Improving Attention and Mood in Heart Failure: Natural Restorative Environment Intervention

by

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DEDICATION

To my mentors, family, and all of my friends

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ABSTRACT

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Impaired attention has been found in approximately 1 out of 4 patients with heart failure (HF). Mechanisms of attention impairment are lowered cerebral oxygen supply due to cardiac dysfunction and increased mental effort from dealing with the fatal disease, HF. Although there is evidence that attention impairment is common in these patients and can affect their HF self-care activities, no interventions to date have directly targeted attention in HF patients.

To improve attention, natural restorative environment (NRE) interventions have been conducted and found to be efficacious in diverse populations. NRE interventions are based on Attention Restoration Theory, which asserts that when directed attention is rested, it can be restored. Whether NRE intervention is efficacious for HF patients is not known. Thus, the primary aim of this study was to examine the efficacy of a NRE intervention for patients with HF on attention. The secondary aim was to examine its efficacy on mood.

A randomized crossover design was used in 20 HF patients and 20 age- and education-matched healthy adults. The NRE intervention involved viewing 50 photographs of nature on a computer and the control condition involved viewing 50 photographs of urban environments. Pre and post intervention, attention was measured by four neuropsychological tests: the Multi-source Interference Task, Trail Making Test, Stroop Test, and Digit Span Test. Mood was measured by the Positive and Negative Affect Schedule. Intervention order was randomly assigned and delivered one week apart.

At baseline, poorer attention was found correlated with lower oxygen saturation and greater mental effort in HF patients compared to healthy adults. Linear mixed models in a pooled sample (n = 40) showed that NRE intervention was efficacious in improving attention, specifically sustained attention compared to the control condition. Attention switching, however, was preserved only in healthy participants after the control condition, but decreased in HF patients. Mood did not differ after interventions.

The NRE intervention is safe and has the potential to be widely disseminated. Future studies are needed on a larger sample with different intervention doses and a longer period of observations, providing knowledge about optimal quality of the intervention.

Word limit (348 / 350)

Chapter 1

Introduction

Why do nurses care about attention that is a part of cognition, and why is attention important specifically in individuals with heart failure? These questions may occur in response to the topic of this dissertation. The answer lies in the fact that nurses have a holistic view of human health including mental, physical, and cognitive health, and they intuitively know that patients have difficulties in getting information and processing it related to their disease management. Educating, thus, is one of the most challenging aspects of the job for nurses. The importance of attention in people with chronic disease, especially heart failure will be presented in following paragraphs.

In general, attention is "a state of focused awareness on a subset of the available perceptual information" (American Psychological Association, n.d.). Without the focused awareness, people cannot process stimuli in the environment to achieve their goals, such as survival and learning. Attention also plays an important role in encoding and retrieving information for memory by organizing information in ways that can facilitate the processes that support human learning and behaviors. Effective learning and behaviors are often critical factors in the survival rate of people with chronic disease, and attention is required in order for this learning to take place. Therefore, the importance of attention cannot be overstated in people with chronic disease, such as heart failure.

Chronic heart failure is a leading cause of death in the United States, and found on one in 9 death certificates (Go et al., 2014). Heart failure patients' survival rate is only 50% after 5 years of diagnosis (Go et al., 2014), and effective self-care activities influence survival. Central to the self-care of heart failure is reducing the burden on their heart workload (e.g., low sodium diet, medication management) and to respond appropriately to serious symptoms of heart failure that need immediate medical attention (e.g., a significant increase in body weight or shortness of breath). Learning and maintaining self-care activities for heart failure that are critical to patients' survival require a high level of attention in these patients. Despite the need, 25% to 50% of patients with heart failure have shown impaired cognition, and impaired attention was one of the most impaired domains, most likely due to an inadequte oxygen supply to the brain caused by cardiac dysfunction (Pressler, 2008).

Because attention to self-care is so essential, impaired attention should be taken into consideration in healthcare for these patients. Essential in this regard are nurses who are on the front line in caring for patients with heart failure from their diagnosis to the end of their lives. Care provided by nurses often includes education, for example, medication instructions focusing on effects and side effects, limiting sodium intake and/or fluid, and mechanisms of cardiac implantation devices. While educating and communicating with heart failure patients, nurses should be aware of possible attention impairment and modify the educational information they provide accordingly. In addition to detecting impaired attention and adjusting their delivery of information, nurses should put more effort into finding ways to improve or preserve attention so that heart failure patients can adhere to their self-care more effectively, thus increasing their survival.

Statement of the Problem

Although many studies have reported impaired attention in heart failure patients, the specific aspects of attention that are affected by heart failure are largely unknown. Most people know what attention is, but no single theory can explain this concept satisfactorily due to its complexity. One well-known classic definition of attention in psychology formulated by William James is that it "is the taking possession of the mind, in clear and vivid form, of one out of what may seem several simultaneously possible objects or trains of thoughts…It implies withdrawal from some things in order to deal effectively with others." (James, 1890, pages 403-404). As the definition indicates, attention is a complex system of information processes with multiple aspects supporting effective behaviors. However, this complexity has not been examined, and thus, which aspects of attention are impaired in heart failure remains unclear. In addition, to our knowledge, no study has directly targeted the issue of how to improve attention in patients with heart failure. Much of the research to date has examined impaired cognition, including attention in heart failure, but little effort has been made to offer interventions for attention. To address this void, the purposes of this dissertation study were to conduct a systematic review of the literature on impaired attention in heart failure and to test efficacy of an intervention based on the Attention Restoration Theory (Kaplan, 1995/2001) on improving attention in patients with heart failure.

Theoretical Perspectives of the Study

The theoretical framework of this dissertation study is based on the Attention Restoration Theory from the field of psychology. Attention Restoration Theory addresses how attention is fatigued and restored. The theory proposes that as the use of directed attention increases, directed attentional fatigue can result and is associated with ineffective behaviors. To avoid the fatigue associated with directed attention, the use of involuntary attention should be increased as a method to restore directed attention. Traditionally, directed and involuntary attention are conceptually defined by the amount of mental effort needed to perform activities. Specifically, directed attention (also called voluntary attention) is activated when a person is required to pay attention to specific stimuli that requires a great deal of mental effort. Involuntary attention, on the other hand, is activated by intriguing or novel stimuli that require little or no mental effort to focus on the stimuli.

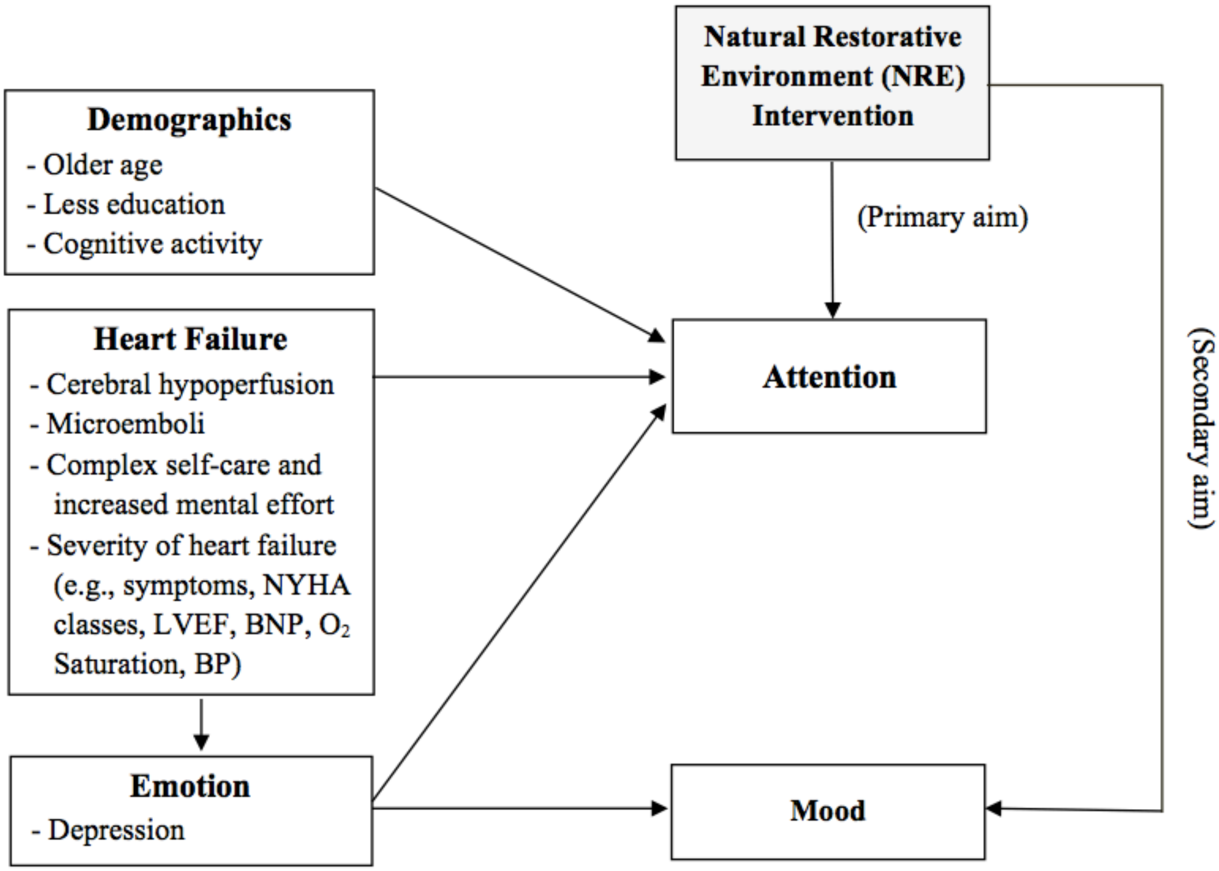
According to Attention Restoration Theory, nature is considered to be a good source for resting directed attention by reducing demands for directed attention. In nature, individuals tend to use more involuntary attention rather than directed attention, leading to restored directed attention and decreasing attentional fatigue. Nature can successfully restore directed attention because of four important characteristics. First, nature provides an environment in which an individual can feel a sense of being away from ordinary activities. Second, nature has what can be described as "soft fascination", the term used in Attention Restoration Theory to refer to nature's aesthetic properties that draw one's attention effortlessly, in a way that is gentle and not upsetting or strong. Third, in nature, a person can feel extended to larger areas mentally and physically. Last, nature can provide an environment in which a person can feel compatible, in other words, function better.

To achieve the purpose of the study that is improving attention in heart failure patients, a theoretical framework has been developed based on the Attention Restoration Theory and literature on cognitive impairment in patients with heart failure (Figure 1). According to the model, three antecedent factors (demographics factors, emotion, and heart failure) have a direct effect on attention. Heart failure also has a direct effect on emotion. As further illustrated in the figure, a natural restorative environment intervention based on the Attention Restoration Theory provides an opportunity to reduce demands for directed attention and improves attention (primary outcome). Although the relationship between the intervention and mood was not described in Attention Restoration Theory, there is some evidence that interventions based on the theory had an influence on improving mood (Berman, Jonides, & Kaplan, 2008; Berman et al., 2012). Mood, which is an emotional state at any given time, has been commonly decreased in heart failure patients, for example, feelings of being depressed or anxious. The decreased mood has a negative impact on mortality and quality of life in heart failure. In the model, the intervention may have a positive impact on mood as a secondary outcome.

Structure of the Dissertation

This dissertation follows a three-manuscript format consisting of five chapters: an introduction; three manuscript-type papers; and an overall discussion. In this first chapter, background knowledge on impaired attention in heart failure, statement of the problem, and the theoretical perspective are presented. Chapter 2, the first manuscript, is a systematic review of current publications that documents attention impairment in heart failure. Chapter 3, the second manuscript, is a report of the efficacy of the natural restorative environment intervention on improving attention and mood in heart failure patients and age- and education-matched healthy adults. The intervention described in Chapter 3 was developed from a study in healthy young adults (Berman, Jonides, & Kaplan, 2008), and adopted for this study. Chapter 4, the third manuscript, is a report of the construct validity of the Multi-source Interference Task, which is one of the attention measures used in the attention intervention in patients with heart failure. The final chapter, Chapter 5, provides an integration of the studies, and discusses the limitations and implications of these three manuscripts, and directions for future studies.

Figure 1.1 Theoretical Framework for Attention Function in Heart Failure



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Chapter 2

Impaired Attention in Individuals with Heart Failure: A Systematic Review and Analysis

Abstract

Objective: Patients with heart failure (HF) are at higher risk of impaired attention that may be caused by reduced cerebral blood flow and increased attentional demands from self-care activities for HF. While many studies have reported attention problems in HF patients, the specific aspects of attention processes that are affected by HF are largely unknown. The purpose of this study was to review existing studies about attention in HF.

Methods: A systematic literature review was conducted with a search of PsycINFO, CINAHL, PubMed, and Medline with dates from 2007 through 2014. Keywords included: heart failure, congestive; cognition; attention; fMRI, diffuse tensor imaging, concentration, and mental fatigue.

Results: Of the 34 studies found and reviewed, approximately 1/4 of HF patients had impaired attention. Compared to healthy adults and patients with other types of cardiovascular disease, HF patients' attention was poorer. Poorer attention was associated with smaller brain size and lower cerebral blood flow in HF. Older age, less education, lower cognitive reserve, gender, and more severe HF were related to poorer attention, and poorer attention had a negative impact on daily activities including self-care for HF. Improved attention was found after cardiac resynchronization therapy. However, no interventions directly targeting attention were found.

Conceptual definitions of attention and theoretical rationales for attention measures were often lacking.

Conclusions: Domain specific research on attention with theoretical perspectives and intervention studies are needed to improve attention, thereby improving self-care and, ultimately, reducing re-hospitalizations and mortality.

