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An examination of the neuropsychological construct executive function and how it may be impacted by cognitive and exercise interventions

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AN EXAMINATION OF THE NEUROPSYCHOLOGICAL CONSTRUCT *EXECUTIVE FUNCTION* AND HOW IT MAY BE IMPACTED BY COGNITIVE AND EXERCISE INTERVENTIONS

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ABSTRACT

Background: There is a growing body of literature supporting the beneficial effects of cognitive training and exercise training on executive function (EF) in older adults. More recently, evidence is amassing that interventions which combine cognitive and physical activity, for example, exergames, may confer even greater cognitive benefits. Comparison of EF interventions for older adults requires more investigation and would benefit from improved operationalization of the EF construct and better understanding of factors which predict baseline EF in older adults.

Methods and Results: Fifty-seven sedentary, non-gamer, community dwelling older adults were randomly assigned to one of three intervention groups (computerized cognitive training, DVD-based exercise program, or combined Xbox Kinect training) or to a no-contact control group. Participant dyads completed supervised training. Forty-nine participants completed baseline and immediate post-training assessments consisting of a large battery of EF measures, psychological and physical health questionnaires, and a treadmill stress test. Forty participants repeated assessments again at a follow-up appointment 6 months after baseline. Results showed that 1) EF measures loaded onto one factor, 2) Caucasian race, greater VO_2max, and lower extraversion were predictive of better EF at baseline, and 3) Cognitive, exercise, and combined groups did not show significant changes in EF after training: The control group showed declines from pre- to post-test, cognitive and exercise groups approximately maintained EF, and the combined group trended toward improvements in EF.

Conclusions: Results lend support to a one-factor conceptualization of EF. Demographic, psychological, and physical health predictors can be used to help identify older adults at risk for executive function decline. Results also support the possibility that older adults could maintain EF through participation in cognitive and exercise training and that combined training activities like those available for Xbox Kinect, may confer improvements in EF. Results need to be replicated in a larger and better powered study before strong conclusions can be drawn.

Keywords: aging, executive function, cognitive training, exercise, randomized controlled trial

DEDICATION

Dedicated to Mom, Dad, Derek, Katie, and Trevor.

And to my friends, old and new.

For your love and support.

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CHAPTER 1

INTRODUCTION

As a result of advances in modern medicine leading to prolonged lifespans, we are left to deal with the challenge of cognitive decline in older adulthood. Executive function (EF) is the cognitive domain involved in support, organization, and control of complex cognitive processes and is disproportionately affected by aging, even in healthy older adults (Buckner, 2004; Hedden & Gabrieli, 2004). The recent unprecedented growth in the number of older Americans, projected to double to 72 million within the next 25 years (Centers for Disease Control and Prevention, 2013), underscores the need to investigate age-related changes in cognition. Following is a more thorough introduction to the EF construct, its measurement, and an overview of factors which may contribute to the prediction of EF in older adults. Interventions thought to promote maintenance of EF in healthy community-dwelling older adults will then be reviewed, focusing on cognitive training, exercise training, and interventions which combine cognitive and exercise components. The final section will summarize the specific aims and hypotheses of this dissertation.

Executive Function as a Construct: Models and Challenges

Since the mid-19th century, scientists and philosophers have postulated that the highest form of human cognition—that which sets humans apart from other animals—resides in the prefrontal cortex (Barkley, 2012; Stuss & Benson, 1986). As physicians first began recording detailed observations of brain injured patients (like the infamous Phineas Gage), a link between prefrontal cortex damage and certain cognitive, emotional, and behavioral abnormalities emerged. Faculties linked to the prefrontal cortex included motivation, goal-directed behavior, abstract thinking, emotional regulation, attention allocation, intentionality, impulse control, moral conduct, independence, self-reliance, and execution of occupational and social transactions (Stuss & Benson, 1986). It was only as recently as 1973 (Pribram) that this collection of higher-order cognitive processes came to be labeled *executive function* (EF).

Given the milieu in which it was conceived, it is not surprising that EF became synonymous with “prefrontal cortical function.” This cross-referencing of levels of analysis (between the neuropsychological function and the anatomical substrate) is not only problematic in its tautology, but is also undermined by the observation that some individuals with clear prefrontal pathology demonstrate intact EF, and some individuals with non-frontal pathology perform poorly on executive tasks (Anderson, Damasio, Jones, & Tranel, 1991; Shallice & Burgess, 1991; Stuss & Benson, 1986). Despite 160 years as a noted and important construct in studies of human cognition, EF still lacks a clear, concise definition that can stand independently of its relation to neural substrates (Barkley, 2012). Operationalization of EF is fundamentally necessary to ensure accurate classification of mental operations and to distinguish uniquely “executive” elements of cognition from “non-executive” elements.

In a broad sense, psychologists agree that EF is a process or set of processes which facilitate purposeful, goal-directed, problem-solving behavior (Barkley, 2012), especially in novel situations (Rabbitt, 1997). In daily interactions with the world, humans cannot solely rely on practiced cognitive skills because they frequently encounter novel situations. A more precise definition of EF has been elusive, however. Even when panels of experts have convened for the purpose of operationalizing EF, resultant definitions have been vague. For instance, a 1994 conference gathering of experts generated a definition which included 33 different components (Eslinger, 1996). In a recent review of the EF literature, Best et al. (2009) reported that a minimum of 15 different executive components are widely researched in contemporary laboratories. As Barkley (2012) pointed out, the prospect of choosing from among several alternate definitions of EF has led some authors to avoid defining the construct altogether, in favor of launching directly into a discussion of whichever component process they have chosen to study.

There are several qualities inherent to the concept of EF which hamper operationalization. First, most theoretical models of EF conceive of it as a *higher-order* construct which modulates *lower-order* cognitive processes such as reception of sensory input (e.g. visual processing) and motor output (e.g. speech production) (Gilbert & Burgess, 2008). Lezak et al. (2012) note that unlike cognitive processes which are concerned with *what* or *how much* a person knows, EF deals with *whether* and *how* a person goes about some task. In other words, lower-order cognitive functions demonstrate high process-behavior correspondence. It is assumed that a specialized cognitive process directly manifests in an individual's behavior which can be observed in a narrow range of situations. Take the cognitive process of mathematical calculation, for instance. If an individual is asked to solve a mathematical equation, his performance is expected to reflect his mathematical processing abilities. If he is then asked to complete a facial recognition task, we would not expect this to elicit his mathematical abilities because recognizing faces would be a separate, “informationally encapsulated” cognitive function. In contrast, EF shows low process-behavior correspondence. EF is not “informationally encapsulated” but rather modulates more fundamental cognitive processes in a wide range of situations. The elusive nature of EF is underscored in the following question: If one is interested in studying EF, one should study an individual who can perform…what exactly?

A related problem is that the language psychologists use to divide up the conscious experience of EF may not map on to the underlying systems which make those behaviors possible. In other words, observed processes are considered logically distinct (e.g. inhibition is different than planning) because they *seem* different. It is possible, however, they may simply reflect different task demands (Rabbitt, 1997). Thus, confusion between task performance and system performance characteristics represents another major challenge to the operationalization of EF.

In light of these challenges, what has research on the structure of EF found? Is it best conceived of as a unified construct or a set of separable components? An exhaustive list of theoretical models will not be provided, but a few of the more influential ones are described. Baddeley & Hitch's (1994) model has been one of the most influential frameworks in the study of EF. In this model, a central executive oversees the phonological loop and visuospatial sketchpad subsystems, which manipulate and store speech and visuo-spatial information, respectively. Norman and Shallice’s (1986) *Supervisory Attention System,* which was originally created as a model of attentional control, was put forth as a potential model of Baddely’s hypothesized central executive. Though Baddeley, Norman, and Shallice's influential theory tended to argue more in favor of one unified executive function, a major question in the neuropsychological study of EF has been whether distinct subcomponents are involved. Evidence from individual studies in a wide range of populations (Burgess, Alderman, Evans, Emslie, & Wilson, 1998; Lowe & Rabbitt, 1997; Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991) has been more supportive of the notion that EF could be fractionated into subcomponents. As such, various models comprised of different EF elements have been postulated. For example, Stuss and Benson's (1986) Hierarchical Model of EF consists of four EF components which they consider essential for novel information processing: anticipation, goal selection, preplanning, and monitoring. Several other EF theorists (Borkowski & Burke, 1996; Butterfield & Albertson, 1995; Fuster, 1997; Mirsky et al., 1991; Posner & Rothbart, 1998) have postulated similar, multi-component models, with variations in component processes typically resulting from divergent conceptualizations about nature of relationships between EFs and different brain regions (Mirsky, 1991).

According to Overton and Lerner (2010) three hypothetical components have received the most attention from contemporary researchers, typically divorced from any particular overarching theory of EF. These include working memory, response control/inhibition, and set shifting/cognitive flexibility. Many researchers consider these processes a core from which other EF "by-products" might manifest. For instance, "planning," a term commonly associated with EF, would theoretically require someone to hold a task-relevant goal in mind (working memory), deliberate on multiple alternative solutions (cognitive flexibility), and resist impulsive or premature responding (inhibition). Redundancy in EF terminology plagues the field and highlights a need to define the most fundamental processes of EF and their interactions.

Because EF is not operationally defined, it is hard to measure. And because it is hard to measure, it is difficult to improve operationalization. Any assessment can be proclaimed a test of EF as long as there is a reasonable argument to be made for its association with any of the processes falling under the EF umbrella. Current “gold standard” assessment practices are necessarily dictated by convenience and tradition rather than solid psychometric support (Barkley, 2012).

In fact, the psychometric properties of EF assessments are quite questionable. One problem is the practice effect. If EF is chiefly involved in novel information processing, then its measurement should always be conducted using a novel task. This is problematic for obvious practical reasons. Well-rehearsed executive tasks are no longer truly executive, so measures tapping a specific executive set may show no deficit in individuals who have a lot of prior experience with that task. Performance on the measure might depend more on the prior experience of the individual being tested, rather than the presence or absence of EF dysfunction.

“Task purity” is another barrier to EF measurement. Currently available executive tasks make demands on several hypothesized sub-processes or even other cognitive skills incidental to the EF of interest. Therefore, indices of performance on a single task may represent the collective outcome of several processes (Barkley, 2012; Overton & Lerner, 2010). Convergent validity of EF measures is poor because an individual’s results across multiple EF measures are contaminated by “runoff” from other cognitive processes required for task completion.

It is also appropriate to question the ecological validity of neuropsychological measures of EF. Is it possible to capture the essence of EF with a “cold” clinical measure? Arguably, it would be more valid and meaningful to conduct naturalistic behavioral observations or to use rating scales completed by patients and/or informants. In fact, some studies of healthy adult and older adult samples have indicated that neuropsychological measures of EF are not as sensitive as everyday problem-solving tests or self-report rating scales for the purpose of capturing real-life executive deficits (Schmitter-Edgecombe, Parsey, & Cook, 2011).

In sum, the concept of EF has existed for over 150 years and is widely regarded as one of the most important constructs in human neuropsychology (Luria, 1966; Stuss & Benson, 1986). Nonetheless, it lacks the basic prerequisite for all scientific investigation: an operational definition. While all of the considerable measurement challenges cannot be overcome, the present study aims to improve upon the limitations of the field through: 1) data-driven analysis of EF structure using a large battery of measures commonly used by neuropsychologists, 2) utilization of alternate form measures whenever possible to limit practice effects, and 3) careful consideration of assessment sub-scores, such that potentially separable and fundamental processes of EF might be accurately reflected.

Predictors of Executive Function in Older Adults

After investigating the nature of the EF construct, the present study aims to identify how over and above demographic characteristics, individual differences in psychological and physical health might predict EF skills. Small sample size limited the number of potential predictors which could be considered. Of physical and psychological characteristics measured in CAPES, hypertension, VO_2max, and depression were of greatest interest based on their putative relationship with EF in the literature. In addition, the relationship between personality characteristics and EF is hinted at in the literature but represents an under-explored line of research. Following is a review of these potential predictors.

Demographic predictors of executive function

Age. Relative to their own younger baseline, all adults undergo cognitive changes (Buckner, 2004). However, overall levels of maintained cognitive ability vary considerably among individuals. Age is consistently one of the strongest predictors of cognitive decline (Lipnicki et al., 2013), and in older adults without symptoms of dementia, EF is disproportionately prone to age-related decline (Buckner, 2004; Craik, 2008; Hedden & Gabrieli, 2004). Though they may display only mild, subclinical EF deficits (relative to a person with dementia), older adults perform worse than younger individuals on average (Royall, Palmer, Chiodo, & Polk, 2005). In cross sectional studies of health and education-matched individuals 20-80 years old, declines in EF are lifelong and linear (Park et al., 1996, 2002). On the other hand, longitudinal data shows that EF may hold relatively stable between ages 20-60, afterward declining at a rate similar to that reported in cross sectional studies (Hedden & Gabrieli, 2004; Schaie, 1996). The mechanism by which age selectively impacts EF is a topic of wide research and has yet to be fully elucidated, though frontal gray matter atrophy (Gunning-Dixon & Raz, 2003; Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998) and changes in functional activity of large-scale neural networks (Andrews-Hanna et al., 2007; Cabeza, 2002; Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008) are strong candidate mechanisms.

Sex. Research on sex differences in EF is scarce. In developmental studies of children, boys and girls develop EFs at approximately the same rate. However, girls have shown slight advantage in verbal fluency and speed of information processing, whereas boys have shown slight advantage in spatial working memory (Anderson, 2008). In older adults, studies on the relationship between sex and EF have partially mirrored the child development literature. In cross sectional analyses, women tended to outperform men on tasks involving verbal fluency and perceptual processing speed, whereas men performed better on tasks with visuospatial demands (Ferreira, Ferreira Santos-Galduróz, Ferri, & Fernandes Galduróz, 2014; McCarrey, An, Kitner-Triolo, Ferrucci, & Resnick, 2016). However, men and women did not differ on other EF tasks thought to involve primarily working memory and attention (Torres et al., 2006). A recent systematic analysis of longitudinal neuropsychological data from adults between 60-80 years of age reported lack of support for sex differences in rate of cognitive decline (Ferreira et al., 2014); however, another large review found that men decline more quickly than women in visuomotor processing speed and visuospatial measures (McCarrey et al., 2016). These reviews indicate the possibility that being a woman confers protection against decline in at least a few cognitive domains, but more research is needed to explore the different cultural and contextual factors experienced by men and women which may explain divergence in age-related trajectories of EF.

Education and Reading Ability. Education is one of the most robust predictors of cross-sectional cognitive ability in older adults, showing consistent positive correlation with performance across multiple cognitive domains, including EF (Ardila, Ostrosky-Solis, Rosselli, & Gomez, 2000; Cagney & Lauderdale, 2002; Sheline et al., 2006;

Wilson et al., 2009). For example, Santos et al. (2014) and Johnson et al. (2006) found that number of school years was the most important discriminatory parameter in predicting cognitive performance in samples of community-dwelling older adults. Education is also one of the most well-established predictors of cognitive reserve capacity in older adults (Alley, Suthers, & Crimmins, 2007). "Cognitive reserve" in older adulthood refers to the notion of protection from age-related cognitive changes through engagement in challenging life experiences, such as education, which help to optimize functioning (Stern, 2012). Experiences and behaviors which come about through educational engagement may create a larger pool of cognitive resources for older adults to draw from and therefore delay age-related cognitive declines. The mechanisms by which cognitive reserve exerts its effects are unclear, however greater education is hypothesized to act via increased density of neural connections from learning and engagement in cognitive activities (Vance et al., 2008; Zahodne et al., 2011). This idea of increased "neural reserves" built from enriching life experiences and upon which older adults can draw to maintain cognitive functioning, is supported by studies showing increased brain activity in older adults related to compensation for age-related cognitive decline (Park & Bischof, 2013).

