1) + $\widehat{\sigma}^2$ (random differences)

Aim 3. Exploratory analyses of cognitive performance on immediate and delayed story recall as a moderator on the relationship between objective and subjective measure of fitness. The hierarchical regression equations are below:

RPE = $\hat{\gamma}_{00}$ (random estimate for VO_2 peak intercept for individuals) + $\hat{\gamma}_{10}$ (random estimate for slope VO_2 peak) + $\hat{\gamma}_{01}$ (Age) + $\hat{\gamma}_{02}$ (Gender) + $\hat{\gamma}_{03}$ (On Medication) + $\hat{\gamma}_{04}$ (Immediate Story Recall)

+ $\hat{\gamma}_{11}$ (VO_2 max*Immediate Story Recall) + $\widehat{\sigma}^2$(random differences)

RPE = $\hat{\gamma}_{00}$ (random estimate for VO_2 peak intercept for individuals) + $\hat{\gamma}_{10}$ (random estimate for slope VO_2 peak) + $\hat{\gamma}_{01}$ (Age) + $\hat{\gamma}_{02}$ (Gender) + $\hat{\gamma}_{03}$ (On Medication) + $\hat{\gamma}_{04}$ (Delayed Story Recall)

+ $\hat{\gamma}_{12}$ (VO_2 peak*Delayed Story Recall) + $\hat{\sigma}^2$(random differences)

Chapter V: Results

Results

Analyses and Outcomes

For all analyses, we used R (R Core Team, 2012) and *lme4* (Bates, Maechler & Bolker, 2012) to perform a linear mixed effects analysis of the relationship between VO_2 peak and RPE. An unstructured correlation matrix was obtained as part of fulfilling the assumption for linearity between the predictors and RPE.

For the primary analyses, as fixed effects, we entered the mean centered VO_2 peak, raw age, gender, CDR, and the mean centered VO_2 peak x CDR interaction term into the model. For exploratory analyses, excluding CDR, the same fixed effects were added as well as immediate or delayed story recall and their respective interaction terms (VO_2 peak x Immediate Story Recall (ISR) or VO_2 peak x Delayed Story Recall (DSR)). As random effects, data driven intercepts and slopes for participants' VO_2 peak were used and enhanced model fit. Visual inspection of residual Q-Q plots indicated a mostly normal distribution of residuals for all analyses. There was some indication of non-normality toward the upper end of the distribution; however, not enough to warrant a different test such as general linear mixed model (GLMM) and MLM is a robust enough test to handle the slight indication of non-normality. P-values were obtained by *t*-tests using Satterhwaite approximations to degree-of-freedom. Chi-square tests were used for each fixed and random effect for model fit.

The first step in using MLM requires a fully unconditional model, which allows us to determine if there is sufficient between- and within-subjects variance in our dependent variable, and the intra-class correlation coefficient (i.e., the percentage of variance explained at the between- and within-subject levels), prior to running models with predictor variables (i.e., a null model).

An intraclass correlation (ICC = 0.0) indicated no variation within the sample on RPE across the GXT stages, which stands to reason with the older adult population. ICC would likely be higher if people across the lifespan were included in the sample. The ICC value indicated even with the non-independence of these data, it would be possible to treat these data as independent measures. However, there are still benefits to using MLM, especially given the nested structure of the data (Hayes, 2006).

Predictors of RPE and moderating effect of cognitive status.

For all analyses, the difference in the -2 log likelihood of the random intercepts model and random slopes model were significantly different, meaning the starting point of VO_2 peak will be allowed to vary for each individual and the slope or steepness of VO_2 peak will be allowed to vary across stages of the GXT. Aims 1 and 2 explored the relationship between objective and subjective measures of fitness and whether cognitive status had a moderating effect on the relationship between VO_2 peak and RPE. Analyses were first performed with all participants regardless of endorsing heart medication usage and/or exceeding RER $\geq$ 1.10 (for gammas, chi-square tests, deviance, and R^2 values, see Table 2 and for RPE means at each stage of the GXT by cognitive status, see Table 8). After model 1, the null model which did not explain any variance in RPE, predictors were entered into the model one at a time and were removed if the predictor did not explain a statistically significant amount of variance. VO_2 peak random intercept and random slope were each supported for better model fit. Models 3-7 indicated VO_2 peak, age, gender, medication usage, and CDR status affected RPE, each with unique contributions to variance. There was no statistically significant interaction effect of VO_2 peak x CDR. Thus, the relationship between VO_2 peak and RPE did not differ by dementia status (see Figure 2). The model with solely fixed effects explained 60.2% of the variance in the relationship between VO_2 peak and RPE and 82.6% of the variance for the full model including a random intercept and random slope, such that increasing VO_2 peak, the physiological intake, usage, and output of carbon dioxide and oxygen via the heart and lungs, leads to greater reported RPE values. Older age, female sex, use of heart medication, and cognitive impairment (CDR 0.5 or 1), all lead to greater reported RPE (see Figure 3).

We found no difference in the pattern of results when including or excluding participants, thus we were justified in including all participants in the analyses: Analyses with only participants that exceeded RER $\geq$ 1.10 (see Table 3) and for participants that exceeded RER $\geq$ 1.10 and were not on medication (see Table 4). For RPE means at each stage of the GXT by cognitive status, see Table 9. The model with solely fixed effects explained 61.4% of the variance in the relationship between VO_2 peak and RPE and 78.9% of the variance for the full model including a random intercept and random slope, such that increasing VO_2 peak, older age, female gender, use of heart medication, and cognitive impairment (CDR 0.5 or 1), all lead to greater reported RPE. The interaction term was not significant, suggesting cognitive status did not moderate the relationship between objective and subjective measures of fitness in our sample.

Exploratory analyses.

Aim 3 was exploratory in nature and we evaluated whether memory performance moderated the relationship between objective and subjective measures of fitness. Immediate Story Recall (ISR) and Delayed Story Recall (DSR) scores were centered and analyses were performed on all cognitively healthy participants (CDR = 0) regardless of endorsing heart medication usage and/or exceeding RER ≥ 1.10 (see Table 5). VO_2 peak random intercept and random slope were each supported for better model fit. Models 3-6 indicated VO_2 peak, age, female gender, and being on heart medication affected RPE, each with unique variance. Models 7 and 8 indicated ISR and the interaction term, VO_2 peak x ISR were not significant predictors in the model, not supporting aim 3. The same process was performed in models 7 and 8, with DSR, and the interaction term VO_2 peak x DSR yielding non-significant results for aim 3. The fixed effect model explained 60.4% and 82.6% of the full model including a random intercept and random slope of the relationship between VO_2 peak and RPE, such that increasing VO_2 peak, older age, female gender, and use of heart medication, all lead to greater reported RPE. However, memory, including immediate or delayed recall, was not a predictor of RPE and the relationship between VO_2 peak and RPE was not dependent on memory.