Introduction

Heart failure (HF) is a prevalent and life-threatening health problem affecting 1 in 5 men and women aged 40 and older in the United States (Mozaffarian et al., 2015). The prevalence of dementia or Alzheimer's disease in patients with HF is almost 3 times higher than that of the general population (27.6% of elderly patients with HF vs 10% of the total elderly population) (Centers for Medicare and Medicaid Services data as cited in Yancy et al., 2013). Even among patients with HF participating in research studies who screened as having no dementia, 25% to 50% of the patients were reported to have impaired cognitive function (Pressler, 2008), which includes deficits in memory, psychomotor speed, executive function, and attention. These findings indicate that cognitive impairment is a serious problem in individuals with HF.

Among the various cognitive impairments, attention is of particular concern because it is fragile, which means it rapidly fatigues with use, but is essential for everyday activity (Kaplan, 2001). More specifically, attention serves as a basic process involved in perceiving the world and regulating thoughts and feelings (Kaplan, 1995; Kaplan & Berman, 2010; Posner, 2004; Posner & Rothbart, 2007; Tennessen & Cimprich, 1995). Poorer attention has been shown to be related to diminished performance in instrumental activities of daily living such as driving, managing finances, and taking medications as prescribed, among elderly people (Carlson et al., 1999; Willis et al., 2006). In patients with HF, attention function is thus particularly important given the required activities related to HF treatment.

Although attention is one of the common cognitive domains reported as impaired in the HF population, the reasons for the attention impairment are not clear. There are two factors which may explain this impairment, one pathophysiological (changes in the brain) and the other psychological (increased attentional demands). First, brain changes might result from reduced cardiac output due to the failure of the heart's blood pumping function given that functional and structural changes in the brain have been found in HF patients. These changes, which can affect attention impairment, might occur due to the inadequate blood supply associated with lowered cardiac output and decreased autoregulation of blood vessels (Alosco et al., 2014; Okonkwo et al., 2010; Zuccalà et al., 1997). The prefrontal cortex, which is the supporting area for attention, has been found to be one of the main areas most likely affected by HF (Pan et al., 2012; Pressler, 2008; Siachos et al., 2005; Woo et al., 2003). Siachos et al. (2005) used brain imaging data from either magnetic resonance imaging or computed tomography and found that roughly one third of the HF patients (40 out of 117) had silent ischemic strokes. Woo et al. (2009) reported brain injuries in multiple areas, including the prefrontal cortex, in HF compared to healthy adults by using whole brain magnetic functional imaging. The changes in the gray and white matter, and the prefrontal and parietal areas may decrease attention function in HF. By using diffusion tensor imaging, Kumar et al. (2011) found altered neurofiber integrity (loss of axons and myelines) in 16 HF patients compared to 26 healthy adults. Alosco et al. (2014) found that lowered cerebral blood flow examined by transcranial doppler ultrasonography was predictive of attention among 145 HF patients. As an index of heart function, left ventricular ejection fraction (LVEF), the percentage of blood amount that leaves ventricle pumps out to the body and brain during each heart contraction (American Heart Association, July 9, 2013), has been examined to find relationships with cognitive function. Pressler et al. (2010a) showed LVEF was predictive of scores of attention measures (Digit Span Test, Trail Making Tests, and the Controlled Oral Word Test) in a longitudinal study with 166 systolic HF patients.

Second, in addition to the pathophysiological changes resulting from HF, patients may have increased demands for attention because of the complex self-care regimen required to manage HF. Increased demands for attention may deplete neural networks and lead to inadequate function of attention (Kaplan, 1995; Lim et al., 2010). HF adds more demands on attention for at least two reasons: the debilitating and confusing symptoms of HF, and the complexity of the HF regimen. Symptoms of HF (e.g., breathlessness, fatigue, and sleep disturbances) are worrisome, even life-threatening at times, and potentially distract patients from attending to their purposive activities (Roger et al., 2012; Yancy, et al., 2013). Pressler et al. (2010b) found that more severe HF symptoms measured by New York Heart Association (NYHA) classification was predictive of worse performance on Trail Making Test B and the Controlled Oral Word Test among 249 systolic HF patients. Beyond the possibility of HF symptoms taxing attention, HF requires patients to follow a complex regime on a daily basis. To adhere to this regimen, for example, in choosing a low sodium diet, and calculating the amount of sodium and water intake, HF patients might have increased demands for attention..

Attention in everyday terms requires no explanation; however, defining attention is not simple because it has multiple aspects. Frequently investigated aspects include the following: directed and involuntary attention, sustained attention, selective attention, divided attention, attentional switching, and the attentional network. Simple definitions of each aspect and its neural basis are summarized in Table 2.1. While a few studies have reported impaired attention in HF patients as a component of cognitive impairment (Bennett & Sauvé, 2003; Vogels et al., 2007c; Zuccalà et al., 1997), the specific aspects of attention that are affected by HF are largely unknown. Accordingly, there is a lack of knowledge about whether all aspects of attention decreased equally or selectively decreased in HF and which aspect is the most important in HF care. The purpose of this study was therefore to review existing empirical research about attention in HF to gain a better understanding of impaired attention and guide future research.

Methods

Search strategies

A literature search was conducted using databases PsycINFO, CINAHL, PubMed, and Medline with dates from August 1, 2007 to September 30, 2014. This time frame was selected because literature reviews on cognitive deficits in HF before 2007 have been published by several study teams (Cohen & Mather, 2007; Pressler, 2008; Vogels, et al., 2007c). The search keywords included: heart failure, congestive, cognition, attention, fMRI, diffuse tensor imaging, concentration, and mental fatigue. The reason why the keyword of 'cognition' was used in the search was because attention was measured as part of cognitive function in the HF literature. Combinations of two or three keywords were entered for data search. The search was limited to the English language and human subjects. Retrieved abstracts were reviewed and data-based publications that examined attention with neuropsychological tests were selected for the final review to describe the current state of knowledge of attention in patients with HF.

Results

The search yielded 316 publications without duplications, and one additional publication was found by reviewing the references (Figure 2.1). A total of 317 abstracts of the publications were reviewed; 279 publications were excluded because they were not data-based, did not examine cognition in HF, or did not use neuropsychological tests. The remaining 39 publications were read and evaluated. Of these 39 studies, 5 publications did not include attention and were excluded from the analysis. The final 34 publications were included in this review. Eight publications were later excluded after the review because attention was not discussed, but results from attention measures were interpreted as other related cognitive domains such as processing speed. Thus, 26 remained in the final review.

Prevalence of Attention Impairment

Impaired attention was reported in 3 studies in 15% to 27% of HF patients (Alosco et al., 2011; Bauer & Pozehl, 2011; Foster et al., 2011). Alosco et al. (2011) found that attention was impaired in 27% of the participants (n = 157) using Trail Making Test A, Digit Symbol Coding, Letter Number Sequencing, and Adaptive Rate Continuous Performance Test Interstimulus Interval score to measure attention. Another study by Bauer and Pozehl (2011) found attention was decreased among 27% of HF patients (n = 26) by administering the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) Attention Index. In comparison, using Digit Span and Digit Symbol test results, Foster et al. (2011) found that 15% of patients with advanced HF (n = 27) had impaired attention.

Not only attention impairment, but also memory impairment (10.2%, 35%, and 59%, in Alosco et. Al, Bauer & Pozehl, and Foster et al., respectively) and executive function impairment (21.7%, 54%, and 33%, respectively) were found in all three studies. Z-scores and t-scores were used based on existing normative data to determine impairments. None of the studies had their own control groups.

Poorer Attention Function in Patients with Heart Failure than in Healthy Individuals and Patients with Other Medical Conditions

Three studies compared the cognitive function of HF patients with healthy participants or patients with cardiovascular disease without HF, and reported significant differences (Hoth et al., 2008; Sauvé et al., 2009; Vogels et al., 2007b). Hoth et al. (2008) recruited 31 HF patients and 31 age- and education- matched cardiac patients without HF as a control group. Executive functioning and psychomotor speed were worse in HF patients than those with cardiovascular disease without HF. However, attention was not significantly different between groups. These authors administered the RBANS Attention Index, and reported low attention function in HF patients on average (z = - 0.7). Sauvé and colleagues (2009) examined prevalence, type, and severity of cognitive impairment by comparing 50 HF patients with 50 age-, gender- and estimated intelligence-matched healthy controls. The results of Symbol Digit Modality and Visual Scanning showed that attention was the second most frequently impaired cognitive domain following memory among patients with HF. In addition, attention (t = 4.70, p = .000) as well as all the domains of cognition were poorer in HF patients compared to healthy participants. Vogels et al. (2007b) compared cognitive performance among three groups comprised of HF patients (n = 63), age-matched cardiovascular disease patients without HF (n = 53), and age-matched healthy participants (n = 42) to investigate patterns of cognitive dysfunction in HF. Attention, measured by the Stroop Test and Trail Making Test A, was significantly lower in HF patients than in participants who were healthy or those with cardiac disease without HF (p = .03, p = .01, respectively). Based on the measurements showed significantly decrease in attention, directed, sustained, selective, and divided attention function appeared to be poorer among HF patients compared to participants who were healthy or had cardiovascular disease other than HF.

Characteristics Associated with Impaired Attention

Eleven publications aimed to investigate relationships between demographic and/or clinical characteristics and cognition in HF, and attention was measured as part of a cognitive battery (Alosco et al., 2011; Alosco et al., 2012a; Alosco et al., 2013a; Alosco et al., 2013b; Alosco et al., 2013d; Bratzke-Bauer et al., 2013; Festa et al., 2011; Foster et al., 2011; Hoth et al., 2008; Miller, et al., 2012; Vogels et al., 2007b). These studies found that poorer attention was associated with older age, fewer years of education, lower level of cognitive reserve, female gender, and more severe HF.

The relationship with demographic characteristics was found in a study by Miller et al. (2012). Community-dwelling HF patients (n = 140) were assigned to three groups based on their cognitive performance on neuropsychological tests: intact, memory reduced, and globally impaired cognition clusters. The globally impaired cognition cluster referred to people with impaired attention/executive function, naming, and impaired memory. The HF patients in the globally impaired cluster were more likely to be older, less educated, and female than those who were in the intact cluster.

A relationship between clinical characteristics and attention was found in ten publications (Alosco et al., 2011; Alosco et al., 2012a; Alosco et al., 2013a; Alosco et al., 2013b; Alosco et al., 2013d; Bratzke-Bauer et al., 2013; Festa et al., 2011; Hoth et al., 2008; Miller et al., 2012; Vogels et al., 2007b). Alosco and his colleagues examined HF severity, hypertension, diabetes, dietary habit, cardiovascular fitness and exercise adherence in the relation to cognition from an NIH-funded study examining cognition among patients with HF. In the 2011 publication, the authors measured HF severity by using physical function data from the 2-minutes Step Test, and found that patients with greater HF severity had poorer attention. In the 2012a publication, Alosco et al. found 70% of the participants had hypertension with HF, and these patients showed lower attention compared to those who did not have hypertension. Similarly, the research group investigated the combined effects of diabetes with HF on cognitive performance and the brain structure, and found smaller brains including reduced cortex size, which was associated with lower attention function (Alosco et al., 2013a). Moderating effects of poor dietary habits on the relationship between HF severity and cognition (Alosco et al., 2013b) and mediating effects of cardiovascular fitness on the relationship between depression and cognition (Alosco et al., 2013d) were also found. There appeared to be different sets of sub-samples from the same sample used for these publications.

In a study by Miller et al. (2012), patients who demonstrated global impairment in cognition showed significantly increased HF severity (worse performance on the 2-minute Step Test) and were more likely to have sleep apnea and be hypertensive. LVEF was associated with attention, global cognition, and executive function (Hoth et al., 2008). Festa et al. (2011) found relationships between poorer memory, and older age and lower LVEF among 207 advanced HF patients. The findings of these authors showed a positive relationship between attention and memory, may indicate that poorer attention was related to older age and lower LVEF. Vogels and colleagues (2007b) found that patients with more serious HF symptoms defined by higher New York Heart Association (NYHA) classes were more likely to have overall impaired cognition ($p = .063$).

Differences in cognition between systolic and diastolic HF were examined by Bratzke-Bauer, et al. (2013). Attention measured by Trail Making Test B was poorer in patients with systolic HF compared to those with diastolic HF. Attention measured by Trail Making Test A and Digit Span Forward did not differ by the groups.

Cognitive reserve has been found to be a moderating factor in the relationship between attention and HF severity among 157 elderly HF patients (Alosco et al., 2011). Vogels et al. (2007b) found that lower premorbid intelligence was a predictor of cognitive impairment ($\beta = .013$, $p = .003$) using regression analysis with age and gender as covariates. However, attention, which was measured by Stroop Test and Trail Making Test A, was not explained by premorbid intelligence. Riegel et al. (2012a) examined changes of cognition over time among 280 patients with HF, and found that attention did not significantly change over time. Patients who had below average psychomotor speed scores had significantly poorer attention scores compared to patients who had above average psychomotor speed scores. Although Riegel et al. (2012b) found relationships among cognitive impairment, sleep disturbance, and health-related quality of life, the authors used composite scores of cognition, so the relationships between these factors and attention were not clear.

Associations of perceived participation in social and leisure activities with cognitive function and depression were examined among 27 advanced HF patients (Foster et al., 2011). The researchers found no significant relationship between attention measured as the average scores of Digit Span and Digit Symbol Tests, and depression and participation. These authors found that individuals who were more active in participation had better executive function ($p < .05$) measured by the Dysexecutive Questionnaire, a self-reported questionnaire on frequencies of listed behaviors related to planning, execution, and regulation of goal-directed behavior.

Three additional studies reported relationships between demographic and clinical characteristics and attention, although this relationship was not the primary aim of these studies. (Bauer et al., 2012; Dickson, McCauley, & Riegel, 2008; Sauvé et al., 2009). Sauvé et al. (2009) found that poorer attention was more likely to be detected among women, people with lower premorbid intelligence, and increased HF severity among 50 HF patients. Bauer et al. (2012) reported a significant correlation between higher NYHA class and poorer attention among 80 HF patients. Dickson, McCauley, and Riegel (2008) compared cognitive function between employed and unemployed HF patients. Forty-eight percent ($n = 20$) of participants were employed. Employed patients showed significantly higher LVEF than unemployed patients (41.35% vs 27.14%, $p = .003$). Subsequently, employed patients performed better on attention as measured by the Digit Symbol Substitution Task compared to unemployed patients.