Because quality of education may be quite variable among adults reporting the same level of education, reading ability may yield a more accurate prediction of cognition than years of school completed (Albert & Teresi, 1999; Manly, Jacobs, Touradji, Small, & Stern, 2002). Brewster et al. (2014) found that single-word reading was one of the best predictors of cognitive decline in older adults, and Schafer-Johnson et al. (2006) found that reading ability mediated the relationship between education and EF performance.

Reading ability has also been shown to explain differences in EF performance between Caucasians and African Americans who have completed the same amount of education (Crowe, Clay, Sawyer, Crowther, & Allman, 2008; Manly et al., 2002; Schneider & Lichtenberg, 2011).

Race. Racial disparities in cognition are widely-reported in cross sectional studies of older adults (Díaz-Venegas, Downer, Langa, & Wong, 2016; Vásquez, Botoseneanu, Bennett, & Shaw, 2015). These differences are sometimes eliminated once lifestyle variables such as early educational experiences and SES have been taken into account (Crowe et al., 2008; Manly et al., 2002; Sisco et al., 2015). However, several researchers have reported that significant racial differences in global cognitive and EF remain even after education is considered (Díaz-Venegas et al., 2016; Vásquez et al., 2015). Longitudinal models, by contrast, tend to show no significant racial differences in trajectory of decline in global cognition and EF, once confounding variables have been included (Castora-Binkley, Peronto, Edwards, & Small, 2015; Early et al., 2013; Masel & Peek, 2009).

Psychological predictors of executive function

Personality factors. Five personality factors comprise the widely-accepted "Big 5" model of personality and include openness to experience, conscientiousness, extraversion, agreeableness, and neuroticism (McCrae & John, 1992). Differences in EF abilities are often highlighted in theoretical conceptualizations of personality, and both EF and personality have been shown to predict cognitive status in older adults (Williams, Suchy, & Kraybill, 2010). Ducheck et al. (2007) examined relationships between older adults' cognitive status and personality and found that personality profiles of demented individuals were characterized by overall greater neuroticism, and lower extraversion, agreeableness, openness, and conscientiousness. Although Ducheck did not examine EF outcomes specifically, findings may hint at the relationship between personality and EF.

According to Williams et al. (2010) neuroticism predicts worse performance on tests of response selection (e.g. Stroop Test) and decision-making tasks, while Boyle et al. (2010) found no association between neuroticism and performance on EF measures. In adults, higher extraversion has been linked to better working memory (Williams et al., 2010). Though less thoroughly investigated than the other personality factors, greater agreeableness has been associated with greater ability to inhibit socially inappropriate behavior (Williams et al., 2010). Parisi et al. (2009) found that self-reported alertness to novelty and intellectual complexity (akin to Openness to Experience) was positively related to fluid intelligence. Some have theorized that openness may confer greater levels of activity engagement which accumulates over the lifespan and contributes to maintenance of cognitive abilities in older age (Ackerman & Heggestad, 1997; Ackerman, 1996). Finally, conscientiousness is, by definition, synonymous with EFs such as inhibition, organization, and self-control. Studies have largely supported this assumed correlation, especially in terms of a negative association between conscientious and symptoms of ADHD (Martel, Nigg, & Lucas, 2008). The few studies which have failed to find an association between conscientiousness and EF have explained this by noting the tendency for individuals low on trait conscientiousness to be insufficiently aware of their deficits to self-report them (Reynolds, Ortengren, Richards, & de Wit, 2006; Williams et al., 2010).

Depression. So widely recognized is the influence of low mood on cognition, that "diminished ability to think and concentrate" is included in the DSM diagnostic criteria for depression (American Psychiatric Association, 2013). The relationship between depression and EF deficits in older adults has a strong footing in the literature (Beats, Sahakian, & Levy, 1996; Potter & Steffens, 2007; Sheline et al., 2006; Shimada et al., 2014; Yochim, MacNeill, & Lictenberg, 2006), particularly when specific symptoms reflecting apathy are present (Feil, Razani, Boone, & Lesser, 2003). In addition, depression severity is an independent predictor of EF in older adults with late-life depression (Sheline et al., 2006).

Physical health predictors of executive function

Hypertension. Though different cut points have been recommended, hypertension is said to be present in older adults when systolic blood pressure $\geq$140 mm Hg and diastolic blood pressure $\geq$ 90 mm Hg (Kovell et al., 2015). Hypertension is associated with detrimental changes in brain structure, such as white matter degeneration (Gunning-Dixon & Raz, 2000; Raz, Rodrigue, & Acker, 2003), which is a candidate pathophysiological explanation for how changes in the aging brain impact EF (Buckner, 2004). Sixty-five percent of individuals 75 and older show white matter abnormalities (Ylikoski et al., 1995), and nearly a third of dementia-free 90-year-olds have a least one brain infarct (DeCarli et al., 2005). One of the most prominent predictors of white matter damage is hypertension (Longstreth et al., 1996) which persists in its relation to EF deficits even while being treated pharmacologically (Raz, Rodrigue, & Acker, 2003). Saxby et al. (2003) reported that hypertensive older adults show deficits in processing speed, working memory, and EF, while Kuo et al. (2004) found that systolic blood pressure predicted speed of processing and performance on Trails B. A review by Schillerstrom et al. (2005) concluded that compared to healthy older adults, individuals with hypertension performed worse on EF measures, deficits which persisted even after accounting for common comorbid conditions such as depression and substance abuse.

Cardiorespiratory Fitness. The positive relationship between physical activity and cognitive functioning is a robust finding in the literature (Brewster et al., 2014; Farina, Tabet, & Rusted, 2014; Hawkes, Manselle, & Woollacott, 2013; Sabia et al., 2009), specifically in regards to the domain of EF (Ble et al., 2005; Colcombe & Kramer, 2003; Eggermont, Milberg, Lipsitz, Scherder, & Leveille, 2009). Newson & Kemps (2006) reported a significant positive relationship between cardiorespiratory fitness (as indicated by maximum oxygen consumption (VO_2 max) during exercise) and performance on measures of EF. Barnes et al.'s (2003) longitudinal analysis showed that older adults' baseline VO_2 max predicted maintenance of both global cognitive function and EF over six years. A recent study by Hayes et al. (2014) demonstrated that in older, but not younger adults, higher VO_2 max was associated with better EF and mitigated cognitive decline.

Interventions Associated with Preserved or Improved Executive Function in Older Adults

Older adults' vulnerability to EF decline has made this cognitive domain a target of much intervention research. Such work must be undertaken with the assumption that change can occur. It is now widely accepted that even older adults maintain brain plasticity, or the ability to acquire cognitive skills beyond those they currently possess (Mercado, 2008; Willis & Schaie, 2009). Predictors of EF reviewed above suggest that health and lifestyle factors may be suitable targets for intervention, and indeed, the cognitive and physical intervention field is booming. Training protocols have ranged widely, from computer and video game training, to aerobic exercise, resistance training, yoga, and square-stepping interventions. Each type of intervention has produced some promising findings; however, much work remains to be done. Conditions under which plasticity is induced must be specified, such that dosage, duration, and intensity needed for change in various populations are clear and replicable. Following is a summary of major findings.

Cognitive training. A search for “brain training” or “cognitive training” will return an overwhelming number of commercially available or research-group-specific programs which claim to preserve or enhance older adults’ cognition. Despite increased awareness and use of these programs by the general public, the efficacy of cognitive training remains controversial (Hardy et al., 2015; Melby-Lervåg & Hulme, 2016; Owen et al., 2010). According to experts in the field of cognitive training, there are several important metrics by which to judge the effectiveness of cognitive training programs (Willis & Schaie, 2009): First, is there evidence of translation of a trained skill to a different task in the same cognitive domain (near transfer) or to an altogether different cognitive domain (far transfer)? In reviewing the field as a whole, it remains unclear that significant cognitive gains resulting from cognitive training interventions extend beyond improvement in the trained task or beyond benefits from general cognitive stimulation such as crossword puzzles (Baniqued et al., 2014; English, 2013; Li, Schmiedek, Huxhold, Rocke, & Smith, 2008; Martin, Clare, Altgassen, Cameron, & Zehnder, 2011; Owen et al., 2010; van Muijden, Band, & Hommel, 2012). Second, the ecological validity of many cognitive training programs is still in question, with transfer of training effects to everyday functioning (e.g. IADLs, driving) representing a large gap in the present research (Kelly et al., 2014; Martin et al., 2011; Papp, Walsh, & Snyder, 2009; Reijnders, van Heugten, & van Boxtel, 2013). Third, it is important to evaluate how long the beneficial effects of training persist after completion of the program. In this regard, there is promising, evidence that gains in training can and do persist beyond the training period (Rebok et al., 2014; Valenzuela & Sachdev, 2009; Wolinsky, Vander Weg, Howren, Jones, & Dotson, 2015), however it is common to see attenuation in gains after a no-contact period (Li et al., 2008; Zelinski et al., 2011).

Posit Science has one of the most promising and thoroughly researched computerized cognitive training programs currently available. In particular, the speed of processing (SOP) module of this program was based on a highly-researched SOP training program, tested against memory and reasoning training in a large, multi-center randomized controlled trial called the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study. The computerized SOP training in ACTIVE targeted participants' visual scanning skills within a format requiring divided attention. After just 10 hours of training, 87% of the SOP group showed improvements in related cognitive functions, compared to 74% of the reasoning group, and 26% of the memory group (Ball et al., 2002). Those in the SOP and reasoning groups who received booster training sessions showed even greater domain-specific gains when they returned for follow-up testing even 10 years post-training (Ball, Ross, Roth, & Edwards, 2013; Rebok et al., 2014; Willis et al., 2006). Further analyses from the ACTIVE trial and other studies of similar Posit Science games have shown transfer of SOP training to other SOP measures

(Edwards et al., 2005), to various measures of EF such as the Trailmaking test, Stroop test, and Symbol Digit Modalities Test (Berry et al., 2010; Wolinsky, Vander Weg, Howren, Jones, & Dotson, 2013), to speedy performance and maintenance of instrumental activities of daily living skills (Edwards et al., 2005; Wolinsky et al., 2015), and to safer driving outcomes and maintained driving mobility (Ball, Edwards, & Ross, 2007; Ball, Edwards, Ross, & McGwin, 2010; Edwards et al., 2009; Ross et al., 2016).

It is clear that the SOP training protocols from the ACTIVE and Posit Science programs have been some of the most successful cognitive training programs available, but what made them so effective? There are several ingredients which likely contributed. In a 2014 systematic review of design factors related to effective computerized cognitive training with healthy older adults, Lampit, Hallock, & Valenzuela (2014) found that group-based training was more effective than at-home interventions and that training three or fewer times per week (for greater than 30 minutes) was more effective than training more often. In terms of intervention content, perhaps it was the dynamic and attention-dividing nature of the SOP training which led to the improvements made by older adults. Several large reviews of cognitive training programs (Bherer et al., 2005; Buitenweg, Murre, & Ridderinkhof, 2012; Kramer, Larish, & Strayer, 1995) have found that variable or flexible protocols confer the greatest degree of improvement and transfer effects. Effective training programs have tended to require simultaneous engagement of several cognitive control processes which have been described in the EF literature (e.g. working memory, shifting, inhibiting, dual-task control) and call for participants to be alert for upcoming novel challenges. Even training that involves more traditional cognitive skills (e.g. memory and psychosocial skills) has been found to improve older adults' EF if practiced simultaneously (Craik et al., 2007; Winocur et al., 2007).

Another type of cognitive training that especially lends itself to a variable or flexible format is video game training (Basak, Boot, Voss, & Kramer, 2008). Action video games have increasingly received attention as a method for promoting cognitive maintenance and improvement in older adults. Training on straightforward first-generation video games (e.g. Tetris) has generally been shown to improve reaction times but not more complex EFs (Dustman, Emmerson, Steinhaus, Shearer, & Dustman, 1992; Goldstein et al., 1997); however, the advent of more complex and rapidly-shifting games requiring integration of several perceptual and cognitive abilities (e.g. Medal of Honor, Space Fortress) has led to findings that beyond enhancing their video game performance, novice gamers improve a wide variety of visual-perceptual, executive, and complex real-world skills (Anguera et al., 2013; Basak et al., 2008; Bavelier et al., 2011; Belchior et al., 2013; Green & Bavelier, 2006, 2012; Green, Pouget, & Bavelier, 2010; Green & Bavelier, 2003; Stern et al., 2011),

One study by Basak and colleagues (2008) found that for novice older adult gamers just over 20 hours of training on a strategy-based video game produced large effects on EF performance, with significant improvement occurring on 4/5 executive measures in the battery. Some researchers have explained such results in terms of "the common demands hypothesis." They have suggested that action and strategy-based video games draw on the same perceptual and attention demands of laboratory-based measures of EF, including multiple object tracking, useful field of view expansion, and rapid attentional shifting, and prioritization of smaller tasks to achieve a larger goal (Bisoglio, Michaels, Mervis, & Ashinoff, 2014; Oei & Patterson, 2014).

The present study includes a cognitive training program similar to that used in the ACTIVE trial, but in addition to completing 10 hours of the Road Tour game (based on the ACTIVE SOP task), current participants also completed five hours each of Jewel Diver and Bird Safari games. The three training games differ in their specific theme and objectives, but all require participants to scan complex visual displays and to hone skills of divided and selective attention to make efficient, accurate responses. In addition, the combined training program in the present study utilizes a number of first-person point-of-view video games, in the form of physical control of an on-screen avatar through the Xbox Kinect gaming platform. Like many of the video games in the literature, this mode of training will demand rapid and adaptive responses to novel challenges.

Exercise training. Evidence continues to amass for the beneficial effects of physical exercise on cognitive function in older adults (Erickson & Kramer, 2009; Erickson, Weinstein, & Lopez, 2012; Flicker, Liu-Ambrose, & Kramer, 2011). Some studies have indicated that preventative physical activity (e.g. before 60) helps slow age-related cognitive decline (Barnes et al., 2013; Bielak, 2010; Geda et al., 2010; Jedrziewski, Ewbank, Wang, & Trojanowski, 2010; Laurin, 2001; Muscari et al., 2010). Chronic physical activity increases expression of brain growth factors (e.g. IGF-1, BDNF) (Dishman et al., 2006; Szuhany, Bugatti, & Otto, 2015), reduces pro-inflammatory cytokines and extracellular beta amyloid (Nascimento et al., 2014), counteracts the stress response (Dishman et al., 2006), and influences molecular pathways involved in synaptic underpinnings of memory and learning (Gomez-Pinilla & Hillman, 2013; Phillips, Baktir, Srivatsan, &

Salehi, 2014), all of which are proposed mechanism of action for the effect of exercise on cognition.