We repeated the analyses for those with a CDR equaling 0.5 (very mild dementia) and CDR = 1 (mild dementia) to explore whether memory explained or moderated the relationship between objective and subjective measure of fitness regardless of endorsing heart medication usage and/or exceeding RER ≥ 1.10 and a similar pattern of results were seen (see Table 6 for ISR and DSR). VO_2 peak random intercept and random slope were each supported for better model fit. Models 3-5 indicated VO_2, age, and female gender affected RPE each with unique variance. Models 6-8 indicated medication, ISR, and the interaction term VO_2 peak x ISR, were not significant predictors of the change in RPE, not supporting our exploratory aim 3. The same process was performed in models 6-8 where medication, DSR, and the interaction term VO_2 peak x DSR were not significant factors in the model. The fixed effect only model explained 57.4% of the change in RPE and 83.1% of the full model including a random intercept and random slope, such that increasing VO_2 peak, older age, and female gender, all lead to greater reported RPE. However, memory, including immediate or delayed recall, did not explain change in RPE in participants with very mild and mild dementia, not supporting our exploratory aim 3.

Finally, among participants with CDR = 0.5, analyses were repeated to evaluate whether memory performance moderated the relationship between objective and subjective measures of fitness regardless of endorsing heart medication usage and/or exceeding RER ≥ 1.10 (see Table 7 for ISR and DSR). VO_2 peak random intercept and random slope were each supported for better model fit. Models 2 and 3 indicated VO_2 peak, and female gender affected RPE each with unique variance. Models 4, 6, and 7, indicated age, medication, ISR and the interaction term VO_2 peak x ISR were not significant predictors of the change in RPE. The same process occurred where models 4, 6, and 8 indicated age, medication, DSR and the interaction term VO_2 peak x DSR were not significant predictors in the model explaining the change in RPE. The fixed effect model explained 59.0% of the change in RPE and 83.0% with the full model including a random intercept and random slope, such that increasing VO_2 peak and female gender lead to greater reported RPE. However, memory, including immediate or delayed recall, was not a predictor for RPE and did not moderate the relationship between VO_2 peak and RPE in participants with very mild dementia. In this subsample, the data suggests VO_2 peak and female gender each accounted for unique variance in greater reported RPE.

Chapter VI: Discussion

Discussion

Few studies have evaluated the relationship between RPE and VO_2 (Chung et al., 2015; Shigematsu et al., 2004); however, no studies to our knowledge have evaluated the relationship between VO_2 peak and RPE measures of fitness to determine whether cognitive status moderates this relationship in older adults. The relationship of objective and subjective measures of fitness is important to determine whether the felt experience during exercise in this population matches physiological ability. Given the cognitive and health benefits of exercise, specifically in this population, it is important to identify physiological and psychological barriers to regular physical activity and exercise engagement.

For the full sample, including individuals with and without AD, the predictors of RPE were mostly as expected. Lower cardiorespiratory fitness (VO_2 peak), older age, female gender, impaired cognitive status, and use of heart or lung medication predicted higher levels of perceived effort. The objective physiological measure of fitness (peak oxygen and carbon dioxide respiratory exchange) accounted for the largest proportion of the variance (57.6%) in RPE, suggesting that self-perceptions are highly dependent on physiological ability levels. In bioscience, effect sizes tend to be larger compared to behavioral sciences likely due to biosciences' larger sample sizes, more narrow scope of the biological organism, and controlled settings compared to behavioral sciences with typically smaller sample sizes and psychological and social variation of people across contexts (Nakagawa & Cuthill, 2007). Therefore, VO_2 peak accounting for such large proportion of variance in RPE stands to reason, with an increasingly effortful exercise test that it would also feel harder with increased demand on the aerobic system.

The individual R^2 information should be interpreted with caution, because the topic of estimating R^2 in multi-level modeling approaches is not fully established. R^2 can be large due to predictors that are not of direct interest in the study and should rely on other model-fit indices as well (e.g., Akaike Information Criterion (AIC) and Bayesian information criterion (BIC); Nakagawa & Schielzeth, 2013). Older age accounted for an additional 0.3% of variance in higher reported RPE after accounting for objective level of fitness. Female gender accounted for 0.7% unique variance in higher reported effortful feeling. Participants' AD cognitive status accounted for 1.8% unique variance in reported RPE, such that greater impairment led to increased reported effortful feeling. Finally, heart or lung medication usage accounted for 0.3% unique variance in reported RPE. Unexpectedly, the relationship between VO_2 peak and RPE was not dependent on cognitive status nor was verbal memory. That suggests that the nature of the relationship between objective and subjective measures of effort are the same for individuals with and without AD or varying levels of memory performance. Surprisingly, the same patterns of main effect results and lack of an interaction were observed for subsamples when excluding participants that endorsed heart or lung medication usage or if they met criteria for a valid exercise test of RER exceeding 1.10.

Objective Predictor of RPE

The physiological response to aerobic exercise undergoes important changes with aging, even in the absence of cardiovascular disease (Fletcher et al., 2001). Allowing estimates of VO_2 peak to vary both at the starting point (intercept) and the magnitude (slope) demonstrated an advantage in model fit through the use of MLM, such that each person was allowed to have their own relationship with VO_2 peak and RPE at each stage of the GXT. The linear pattern of increasing VO_2 peak and increasing RPE seems intuitive with a GXT-- the harder the exercise test, the more demand on the cardiorespiratory system. However, when objective fitness is accounted for, certain demographics predicted a greater effortful feeling.

Age and Gender as Predictors of RPE

Despite evidence that aerobic capacity decreases starting at age 30 (Astrand, 1960) with even greater rates observed over the age of 50 (Rogers et al., 1990), our data suggest when controlling for fitness level, older age still predicted a reported increased effortful feeling. Although physiological fitness may decrease with older age, which our data also suggests, many factors influence attitudes and prejudices about aging (Gilbert & Ricketts, 2008), such as expectations and stereotypes. Indeed, positive expectations regarding aging have been found to be associated with more engagement in physical activity and better physical function among older adults (Breda & Watts, 2017). Negative beliefs about aging are pervasive in Western society via younger adults, media, and diminished social roles leading to negative biases and low expectations that can be internalized by older adults and projected by others about decreased physical ability and function with older age (for a full review, see Maxfield & Bevan, in press). The internalized negative beliefs about function among older adults are associated with a variety of negative outcomes for physical and psychological health (Kim, 2009; Levy, 2009). Aging self-stereotypes have been shown to influence walking behavior, such that participants exposed to positive aging stereotypes showed a significant increase in swing time (i.e., time spent with one foot off the ground while walking) and gait speed compared to participants with negative aging stereotypes (Hausdorff, Levy, & Wei, 1999). The average increase in speed was comparable to the gain observed when older adults participated in rigorous exercise programs for several weeks (e.g., Alexander, 1996; Buchner, Beresford, Larson, LaCroix, & Wagner, 1992). It is possible that negative internalized beliefs primed the expectation that greater subjective feelings of effort occurred when engaging in exercise, which is not a common social expectation for individuals between 60 and 80 years of age. Furthermore, these beliefs may lead individuals to be less active, in turn making the exertion feel more effortful.