Impact of Attention Impairment on Healthcare and Healthcare Outcomes

In four publications from two studies, poorer attention was associated with activities of daily living (ADL) and HF self-care management (Alosco et al., 2012b; Alosco et al., 2012c; Alosco et al., 2014; Dickson, Deatrick, & Reigel, 2008), although the results were inconsistent based on the attention measures. Alosco et al. (2012b) examined basic and instrumental ADLs using the Lawton Brody Activities of Daily Living Scale among 122 HF patients. Patients with HF received much support for ADLs (mean score = 25.19, possible range = 0 ~ 28) including laundry, preparing meals, shopping, managing finances, medication management, and driving. Poorer attention, measured with the Trail Making Test A, was predictive of limited activities on medication management ($\beta = -.24$, $p < .05$). Another publication of Alosco et al. (2014) based on a study of 174 HF patients, did not find a significant association between instrumental ADLs and attention measured by the Digit Symbol Coding, Complex Figure Test, and Animal Fluency Test.

Lower HF self-care adherence was associated with poorer attention from two studies. Dickson, Deatrick, and Riegel (2008) classified 41 HF patients as expert, novice, or inconsistent in self-care. The authors used the Letter Number Sequencing Task and Digit Symbol Substitution Task to measure attention, memory, executive function, and psychomotor speed. The Self-Care of Heart Failure Index was used to examine HF self-care. Patients with poorer attention test scores were more likely to be in the group of inconsistent self-care. Alosco et al. (2012c) found that 49% out of 149 NYHA class II and III patients were not adherent to at least one of the following self-care activities: doctor's appointment, medication management, HF diet, exercise regimen, smoking cessation, and alcohol abstinence. Poorer attention measured by Trail Making Test A and Digit Symbol Coding was a significant factor of overall non-adherence to self-care while Stroop test scores and Trail Making Test B were not predictive of self-care adherence. Individual self-care activity analyses showed keeping doctor's appointment and managing medication were significantly correlated with attention. These studies recruited only NYHA class II and III patients, and thus, knowledge on patients with early and very late stage of HF is limited.

Medical Treatment Having Effects on Attention

Three publications found positive effects of medical treatment with cardiac resynchronization therapy (CRT) on attention (Conti & Sears, 2007; Dixit et al., 2008; Hoth et al., 2010). In the intervention studies by Conti and Sears (2007) and Dixit et al. (2008, an extension of Conti and Sears' study), attention measured by the Digit Span Test improved 3 months after CRT implantation (n = 20). However, Hoth et al. (2010) did not find significantly improved attention as measured by Trail Making Test A and RBANS 3 months after CRT (n = 27). These 3 studies did not include control groups or randomization, and the sample sizes were small. None of these studies directly targeted attention, but the improvement was secondary to improved cardiac function.

Brain Changes and Attention Impairment

Two studies reported changes in the brain by using imaging techniques, and only one of them found that worse brain perfusion was associated with poorer attention (Alosco et al., 2013c). Vogels et al. (2007a) investigated the relationship between brain structural changes and cognitive function among 58 patients with NYHA class II to IV. A brain MRI was conducted after neuropsychological tests were administered. Regions of interest included the white matter hyperintensities (frontal, occipital caps, and periventricular bands) and deep white matter hyperintensities (4 subcortical, 5 basal ganglia, and 4 infratentorial regions). Attention measured by the Stroop Test and Trail Making Test A was not related to any of the brain structural changes in HF. Alosco et al. (2013c) examined relationships between cerebral perfusion, depression, and cognition among 89 patients with NYHA class II and III. Class III participants showed greater decrease in cerebral blood flow velocity measured by Transcranial Doppler ultrasonography. Decreased global cerebral perfusion was predictive of worse attention ($\beta = .21$, $p = .039$). There was an interaction effect of cerebral perfusion and depression on attention ($\beta = .32$, $p = .003$).

Psychometrics of a Neuropsychological Battery

One study examined psychometric properties of a neuropsychological battery in patients with HF (Bauer et al., 2012) and supported reliability and validity of the test. The authors tested the validity and reliability of the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) among 80 patients with HF. When the RBANS Attention Index was administered, scores from HF patients were lower than the published normative data among healthy adults ($p < .001$). The Attention Index scores were significantly correlated with other measures of attention, Trail Making Test A and B, in this study ($r = .50$ and .51, respectively). No significant relationship was found between the Lawton Instrumental Activities of Daily Living questionnaire scores and RBANS Attention Index scores, but significant relationships were found between the instrumental ADL scores and Trail Making Test A, and B ($r = .35$ and $r = .27$, respectively). Test-retest reliability of the Attention Index was established among a subsample of 21 participants. One week lapsed between the initial test and repeat test, and the test-retest correlation was acceptable ($r = .73$). Poorer performance on RBANS Attention Index was significantly correlated with a higher NYHA class representing a more serious HF condition ($r = -.24$).

Lack of Clarity in Theoretical Definitions of Attention in Existing Studies

Theoretical definitions of attention were not provided in the 26 publications. Two out of 26 publications addressed *working definitions* of attention (Table 2.2). Bauer and Pozehl (2011), in their measurement section, described the function of attention as that which "allows individuals to focus on information for further processing". In contrast, Sauvé et al. (2009) provided a working definition of attention as "a complex cognitive function comprised of sustained concentration, working memory, and motor responses (p. 4)", which would not appear to be the most accurate definition of attention because working memory and attention share common components, and attention is more likely to support working memory processes and working memory modulates attentional capture of stimuli (Awh & Jonides, 2001; Baddeley, 1986; Lavie & Fockert, 2005). Although several neuropsychological tests were used to measure attention, the constructs of attention examined by the tests were not described in this literature. Inconsistent findings on attention impairment and improvement might be explained by the different aspects of attention that were measured in these studies.

Measurements of Attention

A total of 12 neuropsychological tests were administered and analyzed across the 26 publications examining attention. These studies measured attention as part of overall cognitive function, which includes memory, executive function, and psychomotor speed, among patients with HF (Table 2.3). The most frequently used neuropsychological test was Trail Making Test A (14 out of 26 publications). The Digit Symbol Coding, Letter Number Sequencing, Trail Making Test B, and RBANS Attention Index, Stroop Test followed. The least frequently administered tests were the Adaptive Rate Continuous Performance Test, Symbol Digit Modalities, and Visual Scanning Test, all three of which were used just once.

Nineteen studies (73%) administered multiple tests to examine attention (Table 2.2). In contrast, five studies (19%) used one neuropsychological test to measure attention and the other cognitive domains of visual scanning and psychomotor speed (Alosco et al. 2012b; Alosco et al., 2013d), memory, executive function, and psychomotor speed (Dickson , Deatrick, & Riegel, 2008; Dickson, McCauley, & Riegel, 2008), and executive function (Miller et al., 2012).

Even among publications that used the same measure, interpretation methods differed based on the purposes of their analyses. For example, Trail Making Test A was administered in 14 publications, and Alosco et al. (2011) used t-scores to define impaired attention. Another study by Alosco et al. (2012b) used raw scores (time taken to finish the task) in a regression model. Vogels et al. (2007a), however, used z-scores from published normative data. For most of the cases, reliability and validity of neuropsychological measures were frequently not reported. The sensitivity and specificity of detecting impaired attention have not been reported as well.

From the review of the measures, the most commonly examined constructs of attention in HF were sustained and directed attention. Based on the definition of directed attention, which is an effortful attention, directed attention appears to be related to all of the neuropsychological tests. Although selective and divided attention, and attentional switching have been examined by the Stroop Test and Trail Making Test B, a few studies defined and described these aspects by distinguishing them from other aspects of attention.

Studies Which Used Attention Measures to Describe Other Cognitive Domains

There were eight studies that administered attention tests but did not explain the results in the framework of attention (Figure 2.1), and instead, these studies focused on other cognitive domains, such as working memory or processing speed. The neuropsychological tests of attention used across the eight studies were Trail Making Test A and B that was most frequently used (6 out of 8 studies), and followed by the Digit Span Test, CogState One Back and Identification Test, and Stroop Test. The main themes from the 8 studies were the following; cognitive impairment (Kindermann et al., 2012; Pressler et al., 2010b), interventions to improve cognition (Carles et al., 2007; Pressler et al., 2011), effects of device implantation on cognition (Petrucci et al., 2009, 2012), a screening measure of cognition (Hammers et al., 2012), and the relationship between cognition and quality of life (Pressler et al., 2010a). The study results were interpreted based on the measures for this review.

Attention impairment was found in the study by Pressler et al. (2010b). Digit Span tests and Trail Making Tests A and B, which are listed as attention measures above, were used to measure working memory, psychomotor speed, and executive function in this study (n = 249 HF patients), respectively. The percentages of HF patients who had z-scores below the cutoff point on the Digit Span test and Trail Making Tests A and B were 1%, 13% and 19%, respectively. Another study examined differences on cognitive function between 20 unstable, 20 stable patients with HF, and 20 age- and gender-matched healthy participants (Kindermann et al., 2012). Unstable HF patients who became stable at the 14-month follow-up showed better performance on the Digit Span Test and Stroop Test compared to their pre-treatment test results. Healthy participants outperformed on these tests compared to the stable and unstable HF participants, except for the Digit Span Forward Test. The Follow-up Digit Span Forward Test, however, did not show a significant difference between stable HF patients and healthy participants.

Three studies used medical and non-medical interventions to improve cognition. Petrucci et al. (2009) evaluated changes after implantation of a left ventricular assist device (LVAD), a mechanical circulatory support to pump blood in left ventricle to aorta) among 93 severe HF patients at 1, 3 , and 6-months after implantation. Performance on Trail Making Test A was improved at the 3 month follow-up compared to the 1 month follow-up, but no differences were found at 6 months. Performance on Trail Making Test B was improved at 3 and 6-month follow-up times. Patients with continuous and pulsatile LVAD did not differ on their Trail Making Test A and B at follow-up. However, the attrition rate was large (53%) mainly due to heart transplants (37%) and death (15%).

Effects of physical exercise (acute and aerobic) on cognition were investigated by Carles et al. (2007). The Trail Making Test was combined with a mental arithmetic test and 2 memory tests to measure information processing. After 2 weeks of exercise training, better information processing was reported. However, detailed test results of the Trail Making Test were not presented because these authors used summed scores to assess information processing.

A computerized cognitive training, which was primarily focused on memory training based on neuroplasticity, was conducted by Pressler et al. (2011). The authors examined effects of the cognitive training at 8 and 12-week follow-ups compared to health education intervention among 34 HF patients. Cogstate Identification and One Back test, which are measures for visual attention/sustained attention and attention/working memory ("Cogstate", n.d.), were used to measure working memory in this study. The cognitive training resulted in improved delayed recall over 12 weeks compared to the education group, but no differences were found in attention between baseline and 8 and 12 week follow-ups.

Hammers et al. (2012) examined the psychometrics of the Cogstate International Shopping List, which is an auditory memory test, as a screening tool predicting functional decline in HF, and sensitivity in myocardial infarction (MI) using the data from the computerized cognitive training study/ using the same data as that used in the computerized cognitive training study (Pressler et al., 2011). Validity and predictability were satisfactory, but sensitivity was not.

Pressler et al. (2010a) examined relationships between cognitive impairments and health-related quality of life. Only three tests were significantly related to healthy-related quality of life: Digit Symbol ($r = -.28$, $p < .001$), Digit Span, scaled ($r = -.15$, $p = .02$), and Trail Making Test B ($r = -.14$, $p = .03$). In other words, HF patients with better attentional capacity and psychomotor speed were more likely to have a better quality of life. However, in a regression model, only memory measured by Hopkins Verbal Learning Test total recall was predictive of health-related quality of life, but had only a minimal effect (increased 1% of variance of explanation).

Discussion

This literature review, to the best of our knowledge, is the first systematic review on attention in patients with HF. Although researchers have found impaired cognition in HF, surprisingly little attention has been given to domain-specific research.

No studies targeted attention primarily, although some studies targeted specific domains addressing cognitive reserve (premorbid intelligence) and memory (Alosco et al., 2011; Festa et al., 2011; Pressler et al., 2012). Almost all studies in this review comprehensively measured cognitive domains that included global cognition, attention, psychomotor speed, and executive function. These studies provided valuable knowledge on cognitive function in HF, but domain specific studies are also needed to design intervention studies. Without detailed information about cognitive domains that are impaired and the relationship between the domains, it is difficult to determine which cognitive interventions are needed for HF patients and, in turn, difficult to evaluate the effects of the interventions. It could be argued that developing an intervention targeting all cognitive domains is ideal, but it is likely to be unrealistic and produce more physical and financial burdens on patients by administering extensive neuropsychological battery for hours.

In addition, theoretical perspectives on attention were not clear in the literature reviewed. Although theoretical perspectives on the *mechanism of cognitive decline* related to HF was mentioned in each research study (e.g., lowered blood flow in the brain may drive cognitive decline), *theoretical perspectives on attention* were rarely found in this literature review. The lack of theoretical or conceptual definitions may lead to problems when designing studies and interpreting study results. For example, when researchers aim to measure specific networks of alerting, orienting, and exercising executive function, the Attentional Network Test would be appropriate, but neither the Trail Making Test or the Digit Span Test measures these networks. The Trail Making Test or Digit Span Test would be more appropriate to measure sustained attention or directed attention. The reason why specific aspects of attention have been selected for investigation in each study, and the impact of the decrease in specific aspects of attention on HF patients' health warrants further analysis.