Other researchers have found links between new engagement in physical activity and maintenance or improvement of EF, memory, or global cognition in both cognitively intact and cognitively impaired populations (Colcombe & Kramer, 2003; Erickson & Kramer, 2009; Heyn, Johnson, & Kramer, 2008; van Uffelen, Chin A Paw, Hopman-Rock, & van Mechelen, 2008; Voss et al., 2010). In addition, aerobic exercise has produced increases in hippocampal gray matter volume (Erickson et al., 2011) reductions in loss of frontal, temporal, and parietal regions associated with EF (Colcombe et al., 2006; Colcombe & Kramer, 2003; Gomez-Pinilla & Hillman, 2013), and increases in density of white matter tracks which have been linked to EF (Colcombe et al., 2006; Oberlin et al., 2015). Resistance training has also been linked to reductions of white matter atrophy (Best, Chiu, Hsu, Nagamatsu, & Liu-Ambrose, 2015).

Nonetheless, research has not definitively proven a causal relationship between exercise and improved cognition (Etnier, Nowell, Landers, & Sibley, 2006; Madden, Blumenthal, Allen, & Emery, 1989). Two large reviews of the extant literature reported that insufficient data still exist to conclude that improvement in cardiovascular functioning via aerobic exercise causes cognitive changes (Angevaren, Aufdemkampe, Verhaar, Aleman, & Vanhees, 2008; Young, Angevaren, Rusted, & Tabet, 2015). Contradictory findings may stem from inconsistencies amongst studies examining the exercise-cognition relationship. Much like in the cognitive training literature, it will be important to refine understanding of the differential effects of program modality, intensity, and duration, as well sample characteristics (i.e. demographic factors, baseline cognitive functioning), and outcome measures utilized (i.e. neuropsychological measures vs. self-report inventories vs. everyday function measures).

While recognizing the variability in current findings, it is still possible to synthesize a picture of what an effective exercise program entails. Moderate intensity aerobic training programs appear to produce moderate improvements in cognition, especially for tasks which require greater amounts of cognitive control (i.e. EF) (Barnes et al., 2003; Bielak, 2010; Colcombe & Kramer, 2003; Erickson & Kramer, 2009; Kramer et al., 1999). Compared to lighter intensity stretching and toning interventions, older adults completing at least moderate intensity aerobic training have shown improvements on several measures of EF (Albinet, Boucard, Bouquet, & Audiffren, 2010; Baker et al., 2010; Kerr et al., 2013; Tseng, Gau, & Lou, 2011). To a lesser degree than EF, memory, visuospatial, and speeded tasks have shown improvement corollary with moderate aerobic activity (Bielak, 2010; Colcombe & Kramer, 2003; Kramer et al., 1999; Prakash et al., 2011).

In addition, aerobic training parameters which have yielded significant cognitive improvements include methodological provisions for supervision by trained exercise leaders, exercise groups, multiple exercise sessions per week, a moderate session duration between 30 and 60 minutes, and total length of the physical training program extending between 3-12 months (Colcombe & Kramer, 2003; Kramer, Erickson, & Colcombe, 2006). Despite these general recommendations, vastly different training protocols have yielded positive results. For instance, one study found significant improvements on community-dwelling older adults' EF, attention, and memory after only 6 days of moderate-intensity water aerobics intervention (Fedor, Garcia, & Gunstad, 2015).

The effects of low to high level resistance training on induction of cognitive change are less studied and more equivocal, but with some studies yielding evidence of cognitive improvement (Anderson-Hanley, Nimon, & Westen, 2010; Brown, 2009; Cassilhas et al., 2007; Teresa Liu-Ambrose et al., 2010; Nagamatsu, Handy, Hsu, Voss, & Liu-Ambrose, 2012). Studies which have demonstrated improvements in EF as a result of resistance training have used a moderate-to-high intensity (progressive loading) protocol and included at least twice-weekly training sessions of at least 30 minutes in duration for at least 6 months (Cassilhas et al., 2007; Davis et al., 2013; Liu-Ambrose & Donaldson, 2009; Liu-Ambrose, Nagamatsu, Voss, Khan, & Handy, 2012; Nagamatsu et al., 2012).

Importantly, multiple studies have demonstrated that healthy, community-dwelling older adults may benefit most from combining elements of aerobic and non-aerobic strength or resistance training (Gregory et al., 2016; Gregory, Gill, & Petrella, 2013; Kramer et al., 2006; Nouchi et al., 2014; Smith et al., 2010). Based on synthesis of the exercise literature, the exercise program in the present study was centered around a DVD series which was selected for its incorporation of moderate-intensity aerobic, resistance, and strength training elements.

Combined training. Despite the finding that total accumulation of mental, social, and physical engagement is the most important factor in reducing risk for dementia (Bielak, 2010), few studies to date have combined cognitive and aerobic training elements into a single intervention. Among the small number of studies which have looked at combined physical and cognitive training, results have been promising, with combined training groups sometimes showing greater cognitive improvements than individual programs of either type assumed separately (Anderson-Hanley, Arciero, Brickman, et al., 2012; Bamidis et al., 2014; Fabre, Chamari, Mucci, Massé-Biron, & Préfaut, 2002; Law, Barnett, Yau, & Gray, 2014; Theill, Schumacher, Adelsberger, Martin, & Jäncke, 2013; van het Reve & de Bruin, 2014), with effects lasting up to five years later (Oswald, Gunzelmann, Rupprecht, & Hagen, 2006).

Despite several promising studies, nearly as many have reported null or inconsistent findings related to the relative merit of combined training over standalone interventions, or even in comparison to control groups (Barnes et al., 2013; Rahe et al., 2015). For instance, in a study comparing cognitive, exercise, combined, and active control groups on various cognitive indices, Shatil (2013) found improvements in the cognitive and combined groups relative to exercise and active controls, concluding that the cognitive training and not physical activity drove the noted improvements. Barnes et al. (2013) failed to find any improvements in global cognition due to combined training as compared to no-contact controls. As highlighted in a recent review (Law et al., 2014) there are so few investigations of the combined training paradigm, and such diversity in methods of training and measurement, that drawing firm conclusions is premature.

Honing in on what positive findings have demonstrated so far, an interesting study in mice suggests that the cognitive effects of combined training may be additive. Fabel et al. (2009) found that exercise primed the acquisition of hippocampal neurogenesis, such that mice who engaged in exercise and were then exposed to enriched environments produced 30% more neural growth than mice who were assigned to either the exercise or cognitively enriching environment alone. As might be expected by the suggestion of improved neurogenesis in the hippocampus, studies of combined training have found improvements in the memory domain. In a study comparing aerobic exercise, cognitively-stimulating activities, and training which combined cognitive and exercise interventions versus a no-contact control, older adults in the combined group showed greater improvements in memory over the three month trial than any other group (Fabre et al., 2002). Researchers have also reported benefits to processing speed and EF. Eggenberger et al. (2015) found that healthy older adults who participated weekly in two hours of a dance exergame or memory training with simultaneous treadmill walking improved on Trails B compared to a group engaging in multi-component (aerobic, stretching, strength) exercise alone. In addition, compared to the treadmill/memory training group, the dance exergame group showed improvements on a working memory task.

Though there is growing support for the notion that cognitive training and exercise are beneficial to older adults' cognition, adherence to training regimens remains a barrier for many older adults. Exergames, which involve interaction of virtual reality and video game features with cognitively stimulating physical activity (Read & Shortell, 2011), can be inherently more appealing to older adults and have shown promising effects on cognition (Anderson-Hanley et al., 2012; Maillot, Perrot, & Hartley, 2012; Van Schaik, Blake, Pernet, Spears, & Fencott, 2008; Vance, McNees, & Meneses, 2009). Exergames are also very conducive to combining cognitive and training elements into an efficient simultaneous intervention.

Multiple studies have examined an intervention involving a cognitively-stimulating, virtual reality display attached to a stationary bike. “Cybercyling” involves a virtual reality road tour, in which participants can navigate different terrains and compete against other virtual bikers. Anderson-Hanley et al. (2012) found that compared to older adults engaged in a three-month intervention involving traditional stationary cycling, cybercyling participants completing the same duration and intensity of intervention demonstrated significantly greater improvements in EF and a 23% reduction in risk of progression to MCI. Another cybercycling study showed that increased complexity of the on-screen task conferred greater improvements in EF, both immediately following a single bout of exercise and after three months of the training program (Barcelos et al., 2015).

Popular video-game platforms like Xbox Kinect and Nintendo Wii use a remote or sensor to detect participants' movements and control an on-screen avatar. There are many sports-based or physically oriented games available for purchase which keep the user moving while navigating through various challenges. One of the very few studies to examine a commercially available exergame produced was conducted by Malliot et al. (2012). In their study, community dwelling older adults were randomized to 12 weeks (24 hours) of partnered, supervised exergaming with the Nintendo Wii Sports game or to a no-contact control group. Participants in the exergame group showed significantly better scores on multiple processing speed and EF measures compared to no-contact controls.

Similarly, the present study builds upon the small combined training literature, utilizing a combined Xbox Kinect training protocol. An advantage of this technology over the Wii is that no extra equipment is needed, as the Kinect sensor detects body movements without a remote or balance board. Pilot testing indicated that older adults found use of the Kinect easier and more acceptable than the Wii. The Xbox training intervention in the present study incorporates many of the efficacious training elements reported in the cognitive literature (e.g. visually complex, variable format, rapidly-shifting requirements) in addition to aerobic physical activity which has shown extensive independent and significant effects on older adults' EF performance. In sum, promotion of healthy cognitive aging through this combined intervention may be a way to efficiently capitalize upon the EF gains resulting from cognitive and exercise training alone (Thom & Clare, 2011).

CHAPTER 2

METHODS

Participants and Study Design

Community-dwelling older adults participated in the Cognitive and Physical Exercise Study (CAPES), a randomized controlled trial conducted at the University of Alabama Birmingham's Center for Research in Applied Gerontology (CRAG). Healthy older adults residing in the Birmingham, Alabama, metropolitan area were recruited via mailings. Experimental procedures were approved and run in accordance with guidelines set forth by the University of Alabama at Birmingham Institutional Review Board for Human Use (See Appendix for IRB Approval). All participants provided written consent prior to enrollment and were compensated for participation in the study.

Criteria for enrollment in the study were as follows: 1) Aged 65-90 years, 2) Available to complete a 10-week, moderate-intensity exercise program, 3) Not currently engaged in an organized exercise program (i.e. no more than 2 hours of organized physical activity per week over the past two years), 4) Novice video-game player (i.e. no more than 2 hours of video game play/week over the past two years), 5) No current or remote history of serious cardiovascular or neurological conditions (i.e. coronary artery disease, myocardial infarction, stroke, traumatic brain injury, epilepsy, multiple sclerosis), 6) No evidence of dementia (i.e. Modified Telephone Interview for Cognitive Status score > 21, no self-report or physician-diagnosed dementia), and 7) No history of substance abuse. Individuals who qualified after screening were required to obtain their personal physician's approval to complete a treadmill stress test.

Qualified participants completed two in-person baseline assessments: a stress test at the Center for Exercise Medicine, and a battery of cognitive and behavioral assessments at CRAG which included neuropsychological measures of EF and self-report measures of psychological and physical health. Next, participants were paired with a partner of their choosing (typically a spouse or friend), as long as both individuals met inclusion criteria, had completed all baseline measurements, and had similar availability for training schedules. For individuals who did not enroll with a partner, a participant of the same sex and approximate age was assigned. Each dyad was randomly assigned to one of three training conditions: Cognitive training (COG), exercise training (EXE), or combined training (COM), or to the no-contact control (NC) condition. Training took place at CRAG in two, one-hour sessions per week for ten weeks (20 total hours). If a participant's partner dropped out prior to completion of at least two weeks of training, a new partner was assigned; otherwise, the participant completed the remainder of the training without a partner. Upon completion of all training sessions, or if randomized to the NC group, approximately 10-12 weeks after baseline assessment, participants underwent another stress test and the same battery of cognitive and behavioral assessments completed at baseline by a blinded assessor.

Measures

Hypertension. During preliminary telephone screening, participants were asked, "Has a doctor or nurse ever told you that you have hypertension? Please remember to count medical conditions for which you take prescribed medications (i.e. report "yes" even if you are taking a blood pressure medication)." The self-reported presence or absence of physician-diagnosed hypertension was utilized in this investigation.

Cardiovascular stress test/ VO_2 max testing. After obtaining physician approval, participants completed a modified Naughton graded treadmill stress test protocol that has been used for other recent studies of older adults (See Table 1) (Colcombe et al., 2004). Under the supervision of a master's level American College of Sports Medicine-Certified Health Fitness Specialist, participants walked on a treadmill as incremental increases in grade or speed were introduced in 2-minutes stages. The exercise test continued to maximum, and expired gases were collected throughout the test to monitor oxygen consumption and carbon dioxide expiration. *Maximum* was defined as either voluntary exhaustion by the participant or the achievement of two of three physiologic criteria: 1) Heart rate = 220 minus age, 2) Respiratory exchange ratio > 1.15, and 3) Leveling off of oxygen consumption with increasing workload. The graded test may have been terminated prior to achieving maximum for one of several reasons, including abnormal blood pressure response or if the participant voluntarily stopped the test.

Table 1

Modified Naughton Treadmill/VO_2max Protocol Used in CAPES Cardiovascular Stress Test

Stage	Time (minutes)	Speed (mph)	Grade (%)
1	2	2	3.5
2	2	2	7
3	2	2	10.5
4	2	2	14
5	2	3	14
6	2	3	17.5
7	2	3	21
8	2	4	21

Note: VO_2 max: Maximum oxygen uptake.

VO_2 max is the maximum amount of oxygen that an individual is able to utilize during exercise and is a valid indicator of cardiovascular fitness level or aerobic endurance (Hawkins, Raven, Snell, Stray-Gundersen, & Levine, 2007). Each participant's VO_2max score was expressed in units of milliliters of oxygen uptake per minute per kilogram of body weight, and was defined for each participant as the highest recorded value. VO_2 max has been the most consistent physical fitness outcome measure across all exercise-cognition studies (Bielak, 2010).

Cognitive and behavioral assessments.

Neuropsychological Assessment Battery (NAB) Mazes Test. The NAB Mazes Test (Stern & White, 2009) is a pencil-and-paper measure in which participants must complete a series of seven increasingly complex mazes. The difficulty level of each 9 inch x 6 inch maze (Exception: 1st maze is only 3 inches high) is manipulated via narrowing of alleyways. Participants are instructed to work as quickly as possible to draw a line through the alley from start point to end point without making errors, stray marks, cutting corners, or crossing over any lines. The test administrator records whether or not the participant completes the maze within the time limit, and time bonus points are awarded for faster completion. Thus, a higher score is indicative of better performance.

The NAB Mazes Test demonstrates strong psychometric properties, including high internal consistency (Cronbach's $\alpha = 0.77$). In a test-retest study with a 6-month inter-test interval, participants showed remarkably small practice effects (Time 1 total score $M = 49.0$; Time 2 total score $M = 50.5$), though the stability coefficient was moderate when corrected for variability ($r = 0.55$). An alternate form of the test, in which mazes were rotated 180 degrees along one axis, demonstrated very high equivalent-forms reliability ($G = .95$). Participants in the present study completed Form 1 at baseline, Form 2 at immediate posttest, and Form 1 again at 6-month follow-up. The high reliability of alternate forms and small practice effects (pertinent to re-administration of Form 1 after 6 months) lends confidence to the reliability of the results obtained from the NAB Mazes Test in the present study. In regards to validity, the NAB Mazes Test was created by a panel of experts to reflect skills related to planning and foresight, but also tapping into impulse control and psychomotor speed. It has shown moderate correlations with the

Wisconsin Card Sorting Test Perseverative Responses score, the Porteus Maze Test, and the Trail-Making Test Part B. The test authors suggest that these relationships indicate shared EF demands of the tasks.