Internalized beliefs of decreased physical ability with older age may also trigger stereotype threat. Stereotype threat occurs when cues in the environment make negative stereotypes associated with an individual's group status salient, triggering physiological and psychological processes that have detrimental consequences for behavior (Steele & Aronson, 1995). Negative stereotype threat has been associated with older adults and women in triggering anxiety (Spencer, Steele, & Quinn, 1999), negative cognitions and emotions (Cadinu, Maass, Rosabianca, & Kiesner, 2005; Keller & Dauenheimer, 2003), physiological arousal (Croizet et al., 2004; Blascovich, Spencer, Quinn, & Steele, 2001), decreased effort (Stone, 2002), and reduction in performance expectations (Cadinu, Maass, Frigerio, Impagliazzo, & Latinotti, 2003; Chasteen, Bhattacharyya, Horhota, Tam, & Hasher, 2007). The current study findings that older age, women, and people taking heart or lung medication reported the treadmill test as more effortful despite controlling for actual fitness level might be attributed to negative expectations or stereotype threat. Perhaps the mere setting, though a positive place for research and engagement of older adults, prompts a psychological process in older adults with and without cognitive impairment leading to self-report greater effortful feelings when engaging in exercise. Another stereotype threat may have included participating in an exercise test similar to that of a stress test for diagnosis of heart disease commonly prescribed for older adults. It is possible that concern about heart disease may also prompt internalized negative beliefs about increased age and decreased function leading to self-report greater effort while exercising. Although we did not measure them here, future studies may benefit from explicit evaluation of the role of expectations regarding aging and stereotype threat in this process. Aligned with stereotype threat literature among older adults (Kim, 2009), perhaps inoculation via positive aging stereotypes, lowering anxiety, psychoeducation about stereotype threat, or by attributing difficulty to external circumstances rather than ability (Abrams et al., 2008; Barber, Selliger, Yen, & Tan, 2018; Burgess et al., 2010; Good, Aronson, & Inzlicht, 2003; Johns, Schmader, & Martens, 2005), may ameliorate negative consequences if it is contributing to a greater effortful feeling, as actual fitness level is not the explanation.

Cognitive Status as a Predictor of RPE

These data contribute an important view of understanding that limited physiological ability is not what may be contributing to barriers in exercise in older adults with and without cognitive impairment. The finding that AD cognitive status explained a significant proportion of variance in reported RPE even when actual fitness level was controlled for may be explained via expectations and stereotype threat; however a pathological brain process related to AD is another important explanation to consider.

Interoception is the ability to consciously perceive internal bodily states that inform felt experiences, which has a regulatory function of maintaining homeostasis (Vaitl, 1996). The regulation of work load relates to RPE, though no studies to date have explored this relationship among older adults or those with AD. Pathological and non-pathological brain processes can influence interoception, such as metabolic changes, brain atrophy, age, and fitness level (Garcia-Cordero et al., 2016; Khalsa et al., 2008; Cantor, Zillmann & Day, 1978). Although the current study did not directly test interoception or its related brain function, it is another possible explanation for the mechanisms that influence RPE in older adults with AD.

Some evidence suggests interoceptive accuracy and learning in those with AD is problematic due to the same widespread brain damage associated with memory and learning deficits (Garcia-Cordero et al., 2016), which also would likely affect RPE. No known research has examined interoception in those with cogntive impairment relating to RPE. People with mild cogntive impairment and AD experience brain atrophy (Sluimer et al., 2009) and metabolic dysregulation in the brain (Cai et al., 2012). It would stand to reason that when older adults with AD and related dsyfunction are asked to rate their perceived exertion, differences in sensing via interoception would impact differences in expressing the sensations. Poor interoceptive awareness can be seen as a potential barrier to exercise as it can lead to overexertion and injury or underexertion.

In AD and mild cogntive impairment due to AD, the first areas of the brain to be affected are usually the medial temporal lobes, including the hippocampus and amygdala (Hyman, Van Hoesen, Damasio, & Barnes, 1984). Decreases in whole brain volume are also common, indicating atrophy and likely loss of function (Wang et al., 2015). These sequelae of brain damange not only affect memory (implicit and explicit), language, executive function, attention, and abstract reasoning, but also interoceptive abilities. The anterior insula and anterior cingulate cortex in the medial temporal lobes have been consistently linked with interoception impairment (Damasio, Damasio, & Tranel, 2012). Hallmark brain regions damaged in AD highlight the importance of future assessment of whether decreasing interoceptive ability is the underlying mechanism of action in the brain by which interoception influences RPE.

Specifically, the insula, located deep within the temporal lobes, has been identified to play a role in body representation, subjective emotional processing of experiences, and mediating interoceptive awareness (Craig, 2009; Critchley et al., 2004; Damasio, 1993; Rozin, Dow, Moscovitch, & Rajaram, 1998; Zaki, Davis, & Ochsner, 2012). Emerging evidence suggests individuals with better interoceptive sensitivity have better implicit memory (Werner, Peres, Duschek, & Schandry, 2010) and show better decision-making on the Iowa Gambling Task, of risk and reward (Dunn et al., 2010). Exercise draws on memory of previous exercise and potentially a decisional balance between barriers to exercise such as immediate discomfort, knee or lower back pain for example, against long-term benefits at each session (Vaughan, Ghosh-Dastidar, & Dubowitz, 2017). Normal aging brain changes may affect interoception as it relates to RPE but specifically, with pathological aging, brain areas most commonly affected overlap with interoception (e.g., insula).

Heart or Lung Medication as a Predictor of RPE

Heart medication usage does physiologically lower cardiac output during increased demand on the body. This may contribute to a more effortful reported feeling for people in the present study. However, not all medications in the same class of drugs result in the same cardiac responses. Thus, the literature is moving toward testing specific heart and respiratory medications' effect on metabolic and respiratory exchange rate. For example, a common medication prescribed to treat high blood pressure, bisoprolol, was found to have no effect on heart rate, VO_2 max, and RPE with the RER threshold exceeding 1.10 in men compared to a placebo (Wonisch et al., 2002). It is reasonable that someone on cardiac mediation may be physiologically limited in their cardiac output and could explain the experience of greater subjective effort during the GXT. Conversely, someone on respiratory medication may increase oxygen consumption and could explain some differences in subjective effort. For some, negative expectations about being on heart or lung medication and exercise may play a role in increased subjective feeling, which can be specifically evaluated.