The degree of impaired attention among patients with HF in research findings ranged from 15% to 27.4% (Alosco et al., 2011; Bauer & Pozehl, 2011; Foster et al., 2011). Given that the HF patients with dementia were excluded from the studies (28 % of HF population, Maslow, 2004), this 15% ~ 27.4% of attention impairment may imply that, in total, almost half of the HF patients had attention impairment. The high prevalence of attention impairment is important because it creates an additional challenge to many HF patients' everyday lives, specifically self-care management for HF (Alosco et al., 2012b; Alosco et al., 2012c; Alosco et al., 2014). Given that attention is a foundational cognitive function of information processing, this could mean that, in terms of initiating and maintaining process of information, impaired attention may lead to impairment in other cognitive domains such as poorer memory and decision making (Dickson, Deatrick, & Riegel, 2008). These findings demonstrate that attention impairment does not only exist cognitively and conceptually, but also affects individuals' daily living with chronic disease.

Studies on exploring mechanisms of cognitive impairment were found. In addition to neuropsychological tests describing the current state of attention, brain imaging techniques were used to explain poorer performance on attention tests in HF. Before 2007, studies have been conducted separately with neuropsychological tests and brain images (e.g. fMRI, DTI), and structural and functional brain changes were suggested as rationales of cognitive impairment in HF. In this review, two studies were found that linked HF patients' brain structure and cerebral perfusion to their performance on neuropsychological tests (Alosco et al., 2013c; Vogels et al., 2007a). The finding of the relationship between lowered cerebral blood flow and poorer attention supported one of the suggested mechanisms on impaired attention in HF. However, studies of finding the etiologies of cognitive impairment in HF showed a tendency of bias to physical changes in the body. Increased demands for mental effort and attention have not been addressed as a possible mechanism of attention impairment in the literature on HF. More efforts are needed to approach attention with diverse perspectives.

Attention impairment was more significant among patients with HF compared to healthy individuals and patients without HF. These findings are consistent with previous studies published before 2007 and provide solid support for the phenomenon that patients with HF are at higher risk of cognitive decline, including decline in attention. Unlike publications before 2007, studies about cognitive impairment placed more focus on multi-morbidity issue. In addition to HF pathophysiology, comorbidity such as hypertension, diabetes, and depression were found to worsen attention (Alosco et al., 2012a; Alosco et al., 2013a; Alosco et al., 2013d). Although the publications were from the same study, increased risk of attention impairment among HF patients with multiple medical conditions should receive more attention.

Factors that might be linked to attention were reviewed and these factors were older age, fewer years of education, female gender, employment status, unhealthy diet (e.g., high in sodium, fat), more severe HF (2-minute step test, NYHA class), and lower cognitive reserve. Education level has been traditionally investigated in cognitive research, but cognitive reserve that might serve as a buffer and protect against attention impairment was a new finding in studies with HF. Employment status may affect attention function because people who work regularly need to use their neural networks, and so have more preserved skills, but employment status may be the result of severe HF and significantly impaired attention. Patients with less severe HF can keep their work, thereby performing better on attention measures. Although direct relationships between attention and specific HF physical symptoms were not described in this review, NYHA class and physical inactivity (measured by the 2-minute Step Test) were correlated with attention. The results were consistent with theories in attention because individuals with HF are required to follow complex regimens that need more attention, paradoxically, decrease attention. The relationships between severity of HF and attention may provide information about target populations for interventions for future research.

Among these factors associated with attention impairment, certain factors, diagnosis of HF, age, gender, and education levels can rarely be changed. However, there is some evidence that attention can be improved. CRT effects on attention were found in the literature, but the attention improvement is a secondary benefit from CRT to stabilize heart function. In addition, not all HF patients are eligible for CRT. Therefore, more generalizable interventions that can be applied to larger HF population are needed. As we found from this review, cognitive training stimulating neuroplasticity (Pressler et al., 2011) and physical activity increasing systemic blood circulation (Carles et al., 2007) may help patients with HF to preserve their ability to attend and improve it.

More diverse approaches to improve attention based on different theoretical perspectives (e.g., attention restoration, cognitive training, and genetic approaches) are needed. There is another compelling intervention based on Attention Restoration Theory (Kaplan, 1995/2001), which contends that directed attention can be refreshed by resting the neural network while using involuntary attention. In other words, when people fully use their involuntary attention, their directed attention is not needed, meaning that directed attention can be in a resting state and has the chance to be restored. In contrast, when people use their directed attention continuously, their directed attention becomes fatigued. Interventions based on this theory were efficacious in improving attention in many populations such as children with attention deficit disorder, pregnant women (Kuo & Taylor, 2004; Stark & Cimprich, 2003; Taylor, Kuo, & Sullivan, 2001). However, no intervention studies have been located that were designed to improve attention in HF. As a basic process of cognition, attention shares some aspects of information processing with other impaired cognitive domains of memory and executive function. Thus, conducting an intervention to improve the HF patients' attention seems to be worthwhile.

There are several methodological concerns regarding attention research in HF. Cross-sectional, descriptive studies with small sample sizes, or no control groups were frequently found in the HF literature. Comparative studies have increased knowledge about HF patients who are at higher risk of attention impairment than healthy adults and patients with other medical conditions. However, attention as well as cognition varies across individuals, and cross-sectional studies may ignore individual differences in attention over time. Taken altogether, the results from this literature review indicate that intervention studies directly targeting attention are needed. Previous intervention studies using medical or non-medical treatments had small sample sizes (n = 10 to 27), and control groups or randomization were not used. A less powered sample size, and lack of control group and randomization weaknesses of these studies decrease the scientific quality of findings.

In addition to the study designs, there was inconsistent use of attention measures in the existing relevant literature. Without theoretical definitions on attention, multiple or different tests of attention have been used in many studies. However, administering multiple and different neuropsychological tests of attention without theoretical definitions may create challenges in the interpretation of results as well as hindering comparisons of the results between studies. The average number of tests administered in each study varied from one to four (mean = 2.4 tests). For example, if a study used 4 tests to examine attention and the results in each test were inconsistent, interpreting the results would be challenging. In addition, among those tests used in a study, which one is more sensitive to impaired attention or improved attention has not been examined. In other cases, only one test was used to measure both attention and other cognitive domains, such as memory, executive function, and psychomotor performance. Similar issues were found in studies that used the same neuropsychological tests but were described as targeting different cognitive domains. For example, one study used Trail Making Test A to examine attention (Alosco et al., 2011), but another study used the test to examine psychomotor speed. (Bauer et al., 2012) This may be inevitable because cognitive domains overlap. Therefore, theoretical perspective on attention and rationales on measurement selections need to be clear. Lastly, it remains unclear which criteria can define impaired or decreased attention in a way that is clinically important.

Studies on attention in HF were mostly biased towards administering neuropsychological tests to estimate attention. One neuroimaging study linking neuropsychological test data to brain structural changes and one blood perfusion test to explain cognition were found. However, studies addressing changes in brain activation among HF patients were not found.

Limitations of the Study

This study is limited to publications that used neuropsychological tests for cognition and excluded publications that only used screening measures. Screening measures for global cognition also raise a few questions for attention. Including the studies with cognitive screening measures may have helped to have more information about attention decrease in HF. However, results from screening measures rarely reported detailed scores of attention apart from the overall score, and thus, studies that used only cognitive screening were excluded from this study. Second, the review did not provide information about the threshold level of attention that is high enough to be effective in HF self-care. Many studies examined attention in HF compared to healthy adults with similar ages. However, attention in healthy adults also decreases with aging. Therefore, further consideration should be given to determining the best, or appropriate level of attention. Third, no genomic or genetic keywords related to HF were entered into the literature search (e.g., ApoE ε4, brain-derived neutrophic factor gene, or dopamine receptor D4 gene). One study by Vogels et al. (2007b), from the searched literature, addressed ApoE ε4 (Vogels et al., 2007b in its examination of the relationship between impaired cognition and the existence of ApoE ε4, with a finding that it was predictive of overall cognitive scores. Knowledge of genetics and genomics in HF related to cognition and attention is sparse so far. Future studies may need to examine the role of genetics or genomics on impaired attention among patients with HF.

Conclusion

Impaired attention is common in patients with HF, and may have a significant impact on their HF management. Domain-specific research that solely focused on attention has not been found in the HF literature. Having precise statements of theoretical perspectives on attention will help in the choice of appropriate measures of attention and interpretation of these measures. No intervention targeted to improve attention was found. The possible interventions that were suggested were physiological intervention by increasing blood perfusion, cognitive training based on neural plasticity, and attention restoration intervention by resting neural networks. Considering the physical limitations in HF and limited applications of medical treatments that have improved attention, an intervention based on Attention Restoration Theory is reasonable because it is safe and requires little physical effort, and has the potential to be widely disseminated.

Table 2.1. Definitions of Diverse Constructs of Attention and Associated Brain Areas

Aspects of attention	Definition	Related regions in the brain
Directed and Involuntary attention	Directed (voluntary) attention is a cognitive-control process that requires a great deal of mental effort to focus on the stimuli. Involuntary attention requires little or no mental effort to focus on the stimuli (James, 1890; Kaplan & Berman, 2010; R. Kaplan & S. Kaplan, 1983).	Directed attention: dorsal frontoparietal area (Parietal cortex and frontal eye field) Iinvoluntary attention: ventral frontoparietal area (temporoparietal junction and ventral fontal cortex) (Corbetta & Shulman, 2002).
Attentional network	The attentional network regulates various brain networks involved in maintaining the alert state, orienting, or regulation of conflict (Posner & Rothbart, 2007)	Alerting: locus coeruleus that is related to norepinephrine release and frontal and parietal cortex (Aston-Jones & Cohen, 2005; Morrison & Foote, 1986; Posner & Rothbart, 2007)
		Orienting: dorsal and ventral frontoparietal network (Corbetta & Shulman, 2002; Posner, 2011)
		Executive control: anterior cingulated cortex and lateral frontal areas (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Dosenbach et al., 2006; Petersen & Posner, 2012)
Sustained attention	Sustained attention is the ability to keep watching for targeted stimuli, which are unpredicted and less frequent, for a prolonged period of time while filtering out distracters (Sarter, Givens, & Bruno, 2001)	Anterior cingulated, dorsolateral prefrontal cortex, and parietal cortical regions (Lawrence, Ross, Hoffmann, Garavan, & Stein, 2003; Posner & Petersen, 1990)
Selective attention	Selective attention refers to differential processing of simultaneous sources of information (Johnston & Dark, 1986)	Sensory-related brain areas and frontal, parietal cortex (Driver, 2001; Kastner & Ungerleider, 2000)
Divided attention	Divided attention refers to the ability to allocate resources between different input stimuli by splitting or rapidly shifting the attentional focus (Parasuraman, 1998)	Similar with selective attention (prefrontal, posterior parietal, premotor cortical areas, and anterior cingulated cortex) (Hahn et al., 2008)
Attention switching	Attention switching is the ability to go back and forth between multiple tasks rapidly (Jersild, 1927; Monsell, 2003; White & Shah, 2006)	The left occipital, medial prefrontal cortex, left and right posterior intra-parietal sulcus, left and right anterior intra-parietal sulcus, and right premotor (Wager, Jonides, & Reading, 2004)

Table 2.2. Summary of Studies Examined Attention in Heart Failure (n = 26 studies)

Author, year	Purpose	Design	Sample	Cognitive domain	Neuropsychological tests	Theoretical definition of attention	Results related to attention
Alosco et al., 2011*	To confirm moderating effect of cognitive reserve on the relationship between HF severity and cognition	(Cross-sectional, secondary data analysis)	157 older HF patients	Attention	Trail Making Test A Digit Symbol Coding Letter Number Sequencing Adaptive Rate Continuous Performance Test Interstimulus Interval score	Not described	Cognitive reserve had moderating effect on the relationship between HF severity and cognitive function. Impairments in attention (27.4%), executive function (21.7%), memory (10.2), and language (8.3%) were found. HF severity that measure by 2-Minute Step Test was positively associated with attention, executive function, and language, but not memory.
				Cognitive reserve	American National Adult Reading Test		
				Executive function	Trail Making Test B Frontal Assessment Battery		
				Memory	California Verbal Learning Test-II (total learning, short delay free recall, long delay free recall, and total hits)		
				Language	Boston Naming Test Animal Fluency		
Alosco et al., 2012a*	To investigate predictive ability of hypertension on cognitive function in HF	(Descriptive), Secondary data analysis	116 HF patients (NYHA class II - III)	Attention/executive function/psychomotor speed	Trail Making Test A and B Digit Symbol Coding Letter Number Sequencing	Not described	Patients with both HF and hypertension (69.8%) showed lower cognitive function in domains of attention, executive function, psychomotor speed and motor functioning compared to those who do not have hypertension. Attention impairment was found in 9.5% of participants, memory impairment was 10.3%, and motor functioning
				Memory	California Verbal Learning Test-II		
				Language	Boston Naming Test Animal Fluency		
				Motor	Grooved Pegboard dominant and non-dominant hand		

							impairment was 34.5%. More years of education and ACE inhibitor medication use were predictive of better attention/executive/psychomotor function.
Alosco et al., 2012b*	To investigate cognitive function as a predictor of IADL	Retrospective observational	122 older HF patients	Attention, visual scanning, and psychomotor speed	Trail Making Test A	Not described	Patients with HF needed assistance in several IADL in terms of laundry (37.7%), housekeeping (34.4%), food preparation (31.3%), shopping (26.2%), finance (12.3%), medication management (7.3%), and driving (5.7%). Higher scores on Trail Making Test A and MMSE were predictive of medication and driving, respectively.
				Global cognition	MMSE		
				Executive function	Trail Making Test B		
Alosco et al., 2012c*	To examine the relationship between cognitive impairment and self-care adherence in HF	Descriptive, secondary data analysis	149 HF patients (NYHA class II - III)	Attention	Trail Making Test A Digit Symbol Coding	Not described	16.1% of HF patients did not adhere to HF self-care, and mostly for dietary and exercise regimen. Patients with lower attention and executive function were more likely to have lower adherence to the self-care.
				Executive function	Trail Making Test B Letter Number Sequencing Stroop Color Word Inference Effect		
				Memory	California Verbal Learning Test-II		
				Language	Boston Naming Test Animal Fluency		
Alosco et al., 2013a*	To examine the effects of Type II diabetes on the brain volume and cognitive function	Descriptive, secondary data analysis (MRI)	75 HF patients (NYHA class II - III)	Global cognition	MMSE	Not described	Patients with both HF and type II diabetes (30%) had smaller brain size and gray matter volume compared to the patients who did not have
				Attention/executive function/psych	Trail Making Test A and B		