Rey Complex Figure Test (RCFT)-Copy Trial. On the RCFT, participants are instructed to copy a complex geometric figure onto a blank sheet of paper as quickly and accurately as possible (Meyers & Meyers, 1995). Participants are awarded a score from 0-2 points for each of the 18 elements comprising the figure, thus, a higher score represents better performance. Two points are awarded for an accurately drawn and correctly placed element, whereas one point is awarded for incorrectly drawn *or* incorrectly placed elements. If an element is recognizable but incorrectly drawn and in the wrong place, 0.5 point is awarded. Time to copy is recorded, with a faster copy time typically indicating better performance. The task is discontinued after 10 minutes if the participant has not finished. The RCFT has demonstrated good inter-scorer reliability (r = .91-.98) (Lezak et al., 2012). It is hypothesized that the copy trial performance reflects skills related to planning and behavioral organization.

Trail Making Test (Parts A & B). The Trail Making Test is a timed paper-and-pencil measure consisting of two parts. In Part A, participants are instructed to connect a series of encircled numbers (1-25) which are arrayed in different locations on a piece of paper. In Part B, they are instructed to alternate between connecting encircled numbers (1-13) and letters (A-L) in ascending order (e.g. 1-A-2-B-3-C, etc.) (Bowie & Harvey, 2006). Better performance is reflected in faster completion times, with no additional penalty assessed for errors (i.e. errors are already penalized via slower completion time). The numbers and letters in the Trail Making Test are splayed in a fixed, semi-random order such that participants will not have to cross over their own lines as they progress through the assessment. Though the Trail Making Test is one of the oldest and most widely used neuropsychological measures, there remains controversy about the specific processes tapped by each part of the test. In general, Part A is thought to reflect visual search and psychomotor speed. Part B is thought to tap several cognitive functions at once and has shown correlation with other measures of EF, including processing speed, attention, episodic memory and working memory (Oosterman et al., 2010).

Wechsler Abbreviated Scale of Intelligence (WASI) Matrix Reasoning. The Matrix Reasoning subtest of the WASI is a measure of non-verbal fluid reasoning involving pattern completion, classification, analogy, and serial reasoning (*Wechsler Abbreviated Scale of Intelligence Manual*, 1999). Participants are presented with a matrix of designs in which one part is missing. They are asked to select the missing part from five possible alternatives, that is, to choose the design that will best complete the overall pattern in the matrix. The test consists of 35 increasingly-difficult items; one point is awarded for each correct answer, and as such, a higher score is indicative of better performance. There is no time limit. The average reliability coefficient for the Matrix Reasoning subtest is .94. In the older adult normative sample (ages 55-89 years), the test-retest stability coefficient was .85.

WASI Block Design. Block Design, another subtest of the WASI, is a measure of non-verbal fluid reasoning in which participants must arrange three-dimensional blocks to replicate two-dimensional pattern illustrations, within a specified amount of time (*Wechsler Abbreviated Scale of Intelligence Manual*, 1999). All blocks are identical, with two red sides, two white sides, and two sides which are half red and half white. The test consists of thirteen increasingly difficult items, and administration is discontinued if three consecutive items are failed. For each item, points are awarded based on correct completion within the time limit. For items 1-4, one point is awarded for a correct answer. For items 5-13, time bonus points are awarded for faster completion. Thus, a higher score is indicative of better performance. The average reliability coefficient for the Block Design subtest is .92. In the older adult normative sample (ages 55-89 years) the corrected test-retest stability coefficient was .79.

Tower of London-Drexel University: 2nd Edition (TOL). The TOL is described by its authors as a measure of executive problem solving, planning, impulse control, attentional allocation, cognitive flexibility, abstraction, rule-governed behavior, and self-monitoring for individuals from 7-80 years old (Culbertson & Zillmer, 2005). The test utilizes two identical wooden boards with three pegs of varying heights. The examiner configures a red, a green, and a blue bead into a pattern on his pegboard. He will have arranged the participant's board in a start configuration, and will reset the beads into this pattern after each trial. The participant must move one bead at a time to make his board identical to the examiner's in as few moves as possible. Participants must not 1) place more beads on a peg than it will hold, or 2) move more than one bead off a peg at a time. Participants must complete each item within 2 minutes, or the item is discontinued, and the maximum move score is awarded (20 moves). A time violation is given for completion times between 1-2 minutes. For each of the ten increasingly difficult trials, the examiner records the following information: Total Moves (number of moves beyond a perfectly-solved problem; lower score indicates better performance), Total Correct (number of items solved with no extra moves; higher score indicates better performance), number of

Rule Violations, number of Time Violations, number of Stimulus-Bound Errors (moving the beads on the examiner's board), Initiation Time (time to make first move; higher number indicates better performance), Execution Time (time from first move to item completion; lower number indicates better performance), and Total Problem Solving Time (initiation time + execution time; lower number indicates better performance).

Wide Range Achievement Test-3rd Edition (WRAT-3) Reading Test: The WRAT-3 Reading Test is a measure of single-word reading (Wilkinson, 1993) in which participants are asked to read a list of increasingly difficult words. A higher score is better, indicating correct pronunciation of more words. Because of its correlation with quality of education experience, the WRAT-3 reading score is often examined in place of years of education (Hedges, Laine, & Greenwald, 1994).

International Personality Item Pool (IPIP). The International Personality Item Pool (IPIP) is a set of over 2000 personality items freely available in the public domain and intended for use in personality research (Goldberg et al., 2006; Goldberg, 1999). Participants in the present study completed a 120-item scale called the IPIP-Representation of the NEO-PI-R. This scale was created as a proxy for the well-established NEO-PI-R inventory, considered by many psychologists to be the gold standard for measurement of the Big 5 personality traits (Costa & McCrae, 1992). Participants rated how accurately each of the items described them as they are now (5-point scale, from very inaccurate to very accurate). A computer program created by Johnson (2011) automatically generates a percentile score for each of the Big 5 personality traits, along with a qualitative label (e.g. low, average, high) based on comparison to the experimental sample. The five domain scales of the IPIP-120 item version are reliable (α = .81-.88) and show high correlation with the original NEO-PI-R (mean correlation corrected for attenuation, $r = .91$) (Johnson, 2011; Maples, Guan, Carter, & Miller, 2014).

Center for Epidemiological Studies Depression Scale (CES-D). The Center for Epidemiological Studies Depression scale is a 20-item self-report measure of current depressive symptomatology designed for quick (5-15 minutes) and easy use by lay interviewers in epidemiological studies (Radloff, 1977). It was intended that the CES-D inform the relationship between depression and other variables of interest across various population subgroups of community-dwelling adults (Olino et al., 2012). The questions that comprise the CES-D were drawn from other, previously validated depression inventories. Four of the questions are worded in a positive direction in attempt to avoid tendencies toward a response set, but also, to assess for the presence of positive affect. Each of the 20 items begins in the following manner: "How often this past week did you…" and is to be rated on a scale of frequency (from rarely to most or all of the time). Scores range from 0-60 with higher scores reflecting greater frequency of symptom occurrence during the past week.

A score of 16 is generally accepted as the cut-point for depression, with scores greater than or equal to 16 indicative of clinically significant depressive symptomology; however, various alternative cutoff scores have been suggested in the literature (Radloff, 1977; Santor, Zuroff, Ramsay, Cervantes, & Palacios, 1995). The CES-D was shown to have high internal consistency in household and patient populations, acceptable test-retest reliability, strong evidence of construct validity, excellent clinical and self-reported concurrent validity, and high discriminant validity between patient and general populations (Radloff, 1977). At one time there was debate as to whether the measure allowed for equal comparison among individuals of different age cohorts: it was feared that questions about somatic symptomatology might over-inflate depression scores in older adults. Numerous studies have rejected this hypothesis, and the CES-D has become widely used in studies of depression and associated variables in older adults (Hertzog, Van Alstine, Usala, Hultsch, & Dixon, 1990).

Training Procedures

The current training protocol called for 20 hours of in-person training over the course of 10 weeks. Participants came in to the CRAG facility and completed two, hour-long training sessions per week. Missed training days were rescheduled. Trained research assistants supervised all training sessions. Individuals randomized to the NC group did not receive an intervention and only came in to CRAG to complete baseline, and post-test measures.

Cognitive training. The Posit Science Cortex Brain Fitness System with InSight (Posit Science Corporation, 2008), hereafter referred to as InSight, is a computer program comprised of activity modules designed to improve cognition. CAPES participants randomized to the COG intervention worked on three InSight modules, with module order standardized. InSight is an adaptive program which automatically adjusts activity difficulty based on participants' performance at any given time. Training took place in a dimly-lit room with two computer stations, one for each participant. Each hour-long session was monitored by a trained and certified research assistant who helped participants log in, navigate through the program, and adjust computer stations as necessary.

Bird Safari. Participants completed a total of 5 hours of the Bird Safari activity, which is aimed at increasing visual precision (quick and accurate perception). The objective is to identify the one bird, out of a group of birds in one's peripheral vision, which matches the central target bird. Over time, task difficulty is increased in several ways: the bird pairs become more similar, the birds spread father apart, the background becomes more complex, and the birds are presented for shorter periods of time.

Jewel Diver. Participants completed a total of 5 hours of the Jewel Diver activity, which is aimed at improving divided attention and visual tracking skills. Jewels are presented in various locations on screen. The jewels are then covered by bubbles which move around the screen. Once the bubbles stop moving, participants must identify which bubbles are hiding jewels. Over time, task difficulty is increased in several ways: the jewels move about more quickly and for longer durations of time, the jewels travel over a larger area of the screen, the bubbles contrast less with the background, and the background becomes more complex. As the participant improves, the program also starts adding more jewels to be tracked.

Road Tour. Participants completed 10 hours of the Road Tour activity, which is aimed at expanding useful field of view, that is, the area over which one can quickly and accurately see details when looking straight ahead. As seen in Figure 1A, a central vehicle is presented briefly in the center of the screen, while a Route 66 sign is presented simultaneously in the periphery. The participant is prompted to recognize which of two cars is the same as the one briefly presented. At the same time, participants are queried for the location of the Route 66 sign. Over time, task difficulty increases via increased similarity of central vehicles, addition of distractor signs in the periphery, and increased distance between the central vehicle and peripheral road sign. The program also adapts to participant performance by increasing speed of stimulus presentation and complexity of the background.

A. B. C.

Figure 1. Screen shots of training games. A) Cognitive training InSight Road Tour game. B) Exercise training Sue Grant DVD Series. C) Combined training Xbox Kinect Adventures River Rush game.

Exercise training. A series of three exercise DVDs entitled *Fit at Any Age*, *Older and Wiser Workout*, and *Older and Much Wiser Workout* (Grant, 2008, 2010a, 2010b) comprised the exercise training intervention. A DVD program was selected for the exercise intervention because it represents an accessible way for older adults to engage in multi-component physical activity independently without leaving home. Each DVD program was 50-60 minutes in duration, including warm up and cool down. This is a session length consistently used throughout the older adult exercise literature and has been shown to yield the highest effect sizes (Colcombe & Kramer, 2003). CAPES participants randomized to the EXE intervention cycled through the three DVDs across the 20 sessions. Training took place in a large open space which allowed participants to move about freely. Small weights, chairs, and fitness bands required for some portions of the workouts were provided.

Fit at Any Age, *Older and Wiser Workout*, and *Older and Much Wiser Workout* were considered a good fit for the present study because they are led by a physical trainer experienced in working with a geriatric population, and they were specifically tailored to safely increase cardiorespiratory fitness in sedentary older adults. The instructor, Sue Grant, is a certified master instructor through the University of California San Diego Fall Proof program, which trains exercise instructors and health care professionals to implement evidence-based balance and mobility programs for people at moderate-to-high risk of falls. Grant is also a certified personal trainer through the American Council of Exercise and the Arthritis Foundation. Directions are given clearly and slowly as the instructor and two additional exercisers demonstrate (See Figure 1B). The programs include elements of low impact aerobics, gentle strength training, balance stabilization, and stretching. Although the programs were created for older adult beginning exercisers, they also offer two levels of modification including restricting range of movements and using a chair for stability. These modifications help ensure that participants are able to keep moving for the entire session at a level which matches their current capability. Each DVD has short built-in break periods at regular intervals. Sessions were monitored by a research assistant who could help participants navigate through the exercise sessions as necessary.

Combined (Xbox) training. CAPES participants randomized to the COM intervention participated in three activities on the Xbox 360 with Kinect (Microsoft Corporation, 2012), as described below. Training took place in a large open space where participants could move about freely. All games utilized the Kinect sensor which captures participants' movements in order to control an on-screen avatar. The activities chosen for this intervention were selected for their hypothesized dual cognitive and aerobic components. To succeed in the Xbox games, participants had to make quick decisions about sensory information displayed in the center and peripheral parts of the screen. Failing to do so, or doing so at a slower speed, would cause the participant to accumulate fewer points or fail to complete the level. Each 60-minute session was monitored by a research assistant who could help participants calibrate the Kinect sensor and navigate through game menus as necessary.

Kinect Adventures! Kinect Adventures (Microsoft Game Studios, 2010) is a game comprised of a series of five related activities. Each activity lasts 4-5 minutes. Participants worked their way through increasing levels of difficulty as they completed more and more activities in pursuit of finishing an adventure. Participants completed 10 sessions on *Adventure Mode*.

20,000 Leaks. In 20,000 Leaks, the participant's avatar is in a glass underwater cube. As crabs, fish, sharks, and swordfish cause cracks in the cube, participants must position their arms, legs, and head to plug leaks. As the difficulty level increases, up to five leaks require plugging at one time. Each game consists of three waves, which end when time expires or when all leaks are plugged.

River Rush. As pictured in Figure 1C, in River Rush participants must work together to navigate their raft through the winding river rapids as they try to collect adventure coins. The raft is controlled by moving left or right to steer or by jumping to catapult the raft out of the water. There are secret passageways along the edge of the river which contain more adventure coins than the river itself. Participants can access these areas by steering onto various ramps.

Rally Ball. Rally Ball is similar to handball in that participants must use their arms and legs to hit balls at targets at the end of a virtual hallway. When certain targets are hit, the ball splits into multiple balls which must be batted simultaneously. Each game consists of three rounds, each with a different set of targets. A round ends when time has expired or when all blocks and targets have been destroyed.

Reflex Ridge. Reflex Ridge is played on a moving platform in an environment similar to a wooden roller coaster or mine cart. Participants race on their platforms, as they jump over hurdles, lean away from obstacles, and duck to avoid hitting their heads on low beams. Jumping in place makes the platform move faster along its rail.

Space Pop. In Space Pop, transparent bubbles float between holes in the walls, floors, and ceilings of a virtual zero-gravity room. Participants pop the bubbles by touching them with their arms, legs, or head in order to earn adventure coins. Space Pop utilizes the illusion of depth, requiring the player to move toward and away from the sensor. To move upwards, participants must flap their arms, or to stay at their current level, hold their arms out to the side.