Limitations and Future Directions

One limitation of the current study is a homogeneous sample made up of mostly White, affluent, and educated older adults in the Kansas and Missouri area. Thus, these findings may not be generalizable to a more diverse population with different psychosocial circumstances. The present study did not directly measure several possible explanatory mechanisms that may contribute to differences in RPE. These include interoception work load tests (Garcia-Cordero et al., 2016), stereotype threat innoculation (Barber et al., 2018; Hausdorff, Levy, & Wei, 1999; Kim, 2009), and exercise self-efficacy (Hu et al., 2007).

On the basis of these data, physiological ability does not explain the increased subjective feeling of exercise in people with AD compared to healthy older adutls, nor does verbal memory. The verbal memory measure we used captures the recall of a story and may not be appropriate for evaluating memory of physical events that require body awareness. We are not aware of any memory measure for recall of physical sensations. Perhaps a measure of executive function such as task switching performance would better tap into the cognitive demand of an exercise test and simultaneous RPE rating for older adults. Previous research on task switching tests has shown a different pattern of errors among different cognitively impaired groups (Belleville et al., 2008; Hutchison, Balota, & Duchek, 2010). Shifting focus beyond verbal memory and physiological ability as an explanation for increased subjective ratings, perhaps interoceptive ability may be an area that can explain these findings. A heart beat detection task or work load studies for older adults with and without AD concurrent with a GXT and RPE would be one way to measure this mechanism. Another method would be to include brain insular deterioration as a possible correlate of RPE.

An area that has not been studied in older adults with and without AD is stereotype threat innoculation. During a GXT, along with an explantion and orientation about the treadmill test and the Borg RPE scale, reading, watching or listening to a short snipet about the ease of the test and how older adults did much better than anticipated may prime older adutls with a postive valance as opposed to a potentially negative prime to begin with (Barber et al., 2018; Hausdorff et al., 1999; Johns et al., 2005). Examining this frame may lend insight into stereotype threat and expectations related to the subjective RPE scale. The felt expereience is an important factor in the engagement of exercise for anyone, especially older adults, and even more so for those with cognitive impairment.

If the felt experience acts as a barrier for exercise engagment for people with cogntive impairment rather than actual physiological fitness, this is a promising platform for interventions. Extra support and encouragment during an exercise session for this popu20uation may prove helpful for exercsie adherence. Psychoeducation and prediction of subjective difficulty about exercise may alleviate the effortful feeling and enable people to still participate in exercise. The benefits of exercise on overall health and brain health in this population is an identifiable and actionable lifestyle change that has the potential to forestall cogntive decline or preserve cogntive health (Colcombe & Kramer, 2003). These data are important because they highlight that physiolgoical fitness is not a limiting factor for exercise and because these data can help inform exercise perscription in this population.

Greater exercsie self-effacy has been shown to influence RPE (Hu et al., 2007), which may explain the changes in RPE among older adults. Exposure and positive experiences of exercise may improve exercsie self-efficacy through progressive mastery of exercise behavior in older adults. If this is the case, exposure and support may help initiation and sustain exercise behavior.

The field of psychology has a unique oppurtunity to intervene on exercise change among older adtuls with and without AD known to increase overall health and brain health. These data are the first to indicate that the relationship between physiological fitness and social constructs contribute to perceived difficulty of exercise. These data also pave the directional next steps in understanding how AD may impact how exercise feels. Importantly, physiolgical fitness may not be the limiting factor in exercise behavior, therefore factors related to beleifs, expectations, and interoceptive abilites are possible next steps.

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Figure 1. Sample Flow

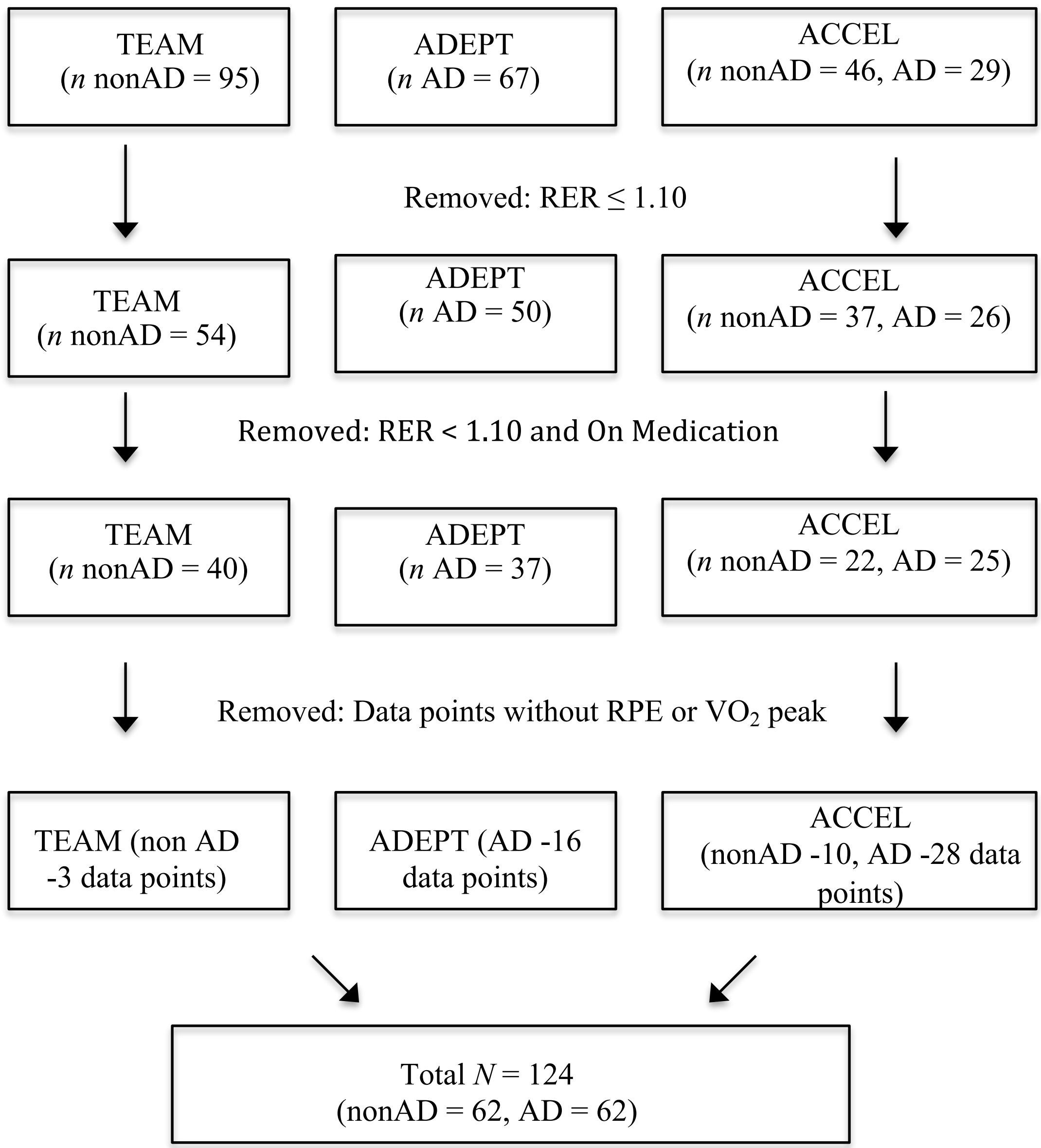

Figure 1. Sample flow of participants for analyses.