	in HF			omotor speed	Digit Symbol Coding Letter Number Sequencing		diabetes. White matter did not differ between the groups. Smaller brain size, gray matter volume, and less white matter hyperintensity were predictive of lower function of global cognition, attention, executive function, and memory.
				Memory	California Verbal Learning Test-II		
				Language	Boston Naming Test Animal Fluency		
				Motor	Grooved Pegboard dominant and non-dominant hand		
Alosco et al., 2013b*	To examine moderating effects of dietary habit on the relationship between HF severity and cognitive function in HF	Descriptive, secondary data analysis	152 HF patients (NYHA class II - III)	Global cognition	The Modified Mini Mental State Examination (3MS)	Not described	Poor dietary habits and HF severity measured by 2-minute step test (2MST) were associated with worse attention/executive function after controlling covariates. The interaction between dietary habit and 2MST was significant predicting attention/executive function. Patients with poor dietary habits were more likely to have worse quality life and more depressive symptoms.
				Attention/ Executive function	Trail Making Test A Digit Symbol Coding Trail Making Test B Letter Number Sequencing Stroop Color Word Inference Effect		
				Memory	California Verbal Learning Test-II		
				Language	Boston Naming Test Animal Fluency		
Alosco et al., 2013c*	To examine moderating effects of cerebral perfusion between depressive symptom and cognitive function in HF	Descriptive, secondary data analysis (TCD ultrasonography)	89 HF patients (NYHA class II - III)	Global cognition	The Modified Mini Mental State Examination (3MS)	Not described	Depressive symptom was prevalent (84.3%) and correlated with cerebral blood flow velocity in the middle cerebral artery. Decreased global cerebral blood flow velocity was associated with worse attention, executive function and memory. The interaction between
				Attention/ Executive function	Trail Making Test A Digit Symbol Coding Trail Making Test B Letter Number Sequencing Frontal Assessment Battery		
				Memory	California Verbal Learning Test-II		
				Language	Boston Naming Test Animal Fluency		

				Motor speed and dexterity	Grooved Pegboard dominant and non-dominant hand		depressive symptom and global cerebral blood flow velocity was significant in predicting attention/executive function.
Alosco et al., 2013d*	To examine mediating effects of reduced cardiovascular fitness between depression and cognitive dysfunction	(Cross-sectional, secondary data analysis)	158 HF patients (NYHA class II - III)	Attention/complex visual scanning/psychomotor speed	Trail Making Test A	Not described	From structural equation modeling analyses, depression has significant direct pathway to cognitive function (all tests except animal fluency test), and indirect pathway thorough cardiovascular fitness measured by 2-minute step test. Exercise adherence did not have direct pathway to cognitive function.
				Executive function/cognitive set switching	Trail Making Test B		
				Executive function	Frontal Assessment Battery		
				Memory	California Verbal Learning Test-II		
				Language	Animal Fluency Test		
Alosco et al., 2014*	To examine the relationship between executive function and IADL and unhealthy lifestyle	Descriptive, secondary data analysis	174 HF patients (NYHA class II - III)	Executive function	Frontal Assessment Battery Letter Number Sequencing	Not described	No association was found between IADL and attention/psychomotor speed, memory, and language. Executive function was associated with total IADL score, and specifically, food preparation, housekeeping, laundry, and medication management in an item analysis.
				Attention/psychomotor speed	Digit Symbol Coding		
				Memory	Complex Figure Test		
				Language	Animal Fluency Test		
Bauer et al,. 2012	To evaluate psychometric properties of RBANS in chronic HF	Psychometric test	80 stable HF patients	Attention	RBANS Attention Index	Not described	Compared to normative data, patients with HF showed lower attention, immediate and delayed memory, executive function,
				Global cognition	RBANS Total Scale		
				Immediate memory	RBANS Immediate Memory		

				Delayed memory	RBANS Delayed Memory		psychomotor speed, and language scores. NYHA classes showed negative correlations with attention, psychomotor speed, executive function, and global cognition. Other clinical characteristics such as sleep disturbance, physical activity function, depressive symptoms were not correlated. Concurrent and convergent validities, and reliability among a subsample of 21 HF patients were acceptable.
				Visual/Constructional domain	RBANS Visual/Constructional Index		
				Language	RBANS Language Index		
				Executive function	Trail Making Test B Letter Fluency "D"		
				Psychomotor speed	Trail Making Test A		
Bauer & Pozehl, 2011	To test feasibility of a brief neuropsychological battery measuring all 6 cognitive domains in HF	Descriptive feasibility study of a brief neuropsychological battery, part of a larger study	26 community-dwelling CHF patients	Attention	RBANS Attention Index	Domain function of attention was described as 'allows individual to focus on information for further processing'	Cognitive impairment (Z score < -1.5) was found in the domains of executive function (54%), immediate memory (35%), attention (27%), and delayed memory (23%). The battery was described appropriate length, not tired, and enjoyable. All 26 participants completed the battery, and mean average time taken was 38 ± 6.5 minutes (range = 25 – 50 minutes). Finger Tapping Test for psychomotor speed could not be performed due to medical condition such as arthritis, thus, substituted to
				Working memory	Trail Making Test B		
				Immediate memory	RBANS Immediate Memory		
				Delayed memory	RBANS Delayed Memory		
				Learning	RBANS List Learning		
				Executive function	Letter Fluency "D"		
				Psychomotor speed	Finger Tapping Test Trail Making Test A		
					From CAMCOG (Cambridge Examination for Mental Disorders of the Elderly) section B		

							Trail Making Test A.
Bratzke-Bauer et al., 2013	To compare cognitive profiles between systolic and diastolic HF patients	Prospective, descriptive design	47 systolic and 33 diastolic HF patients	Attention Immediate memory Delayed memory Visual/spatial construction Language	RBANS	Not described	Patients with systolic HF had worse memory function compared to diastolic HF patients, but not for visuospatial skills, letter fluency. Mixed results were shown in attention and language domains. Simple attention tests (Trail Making Test A, Digit Span Forward) did not show different results, but patients with systolic HF had worse scores on the complex attention test (Trail Making Test B).
				Processing speed and switching	Trail Making Test A, B		
				Global cognition	MMSE		
Conti & Sears, 2007[§]	To examine the effects of cardiac resynchronization therapy (CRT) on attention and cognition	Pre-post experimental (Quasi-experimental)	10 HF patients with CRT	Attention	Digit Span Subtest of WAIS-III	Not described	3-month after the CRT treatment, attention and processing speed significantly improved compared to before CRT, but memory. Quality of life also improved at 3-month follow-up of CRT. Depression, measured by CES-D, did not change.
				Verbal memory	Hopkins Verbal Learning Test		
				Processing speed	Symbol Digit Modalities Subtest of WAIS-III		
Dickson, Deatrick, & Riegel, 2008	To explore the influence of attitudes, self-efficacy, and cognitive function on self-care decision making	Mixed method	41 CHF patients	Attention, psychomotor performance, ability to remember and operate using complex	Digit Symbol Substitution Task	Not described	Three typology of self-care were found: experts, novices, and inconsistent. 71% were inconsistent in self-care with many barriers to self-care and negative attitudes.

	process			symbols			46.3% had impaired memory and 75.6% had impaired working memory. Working memory performance was different between the 3 groups, and Digit Symbol Substitution Task scores were significantly lower in the inconsistent group than in expert and novice groups.
				Attention, memory, and executive function (working memory)	Letter-Number Sequencing task		
				Memory	Probed Memory Recall test		
Dickson, McCauley, & Riegel, 2008	To explore the influence of attitude, self-efficacy, cognitive function, and physical function on self-care management among employed HF patients	Mixed method	41 CHF patients	Attention, psychomotor performance, ability to remember and operate using complex symbols	Digit Symbol Substitution Task	Not described	20 patients were employed. Unemployed patients had more impairment in psychomotor performance and memory (14% and 52.4%, respectively) than employed patients (0% and 40%, respectively). 16 patients (80%) employed showed poorer self-care than those unemployed.
				Attention, memory, and executive function (working memory)	Letter-Number Sequencing task		
				Memory	Probed Memory Recall test		
Dixit et al., 2010[§]	To examine changes in attention, cognition, and quality of life before and after CRT	Prospective, pre-post (extension of a study by Conti & Sears (2007) in a bigger sample size) (Quasi-	20 CHF patients	Attention	Digit Span Trail Making Test A	Not described	3-month after CRT, attention (only Digit Span test), processing speed, and langue increased. Quality of life, measured LHFQ and LVD-36, was improved, but depression and
				Executive function	Trail Making Test B		
				Processing speed	Digit Symbol test		
				Declarative	Hopkins Verbal Learning		

		experimental)		memory	Test-revised		anxiety were not significantly changed during the follow-up.
				Language	Controlled Oral Word Association test		
Festa et al., 2011	To examine the associations among age, LVEF, and memory function	Retrospective	207 end-stage HF patients	Attention	Digit Span Trail Making Test A	Not described	Age and LVEF were correlated with composite memory scores. In multivariate analysis, interaction between age and LVEF was predictive of verbal memory. For, patient with 63 years or older, lower LVEF was related to worse verbal memory, but not in patients with younger than 63. Lower attention and executive function were associated with lower memory.
				Verbal memory	Hopkins Verbal Learning Test		
				Visual memory	Brief Visuospatial Memory Test-Revised		
				Executive function	Trail Making Test B Controlled Oral Word Association test		
Foster et al., 2011	To describe perceived participation level (instrumental, leisure, and social activities), and to examine the relationships among cognition, depression, and participation level	Descriptive, correlational	27 CHF, NYHA class III and IV	Attention	Digit Span Digit Symbol	Not described	59% had impaired memory, 33% had impaired executive functioning, and 15% had impaired attention. Worse executive dysfunction and depressive symptoms were associated with reduced participation.
				Verbal memory	Logical Memory Immediate and Delayed recall (LM I and II) test		
				Executive functioning	Letter Fluency and Category Fluency tests Dysexecutive Questionnaire		
Hoth et al., 2010	To investigate the relationship between improved LVEF after CRT and cognition	Controlled intervention (Quasi-experimental)	27 HF patients (NYHA class > II)	Attention	RBANS	Not described	17 patients (63%) had improved LVEF after CRT. Cognitive performance was not significantly changed after 3-month after CRT in t-
				Global cognition			
				Immediate memory			

				Delayed memory			test of overall sample. In repeated measure MANOVA, significant improvement of executive functioning and visuospatial skills and less decline in global cognition were experienced in LVEF increase group compared to no LVEF increase group.
				Language			
				Visuospatial/ constructional			
				Executive functioning	Average score of RBANS Trail Making Test B Controlled Oral Word Association test		
Hoth et al., 2008	To compare cognition between HF and non-HF cardiac disease patients, and to investigate the relationship between cognition and heart function (LVEF and cardiac index)	Comparative, correlational	31 HF (NYHA class > II, LVEF < 40%) and 31 age- and education-matched cardiac patients without HF as a control	Attention	RBANS	Not described	Executive functioning and psychomotor speed were worse in HF group than non-HF cardiac disease group. Among HF patients, LVEF was associated with global cognition, attention, and 2 measures of executive functioning and psychomotor speed. Cardiac index was associated with immediate memory.
				Global cognition			
				Immediate memory			
				Delayed memory			
				Language			
				Visuospatial/constructional			
				Executive function and psychomotor speed	Trail Making Test A and B Letter Number Sequencing (WAIS-III) Controlled Oral Word Association test Stroop Color Word test		
Miller et al., 2012	To investigate cognitive profiles in HF by using a cluster analytic approach and characterizing each profile	Longitudinal, secondary data analysis (cross-sectional data)	140 older HF patients from a outpatient clinic	Attention/executive function	Trail Making Test A & B Frontal Assessment Battery Letter-Number Sequencing Stroop Test	Not described	Within the domains of memory, naming, and attention/executive function, 3 cluster of intact, memory reduced, and globally impaired were suggested. Intact cluster had better global cognition and
				Global cognition	Modified Mini Mental Status Examination (3MS)		
				Memory	California Verbal Learning Test		