Body and Brain Connection. Body and Brain Connection (Bandai, 2011) challenges participants to think and act quickly as they compete in twenty unique activities involving math, logic, and memory. All activities involve physical movements to answer questions or complete challenges. For example, one activity involves popping a series of balloons with numbers on them, working from lowest to highest. In another activity, participants must attend to the location of pizzas moving quickly down a series of assembly lines, before they are hidden from view. The participant must then remember the pizza location and move to catch it before it falls on the floor. Participants completed 5 sessions of Body and Brain Connection on *Group Exercise, Two Player Mode*.

Just Dance 4. In Just Dance 4 (Ubisoft, 2012), participants must dance along to a variety of songs as on-screen coaches demonstrate choreographed dance moves in real-time. Small icons with arrows appear on-screen to alert participants to upcoming moves. The Kinect sensor registers each participant's movements and compares them to the choreography on screen. Level of energy can even be detected and affects participants' scores. The system gives participants feedback such as "Move missed, try again!" or "Great style! Keep up the good work!" so participants are able to gauge their performance. Participants completed 5 sessions of Just Dance 4. The first 25 minutes were played on *Just Sweat Mode,* in which they could choose from *Latin Around the World, Aerobics in Space, Cardio Fighting Electro, or Extreme Training Punk Rock* dance workouts. For the remainder of the session, participants were allowed to pick their favorite dance songs under *Just Dance Mode.*

Aims and Statistical Analyses

Aim 1. The first aim of this study was to understand the latent structure of *executive function* through exploratory factor analysis of EF measures administered as part of the CAPES baseline assessment battery. Different conceptualizations of EF in the literature suggest it may consist of separable factors or one general factor. Though Aim 1 was not based on any *a priori* model, prior to entering test scores into a factor analysis, all EF scores generated in the baseline assessment were scrutinized on the basis of: 1) the purported meaning of the score as outlined in testing manuals, peer-reviewed journal articles, and based on clinical judgment, 2) score range, variability, and normality of distribution, and 3) bivariate correlations.

To address the first aim, an exploratory factor analysis was conducted in SPSS, Version 22, using principal axis factoring extraction. This method was chosen to accommodate non-normally-distributed data (Costello & Osborne, 2005). Oblimin oblique rotation was used to identify factors, which were expected to correlate with one another. According to Costello and Osborne (2005) although orthogonal rotation is typically favored for its more easily-interpretable results which produce uncorrelated factors, it is rare for factors in the social sciences to be truly independent. Oblique rotation was considered more appropriate for the observed data in the present investigation. Furthermore, if multiple factors are truly uncorrelated with one another, then oblique and orthogonal solutions should produce approximately the same results.

In step 1, the number of factors extracted was based on the scree plot and eigenvalues > 1. Item correlations and the rotated pattern matrix were examined. Item removal was based on the following pre-determined criteria: items with low correlations among all other items ($r < 0.20$), items with high loading on a factor (> 0.30) with no other loading items, items with low loadings on a factor (< 0.30) and low communality ($h^2 < 0.20$), and items with cross-loadings (Costello & Osborne, 2005).

Overall sample size < 100 is considered poor (Comrey & Lee, 1992). However, Costello and Osborne (2005) note that for exploratory factor analysis there are no strict rules regarding sample size and that, like the present study, a majority of studies they reviewed had a participant to item ration of 10:1 or less. Factor loadings and communalities may influence reliability regardless of sample size (Guadagnoli & Velicer, 1988; MacCallum, Widaman, Zhang, & Hong, 1999). “Strong data” can tolerate a smaller sample size and is indicated by higher communalities (>.40) and an absence of crossloadings (Costello & Osborne, 2005).

Aim 2. The second aim of this study was to determine if information about psychological and physical characteristics improved prediction of older adults' EF performance beyond what was predicted by demographic information alone. It was hypothesized that demographic predictors of better EF at baseline would be younger age, female sex, Caucasian race, and greater education (as indicated by better reading ability). Over and above demographic factors, greater VO_2max, the absence of hypertension, having fewer depressive symptoms, and having lower neuroticism, higher conscientiousness, higher openness to experience, higher agreeableness, and higher extraversion were hypothesized to predict a higher baseline EF composite score. These predictor variables were chosen on the basis of their hypothesized theoretical importance with regards to EF. Various rules of thumb exist in regards to the appropriate ratio of participants to predictors. The present analysis falls within the bounds of Tabachnick and Fidell's (2007) suggested minimum of five participants per predictor variable. The EF composite score, which served as the dependent variable in the regression model, was calculated by multiplying the participant's score on each EF measure by its factor loading derived from the Aim 1 analysis.

Multiple regression, conducted in SPSS, was used to construct a model for predicting baseline EF performance. First, distribution information for each predictor variable was examined. Pearson correlations were used to assess the bivariate relationships amongst the predictors and of predictors with the EF composite. Variables without significant and/or meaningful relationships to other variables were not considered in the regression model. All continuous predictor variables were centered. Categorical independent variables were dichotomized.

Demographic predictors were entered in Step 1. In step 2, the main effects of physical and psychological factors of interest were entered. In the third step, the interaction of personality factors was entered. Non-significant variables were removed from the model in an iterative fashion until the most parsimonious model was achieved.

Aim 3. The third aim of this study was to assess the impact of COG training, EXE training, or COM training versus NC on older adults' EF performance. It was hypothesized that 3.1) Individuals randomized to the COM training intervention would show greater improvement in EF factor scores from baseline to post-training assessment than individuals in the COG or EXE interventions alone, 3.2) All training groups would show greater improvements in EF from baseline to post-training assessment than individuals in the NC control group, and 3.3) EF would be maintained at 6 month follow-up for all training groups.

A mixed measures repeated measures ANOVA was conducted in SPSS. Time was the within-subjects factor (baseline, immediate post-training, and 6-month follow-up), and intervention group (COG, EXE, COM, or NC) was the between-subjects factor. The dependent variable was the EF composite score at each time point. The composite score was derived by multiplying the participant's score on each EF measure by its factor loading derived from the Aim 1 analysis. The factor-weighted scores were then averaged to make one composite factor score for that time point. The procedure for creating a composite factor score was repeated for immediate post-training and 6 month follow-up assessments. Comparison of the calculated EF composite score with the computer-generated factor score revealed a correlation of $r = .999$, indicating that these methods of generating a summary score were essentially equivalent.

Data of all participants who completed training was included in the repeated measures ANOVA ($N = 49$). Because of limited resources, only a subset of the sample were invited to be reassessed at 6-months post-baseline ($n = 40$). Due to already limited sample size, post-training scores were carried forward for all participants who had complete data (pre- and post-training) but did not complete a six-month follow-up assessment. As recommended by Tabachnick and Fidell (2007), analyses were repeated using only complete cases. The same pattern of results was obtained in both analyses, lending confidence to the findings of analyses with values carried forward.

CHAPTER 3

RESULTS

Sample Descriptives

Participant flow through the study is presented in Figure 2. Fifty-seven older adults completed the full baseline battery of assessments. Two individuals dropped out of the study prior to randomization. Six participants withdrew from the study prior to completion of all training sessions, for personal and health reasons. One participant opted to withdraw from the study after a minor twisted ankle sustained during Xbox training.

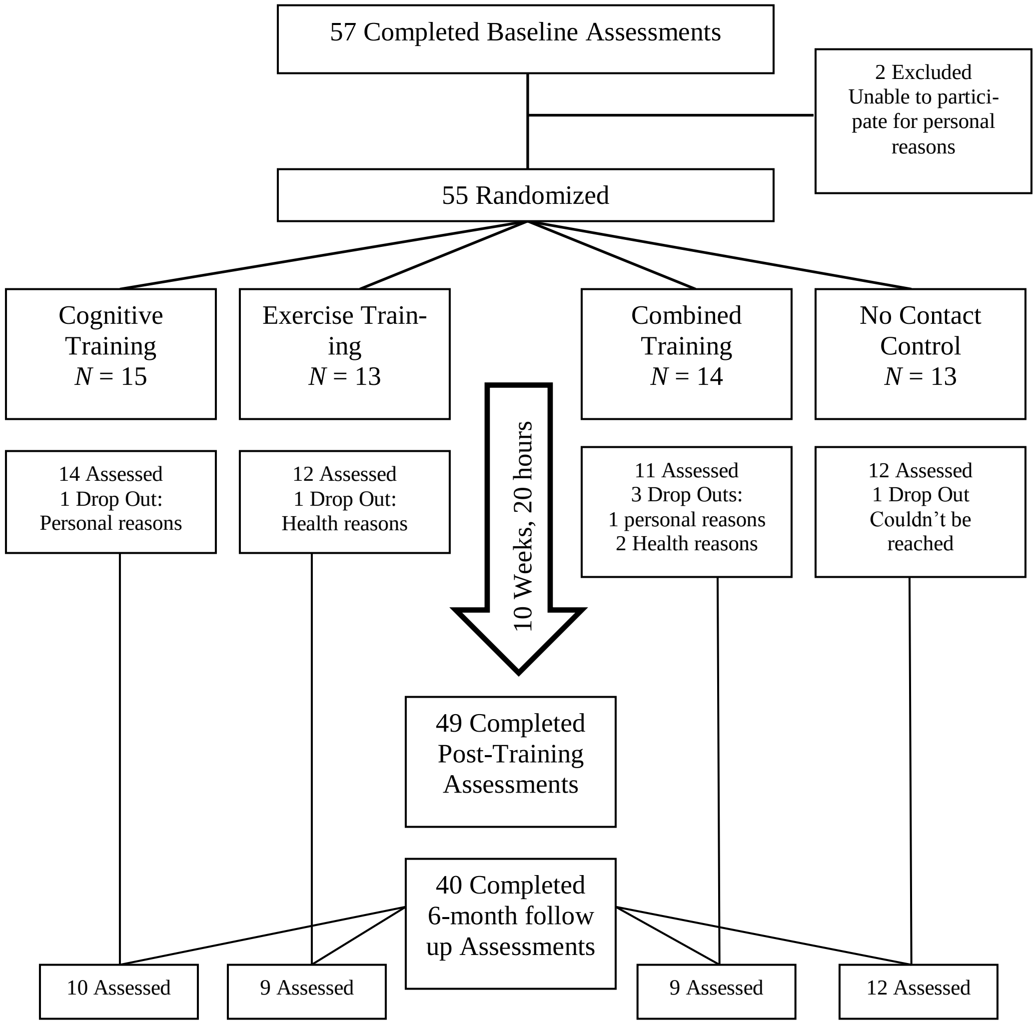

Figure 2. Participant flow through CAPES.

All partners of dropouts completed some training sessions independently (i.e. because the dropouts occurred later than two full weeks into training), however, training was paired in 87% of sessions. There were no significant differences in demographic variables or baseline EF score between those who completed training versus those who dropped out ($p > .05$ for all variables). Number of dropouts was not significantly different between the four groups $X^2(3, N = 55) = 3.85$, $p > .05$. Of participants who completed training and immediate post-training assessments ($n = 49$) all but one completed all 20 training sessions (One participant completed 19/20 sessions). A subset of participants (*n* = 40) completed an additional cognitive and behavioral assessment 6 months after completion of their baseline assessment.

Characteristics of the sample at each time point are summarized in Table 2. Overall, the sample were highly educated (mean and modal years of education equal to a college degree), community dwelling older adults. Participant age was slightly positively skewed toward the younger end of the 65-85 year range. Caucasians were overrepresented in the sample. Men and women were represented approximately equally.

Table 2

Mean (SD) Sample Characteristics by Time Point

Sample	Baseline	Immediate Post-Training	6-Month Follow-Up	Drop Outs
N	57	49	40	8
Age in Years	71.39 (5.21)	71.14 (4.90)	71.55 (5.07)	72.87 (7.04)
Men (%)	54.4	53.1	55.0	62.5
Caucasian (%)	86	85.7	85.0	87.5
Years Education	16.05 (2.32)	15.98 (2.13)	15.90 (2.24)	16.50 (3.46)
WRAT Reading Score	48.12 (4.58)	47.92 (4.85)	47.80 (5.00)	49.37 (2.13)
Baseline EF Composite Score	-0.13 (0.55)	-0.09 (0.54)	-0.11 (0.57)	-0.41 (.56)

Note: Due to limited resources, only 40 participants were invited to complete a 6-month follow up appointment. *Drop outs* refers to participants who ended the study prior to completion of training. There were no significant differences in demographics or baseline EF scores between those who completed training versus drop-outs. Non-Caucasian participants were African American (*n* = 8) and Asian (*n* = 1).

Aim 1

There was no missing baseline data. During preliminary data screening, four outliers were detected and truncated to the highest value within 3 SD above the mean. Truncation was performed on one participant’s Trails B score, one participant’s TOL Total

Moves score, and two participants' TOL Initiation Time score. Inspection of descriptives (See Table 3) and histograms revealed a good range of performances on each measure.

Table 3

Sample Descriptives for Baseline EF Measures

Measures	Minimum	Maximum	Mean	SD	Skewness	Kurtosis
NAB Mazes Total Score	0	23	8.00	5.00	.860	.399
RCFT Total Correct	20	36	30.63	4.38	-.812	-.315
RCFT Time-to-Copy	121.78	600.00	243.00	111.61	1.76	2.858
Revised RCFT Copy Score	16.62	36.00	30.09	4.73	-.704	-.231
Trails A Time	21.87	118.89	40.94	17.10	2.441	8.049
Trails B Time	43.94	254.10	102.34	51.72	1.666	2.527
Block Design Raw Score	2	59	29.72	13.73	-.050	-.640
Matrix Reasoning Raw Score	5	29	20.42	7.14	-.776	-.769
TOL: Total Moves	0	85	36.68	19.46	.341	.148
TOL: Total Correct	0	10	4.14	2.36	.558	-.360
TOL: Rule Violations	0	6	.70	1.35	2.244	4.964
TOL: Time Violations	0	8	1.72	1.96	1.409	1.561
TOL: Initiation Time	13	177	64.72	39.83	1.294	1.618
TOL: Execution Time	95	918	297.23	151.01	1.798	4.416
TOL: Problem Solving Time	139	976	363.37	163.92	1.694	3.214
UFOV 1-4	334.00	1534.00	837.09	285.58	.280	-.705
Eriksen Flanker Task	10.00	166.00	87.20	33.83	.434	.280

Note: Measures in bold were entered into the Aim 1 factor analysis. *EF:* Executive Function; *NAB:* Neuropsychological Assessment Battery; *RCFT:* Rey Complex Figure Test; *TOL:* Tower of London; *UFOV1-4:* Useful Field of View Sum of Tasks 1-4

As seen in Table 4, most measures correlated at least moderately (>.30) with some or all other measures. An exception to this was the Eriksen Flanker Task score (i.e. reaction time on incongruent trials - congruent trials), which was not significantly correlated with any other score. For this reason, the Eriksen Flanker task was excluded from the factor analysis.

Table 5 shows a matrix of potential component EF processes tapped by each EF measure in the CAPES battery. It is evident that any one EF measure could potentially reflect multiple executive demands. For example, completion of the NAB Mazes Test required participants to initiate a search, hold several alternative maze routes in mind, inhibit impulsive or erroneous movement through the maze, and to catch and correct course errors when they occurred. The table shows that all EF measures were thought to tap into at least two potentially separable executive processes, and at least two measures were thought to involve each hypothesized EF component. It is important to note that no *a priori* hypothesis about a particular factor structure was generated. This matrix allowed for the systematic consideration of all EF measures so as to increase the likelihood of entering quality, potentially factorable data into the analysis.