Figure 2. Main Effect for Alzheimer's Disease Status on RPE

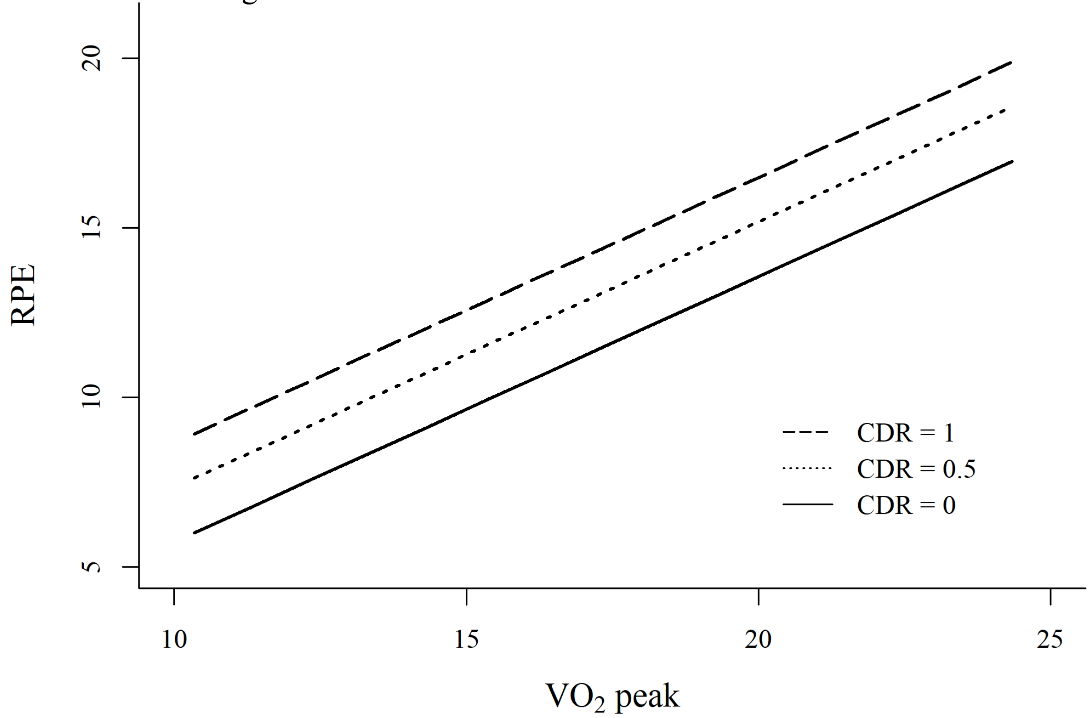

Figure 2. Main effect for Alzheimer's Disease (AD) status on rate of perceived exertion (RPE) where the use of random intercepts for VO_2 peak showed a stepwise increase of greater cognitive impairment and a higher starting point of perceived effort when starting the graded exercise test (GXT).

Figure 3. Main Effects for Rate of Perceived Exertion (RPE)

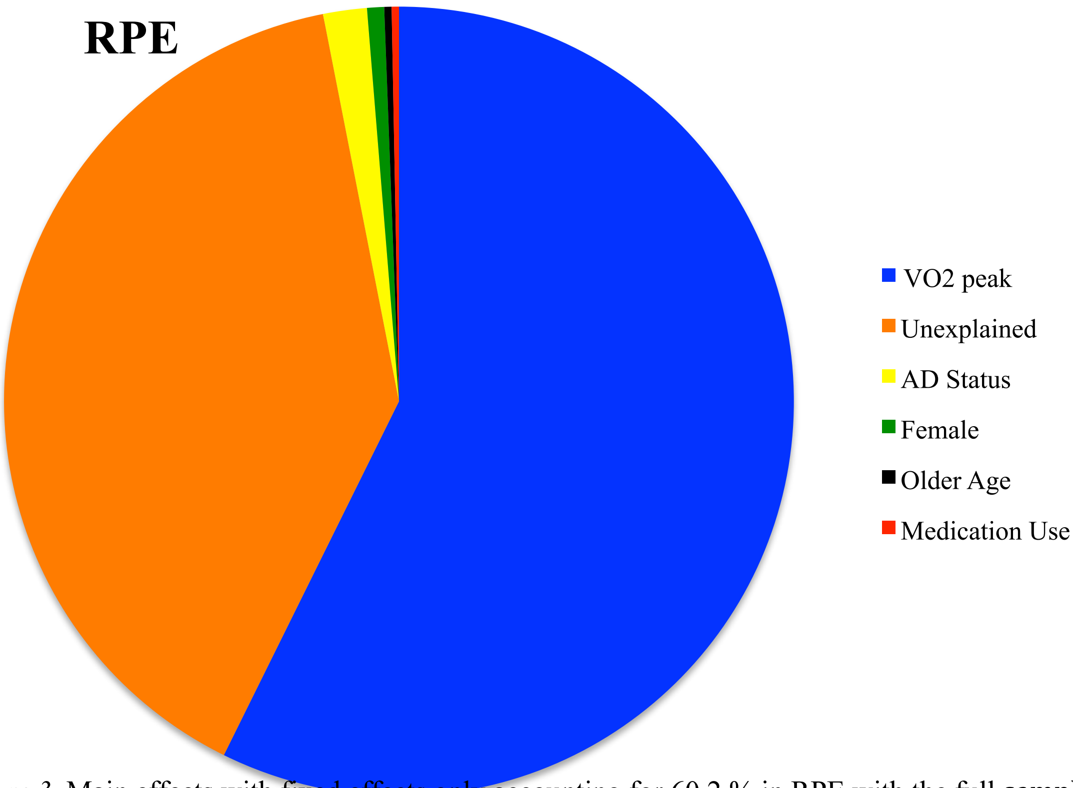

Figure 3. Main effects with fixed effects only accounting for 60.2 % in RPE with the full sample.