				Naming (verbal fluency and language)	Animal Naming Boston Naming Test		premorbid intelligence. Older age, female, and less education were shown in reduced memory and impaired clusters. Globally impaired cluster was likely to be hypertensive, worse in cardiovascular fitness test, and experience sleep apnea.
				Premorbid intelligence	North American Adult Reading Test		
Riegel et al., 2012a	To describe changes in cognition over time at baseline, 3 and 6 months	Prospective cohort	280 systolic and diastolic HF	Attention, simple	Psychomotor Vigilance Task	Not described	Growth mixture modeling showed 2 trajectories of DSST; smaller (averaging processing speed group) and larger (below average processing group). Factors increasing possibilities of being in a below average group were older age, male, non-White race, less education, higher ejection fraction, more comorbid status, more daytime sleepiness, and higher BMI scores.
				Attention, complex	Trail Making Test B		
				Processing and psychomotor speed	Digit Symbol Substitution Test (DSST)		
				Working memory	Probed Recall Memory Test		
				Short-term memory	Letter Number Sequencing test		
				Premorbid intellect	American National Adult Reading Test		
Riegel et al., 2012b	To examine excessive daytime sleepiness (EDS) and cognitive impairment as predictors of HRQL.	Prospective cohort, comparative	280 symptomatic (currently or previously) HF patients	Attention, simple	Psychomotor Vigilance Task	Not described	HRQL improved over 6 moths follow-up with no intervention. Cognitively impaired cohort was more likely to be older, non-white, less educated, and not employed. Perceived health was found highest in cohort with EDS and no impaired cognition.
				Attention, complex	Trail Making Test B		
				Processing and psychomotor speed	Digit Symbol Substitution Test		
				Working memory	Probed Recall Memory Test		
				Short-term	Letter Number Sequencing		

				memory	test		HRQL was lowest in cohort with EDS and impaired cognition.
Sauvé et al., 2009	To describe cognitive impairment (prevalence, type severity) in HF compared to healthy people.	Case controlled	50 HF and 50 matched healthy control	Attention	Symbol Digit Modalities Test Visual Scanning Test	Working definition of attention as 'complex function, including sustained concentration, working memory, and motor responses'	23 patients with HF (46%) had impaired cognition. HF patients were 4 times more likely to be impaired in cognition than healthy control. Memory was most frequently impaired, and attention, problem solving (executive function), motor performance followed. Poor attention function was associated with being female, more severe HF, and estimated IQ. Severity of cognitive impairment was associated with depressed learning curve and MI history, but no associated was found with emotional status (anxiety, depression, and positive affect).
				Orientation	Neurobehavioral Cognitive Status Examination, subscale for orientation		
				Memory	Rey Auditory Verbal Learning Test Memory Scanning Test		
				Executive function	Neurobehavioral Cognitive Status Examination, subscale for executive function Controlled Oral Word Association Test		
				Motor performance	Finger Tapping Test		
				Estimated IQ	WAIS-R Vocabulary subtest		
Vogels et al., 2007a	To examine relationship between cognitive neuropsychological performance and cerebral abnormalities detected by MRI	Cross-sectional, correlational	58 stable HF patients (NYHA classes II - IV)	Attention/ mental speed	Stroop Test Trail Making Test A	Not described	Neuropsychological tests were administered before MRI. Medial temporal lobe atrophy was negatively associated with memory, executive function, and global cognition, but not with attention. In a regression analysis, medial temporal lobe atrophy, age, and
				Memory	Rey Auditory Verbal Learning Test Digit Span Pattern Recognition		
				Executive function	Intra-Extra Dimensional Set Shift Stocking of Cambridge Trail Making Test B		
				Language	Letter Fluency and		

					Categorical Fluency		premorbid intelligence were predictive of cognitive performance. White matter and deep white matter hyperintensities were not correlated with cognition, but depression and anxiety.
				Visuospatial function	Fragmented Line Drawings and object recognition		
				Overall cognition	MMSE		
				Premorbid intelligence	Dutch versicon of the National Adult Reading Test		
Vogels et al., 2007b	To describe the profile of cognitive dysfunction in HF compared with people with other cardiovascular disease and healthy people, and to examine relationships with patients' demographic and clinical characteristics	Case-controlled	62 HF patients (NYHA II – IV, aged over 50, LVEF ≤ 40%), 53 age-matched patients with cardiovascular disease (no HF), and 42 age-matched healthy controls, a total of 157 participants	Attention/ mental speed and	Stroop Test Trail Making Test A Memory from Cambridge Neuropsychological Test Automated Battery	Not described	Cognitive impairment was more prevalent in patients with HF (25%) compared to cardiac control (15%) and healthy controls (4%). Executive function, memory, language, mental speed, and attention were decreased in HF. Predictors of cognitive impairment were lower premorbid intelligence, higher HF severity, and having ApoE ε4.
				Executive Function	Intra-Extra Dimensional Set Shift Stocking of Cambridge Trail Making Test B		
				Visuospatial function	Fragmented Line Drawings MMSE subscore of visual figure copy		
				Language	Letter Fluency and Categorical Fluency MMSE subscore of naming, reading and writing		
				Memory	Rey Auditory Verbal Learning Test Digit Span Pattern Recognition		
				Overall cognition	MMSE		
				Premorbid intelligence	Dutch version of the National Adult Reading Test		

Note: ApoE = Apolipoprotein E; BMI = body mass index; CES-D = Center for Epidemiologic Studies Depression Scale; CHF = chronic heart failure; COG = Cognitive Solicitation; CRT = cardiac resynchronization therapy; HF = heart failure; IADL = instrumental activities of daily living; IQ = intelligence quotient; LVAD = left ventricular assist devices; LEVF = left ventricular ejection fraction; LVD-36 = Left Ventricular Dysfunction Questionnaire; MANOVA = multivariate analysis of variance; MI = myocardial infarction; MMSE = Mini-Mental State Examination; MRI = magnetic resonance imaging; NYHA = New York Heart Association; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status.

* , § = each symbol represents publications from the same study

Table 2.3. Summary of Neuropsychological Tests for Attention Used in Heart Failure (n = 26 studies)

Neuropsychological tests	Constructs of attention (related cognitive domain)	Number of publications	Time to finish	Rating / Interpretation	Reliability	Validity
Trail Making Test A	Sustained attention (processing speed)	14 Alosco et al., 2011; Alosco et al.,2012a; Alosco et al., 2012b; Alosco et al.,2012c; Alosco et al.,2012c; Alosco et al.,2013a; Alosco et al.,2013b; Alosco et al.,2013c; Alosco et al.,2013d; Dixit et al., 2010; Festa et al., 2011; Miller et al., 2012; Vogel et al., 2007a; Vogel et al., 2007b	5 minutes*	• Raw score (Alosco et al., 2011; Alosco et al.,2013a) • t-score (Alosco et al., 2012a; Alosco et al., 2012b; Alosco et al.,2012c; Alosco et al.,2013b; Alosco et al.,2013c; Alosco et al.,2013d; Dixit et al., 2010; Miller et al., 2012). • z-score (Alosco et al., 2012; Festa et al. 2011) • Mean overall cognitive z-score (Vogelt et al. 2007b) • Mean overall cognitive z-score and a cutoff z-score defining cognitive impairment (-0.45) (Vogels et al., 2007a)	Not described	Not described
Digit Symbol Coding (Substitution Test)	Possibly sustained attention based on interpretation methods (Psychomotor speed)	10 Alosco et al., 2011; Alosco et al.,2012a; Alosco et al.,2012c; Alosco et al.,2013a; Alosco et al.,2013b; Alosco et al.,2013c; Alosco et al.,2014; Dickson, Deatrick, & Riegel, 2008;	90 seconds* 120 seconds*	• Raw score (Alosco et al.,2013a; Dickson, Deatrick, & Riegel, 2008; Dickson, McCauley, & Riegel, 2008) • Composite index scores with another measure of attention in a study, and a cutoff score below 7 defined attention impairment (Foster et al., 2011) • t-score (Alosco et al., 2012a;	Test-retest reliability was .86 (Dickson, Deatrick, & Riegel, 2008; Dickson, McCauley, &	Not described

		Dickson, McCauley, & Riegel, 2008; Foster et al., 2011		Alosco et al.,2012c; Alosco et al.,2013b; Alosco et al.,2013c; Alosco et al.,2014) • z-score (Alosco et al., 2011)	Riegel, 2008)	
Letter Number Sequencing	Sustained attention (working memory)	8 Alosco et al., 2011; Alosco et al.,2012a; Alosco et al.,2013a; Alosco et al.,2013b; Alosco et al.,2013c; Dickson, Deatrick, & Riegel, 2008; Dickson, McCauley, & Riegel, 2008; Miller et al., 2012	Not described	• Raw score (Alosco et al.,2013a; Dickson, Deatrick, & Riegel, 2008; Dickson, McCauley, & Riegel, 2008) • t-score (Alosco et al., 2011; Alosco et al., 2012a; Alosco et al.,2013b; Alosco et al.,2013c; Miller et al., 2012) • z-score (Alosco et al., 2011)	Test-retest reliability was .73 - .77 in middle-age elderly. (Dickson, Deatrick, & Riegel, 2008; Dickson, McCauley , & Riegel, 2008)	Not described
Trail Making Test B	Attentional switching, directed attention, sustained attention (cognitive flexibility)	6 Alosco et al.,2012a; Alosco et al.,2013a; Alosco et al.,2013b; Alosco et al.,2013c; Riegel et al., 2012a; Riegel et al., 2012b	5 minutes*	• Raw score (completion time) (Reigel et al., 2012a) • Raw scores worse than age-corrected norm was counted to define cognitive impairment (Riegel et al., 2012b). • t-score (Alosco et al.,2013b; Alosco et al.,2013c;	Not described	Not described

RBANS Attention Index (Digit Span and Coding)	Sustained attention (working memory and processing speed)	5 Bauer et al., 2012; Bauer & Pozehl, 2011; Bratzke-Bauer et al., 2013; Hoth et al., 2008; Hoth et al., 2010	20 – 30 minutes for the 12 RBANS subsets.	• Raw score (Bauer et al., 2012) • Standardized index score with mean of 100, and standard deviation of 15 (Bratzke-Bauer et al., 2013; Hoth et al., 2010) • z-score (Bauer et al., 2012; Bauer & Pozehl, 2011; Hoth et al., 2008)	Test-retest reliability was reported as acceptable (r = .73) (Bauer et al., 2012) Good reliability with references (Bratzke-Bauer et al., 2013)	Concurrent validity was reported as acceptable. (Bauer et al., 2012) Good vaidity with references (Bratzke-Bauer et al., 2013)
Digit Span Test	Sustained attention (working memory and executive function)	4 Conti & Sears, 2007; Dixit et al., 2010; Festa et al., 2011; Foster et al., 2011	5 minutes	• Composite index score with another measure of attention in a study, and a cutoff score below 7 defined attention impairment (Foster et al., 2011) • t-score (Conti & Sears, 2007; Dixit et al., 2010) • z-score (Festa et al. 2011)	Not described	Not described
Stroop Test	Selective – focused-attention, directed attention (executive function)	4 Alosco et al.,2013b; Miller et al., 2012; Vogel et al., 2007a; Vogel et al., 2007b	Not described	• t-score (Alosco et al.,2013b; Miller et al., 2012) • Mean overall cognitive z-scores (Vogels et al., 2007b) • Mean overall cognitive z-scores and a cutoff z-score defining cognitive impairment (-0.45)	Not described	Validity of the tests was reported as satisfactory (Vogels et al., 2007b)

				(Vogels et al., 2007a)		
Psychomotor Vigilance Task	Sustained attention, especially in research on sleep	2 Riegel et al., 2012a; Riegel et al., 2012b	Not described	• Raw score (Alosco et al.,2013a; Reigel et al., 2012a) • Raw scores worse than age-corrected norm were counted to define cognitive impairment (Riegel et al., 2012b).	Not described	Not described
Frontal Assessment Battery	(Executive function)	2 Alosco et al.,2013c; Miller et al., 2012	Not described	• t-score	Not described	Not described
Adaptive Rate Continuous Performance Test	Sustained attention	1 Alosco et al., 2012b	Not described	• t-score and z-score	Not described	Not described
Symbol Digit Modalities Test	Possibly sustained attention (Psychomotor speed)	1 Sauvé et al., 2009	90 seconds*	• t-score	Not described	Not described
Visual Scanning Test	Possibly selective visual attention, involuntary attention (Perception)	1 Sauvé et al., 2009	Not described	• t-score	Not described	Not described

Note: RBANS = Repeatable Battery for the Assessment of Neurocognitive Status.

* Timed test.

Table 2.4. Summary of studies that Used Neuropsychological Tests that measure Attention but Not Described Attention (n = 8 studies)

Author and year	Purpose	Design	Participants	Cognitive domain	Cognition measures	Attention tests	Findings
Carles et al., 2007	To examine the effects of 2-week exercise training on cognition in terms of acute exercise and aerobic physical training.	Pre-post	24 male CAD (n = 12) and HF (n = 12) patients in France	Information-processing	COG (mental arithmetic test, Trail Making Test, and 2 memory tests)	Trail Making Test	Cognition was measured four times at resting and exercising before and after the training program, and significant increases for COG were found at both states of resting and exercise before and after the training, but not for Tracking task. For Tracking task, significant improvement was only found at resting state after the training.
				Psychomotor (precision of movement)	Tracking task		
Hammers et al., 2012[a]	To examine the validity, stability, and sensitivity of the Cogstate International Shopping List test as a screening cognitive test in HF.	Longitudinal, secondary data analysis from MEMOIR study	17 HF patients	Global cognition	MMSE	Cogstate One Back Test and Identification test	Cogstate International Shopping List test was comparable to Hopkins Verbal Learning test which is a traditional neuropsychological test. Stability (test-retest reliabilities) of the test was adequate (r = .53 ~ .68). Predictability of the test on physical function measured by activities of daily living has been supported over 8 weeks (delayed recall, $\beta = .47$, $p < .001$). No differences on International Shopping List and Hopkins Verbal Learning Test results between patients with and without
				Memory	Hopkins Verbal Learning Test Cogstate International Shopping List test		
				Working memory	Cogstate One Back test Cogstate Identification test		
				Psychomotor speed	Cogstate Detection test		
				Executive function	Controlled Oral Word Association test		

							myocardial infarction.
Kindermann et al., 2012	To examine cognitive function among compensated and decompensated HF patients and healthy control, the effects of cardiac compensation on cognitive function, and risk factor of mortality and rehospitalization at 14-month follow-up.	Pre-test-treatment-post-test design	40 HF (NYHA class III and IV, 20 decompensated and 20 compensated) and 20 age- and gender-matched healthy controls in Germany; CogImpair-HF study	Short-term memory Working memory Episodic memory Executive control Speed Intelligence	Digit Span Forward test Digit Span Backward test Logical Memory Test II Stroop test Digit Symbol Substitution test Raven Standard Progressive Matrices	Digit Span Test and Stroop Test	Memory, processing speed, executive control, performance was worse in decompensated HF patients than stable HF and healthy controls. Fluid intelligence was not different between compensated and decompensated HF groups, but the patients group had poorer fluid intelligence than healthy control. Short-term, working, and episodic memory, processing speed, and executive control improved after compensation period in decompensated group but not stable group. No difference was found in fluid intelligence. Rehospitalization rates did not differ in HF patients groups, and the average was 2.16 ± 2. Ejection fraction was predictive of rehospitalization, and worse memory, processing speed, and executive control were related to more rehospitalization.
Petrucci et al., 2009[b]	To describe change in cognition after	Longitudinal, secondary data analysis	93 end-stage HF patients receiving	Visual spatial perception	Clock Drawing WAIS-III Block Design	Trail Making Test A and	In a paired analysis of neuropsychological tests at 1 to 3, and 1 to 6 months, visual memory