Table 4

Bivariate Correlation Matrix of CAPES EF Measures

Measure	**NAB Mazes Total**	**RCFT Revised Score**	**Matrix Reasoning**	**Block Design**	Trails A	**Trails B**	UFOV 1-4	Eriksen Flanker	**TOL Total Moves**	TOL Total Correct	**TOL Initiation Time**	TOL Execution Time	TOL Problem Solving Time	TOL Time Violations	TOL Rule Violations
NAB Mazes Total	1	.432**	.530**	.686**	-.342*	-.461**	-.523**	.163	-.330*	.291*	-.162	-.434**	-.431**	-.418**	-.450**
RCFT Revised Score	.432**	1	.520**	.541**	-.313*	-.406*	-.502**	.118	-.479**	.374*	.098	-.430**	-.360*	-.323*	-.380*
Matrix Reasoning	.530**	.520**	1	.600**	-.458**	-.533**	-.403*	.018	-.399*	.282*	-.117	-.518**	-.517**	-.575**	-.570**
Block Design	.686**	.541**	.600**	1	-.484**	-.437**	-.526**	.107	-.395*	.428**	.154	-.388**	-.314*	-.311*	-.514**
Trails A	-.342*	-.313*	-.458**	-.484**	1	.595**	.366*	.088	.120	-.182	.068	.458**	.419**	.462**	.502**
Trails B	-.461**	-.406*	-.533**	-.437**	.595**	1	.400*	-.130	.396*	-.290*	.211	.657**	.685**	.697**	.496**
UFOV 1-4	-.523**	-.502**	-.403*	-.526**	.366*	.400*	1	-.146	.272*	-.305*	-.079	.419**	.347*	.374*	.457**
Eriksen Flanker	.163	.118	.018	.107	.088	-.130	-.146	1	-.111	.029	-.105	.008	-.042	-.018	.230
TOL Total Moves	-.330*	-.479**	-.399*	-.395*	.120	.396*	.272*	-.111	1	-.801**	-.185	.727**	.624**	.536**	.336*
TOL Total Correct	.291*	.374*	.282*	.428*	-.182	-.290*	-.305*	.029	-.801**	1	.249~	-.599**	-.456**	-.380*	-.295*
TOL Initiation Time	-.162	.098	-.117	.154	.068	.211	-.079	-.105	-.185	.249~	1	.175	.407*	.379*	.032
TOL Execution Time	-.434**	-.430**	-.518**	-.388**	.458**	.657**	.419**	.008	.727**	-.599**	.175	1	.948**	.883**	.536**
TOL Problem Solving Time	-.431**	-.360*	-.517**	-.314*	.419**	.685**	.347*	-.042	.624**	-.456**	.407*	.948**	1	.926**	.486**
TOL Time Violations	-.418**	-.323*	-.575**	-.311*	.462**	.697**	.374*	-.018	.536**	-.380*	.379*	.883**	.926**	1	.521**
TOL Rule Violations	-.450**	-.380*	-.570**	-.514**	.502**	.496**	.457**	.230*	.336*	-.295*	.032	.536**	.486**	.521**	1

Note: Measures in bold were entered into the factor analysis. *EF:* Executive Function; *NAB:* Neuropsychological Assessment Battery; *RCFT:* Rey Complex Figure Test*;* *UFOV1-4:* Useful Field of View Sum of Tasks 1-4. *TOL:* Tower of London
~$p \leq .10$. *$p < .05$. **$p \leq .001$.

Table 5

CAPES EF Score Characteristics

Measure/Score	Score type			Potential EF Demands						Task Directions
	Correct/ Incorrect	Time	Sum Score	Working Memory	Initiation/ Inhibition	Cognitive flexibility	Planning	Error/ Self Monitor	Search	Task Goal Made Clear?
NAB Mazes Total	1	1	1	1	1		1	1	1	Time=Yes; Correct=Yes
***RCFT Copy Total Correct**			1		1		1	1	1	Correct=Yes
***RCFT Time-to-Copy**		1			1		1			Time=Yes (but priority is correctness)
Matrix Reasoning			1	1				1	1	Correct=Yes
Block Design	1	1	1	1	0.5		1	1		Time=Yes; Correct=Yes
Trails A		1						1	1	Time=Yes
Trails B		1		1	1	1			1	Time=Yes
UFOV1-4			1		1	1		1		Correct=Yes
Eriksen Flanker Task		1			1			0.5		Time= Yes
TOL Total Moves			1	1	1		1	1		Fewest moves possible= Yes
TOL Total Correct	1		1	1	1		1	1		Correct=Yes
TOL Initiation Time		1	1	1	1		1			Time until start= No, not told
TOL Execution Time		1	1	1	1		1	1		Time to work= No, not told
TOL Problem Solving Time		1	1	1	1		1	1		Time to complete= No, not told
TOL Time Viola-tions		1	1	1	1		1	1		Penalty for over one minute= No, not told
TOL Rule Viola-tions	1		1	1	1					Penalty for breaking rules = Yes (told rules count)

Note: Measures in bold were entered into the factor analysis. *EF:* Executive Function; *NAB:* Neuropsychological Assessment Battery; *RCFT:* Rey Complex Figure Test; *UFOV1-4:* Useful Field of View Sum of Tasks 1-4; *TOL:* Tower of London. *Task Directions* explain what type of instructions participants were given for each task.
*Scores later combined into one, Revised RCFT score.

Score type was important, in terms of identifying the nature of information conveyed by the score. For example, on the NAB Mazes Test, the participant's ability to carry out the task is captured in one score (NAB Mazes Total score), reflecting both speed and accuracy of performance. Although this score could technically be parsed into separate time and accuracy components, this is not how the test creators have chosen to capture task performance. Perhaps this is because separating speed and accuracy would be artificial, that is, less reflective of the executive skill needed to complete the task.

Through similar reasoning, it was decided that instead of considering RCFT Copy Total Correct and Time-to-Copy scores separately, a better way to capture the executive nature of the task would be to combine them into one score. To further explain this reasoning, an accurate rendering of the figure, copied in 60 seconds and an equally accurate figure copied in 10 minutes would receive the same accuracy score, failing to capture the difference in the participants' performances. Likewise, considering Time-to-Copy score in isolation would fail to distinguish between an individual who quickly drew a poor figure and an individual who quickly drew a perfect figure. Thus, a RCFT Revised score was created, which adjusted the Total Correct score to account for impaired performance speed. Participants who performed accurately (Total Correct >16th percentile for age) but were impaired in terms of speed (Time-to-Copy <16th percentile for age) were penalized for slowness by subtracting 1 standard deviation from the Total Correct score (based on the statistic of the entire baseline sample). Participants whose Time-to-Copy score was not impaired retained their raw Total Correct score.

Several scores were excluded from the factor analysis based on criteria outlined in the analysis plan (see Methods). Although Trails A may arguably have some executive demands, it was ultimately excluded because of high positive skew and the fact that research has shown it to be more reflective of processing speed than EF per se (Bowie & Harvey, 2006; Sánchez-Cubillo et al., 2009). Similarly, although the UFOV summary score showed moderate correlations with other measures, it was excluded from the factor analysis because it is thought to be more reflective of processing speed, visual perceptual processes, and divided attention, rather than EF (Edwards et al., 2006). For the purposes of this study, tasks involving EF were broadly defined as higher-order processes which facilitate purposeful, goal-directed, problem-solving behavior through modulation of lower-order processes such as reception of sensory input.

Time Violation and Rule Violation scores were excluded from the factor analysis due to high positive skew and very low occurrence rates. Amongst the three time-related scores of the TOL, Total Problem Solving Time was eliminated from consideration in the factor analysis, as it is simply a sum of the two other time scores. TOL Initiation Time was not significantly correlated with other EF measures except for TOL Time Violations, while TOL Execution Time was highly correlated with almost all other scores. However, Initiation Time was retained in the factor analysis because conceptually, it seemed to serve as a marker variable, capturing the pure "pre-planning" aspect of the TOL task. Execution Time, or time from first to last move, was not retained due to potential redundancy (i.e. time to execute task related to number of moves made, already reflected in Total Moves score).

Based upon the aforementioned considerations, a total of seven scores were identified for inclusion in the factor analysis model (bolded in Tables 3-5). Although distributions were slightly positively skewed for Trails B (Skewness = 1.67) and TOL Initiation

Time (Skewness = 1.29), no transformations were performed, in favor of interpretability of results. All scores were converted to z scores (*M* = 0, *SD* = 1). Trails B and TOL Total Moves scores were reverse coded (multiplied by -1) so as to be in the positive direction. This was necessary because higher scores on these measures are indicative of worse performance.

Factor analysis of baseline EF measures was performed using principal axis factoring extraction with oblique rotation. The appropriateness of factor analysis for the current battery of EF measures was supported by the Kaiser-Meyer-Olkin Measure of Sampling Adequacy > 0.6 (KMO = 0.84) and Bartlett's test of sphericity ($p < .001$). Two factors were extracted in three iterations, based upon the criteria of Eigenvalues >1 and examination of the scree plot. Inspection of the pattern matrix revealed no split factor loadings or low factor loadings. However, TOL Initiation Time was the only score with a high loading on Factor 2. All other items strongly loaded onto Factor 1. Therefore, the TOL Initiation Time score was removed, and a final one-factor solution was obtained. When orthogonal rotation was requested, the same solution was found.

As seen in Table 6, the six EF scores showed good to excellent factor loadings on the one factor. The factor is interpreted as reflecting the underlying process of executive function which produced participants' scores on the EF measures. Communalities indicate that between 30 and 65 percent of the variance in each measure is accounted for by the EF factor. The EF factor accounts for 48.43% of the variance in scores.

Table 6

Factor Loadings of CAPES EF Measures

Measure	Communalities	Factor 1
NAB Mazes	.520	.721
RCFT Revised Score	.462	.680
*Trails B	.398	.631
Matrix Reasoning	.581	.762
Block Design	.641	.801
*TOL Total Moves	.304	.551
Eigenvalue		2.91
% of Variance		48.43

Note: CAPES: Cognitive and Physical Exercise Study; *EF:* Executive Function; *NAB:* Neuropsychological Assessment Battery; *RCFT:* Rey Complex Figure Test; *TOL:* Tower of London
*Scores reversed to be in positive direction (i.e. higher scores indicate better performance).

Aim 2

Assumptions of multiple regression were tested via inspection of descriptive statistics and residual plots for 13 predictor variables and the dependent variable (EF composite, generated in Aim 1 analysis). One participant's VO_2max score was an extreme outlier and was therefore truncated to the highest value within 3 standard deviations of the mean. As presented in Table 7, VO_2max and all five IPIP scales demonstrated a reasonable range of scores. Scores were approximately normally distributed. CES-D scores were highly positively skewed, with only two individuals reporting depressive symptomology above the accepted cutoff for clinical significance (CES-D Total $\geq$ 16) (Radloff, 1977). The pattern of bivariate correlations between the log transformed CES-D score and other predictor variables was not different from when the raw score was used.

Therefore, the CES-D Total Raw score was retained for analyses for ease of interpretation. Approximately half of the sample self-reported the presence of physician-diagnosed hypertension.

Table 7

Sample Descriptives for Baseline Psychological and Physical Measures

	Minimum	Maximum	Mean	SD	Skewness	Kurtosis
Extraversion Percentile	2	99	54.55	26.83	-.007	-.847
Neuroticism Percentile	0	88	36.27	25.23	.382	-.892
Agreeableness Percentile	0	97	61.98	24.22	-.855	.485
Conscientiousness Percentile	1	97	54.29	27.67	-.250	-.955
Openness to Experience Percentile	0	99	44.18	25.73	.195	-.792
CES-D Total Raw Score	0	25	4.61	5.00	2.35	7.21
VO_2max (ml/min/kg)	5.20	35.30	22.02	6.53	-.164	-.105
	Present	Absent				
Hypertension	45.6%	54.4%				

Note: CES-D: Center for Epidemiological Studies-Depression Scale; *VO2max*: Maximum oxygen uptake

The assumptions of homoscedasticity, normality, and linearity were upheld in examination of residual plots. The Durbin-Watson statistic of the final model approached 2 (1.89), indicating the assumption of independence of errors was likely met. No multivariate outliers (Mahalanobis Distance > 15) were identified. The assumption of the absence of multicollinearity and singularity was upheld (no IVs correlated >.70, low variance inflation factors, high tolerance).

Bivariate Pearson correlations, presented in Table 8, show that sex was significantly associated with VO_2 max but not with baseline EF or any other predictor variable.

Participant age showed a negative association with VO_2max and baseline EF. African American race was significantly negatively associated with WRAT-Reading score, VO_2max, and baseline EF. Years of education was correlated only with reading ability. Given that the literature suggests reading ability may be a better indicator of educational quality than years of school, and the finding here that reading score, but not education was significantly correlated with baseline EF and race, the participants' reading scores may be a proxy for educational attainment. The five personality scales tended to show small to moderate correlations with one another, but only extraversion and neuroticism were significantly related to baseline EF. VO_2 max was significantly positively associated with male sex, Caucasian race, and baseline EF, and significantly negatively associated with age.

Table 8

Bivariate Correlations Among Predictors of EF and of Predictors with Baseline EF Composite Score

Predictor	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
1 Sex	1	.048	-.238~	.051	.141	-.048	.156	.168	.098	-.086	.028	.471**	.132	.211
2 Age	.048	1	.077	-.134	-.072	.056	-.139	-.104	-.123	-.130	-.050	-.295*	.184	-.300*
3 Race	-.238~	.077	1	-.009	-.356*	.084	-.200	-.088	.177	.095	-.060	-.424**	.137	-.504**
4 Education	.051	-.134	-.009	1	.316*	-.098	.106	.077	-.183	.083	-.096	.171	-.296*	.102
5 Reading	.141	-.072	-.356*	.316*	1	-.106	-.056	.247~	-.247~	.274*	-.265*	.231~	.092	.241~
6 Extraversion	-.048	.056	.084	-.098	-.106	1	-.534**	.303*	.544**	.294*	-.356*	.032	-.003	-.246~
7 Neuroticism	.156	-.139	-.200	.106	-.056	-.534**	1	-.433**	-.514**	-.073	.595**	.099	.050	.263*
8 Agreeableness	.168	-.104	-.088	.077	.247~	.303*	-.433**	1	.394*	.346*	-.084	.145	-.146	.063
9 Conscientiousness	.098	-.123	.177	-.183	-.247~	.544**	-.514**	.394*	1	.013	-.256~	.106	-.032	.009
10 Open to Experience	-.086	-.130	.095	.083	.274*	.294*	-.073	.346*	.013	1	.042	-.057	.028	-.130
11 Depression	.028	-.050	-.060	-.096	-.265*	-.356*	.595**	-.084	-.256~	.042	1	-.109	-.028	.142
12 VO_2max	.471**	-.295*	-.424**	.171	.231~	.032	.099	.145	.106	-.057	-.109	1	-.150	.485**
13 Hypertension	.132	.184	.137	-.296*	.092	-.003	.050	-.146	-.032	.028	-.028	-.150	1	-.119
14 Baseline EF	.211	-.300*	-.504**	.102	.241~	-.246~	.263*	.063	.009	-.130	.142	.485**	-.119	1

Note: EF : Executive Function ; *VO_2 max*: Maximum oxygen uptake.
~$p \leq .10$. *$p < .05$. **$p \leq .001$.