Table 1 *Sample Characteristics*

	Total Sample (N= 237)		CDR = 0 (n = 141)		CDR = 0.5		CDR = 1		CDR = 0.5 or 1 (n = 96)
	M (SD)	%	*M (SD)*	%	*M (SD)*	%	*M (SD)*	%	*M (SD)*
Descriptives									
Age	71.47 (6.85)		72.12 (6.45)		69.34 (6.68)		73.49 (7.56)		70.67 (7.23)
Gender									
Female		48.1		58.0		42.4		21.9	
Reached VO_2 max		82.8		94.7		68.3		67.2	
On Heart Medication		25.3		30.6		19.7		16.8	
CDR = 0		55.5							
CDR = 0.5		30.0							
CDR = 1		14.5							
	Sample that Reached RER $\geq$ 1.1 (N = 167)								
			CDR = 0 (n = 91)		CDR = 0.5 (n = 49)		CDR = 1 (n = 27)		CDR = 0.5 or 1 (n = 76)
	M (SD)	%	*M (SD)*	%	*M (SD)*	%	*M (SD)*	%	*M (SD)*
VO_2 max			23.22* (5.37)						21.35* (4.93)
VO_2 peak			17.30* (5.28)		16.85* (5.16)		15.98* (5.24)		

Note. * $p < 0.05$

Table 2 *Predictors of Subjective Fitness (RPE) for All Participants*

		Model 1	Model 2	Model 3[d]	Model 4	Model 5	Model 6	**Model 7**	Model 8
Fixed components[a]									
Intercept	γ_{00}	12.534 (0.114)***	12.88 (0.173)***	13.161 (0.184)***	6.929 (1.842)***	5.059 (1.853)**	3.921 (1.738)*	**4.213 (1.693)***	4.260 (1.686)*
VO_2 peak	γ_{10}		0.693 (0.693***	0.794 (0.022)***	0.792 (0.022)***	0.786 (0.022)***	0.783 (0.021)***	**0.783 (0.021)*****	0.798 (0.026)***
Age	γ_{01}				0.086 (0.025)***	0.102 (0.025)***	0.103 (0.023)***	**0.094 (0.023)*****	0.093 (0.093)***
Gender	γ_{02}					1.176 (0.336)***	1.765 (0.324)***	**1.709 (0.315)*****	1.711 (0.314)***
CDR = 0.5	γ_{03}						1.542 (0.361)***	**1.616 (0.351)*****	1.588 (0.361)***
CDR = 1.0	γ_{04}						2.812 (0.474)***	**2.920 (0.463)*****	2.609 (0.497)***
On Medication	γ_{05}							**1.140 (0.322)*****	1.134 (0.321)***
VO_2 peak X CDR = 0.5	γ_{11}								-0.019 (0.048)
VO_2 peak X CDR = 1.0	γ_{12}								-0.119 (0.072)
Variance of random components[b]									
Random intercept	τ_{00}	0.00	5.978	6.818	6.375	5.700	4.816	**4.491**	4.266
Random slope (VO_2 peak)	τ_{10}			0.046	0.046	0.046	0.044	**0.043**	0.042
$Cor(\tau_{00}, \tau_{10})$				0.41	0.38	0.28	0.33	**0.32**	0.31
Sigma (e)	σ^2	16.44	5.439	4.332	4.338	4.354	4.372	**4.380**	4.395
Deviance (-2LL)		7153.0	6195.9	6112.1	6093.5	6082.6	6043.4	**6031.3**	6028.5
$\Delta\chi^2$ (df)			957.12*** (1)	92.003*** (2)	11.129*** (1)	10.843*** (1)	39.191*** (2)	**12.17*** (1)**	2.733 (2)
R^2 marginal[c] (conditional)			0.529 (0.775)	0.576 (0.852)	0.579 (0.847)	0.581 (0.838)	0.599 (0.831)	**0.602 (0.826)**	0.602 (0.825)

Note. * $p < 0.05$, ** $p \leq 0.01$, *** $p < 0.001$
[a]Fixed effects estimated using maximum likelihood, gamma, standard error, and significance reported; [b]Random components estimated using restricted estimation maximum likelihood
[c] pseudo R^2 was estimated using REML
[d] Deviance and corresponding χ^2 difference test calculated using REML; CDR = Clinical Dementia Rating
Bolded model = final model

Table 3 *Predictors of Subjective Fitness (RPE) for Participants Who Reached RER ≥ 1.1*

		Model 1	Model 2	Model 3[d]	Model 4	Model 5	Model 6	**Model 7**	Model 8
Fixed Components[a]									
Intercept	γ_{00}	12.653***	12.739***	12.930***	7.695***	5.204**	3.568	**3.903***	3.981*
VO_2 peak	γ_{10}		0.670***	0.760***	0.760***	0.750***	0.748***	**0.747*****	0.776***
Age	γ_{01}				0.073**	0.093***	0.100***	**0.091*****	0.090***
Gender	γ_{02}					1.834***	2.306***	**2.225*****	2.229***
CDR = 0.5	γ_{03}						1.635***	**1.733*****	1.730***
CDR = 1.0	γ_{04}						2.564***	**2.694*****	2.546***
On Medication	γ_{05}							**1.246*****	1.253***
VO_2 peak X CDR = 0.5	γ_{11}								-0.051
VO_2 peak X CDR = 1.0	γ_{12}								-0.139
Variance of Random Components[b]									
Random Intercept	τ_{00}	0.00	5.156	5.443	5.282	4.194	3.343	**3.053**	2.984
Random Slope (VO_2 peak)	τ_{10}			0.049	0.048	0.049	0.046	**0.046**	0.045
$Cor(\tau_{00}, \tau_{10})$				0.24	0.23	-0.01	0.05	**0.01**	-0.01
Sigma (e)	σ^2	16.43	5.797	4.657	4.657	4.677	4.701	**4.706**	4.720
Deviance (-2LL)		5083.7	4429.9	4380.7	4367.0	4346.1	4313.2	**4301.9**	4298.6
$\Delta\chi^2$ (df)			653.83*** (1)	56.893*** (2)	6.791** (1)	20.91*** (1)	32.9*** (2)	**11.307*** (1)**	3.330 (2)
R^2 marginal[c] (conditional)			0.533 (0.753)	0.582 (0.832)	0.584 (0.829)	0.590 (0.813)	0.610 (0.804)	**0.614 (0.799)**	0.614 (0.797)

Note. * $p < 0.05$, ** $p \leq 0.01$, *** $p < 0.001$
[a]Fixed effects estimated using maximum likelihood, gamma, standard error, and significance reported; [b]Random components estimated using restricted estimation maximum likelihood
[c] pseudo R^2 was estimated using REML
[d] Deviance and corresponding χ^2 difference test calculated using REML; CDR = Clinical Dementia Rating
Bolded model = final model

Table 4 *Predictors of Subjective Fitness (RPE) for Participants Who Reached RER ≥ 1.1 and Are Not on Medication*