	left ventricular assist devices implantation.		LVAD implantation from 11 clinics	Memory	WAIS-II Logical Memory WAIS-II Visual Reproduction	B	and executive function improved in both follow-up periods. Among participants who completed all 3 time points, visual-spatial perception, executive function, and processing speed were significantly improved, and no significant decline was observed in all cognitive domains.
				Executive function	Trail Making Test B WAIS-III Digit Symbol		
				Language	Abbreviated Boston Naming Test		
				Processing speed	Trail Making Test A		
Petrucci et al., 2012[b]	To compare the impacts of continuous-flow versus pulsatile-flow LVAD on cognition among destination therapy HF patients	Sub-study from the HeartMate II DT Trial (neuropsychological tests at 1, 3, 6, 12, and 24 months after LVAD implantation)	126 HF patients(96 continuous and 30 pulsatile flow LVAD) from 12 clinics	Visual-spatial perception	Clock Drawing WAIS-III Block Design	Trail Making Test A and B	No significant deterioration in all 6 domains of cognition. Performance on Trail Making Test A and B was improved over time ($p < .0001$, $p = .006$, respectively), but no group effects were found on these tests. No difference in cognitive function between patients with continuous vs pulsatile LVAD implantation.
				Auditory memory	Wechsler Memory Scale (WMS)-III Logical Memory (modified)		
				Visual memory	WMS-III Visual Reproduction and delay		
				Executive function	Trail Making Test B WAIS-III Digit Symbol		
				Confrontational language	Abbreviated Boston Naming Test		
				Processing speed	Trail Making Test A		
Pressler et al., 2010a[c]	To investigate the relationship between cognitive deficit and HRQL in	Substudy of a larger comparative and explanatory study	249 HF patients (LVEF < 40%)	Global cognition	MMSE	Digit Span and Trail Making Test A and B	Psychomotor speed, working memory, and executive function were negatively correlated with HRQL. Patients with better HRQL were
				Premorbid intellect	Wechsler Test of Adult Reading		
				Language	Boston Naming Test		
				Working memory	Digit Span		

	HF and mediating effect of cognitive deficit between HF severity and HRQL.			Declarative verbal memory Visuospatial ability Psychomotor speed Executive function	Hopkins Verbal Learning Test Figure Copy, Figure Memory recall Digit Symbol, Trail Making Test A Trail Making Test B, Controlled Oral Word Association		more likely being older, less functionally limited and perceived more functional capacity, less depressive, and had more memory performance. No mediating effect of cognitive deficit in the relationship between HF severity and HRQL was found.
Pressler et al., 2010b[c]	To evaluate cognitive deficits in terms of type, frequency and severity compared to medical patients without HF and healthy controls, and the associations between HF severity, age, comorbidities and cognitive deficits.	Comparative design	249 HF, 102 medical patients, and 63 healthy participants, a total of 414.	Global cognition Premorbid intellect Language Working memory Declarative verbal memory Visuospatial ability Psychomotor speed Executive function	MMSE Wechsler Test of Adult Reading Boston Naming Test Digit Span Hopkins Verbal Learning Test Figure Copy, Figure Memory recall Digit Symbol, Trail Making Test A Trail Making Test B, Controlled Oral Word Association	Digit Span and Trail Making Test A and B	24% of HF patients had impaired cognition in 3 or more domains: verbal memory (23%), psychomotor speed (19%), and executive function (16-19%). HF patients showed more cognitive deficits than medical and healthy controls. Worse heart function was associated with poorer memory, visouspatial ability, psychomotor speed, and executive function. Being older was positively related with executive function, being male was negatively related with worse memory, psychomotor speed, and visuospatial memory. Comorbidity was not a factor explaining cognitive deficits.
Pressler et al.,	To examine cognitive	Pilot randomized	34 HF patients (17 for each	Memory (list learning and recall)	Hopkins Verbal Learning Test-	Cogstate One Back	Cognitive training, BrainFitness, was provided during 8 weeks (I

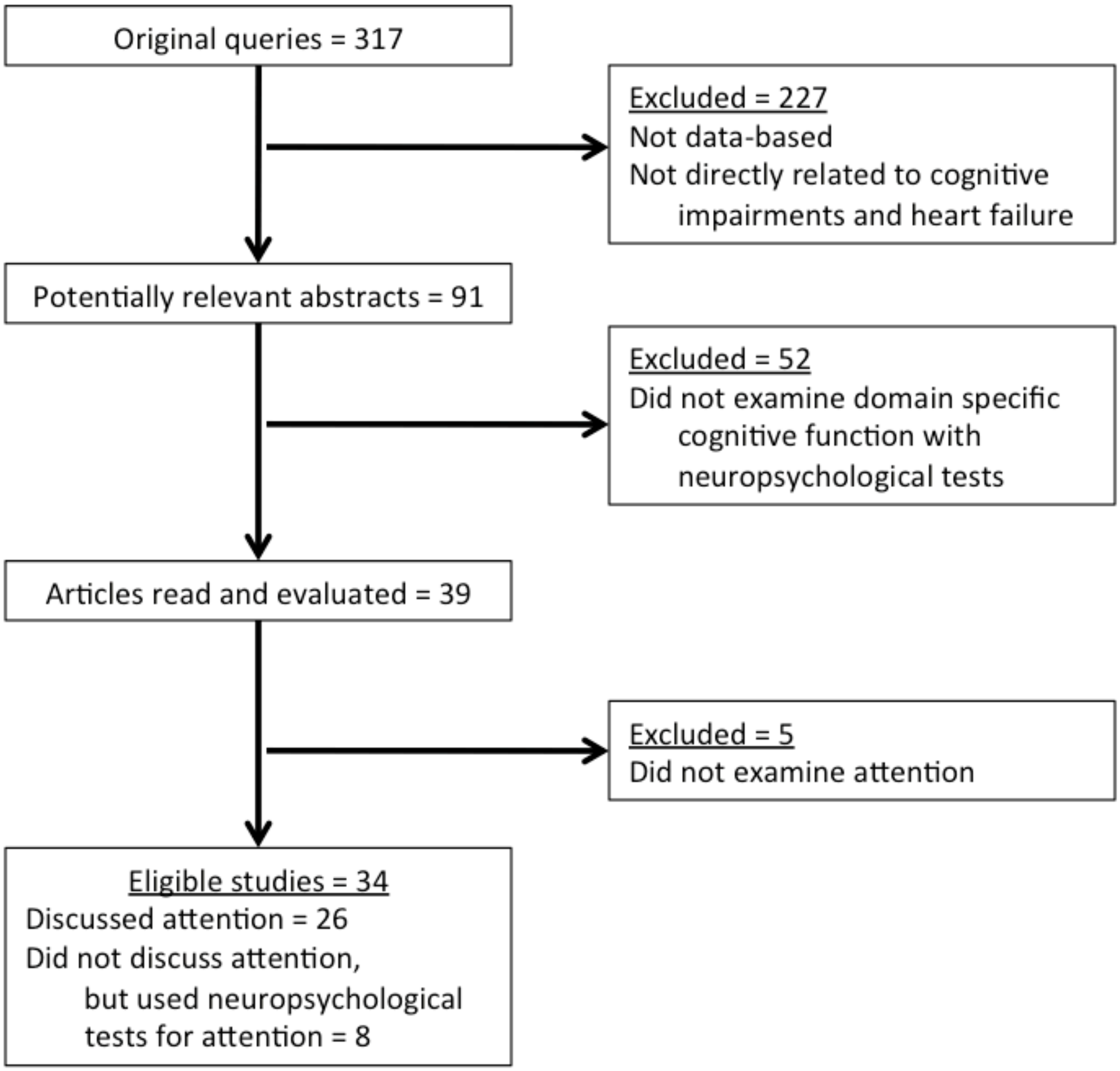
2011[a]	training intervention efficacy on cognition, primarily memory, and activities in HF.	controlled trial	intervention and control group)		Revised Cogstate International Shopping List	Test and Identificati on Test	hour per day, 5 days per week). HF patients in intervention group showed significantly better performance of delayed recall memory (p = .032) compared to control group (health education) over 12 weeks. Performance on list learning (P= .001), psychomotor speed (P = .029), and IADLs (P = .006) became better over time, but no group differences were found.
				Working memory	Cogstate Identification Cogstate One Back		
				Psychomotor speed	Digit Symbol Subtest of WAIS-III Cogstate Detection		
				Executive function (verbal fluency)	Controlled Oral Word Association Test		

Note. * Neuropsychological tests that measure attention

[a, b, c] Each symbol represents publications from the same study

COG = Cognitive Solicitation; HF = heart failure; IADL = instrumental activities of daily living; LVAD = left ventricular assist devices; LEVF = left ventricular ejection fraction; MMSE = Mini-Mental State Examination.

Figure 2.1. Literature Search Results



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Chapter 3

Improving Attention and Mood in Heart Failure: Natural Restorative Environment Intervention

Abstract

Background: Attention impairment in patients with heart failure (HF) can occur possibly due to lowered cerebral blood flow and increased mental effort from HF. However, no interventions were found that were conducted to improve attention in these patients. The primary aim of this study was to examine the efficacy of the natural restorative environment (NRE) intervention on attention compared with the active control condition in HF patients and healthy adults. The secondary aim was to examine its efficacy on mood. The influence of having HF and intervention preference on intervention efficacy was examined.

Methods/Results: A randomized crossover design was used in 20 HF patients and 20 age-, education-matched healthy adults. At baseline, HF patients had poorer attention, lower SpO_2, and greater mental effort related to chronic disease than healthy adults. Linear mixed models for the primary aim indicated that there was no significant difference in attention after the NRE intervention compared to the control condition in HF and healthy participants. Results of the secondary aim indicated that there was no significant difference in mood after the NRE intervention compared to the control condition in both groups. However, final linear mixed models, which were built with preference and group effects in a pooled sample with both HF and healthy participants, showed improved sustained attention after the NRE intervention compared to the control condition. Healthy participants better preserved their attention switching responding to the control condition than HF patients. Mood was unchanged after interventions. **Conclusions**: Preliminary support for the NRE intervention efficacy in improving attention was provided. Future studies on a larger scale providing knowledge about optimal intervention dose to improve attention are needed.

Keywords: psychophysiology; attention, heart failure, intervention studies, neuropsychological tests

Introduction

Heart failure (HF) is a detrimental and prevalent public health concern affecting 5.7 million adults in the United States (Mozaffarian et al., 2015). Although survival after HF diagnosis has improved, death and re-hospitalization rates remain high. Over 80% of HF patients are hospitalized at least once annually, 43% are hospitalized more than 4 times annually, and the mortality rate is 50% at five years after diagnosis (Mozaffarian et al., 2015). These serious consequences suggest that there are barriers to HF care including cognitive deficits (Nancy et al., 2015; Pressler et al., 2010c; Riegel et al., 2009), one of which is decreased attention (Dickson, Tkacs, & Riegel, 2007).

Cognitive Deficits in Heart Failure Cognitive deficits have been reported in 25% to 50% of HF patients, and impairments are often found in attention, memory, and executive function (Pressler, 2008). The reasons proposed for cognitive deficits in HF are inadequate cerebral perfusion associated with lowered cardiac output and impaired cerebral autoregulation and microemboli (Alosco et al., 2014; Alves, et al., 2005; Gottesman, et al., 2010; Jefferson, 2010; Jesus et al., 2006; Siachos et al., 2005). Structural brain changes have been documented in HF with brain imaging studies showing broad neurofiber injury (Kumar et al., 2011; Pan et al., 2012) in the hippocampus and prefrontal cortex (Pan et al., 2012; Pressler, 2008; Woo et al., 2009). Cognitive deficits have important implications in terms of self-care (Nancy et al., 2015; Riegel et al., 2009). The HF self-care regimen, which includes restricting dietary sodium intake and monitoring symptoms of dyspnea and fatigue, is so complex that the process of learning and applying self-care is not spontaneous and requires substantial cognitive effort every day (Moser & Watkins, 2008; Pressler et al., 2010b). Adherence to self-care regimens is low in almost a third of HF patients, and the adherence rate varied based on the self-care domain and the measurements (2% - 90%) (Cline et al., 1999; Riegel et al., 2009), Cognitively impaired patients may be at particular risk for not being able to adhere to self-care (Cameron et al., 2010; Dickson, Tkacs, & Riegel, 2007; Moser & Watkins, 2008; Riegel, Vaughan Dickson, Goldberg, & Deatrick, 2007; Sloan & Pressler, 2009) and thus at risk for higher mortality (Pressler et al., 2010a).

Decreased Attention in Heart Failure Attention is defined as "the regulating of various brain networks by attentional networks involved in maintaining the alert state, orienting, or regulation of conflict" (Posner & Rothbard, 2007, p2), and it serves as a basic set of mechanisms involved in perceiving the world and regulating our thoughts and feelings (Kaplan, 1995; Posner, 2004; Posner & Rothbard, 2007). Thus, attention is essential for performance of daily activities such as self-care (Posner & Rothbard, 2007; Tennessen & Cimprich, 1995). Despite the importance, attention has been reported as impaired, and 3 important factors of HF may be involved: pathophysiology of HF resulting in low blood and oxygen supply to the brain; HF symptoms distracting and interfering with patients' daily activities; and complex HF treatment. Specifically, the neural basis of attention is the prefrontal cortex (Posner & Rothbart, 2007) and this area has been reported as impaired among patients with HF (Kumar et al., 2011; Pan et al., 2012). Due to the symptomatology of HF and the complexity of the HF treatment regimen, increased demands for attention are placed on the very patients who may already have decreased attention (Bennett et al., 2000; Riegel et al., 2007). These increased attentional demands may deplete neural networks and lead to attentional fatigue manifested as decreased attention to concentrate on tasks (Pressler et al., 2010c; Tennessen & Cimprich, 1995).