Based on correlational data, demographic variables age, race, and reading score (as an indicator of educational attainment) were entered into the regression model. VO_2max, extraversion, and neuroticism were entered in step 2 to determine if the addition of psychological and cardiorespiratory health information would improve prediction of EF beyond demographic information alone. In step 3, the interaction of extraversion and neuroticism was entered. This interaction was of particular interest, as it has been suggested that a combination of high neuroticism-low extraversion may predict poorer EF (LeMonda, Mahoney, Verghese, & Holtzer, 2015). Inclusion of seven predictors falls within the accepted range of ratios of cases to predictors (5:1) (Field, 2013; Tabachnick & Fidell, 2007).

After generating the initial model, variables were removed in an iterative fashion until the most parsimonious model was attained. The interaction of extraversion and neuroticism did not significantly improve the model, $R^2\Delta = .00$, $p = .95$, and was removed first. Reading score, age, and neuroticism were removed in each of the next steps, as they were not significantly predictive of EF in the model. As seen in Table 9, race was a significant predictor, $F(1, 55) = 18.72$, $p < .001$, accounting for approximately 25% of the variance in baseline EF. Over and above race alone, VO_2max and extraversion accounted for an additional approximately 14% of the variance in baseline EF (*F* Change = 6.21, $p = .004$). In the final model, $F(3, 53) = 11.56$, $p < .001$, the best linear combination of race, VO_2max, and extraversion accounted for approximately 40% of the variance in EF scores ($R^2 = .396$). Non-Caucasian race was associated with 0.34 standard deviation decrease EF composite score at baseline. A one standard deviation increase in VO_2 max predicted a 0.35 standard deviation increase in baseline EF. A one standard deviation decrease in extraversion predicted a 0.23 standard deviation increase in EF composite score.

Table 9

Regression Model for Predictors of EF at Baseline

Step	Predictor	B (SE)	95% CI	β	t	*sr^2*	*R^2*	*Adjusted R^2*	*R^2 Change*	*F* Change
1	Non-Caucasian Race	-.79 (.18)	-1.160- -.426	-.504	-4.327**	.254	.254	.240	.254	18.72**
2	Non-Caucasian Race	-.53 (.19)	-.904- -.155	-.336	-2.84*	.112	.396	.361	.142	11.56*
	VO_2 Max	.03 (.01)	.010- .050	.350	2.96*	.123				
	Extraversion	-.005 (.002)	-.009- .001	-.229	-2.13*	.052				

Note: EF: Executive Function; VO_2 Max: Maximum oxygen uptake
*$p < .05$. **$p \leq .001$.

Aim 3.

A mixed repeated measures ANOVA was performed, with EF composite as the continuous dependent variable. The within-subjects factor was time (baseline, immediate post-training, and 6-month follow-up). The between-subjects factor was group (COG, EXE, COM, and NC). There were no cases of missing data. For immediate post-training data, one outlier on each Trails B and RCFT were truncated prior to calculation of the composite score. No outliers were detected in any of the 6-month data. Examination of composite scores showed no outliers and approximately normal distribution at each time point. Composite scores for each group at each time point were also approximately normally distributed (Shapiro-Wilk, $p > .05$). Levene's Test indicated that the homogeneity of variance was equal across groups, $p > .05$**.** Mauchly's Test of Sphericity indicated the assumption of sphericity was upheld, $\chi^2 = 5.54$, $p = .06$.

Analysis revealed no main effect of group, $F(3, 45) = .08$, $p = .97$, or time, $F(2, 90) = 2.24$, $p = .11$, on the EF composite. The interaction of group and time was also not significant, $F(6, 90) = 1.77$, $p = .11$. Results were approximately the same when repeated without immediate post-training values carried forward for participants without 6-month follow-up data (Between subjects effects, $F(3, 36) = .19$, $p = .90$; Within subjects effects, $F(2, 72) = 1.24$, $p = .30$; Interaction (Time x Group), $F(6, 72) = 1.98$, $p = .08$). This lends confidence to the results incorporating the *last value carried forward* method for dealing with missing data.

Despite the non-significant interaction of group and time, a plot of EF composite scores (See Figure 3) clearly shows unique trends amongst the groups over time.

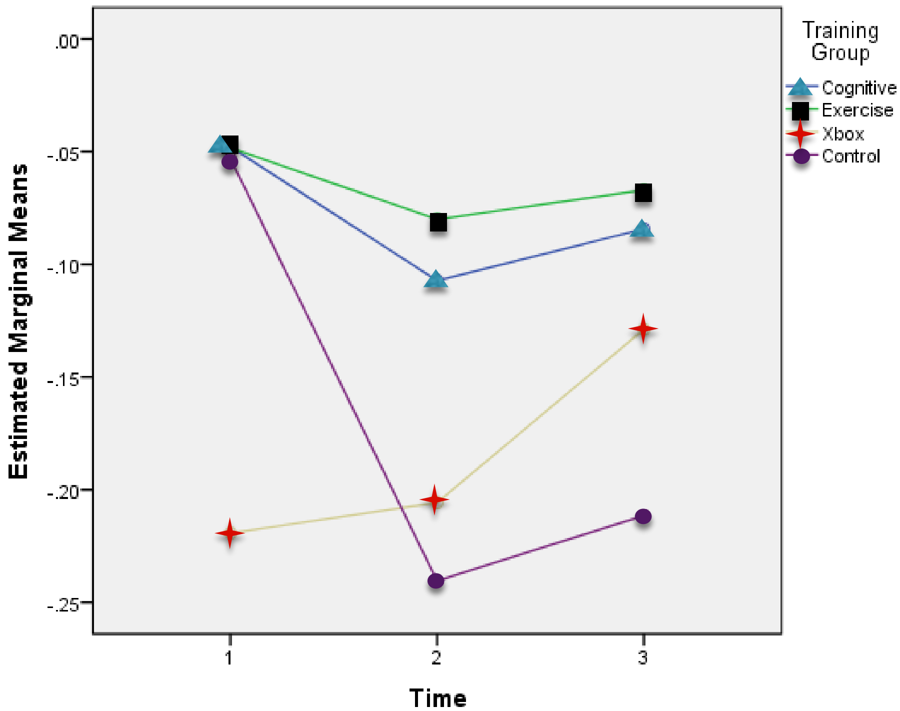

Figure 3. Trends in EF composite scores by training group. Time 1: Baseline; Time 2: Immediate post-training; Time 3: 6-month follow-up (last value carried forward for 9 participants, N = 49). Higher scores indicate better performance on the EF composite, which was calculated as the average of factor-weighted scores from six neuropsychological measures of EF. The baseline EF composite was not statistically different among groups.

The NC group declined from baseline to immediate post-training and then improved slightly at 6-month follow-up The EXE and COG groups declined slightly from baseline to immediate post-training and improved slightly at 6-month follow-up. The COM group stayed approximately the same or improved slightly from baseline to immediate post-training and improved performance to an even greater extent at 6-month follow-up. Groups did not differ significantly at baseline on the EF composite, $F(3, 48) = .405$, $p = .75$. Average EF composite scores by training group at each time point are presented in Table 10.

Table 10

Mean Composite EF at Each Time Point by Group

Time	Training Group	*N*	Mean	*SD*
Baseline	Cognitive	14	-.0676	.50874
	Exercise	12	-.1049	.57536
	Xbox	11	-.2223	.51823
	Control	12	.0291	.60896
	Total	49	-.0878	.54281
Immediate Post-Training	Cognitive	14	-.1311	.52840
	Exercise	12	-.1173	.50993
	Xbox	11	-.2116	.31348
	Control	12	-.1699	.64563
	Total	49	-.1553	.50251
6-Month Follow-Up	Cognitive	14	-.0950	.58673
	Exercise	12	-.1346	.59287
	Xbox	11	-.1262	.35479
	Control	12	-.1340	.57468
	Total	49	-.1212	.52535

Note: EF: Executive Function. At 6-month follow-up, the immediate post-training score was carried forward for 9 participants. Higher scores indicate better performance on the EF composite, which was calculated as the average of factor-weighted scores from six neuropsychological measures of EF.

CHAPTER 4

DISCUSSION

This study investigated 1) the latent factor structure of a large EF battery, 2) demographic, psychological, and health predictors of EF in older adults, and 3) the impact of cognitive, exercise, and combined training interventions on EF.

Aim 1

Factor analysis of the CAPES EF battery produced a one-factor solution, in which NAB Mazes Total score, RCFT Revised score, Trails B, Matrix Reasoning, Block Design, and TOL Total Moves scores loaded onto one factor. The existing body of literature is mixed in terms of support for EF as a unified construct or one with separable components. It is difficult to objectively assess the strength of the one-factor solution resulting from this analysis. However, according to the criteria put forth by Comrey and Lee (1992), the size of factor loadings (See Table 6) for NAB Mazes, Matrix Reasoning, and Block Design (>.71) indicate that they were excellent measures of the EF factor. The RCFT Revised score and Trails B score showed very good loadings (.63-.71) onto the factor, and the TOL Total Moves score showed good loading on the factor (.55-.63). In addition 30-64% of the variance in each measure was accounted for by the EF factor. These strong loadings and high communalities support the validity of the one-factor solution and the notion of EF as a unified construct.

Because exploratory factor analysis “lets the data do the talking,” the strategy chosen for entering data into the model is of utmost importance for its influence on the final solution. Care was taken to choose what were thought to be the most meaningful, non-redundant scores out of the large CAPES EF battery. Nonetheless, it is important to consider how selection of measures for the factor analysis may have influenced the finding here of a unified EF construct.

A look at Table 5 immediately alerts the reader to the fact that the EF scores were complex, and this may be one reason a one-factor solution was returned. For example, the NAB Mazes, Trails B, and Block Design scores are summaries of both efficiency and accuracy of complex task performance. When simpler scores were available, as in the case of the RCFT copy task, the decision was made to combine Total Correct and Time-to-Copy scores into one score, rather than considering them separately. This choice was based on the notion that the executive nature of the task would be more realistically captured in a score which jointly accounted for speed and accuracy (i.e. improving ecological validity). In everyday life, these elements are not divorced from one another. To be effective, one must complete a task effectively *and* efficiently. As a consequence, however, the one-factor model may actually be capturing the quality of complexity (i.e. task purity problem), masking potentially separable underlying executive demands. Had we taken the approach of dividing test scores up into the most fundamental elements, it is possible that a multiple-factor structure would have emerged.

It was interesting that TOL Initiation Time loaded highly onto a separate factor from all other measures included in the factor analysis. This indicates that the time participants took to think about their response ahead of actually making a move was capturing a different executive demand than any other measures. At face value, one might interpret Initiation Time as an indication of planning ability, such that those who took longer to start moving pegs on the board were demonstrating strong EF skills. However, the TOL Initiation Time score showed a significant positive correlation with TOL Time Violations and Total Time, indicating that those who took longer to think about their moves tended to take longer to complete the whole task overall. Thus, longer time thinking about one's first move did not necessarily translate into more success on the task. As Koppenol-Gonzalez et al. (2010) found, combining information about total moves, pre-planning time, problem difficulty, and strategic approach may better distinguish individuals' planning performance. In their study, individual scores were insufficient to characterize participants' success on the task. In future studies, a productive avenue may be to explore composite TOL scores which account for various aspects contributing to participants' success on a task.

It is possible that fundamental and separable EFs exist within this battery and are simply not reflected in the results due to lack of power to detect a true effect (Type 2 error). CAPES was a small pilot study, and sample size was very small in relation to the large number of measures under consideration. According to Tabachnick and Fidell (2007), if there are strong correlations and truly a few distinct factors, a smaller sample size is generally adequate. Even so, they recommend 150 cases minimum, which is almost three times the current sample size. Clearly, future studies should examine the present measures in a larger sample size.

In a large study of EF in older adults, de Frias et al. (2009) found that a one-factor solution best described the overall sample's performance. However, when divided into sub-groups of overall cognitive performance, a three-factor structure better fit the cognitively elite group but neither of the other two groups. Compared to age-matched norms, the average CAPES participant was within the average range of functioning (See Table 3). However, the CAPES sample did show a good amount of variability on EF measures, and future studies might consider how different levels of baseline functioning impacts the factor structure of EF.

Within the EF literature, there is a sense that fundamentally different EFs must exist. There is a desire to tease out individual functions within the EF family, so that the construct may become more concretely defined. Another possible benefit of separating EF into more fundamental components would be that particular subdomains of EF could be targeted in training, depending on the particular strengths and weaknesses of the individual. Yet, it seems that a one-factor solution does say, in a concise way, something useful about an individual's general ability to marshal cognitive resources effectively in situations of novelty or weak environmental support. In clinical neuropsychology, a main goal of assessment is to obtain some idea about how the individual will function on complex novel tasks. Results of the present study suggest that several common measures are good to excellent indicators of such ability.

Aim 2

Results of Aim 2 analyses indicated that non-Caucasian race predicted worse baseline EF. Over and above race, having a lower VO_2max and being more extraverted predicted worse EF at baseline. The finding that race was the strongest predictor of baseline EF in the CAPES sample mirrors findings in the literature. Many large cross sectional studies of diverse older adults have reported racial disparities favoring Caucasians, both in global cognition (Brewster et al., 2014; Díaz-Venegas et al., 2016; Manly et al., 2002; Shadlen et al., 2001; Sisco et al., 2015; Sloan & Wang, 2005) and on EF tasks (Early et al., 2013; Rexroth et al., 2013). In contrast, longitudinal studies tend to find that the rate or likelihood of cognitive decline is not significantly related to race (Castora-

Binkley et al., 2015; Early et al., 2013; Masel & Peek, 2009). This discrepancy suggests that it may be differences in life experiences or access to resources, not greater disease processes, that are driving the racial disparities evident in studies of cognitive aging. Indeed, in many of these studies, there is an attenuation (Manly et al., 2002; Shadlen et al., 2001; Sisco et al., 2015; Vásquez et al., 2015) or negation of significant cognitive differences (Castora-Binkley et al., 2015; Early et al., 2013; Masel & Peek, 2009) once education or educational quality is taken into account.

Interestingly, a significant correlation between race and reading score was observed. An ANOVA showed that non-Caucasian participants had significantly lower WRAT-Reading scores (*M* = 44.13, *SD* = 4.60) than Caucasians (*M* = 48.78, *SD* = 4.27) at baseline, $F(1, 55) = 7.98$, $p = .007$). Reading score was marginally correlated with EF, but was not significant in the regression model and did not attenuate the significance of race as a predictor of baseline EF.

Race was also significantly negatively correlated with VO_2 max, which was itself an independent predictor of EF in the final model. An ANOVA showed that non-Caucasian participants had significantly lower baseline VO_2max (*M* = 15.23, *SD* = 6.48) than Caucasians (*M* = 23.13, *SD* = 5.90), $F(1, 55) = 12.03$, $p = .001$). The average baseline VO_2max of non-Caucasian participants is particularly remarkable, because it falls in a range that is considered at-risk for loss of ability to carry out IADL (Shephard, 2009).

The observed racial disparities in EF, as well as other variables significantly related to EF at baseline, adds to the extant literature showing that non-Cacuasians are especially vulnerable to deficits in EF. Mechanisms by which these vulnerabilities disproportionally affect non-Caucasians is beyond the scope of this study, but current findings raise questions about disparities in quality of educational and recreational resources available to non-Caucasian older adults (Bleich, Jarlenski, Bell, & LaVeist, 2012; Jones et al., 2015) which should be explored further in future studies.