		Model 1	Model 2	Model 3[d]	Model 4	Model 5	**Model 6**	Model 7
Fixed components[a]								
Intercept	γ_{00}	12.594 (0.157)***	12.384 (0.214)***	12.534 (0.215)***	6.291 (2.180)**	5.03 (2.074)*	**3.390 (1.917)**	3.498 (1.904)*
VO_2 peak	γ_{10}		0.636 (0.020)***	0.719 (0.030)***	0.718 (0.030)***	0.710 (0.030)***	**0.707 (0.029)*****	0.723 (0.038)***
Age	γ_{01}				0.087 (0.030)**	0.094 (0.029)**	**0.101 (0.026)*****	0.099 (0.026)***
Gender	γ_{02}					1.481 (0.391)***	**1.853 (0.356)*****	1.862 (0.353)***
CDR = 0.5	γ_{03}						**1.794 (0.395)*****	1.797 (0.391)***
CDR = 1.0	γ_{04}						**2.510 (0.511)*****	2.432 (0.510)***
VO_2 peak X CDR = 0.5	γ_{11}							-0.010 (0.064)
VO_2 peak X CDR = 1.0	γ_{12}							-0.112 (0.088)
Variance of random components[b]								
Random intercept	τ_{00}	0.00	4.495	4.551	4.249	3.614	**2.693**	2.630
Random slope (VO_2 peak)	τ_{10}			0.047	0.048	0.048	**0.044**	0.045
$Cor(\tau_{00}, \tau_{10})$				0.18	0.13	-0.05	**-0.03**	-0.05
Sigma (e)	σ^2	16.26	5.895	4.770	4.751	4.779	**4.787**	4.798
Deviance (-2LL)		3729.5	3251.9	3218.8	3204.4	3191.9	**3160.6**	3158.9
$\Delta\chi^2$ (df)			477.61*** (1)	40.332*** (2)	7.980** (1)	12.47*** (1)	**31.346*** (2)**	1.637 (2)
R^2 marginal[c] (conditional)			0.531 (0.734)	0.581 (0.816)	0.586 (0.813)	0.589 (0.799)	**0.614 (0.789)**	0.612 (0.787)

Note . * $p < 0.05$, ** $p \leq 0.01$, *** $p < 0.001$
[a]Fixed effects estimated using maximum likelihood, gamma, standard error, and significance reported; [b]Random components estimated using restricted estimation maximum likelihood
[c] pseudo R^2 was estimated using REML
[d] Deviance and corresponding χ^2 difference test calculated using REML; CDR = Clinical Dementia Rating
Bolded model = final model

Table 5 *Predictors of Subjective Fitness (RPE) for Cognitively Healthy Participants (CDR =0)*

		Model 1	Model 2	Model 3[d]	Model 4	Model 5	**Model 6**	Model 7	Model 8
Fixed components[a]									
Intercept	γ_{00}	12.270 (0.146)***	12.347 (0.215)***	12.639 (0.230)***	6.802 (2.422)**	3.963 (2.433)	**4.276 (2.348)**	4.083 (2.684)	5.319 (2.531)*
VO_2 peak	γ_{10}		0.720 (0.019)***	0.804 (0.025)***	0.802 (0.025)***	0.794 (0.025)***	**0.794 (0.025)*****	0.642 (0.120)***	0.668 (0.094)***
Age	γ_{01}				0.080 (0.033)*	0.105 (0.032)**	**0.096 (0.031)****	0.094 (0.032)**	0.088 (0.032)**
Gender	γ_{02}					1.539 (0.427)***	**1.411 (0.414)*****	1.422 (0.419)***	1.489 (0.417)***
On Medication	γ_{03}						**1.259 (0.401)****	1.254 (0.400)**	1.312 (0.400)**
ISR	γ_{04}							.017 (0.066)	
DSR	γ_{05}								-0.042 (0.053)
VO_2 peak X ISR	γ_{11}							.010 (0.008)	
VO_2 peak X DSR	γ_{12}								0.009 (0.006)
Variance of random components[b]									
Random Intercept	τ_{00}	0.00	5.582	6.477	6.153	5.158	**4.757**	4.734	4.725
Random Slope (VO_2 peak)	τ_{10}			0.034	0.033	0.032	**0.032**	0.032	0.032
$Cor(\tau_{00}, \tau_{10})$				0.60	0.59	0.46	**0.46**	0.44	0.46
Sigma (e)	σ^2	17.01	5.202	4.382	4.389	4.419	**4.432**	4.430	4.422
Deviance (-2LL)		4496.5	3828.0	3789.2	3776.7	3765.6	**3756.1**	3754.4	3752.3
$\Delta\chi^2$ (df)			668.49*** (1)	46.204*** (2)	5.691* (1)	11.159*** (1)	**9.503** (1)**	1.650 (2)	3.721 (2)
R^2 marginal[c] (conditional)			0.561 (0.788)	0.591 (0.849)	0.592 (0.845)	0.599 (0.831)	**0.604 (0.826)**	0.604 (0.826)	0.603 (0.826)

Note. * $p < 0.05$, ** $p \leq 0.01$, *** $p < 0.001$

[a]Fixed effects estimated using maximum likelihood, gamma, standard error, and significance reported; [b]Random components estimated using restricted estimation maximum likelihood

[c] pseudo R^2 was estimated using REML

[d] Deviance and corresponding χ^2 difference test calculated using REML; CDR = Clinical Dementia Rating; ISR = Immediate Story Recall; DSR = Delayed Story Recall

Bolded model = final model

Table 6 *Predictors of Subjective Fitness (RPE) for Participants (CDR 0.5 and 1)*

		Model 1	Model 2	Model 3[d]	Model 4	**Model 5**	Model 6	Model 7	Model 8
Fixed components[a]									
Intercept	γ_{00}	12.973 (0.179)***	13.639 (0.367)***	13.927 (0.235)***	6.945 (2.597)**	**4.408 (2.453)**	4.725 (2.417)	5.676 (2.514)*	5.601 (2.509)*
VO_2 peak	γ_{10}		0.641 (0.025)***	0.765 (0.039)***	0.762 (0.039)***	**0.752 (0.039)*** **	0.753 (0.039)***	0.670 (0.075)***	0.692 (0.056)***
Age	γ_{01}				0.096 (0.036)**	**0.120 (0.033))** **	0.112 (0.033)**	0.109 (0.033)**	0.107 (0.033)**
Gender	γ_{02}					**2.063 (0.508)*** **	2.067 (0.499)***	2.020 (0.500)***	2.043 (0.500)***
On Medication	γ_{03}						0.982 (0.556)		
ISR	γ_{04}							-0.071 (0.053)	
DSR	γ_{05}								-0.053 (0.050)
VO_2 peak X ISR	γ_{11}							0.011 (0.009)	
VO_2 peak X DSR	γ_{12}								0.012 (0.008)
Variance of random components[b]									
Random Intercept	τ_{00}	0.00	5.514	6.366	5.795	**4.509**	4.338	4.453	4.468
Random Slope (VO_2 peak)	τ_{10}			0.069	0.068	**0.071**	0.072	0.073	0.072
$Cor(\tau_{00}, \tau_{10})$				0.26	0.20	**0.05**	0.03	0.08	0.09
Sigma (e)	σ^2	15.21	5.786	4.209	4.209	**4.216**	4.207	4.195	4.201
Deviance (-2LL)		2645.6	2345.9	2303.0	2290.7	**2276.4**	2273.4	2272.8	2272.8
$\Delta\chi^2$ (df)			299.69*** (1)	49.197*** (2)	6.898** (1)	**14.286*** (1)**	3.033 (1)	3.643 (2)	3.615 (2)
R^2 marginal[c] (conditional)			0.494 (0.741)	0.562 (0.850)	0.566 (0.844)	**0.574 (0.831)**	0.573 (0.829)	0.578 (0.833)	0.577 (0.832)