Next, the observed relationship between higher VO_2max and better EF is commensurate with findings in the literature. Cross-sectional (Hayes et al., 2014; Newson & Kemps, 2006) and longitudinal studies (Barnes et al., 2003) have also linked greater VO_2max to greater EF. In addition, VO_2max has been associated with increased gray matter thickness in the prefrontal cortex and hippocampus, brain areas responsible for memory and EF (Erickson, Leckie, & Weinstein, 2014; Szabo et al., 2011; Weinstein et al., 2012).

According to a review by Shepard (2009), beginning in middle age, maximal oxygen consumption declines steadily at a rate of about 5ml/kg/minute each decade. Near age 60, men's VO_2 max is expected to have decreased from about 45 ml/kg/min to around 25 ml/kg/minute, and for women, from 38 ml/kg/min to approximately 25 ml/kg/min. Thus, as seen in Table 7, CAPES participants' average baseline VO_2 max of 22.02 ml/min/kg is in line with expectations for sedentary adults of that age. Shepard (2009) indicates that if VO_2max drops below 15-18 ml/kg/min, individuals are at risk for loss of independence.

Highlighted in Table 8, results showed significant correlation between male sex and better VO_2max. This finding replicates a commonly-reported sex difference attributable to differences in total body fat and heart size between men and women (Hutchinson, Cureton, Outz, & Wilson, 1991). In CAPES participants, VO_2 max was also significantly negatively associated with age, which in turn was significantly negatively associated with baseline EF. The finding that age became a non-significant predictor of EF with the addition of VO_2max into the model suggests that age-related declines in cardiorespiratory fitness might be driving the observed negative relationship between age and EF.

In sum, the finding that VO_2max was a strong predictor of baseline EF in the present study underscores the need to emphasize exercise as part of a healthy aging regimen. Findings that female sex, non-Caucasian race, and increasing age were significantly negatively associated with VO_2max indicate that promotion of cardiorespiratory fitness in older women and minorities may be particularly important.

As seen in Table 7, almost half of CAPES participants reported physician-diagnosed hypertension, however no relationship between hypertension and VO2 max or baseline EF was found. Table 8 shows the only significant correlation of hypertension was with years of education. The lack of significant relationships is perplexing given findings in the literature linking cardiovascular health and cognitive outcomes in older adults. A possible explanation may be that the current study's presence/absence measure of hypertension may have been too gross an indicator. Research has shown that there may be distinct relationships between systolic hypertension and diastolic hypertension and EF respectively (Ogliari et al., 2016). It may also be that blood pressure variability over time (Ogliari et al., 2016) or hypertension- related pathologies affecting brain structures (e.g. white matter deficits, TIA, level of oxidative stress etc.) (Buford, 2016; Li et al., 2015; Raz et al., 2003; Schillerstrom et al., 2005) are more predictive of EF than presence/absence of hypertension alone.

Results of the present study also showed that lower extraversion significantly predicted better baseline EF scores. According to Costa and McCrae (1992), extraversion may be thought of as the degree to which an individual is motivated for external interaction. Researchers have linked EF and the introversion/extraversion personality spectrum to similar underlying neurological substrates and neurotransmitter systems (Campbell, Davalos, McCabe, & Troup, 2011), namely the behavioral inhibition system (BIS) and behavioral activation system (BAS) (Gray, 1970). According to Gray’s theory, more extraverted individuals have a more highly active BAS and are sensitive to reward and approach motivation. More introverted individuals have a more highly activated BIS, sensitizing them to punishment cues and avoidance motivation. Thus, individual differences in BAS and BIS may manifest in individual differences in expressed personality traits and action control (i.e. EF).

The present result, indicating that being less extraverted may predict better baseline EF, is supported by a few investigations: In two longitudinal studies, lower extraversion predicted higher global cognition and less decline over 4 years (Luchetti, Terracciano, Stephan, & Sutin, 2015) and over 7 years (Chapman et al., 2012) respectively. Campbell et al. (2011) found that introverts performed better than extraverts on shifting tasks and that they may be less prone to impulsivity. Campbell et al. (2011) and Gray (1970) posit that extraverts may be more impulsive because of their drive to seek reward.

Contrary to CAPES findings, some studies have shown that greater extraversion actually confers an advantage to EF (Gray & Braver, 2002; Liberman, 2000). These studies reported an advantage for more extraverted individuals on working memory tasks, especially as task load increased. Similarly, Lieberman and Rosenthal (2001) postulated that the reason extraverted individuals may be more facile in social situations is that their better working memory allows them to coordinate simultaneous social tasks. Gray and Braver (2002) argue that under high loads, more introverted individuals need to exert greater mental effort to achieve the same level of performance as more extraverted individuals. In CAPES, EF tasks were fairly structured (low-load) and given under relaxed conditions, such that conditions may have been conducive to eliciting the introverts' EF strengths. As seen in Table 9, the regression beta coefficient for extraversion was very small and should be studied in a bigger sample. If relative introversion/extraversion truly does influence EF, this has implications for how interventions to improve EF might approach the differential strengths and weaknesses of people on either end of the spectrum.

Contrary to our hypothesis, no relationship between depression and baseline EF was observed, however, this may have been confounded by the restricted range of depression scores in the CAPES sample. As seen in Table 7, 96.5% of participants were below the cutoff for clinically significant depressive symptomology (Radloff, 1977). In a large sample of adults aged 55 and older, Zahodne et al. (2014) also did not find a significant relationship between depression and EF or other cognitive domains. Instead, they found that greater emotional support and self-efficacy predicted better EF. This is an indication that in addition to negative affective factors, positive factors may have just as much influence on cognitive function. Future studies would benefit from inclusion of measures of positive affect and social support.

Aim 3

Contrary to hypothesized effects, older adults in the COG, EXE, and COM groups did not show significant improvements in EF after training. Though non-significant, results did show some distinct trends. The NC group declined from baseline to immediate post-training and then improved slightly (still below baseline performance) at 6-month follow-up. The EXE and COG groups declined slightly from baseline to immediate post-training, and improved slightly (not quite to baseline level) at 6-month follow-up. The COM group stayed approximately the same or improved slightly from baseline to immediate post-training and improved performance to an even greater extent at 6-month follow-up.

The literature on combined training is still in its infancy. CAPES tested a combined intervention against more traditional interventions about which more is known. Examining differences in group trends serves as a starting point for comparing the various interventions and helps to identify further lines of inquiry that will need to be pursued in future investigations of EF interventions in older adults.

Regarding the observed trends, the rate of cognitive decline in the NC group is likely greater than would be expected over a 10 week period for healthy older adults (Ball et al., 2002). As seen in Table 10, over the 10 week period between baseline and post-test assessment, NC participants' average EF composite score declined by approximately .25 SD, a magnitude of change that would be expected to occur over a 7-year period, based on the literature (Schaie, 1996). This decline also does not fit with the expectation of observing practice effects at later assessments. This trend needs to be confirmed in a larger sample and may be an artifact of small sample size and large standard deviation of baseline EF composite scores in the NC group.

The COM group showed the expected trend of improvement over time. COM participants' composite EF scores improved slightly from baseline to immediate training, but then jumped up noticeably at 6-month follow-up. Why might this be? Because the literature of combined training is so young, it is hard to say what magnitude and time course of change is expected with this type of intervention. Perhaps training-related improvements unfold in a non-linear pattern. One possibility is that Xbox training prompted sedentary adults to become more engaged in activities outside of training or to practice more complex tasks on their own as they improve. Older adults in the present study were asked to keep activity logs over the 6 months they were involved in the study, and examination of these logs could give clues about what contributed to the jump in scores from post-training to 6-month follow up in the COM group versus other training groups.

As seen in Figure 3, the COM training group's average baseline EF appears lower than all other groups. It was not statistically different than other groups, but if clinically meaningful differences did exist, this confounds interpretation of results. Is it possible the COM group was more impaired at baseline, and thus, had more room to improve? Some studies of COG, EXE, and COM interventions have found larger training effects in individuals who were older or more physically or cognitively impaired (Anderson-Hanley, Arciero, Westen, Nimon, & Zimmerman, 2012; Baniqued et al., 2014; Edwards et al., 2005; Leckie et al., 2014; Lee et al., 2012; Sink et al., 2015) at baseline. Even with randomization to groups, with such a small sample size and randomization done in pairs, it is possible that groups could have differed in a meaningful (yet statistically non-significant) way at baseline. This is a question that should be addressed in future studies with a larger sample.

Because of the consistent finding that 10 hours of on-site, group-based SOP training similar to the Posit Science Road Tour program used in CAPES (Ball et al., 2002; Edwards et al., 2009; Rebok et al., 2014; Willis et al., 2006; Wolinsky et al., 2013), it is puzzling that we did not find similar effects in the CAPES COG group, with participants completing more total hours of training. It could be that having participants practice on multiple tasks instead of just one game as in ACTIVE 13)271.", "ISBN" : "00987484\ffects, that is, training could have been too unfocused to produce changes in EF. This seems unlikely though. Another possibility is a lack of transfer of trained skills to the particular battery of EF measures used in CAPES. Differences in findings could be an artifact of using a different EF battery than past studies of similar cognitive training paradigms. It is also possible that the COG (and other) intervention(s) may have conferred more or less benefit on individual tests of EF, which became obscured by the use of a summary score. In addition, a composite score can mask the variability in time course of improvements on specific measures. Despite the usefulness of a composite to reduce data into a manageable form, and the strength of loadings on the factor, the relative merit of individual tests to pick up on changes in EF may have been lost. There is evidence from the cognitive literature that this can happen: Wolinsky et al. (2013) found that compared to an intervention involving completion of crossword puzzles, 14 hours of speed of processing training led to maintenance or improvement on several individual measures of EF. However, in a later factor analysis which combined EF measures into one factor score, there were no longer significant differences between the crossword puzzle and speed of processing training groups.

There are several additional issues, related to intervention design, that deserve mentioning. One challenge of running three different simultaneous interventions is that the dosage of interventions has to be standardized for practical reasons, even if the interventions may have different ideal dosages or exert their effects over a different time course. What is the ideal "dose" of each intervention? Within the limitations of a pilot study's resources, we chose 20 total hours based on suggestions in the exercise literature for 2-3 weekly sessions for 3-12 months, with most studies involving training of at least 6 months. Again, the cognitive literature suggests a 10-hour dosage. Did compromising on the two schedules harm the chance to see effects of one or both interventions? How does one compare the effectiveness of interventions which exert their effects differently across time, if that truly is the case? Building off of CAPES, future studies would benefit from looking at longer training periods and longer longitudinal follow-up so that trajectory and durability of training effects could be better understood.

Another issue is that of training intensity. With multi-component programs showing the most promising effects (Gregory et al., 2016; Smith et al., 2010), the exercise literature calls for moderate-intensity aerobic training and progressive-load resistance training. The current EXE intervention involved use of small hand-held weights, but weight was not increased over the course of the program. Heart rate data, should be scrutinized so that all training programs can be compared in terms of cardiovascular intensity. In addition to gauging overall intensity of the programs, it would be useful to know if the COM and EXE groups were operating under a similar level of aerobic demand. For participants in the exercise group, the DVD programs required fairly constant movement. In contrast, it seemed as if the participants in the Xbox group may have had more down time within each session, as they had to navigate through more program menus and play games of inherently varying intensities. Future studies should also examine changes in VO_2max from baseline to post-training assessments. As results of Aim 2 suggested, changes in VO_2max could be driving any observed training-related changes in the composite EF.

Finally, the “active ingredients” in each of the multifaceted training programs are difficult to isolate. Individuals in the COG group played three different games, the EXE group worked with three different DVDs, and the COM group worked with three different Xbox games. Therefore, it is difficult to know what particular games or facets of training were most driving the observed trends. Eventually, it may be useful to narrow down training to one game or type of exercise. However, the disadvantage of that approach is that training will no longer be as dynamic or novel, the very elements which might be driving positive training effects (Bherer et al., 2005; Buitenweg et al., 2012). Teasing out the active ingredients of training will likely take successive study trials and comparison of trials to other, similar studies.

Taking into account the results of Aim 2, future iterations of the CAPES study should include a more racially diverse sample. It would also be interesting to conduct training with populations more impaired at baseline, to maximize the potential for seeing training-related change. CAPES participants were healthy, community-dwelling older adults, many of whom, we learned over the course of working with them for several months, tended to be very engaged in family and community activities despite reporting a sedentary lifestyle (no formal cognitive or physical training program). As seen in Table 3, CAPES participants performed within the average range for their age group on all measures of EF. This level of performance could have limited the ability to find significant effects of training that may have been found in a more impaired sample. In addition, it would be helpful in future studies to include an active control group (i.e attending sessions at CRAG, working on crossword puzzles or brain teasers) to control for general cognitive and social stimulation.

CAPES had several strengths. It was a randomized controlled trial in which space was provided for participants to attend group sessions and work on interventions under supervision. The study design allowed participants to work with a partner of their choosing, assuming both met criteria for inclusion in the study. Program adherence in the present study was high. Participants generally reported enjoying the interventions, which is an important qualitative note, given that attrition is a problem in many intervention studies and is also very important clinically in terms of prescribing intervention activities which older adults enjoy enough to carry out regularly (Van Schaik et al., 2008). In addition, CAPES investigated simultaneous cognitive and physical training versus a design in which dosage is confounded by sequential administration.

Adding to that, CAPES was an investigation of commercially available and accessible interventions suitable for older adults of various physical ability levels and financial resources. Studies have shown that individuals most at risk for cognitive decline, including those with poor mobility and lower levels of IADL /ADL performance are less likely to attend training interventions (Van Schaik et al., 2008). All three CAPES interventions would be suitable for such individuals because of their ability to be implemented in homes and modifiable difficulty levels (e.g. the exercise DVD modeled exercises for people with restricted range of arm motion).

A final strength of CAPES was that it included cognitive and behavioral measurements which were comprehensive and captured diverse demographic, cognitive, physical, and psychological characteristics of the participants. Alternate form measures were used for many of the EF tests, limiting practice effects to a greater extent than usually seen in similar studies. Ultimately, the results of this investigation show that there is promise for COG, EXE, and especially COM interventions to promote the halting or reversal of EF declines in aging and suggest several lines of further inquiry for future investigations in this area. Practically speaking, advising older adults to maintain any form of active lifestyle engagement, including cognitive, physical, or combined activities, would be appropriate.

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APPENDIX

IRB IDENTIFICATION AND CERTIFICATION OF RESEARCH APPROVAL FORM

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The Assurance number is FWA00005960 and it expires on January 24, 2017. The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56.

Principal Investigator:	SCHMIDT, ERICA L
Co-Investigator(s):	BALL, KARLENE K ROSS, LESLEY
Protocol Number:	**E150511008**
Protocol Title:	*"An Examination of the Neuropsychological Construct Executive Function and How it May Be Impacted by Cognitive and Exercise Interventions."*

The above project was reviewed on 5/26/15. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This project qualifies as an exemption as defined in 45CF46.101, paragraph 4.

This project received EXEMPT review.

IRB Approval Date: 5/26/15

Date IRB Approval Issued: 5/26/15

Cari Oliver
Assistant Director, Office of the
Institutional Review Board for Human Use
(IRB)

Investigators please note:

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

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