Note. * $p < 0.05$, ** $p \leq 0.01$, *** $p < 0.001$
[a]Fixed effects estimated using maximum likelihood, gamma, standard error, and significance reported; [b]Random components estimated using restricted estimation maximum likelihood
[c] pseudo R^2 was estimated using REML
[d] Deviance and corresponding χ^2 difference test calculated using REML
Bolded model = final model

Table 7 *Predictors of Subjective Fitness (RPE) for Participants (CDR 0.5)*

		Model 1	Model 2	Model 3[d]	Model 4	**Model 5**	Model 6	Model 7	Model 8
Fixed components[a]									
Intercept	γ_{00}	12.877 (0.219)***	13.202 (0.301)***	13.538 (0.334)***	8.932 (3.125)**	**12.709 (0.385)*** **	12.369 (0.419)***	13.162 (0.656)***	13.086 (0.511)***
VO_2 peak	γ_{10}		0.654 (0.030)***	0.796 (0.045)***	0.794 (0.045)***	**0.785 (0.785)*** **	0.787 (0.045)***	0.737 (0.091)***	0.743 (0.071)***
Age	γ_{01}				0.064 (0.043)				
Gender	γ_{02}					**1.887 (0.586)** **	2.022 (0.578)***	1.865 (0.580)**	1.893 (0.574)**
On Medication	γ_{03}						1.077 (0.641)		
ISR	γ_{04}							-0.052 (0.063)	
DSR	γ_{05}								-0.065 (0.058)
VO_2 peak X ISR	γ_{11}							0.006 (0.009)	
VO_2 peak X DSR	γ_{12}								0.007 (0.009)
Variance of random components[b]									
Random Intercept	τ_{00}	0.00	4.571	5.949	5.698	**4.737**	4.502	4.767	4.678
Random Slope (VO_2 peak)	τ_{10}			0.062	0.062	**0.062**	0.062	0.066	0.065
$Cor(\tau_{00}, \tau_{10})$				0.40	0.35	**0.32**	0.27	0.32	0.33
Sigma (e)	σ^2	16.35	6.179	4.397	4.395	**4.425**	4.416	4.405	4.413
Deviance (-2LL)		1919.5	1686.4	1649.2	1642.2	**1635.1**	1632.3	1633.8	1632.8
$\Delta\chi^2$ (df)			233.12*** (1)	42.978*** (2)	2.079 (1)	**9.271** (1)**	2.723 (1)	1.304 (2)	2.291 (2)
R^2 marginal[c] (conditional)			0.505 (0.715)	0.578 (0.844)	0.579 (0.841)	**0.590 (0.830)**	0.592 (0.828)	0.589 (0.833)	0.591 (0.831)

Note. * $p < 0.05$, ** $p \leq 0.01$, *** $p < 0.001$
[a]Fixed effects estimated using maximum likelihood, gamma, standard error, and significance reported; [b]Random components estimated using restricted estimation maximum likelihood
[c] pseudo R^2 was estimated using REML
[d] Deviance and corresponding χ^2 difference test calculated using REML; CDR = Clinical Dementia Rating; ISR = Immediate Story Recall; DSR = Delayed Story Recall
Bolded model = final model

Table 8 *RPE Means for Stages of the Graded Exercise Test (GXT) on the Full Sample of Participants*

	AD				Non-AD			
	n	***M* (*SD*)**	**Min**	**Max**	***n***	***M*(*SD*)**	**Min**	**Max**
Stage 1	83	8.23 (1.85)	6.00	14.00	137	7.31 (1.20)	6.00	11.00
Stage 2	82	10.26 (2.22)	6.00	15.00	138	9.22 (2.07)	6.00	17.00
Stage 3	84	12.46 (2.51)	6.00	17.00	140	11.54 (2.63)	6.00	17.00
Stage 4	81	14.63 (2.63)	6.00	20.00	131	13.83 (2.87)	6.00	20.00
Stage 5	65	15.97 (2.45)	7.00	20.00	114	15.55 (2.67)	7.00	20.00
Stage 6	44	16.66 (2.38)	7.00	20.00	69	16.22 (2.35)	8.00	20.00
Stage 7	26	17.42 (2.19)	9.00	20.00	48	17.56 (1.83)	12.00	20.00
Stage 8	8	17.50 (2.88)	11.00	20.00	15	18.27 (1.53)	14.00	20.00
Stage 9	2	18.50 (0.71)	18.00	19.00	1	19.00 (--)	19.00	19.00
Stage 10	1	18.00 (--)	18.00	18.00	0	--	--	--

Note. -- reflects no data available for that stage or there was only 1 participant the standard deviation could not be calculated

Table 9 *RPE Means for Stages of the Graded Exercise Test (GXT) on Participants Exceeding RER of 1.10*

	AD				**Non-AD**			
	n	***M* (*SD*)**	**Min**	**Max**	**n**	***M* (*SD*)**	**Min**	**Max**
Stage 1	65	8.32 (1.95)	6.00	14.00	88	7.24 (1.10)	6.00	11.00
Stage 2	65	10.23 (2.20)	7.00	15.00	89	9.20 (1.97)	6.00	17.00
Stage 3	67	12.42 (2.49)	6.00	17.00	90	11.50 (2.51)	6.00	17.00
Stage 4	65	14.62 (2.52)	9.00	20.00	84	13.71 (2.84)	6.00	19.00
Stage 5	52	16.08 (2.28)	12.00	20.00	76	15.58 (2.74)	7.00	20.00
Stage 6	36	16.81 (1.92)	13.00	20.00	45	16.09 (2.47)	8.00	20.00
Stage 7	23	17.74 (1.45)	15.00	20.00	36	17.78 (1.79)	12.00	20.00
Stage 8	7	18.43 (1.27)	17.00	20.00	10	18.20 (1.75)	14.00	20.00
Stage 9	2	18.50 (0.71)	18.00	19.00	1	19.00 (--)	19.00	19.00
Stage 10	1	18.00 (--)	18.00	18.00	0	--	--	--

Note. -- reflects no data available for that stage or there was only 1 participant the standard deviation could not be calculated