Attention is one of the most commonly impaired cognitive domains in HF, occurring in 15% to 27.4% of HF patients (Jung et al., 2015). Compared with healthy and cardiac patients without HF, HF patients had significantly worse attention (Sauvé et al., 2009; Vogels et al., 2007). Clinical characteristics of HF related to decreased attention were lowered LVEF and increased HF severity (Alosco et al., 2011; Hoth et al., 2008; Jung et al., 2015). These findings were consistent with the results of a literature review of previous studies showing HF as a factor of cognitive impairment (Pressler et al., 2010c). Importantly, impaired attention was associated with poorer medication management and inconsistent self-care behaviors (Alosco et al., 2012; Dickson et al., 2007).

Despite the finding that decreased attention is documented in HF, there is a lack of knowledge about the specific aspects of attention that are decreased. Attention is a complex concept with several sub-domains, which include directed attention, sustained attention, attention switching, and selective attention (James, 1890). However, no studies investigated attention in detail to investigate which aspects of attention are more diminished in HF. Furthermore, the HF literature on decreased attention focused on physiological changes in the heart and the brain, and has not included increased attentional demands as a variable that would influence attention. Thus, attentional demands should be considered while discussing changes in attention in HF.

Moreover, no interventions directed at improving attention were found. There were some interventions to improve cognitive function in HF. Cardiac resynchronization therapy had some impact on attention improvement (Dixit et al., 2010; Hoth et al., 2010), but the treatment is applicable to only a limited number of HF patients and hard to be generalized. The MEMOIR studies, which targeted memory with computerized cognitive training, have shown some improvement in memory, working memory, and processing speed among HF patients, but not improvement in attention (Pressler et al., 2011; Pressler et al., 2015). The ACTIVE trial in healthy older adults found that the cognitive training delayed declines in reasoning and processing speed, but memory declined at 10-year follow-up (Rebok et al., 2014). These interventions were about training cognitive skills at their threshold and helping cognitive plasticity or neuroplasticity. Besides cognitive training, there is an attention intervention, called natural restorative environment intervention (NRE), based on a theory that has shown efficacy in improving attention even without any training.

Theoretical Background of Improving Attention The theoretical foundation of attention interventions can be found in the Attention Restoration Theory, in which increased exposure to nature is proposed to significantly decrease unnecessary use of attention and thereby refresh attentional resources and improve attention (Kaplan, 1995). In the theory, attention is conceptualized into two components: directed and involuntary attention. Directed attention is conceptually defined as a cognitive-control process that requires a great deal of mental effort to focus on something that is not particularly interesting by ignoring competing stimuli (James, 1890; Kaplan, 1995/2001). Directed attention, unlike other cognitive domains, is fragile and easily becomes fatigued (Kaplan, 1995). In contrast to directed attention, involuntary attention is conceptually defined as attention that is captured by intriguing or novel stimuli, such as moving objects and wild animals (James, 1890; Kaplan, 1995). Involuntary attention requires little or no mental effort to focus on stimuli and is never fatigued. The requirement of little or no mental effort is important because it serves as the basis for using involuntary attention as an intervention to restore attention by resting the neural network for directed attention (Kaplan, 1995; Kaplan & Berman, 2010).

In nature, individuals often feel comfortable and are able to rest because nature does not force individuals to use cognitive effort (Kaplan, 1995; R. Kaplan & S. Kaplan, 1989). Attention Restoration Theory posits that nature might be the best source for improving attention because nature contains four elements of attention restorative stimuli (Table 2.1): 1) a sense of being away from routine daily life; 2) "soft fascination", the term the theory uses for the attraction to the aesthetically pleasing qualities of nature that requires little or no effort; 3) extended feelings in a broader area, physically and conceptually; and 4) a sense of high compatibility, through which one functions at a higher level when in a desirable situation (Kaplan, 1995; R. Kaplan & S. Kaplan, 1989). Due to these elements in nature, attentional fatigue can be reduced and attention can be restored while interacting with nature (Kaplan, 1995). Overall, in Attention Restoration Theory, it is proposed that interactions with the natural environment can enhance subsequent performance on tasks that depend on attention function, specifically directed attention (Kaplan, 1995; R. Kaplan & S. Kaplan, 1989).

Based on Attention Restoration Theory, various formats of interventions using the natural environment have been tested and found to be efficacious in improving attention in diverse populations (Kaplan & Berman, 2010). For example, children with attention deficit hyperactivity disorder (n = 17) showed improved attention immediately after a 20-minute walk in the park compared to a 20-minute walk in a downtown area or a neighborhood (effect size Cohen's d = .52 and .77) (Faber Taylor & Kuo, 2009). Women with early breast cancer (n = 157) were randomly assigned to the intervention or control group before their scheduled breast cancer surgery. After the surgeries, women who participated in nature activities (e.g., gardening, walking) for 120 minutes per week showed more improved attention compared to women who did not participate in nature activity (n = 74) (Cimprich & Ronis, 2003). Another form of the nature intervention was conducted using a randomized cross-over design with university students (n = 12) to compare restorative effects of pictures of natural environments and urban environments (Berman, Jonides, & Kaplan, 2008). The authors found that viewing pictures of nature improved attention as well (Berman et al., 2008). The NRE interventions, overall, improved attention, but the studies had limitations in that, first, the optimal dose of the intervention was not explored, and, second, control groups were recruited from the same populations so that comparisons of intervention responsiveness between people with and without attention impairment was not examined.

Attention Restoration and Improved Mood. In addition to improved attention, improved mood was found in two NRE intervention studies (Berman et al., 2008; Berman et al., 2012). In a randomized cross-over study of 28 university students, students had increased positive mood after a 50-minute walk in a natural environment (arboretum in this study) compared to a 50-minute walk in the downtown area (Berman et al., 2008). The same intervention was conducted with 20 patients with major depression, and the patients' mood improved after a 50-minute walk in an arboretum compared to a 50-minute walk in downtown, which was a consistent result with the previous study (Berman et al., 2012). The studies did not find correlations between improvements in attention and mood, indicating that improved attention was not driven by mood. Instead, improved attention, which results from reducing attentional fatigue from the NRE interventions, may improve mood because decreased mood such as irritability and anxiety can be caused as symptoms of attentional fatigue (Kaplan, 1995). Therefore, the positive effects on mood from interactions with nature would be consequences of the interventions.

Mood is conceptually defined as an emotional state at any given time (Ekkekakis, 2013), and it has been shown that some impact on health behaviors may be due to disrupted attention focus or arousal (Salovey & Birnbaum, 1989). In HF, depressed mood and anxiety were most investigated in the relationship with health outcomes such as functional status, mortality, and quality of life (MacMahon & Lip, 2002). Another line of investigation is the impact of positive mood on inflammatory biomarkers and compliance with self-care (Brouwers et al., 2013; Kessing, Pelle, Kupper Szabó, & Denollet, 2014). Relationships between mood and attention and/or attentional fatigue have not been investigated in HF.

In summary, decreased attention and mood are common in HF patients. Past studies were limited by a lack of focus on sub-domains of attention, and interventions directly targeted to improved attention were not reported in HF. The NRE intervention can be widely disseminated at low cost, and it is safe and has been efficacious in many populations in improving attention, as discussed earlier. Improved attention may have a positive impact on HF self-care activities, such as medication management, for example. However, the efficacy of the NRE intervention in improving attention and mood among HF patients has not been tested.

The primary aim of this randomized cross-over study was to examine the efficacy of the theory-based natural restorative environment (NRE) intervention compared with the urban environment control condition on attention in HF patients and healthy age- and education-matched adults. The secondary aim was to examine its efficacy on mood. The four hypotheses were: 1) HF patients have greater improvement in attention after NRE intervention compared to the urban control condition; 2) HF patients have greater improvement in mood after NRE intervention compared to the urban control condition; 3) healthy participants have greater improvement in attention after NRE intervention compared to the urban control condition; and 4) healthy participants have greater improvement in mood after NRE intervention compared to the urban control condition. Two research questions were addressed to further examine the efficacy: 1) does the individual's preference (how much the participant likes the pictures that are used for each intervention) affect the efficacy of the NRE intervention?; and 2) is the amount of attention improvement after NRE intervention in HF patients different from the amount of attention improvement in healthy participants?

Methods

Design and Procedures

A randomized crossover design (within-subject, 2-treatments, 4-observations) was used to examine intervention efficacy in HF patients and age- and education-matched healthy adults. Data collection was conducted at participants' homes or a mutually agreed upon place (e.g., a research office at the school or hospital). A 1:1 ratio randomization was utilized based on a computer-generated random list, and the allocation sequence was enclosed in an envelope with study identification numbers. After the written informed consent was obtained, participants completed baseline surveys and tests and the envelope with the allocation sequence was opened. The tester in each research visit was blinded to the random group sequence, and only the interventionist knew the sequence. Although blinding was difficult to achieve for 4 patients because those participants talked about the pictures during tests and the tester overheard their comments, they were retained in the study. This study was approved by the Institutional Review Board at the University of Michigan, and all participants provided written consents.

Sample

From April 2014 to May 2015, 48 participants (27 HF, 21 healthy) were recruited from a cardiology outpatient clinic and a university research recruiting registry, and 40 completed the study (20 HF, 20 healthy). The sample size of 20 for each group was calculated from a previous study in which the same intervention was tested among university students (Berman, et al., 2008). Patients with HF were recruited first, and healthy participants recruited later to match age and education years to the HF participants.

Inclusion criteria for HF participants were: 1) adults over 21 years old; 2) diagnosed with HF by echocardiography, nuclear imaging, or cardiac catheterization; and 3) able to read and hear the English language. Inclusion criteria for healthy adults were the same except for the diagnosis of HF. Exclusion criteria for both groups were: 1) having conditions known to be related to cognitive or attention deficits such as a history of dementia, stroke in the past 5 years, major neurological and psychiatric disorders (amnesia, schizophrenia, or major depression), or attention deficit and hyperactivity disorder (ADHD); 2) uncorrected visual impairment; 3) color blindness; and 4) a Mini-Mental State Exam (MMSE) score less than 24 in order to screen cognitive deficits including possible dementia (cutoff point of 22 for participants with less than 9th grade education) (M. Folstein, S. Folstein, & McHugh, 1975; Tombaugh, McDowell, Kristjansson, & Hubley, 1996).

Interventions

Natural restorative environment intervention. The NRE intervention consisted of 50 photographs of nature (scenery of Nova Scotia with sea, woods, mountains, rocks, and flowers) that have been tested and were efficacious in improving attention and mood in healthy undergraduate students in a study by Berman et al (Berman et al., 2008). Each photograph was displayed once for 7 seconds on a laptop computer screen, and, to assess their preference, participants rated each picture on a scale of 1 to 3, indicating how much they liked each one.

Active control condition. The active control intervention consisted of 50 photographs of urban views from 3 cities in the Midwest. The photographs of urban areas were of buildings, streets with cars and pedestrians, or parking spaces with little color or nature that are less interesting or fascinating, and were mostly in muted grays rather than green or colors. This control condition had the same features as the NRE intervention in terms of time (7 seconds for each picture), dose (50 photographs, one time intervention), and mode (computer-based), but the content of the pictures (natural versus urban views) differed. Examples of photographs of each intervention are shown in Table 2.1.

Measures

Attention (primary outcome). Four neuropsychological tests of attention were administered: the Multi-Source Interference Task, Digit Span Test, Trail Making Test, and Stroop Test. These are performance-based objective measures of attention. A solitary measure of attention as an outcome variable could result in a limited assessment of the efficacy of the intervention on attention because attention involves various skills in different contexts, and different neuropsychological tests measure different aspects of attention (Kindlon, 1998; Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991) Therefore, 4 validated neuropsychological tests measuring directed, sustained attention, attention switching, and attentional span were selected to examine the intervention efficacy. All tests were treated equally in the analysis, and individual and composite scores of the attention tests were analyzed. Composite scores were calculated to examine interference skills representing directed attention function, sustained attention, and attention switching.

The Multi-Source Interference Task (MSIT) was designed to indirectly examine the function of the cingulo-fronto-parietal cognitive/attention network (Bush & Shin, 2006; Bush, Shin, Holmes, Rosen, Vogt, 2003), supporting directed attention. On the computer screen, three numbers and/or letters were displayed, and participants were instructed to identify the number that is different from the other two numbers within 2 seconds. The numbers are the combinations of 1, 2, and 3, and only 3 buttons were used to report. Handedness was identified before the test, and participants were asked to use their index, middle, and ring fingers to respond. There are two types of trials, congruent and incongruent. Congruent trials have a target number that is always matched in position (e.g., 1XX, X2X, or XX3) with two X letters (Figure 3.1-A). In contrast, incongruent trials have only numbers and the target number is never matched with its position (e.g., 212, 233, or 332) (Figure 3.1-B) (Bush et al., 2003). The test consisted of 8 sessions, and each session had 24 trials with the same proportion of congruent and incongruent trials. A total of 192 trials were administered at each observation. Practice sessions were provided before the actual trials and participants moved on to the actual trials when they felt comfortable doing so.

Error rates (number of trials with incorrect answers out of the total number of trials) and response time were calculated separately for congruent and incongruent trials. To examine interference skills, differences on test performance between congruent and incongruent trials were computed. Standardized z scores were then calculated with baseline mean scores of the entire sample in this study. Next, error rate z scores and response time z scores were averaged for each individual to calculate one z score summarizing interference skills. Lower z scores indicate better directed attention. Content validity of MSIT examining cingulo-fronto-parietal cognitive/attention network has been supported with fMRI in healthy individuals (Bush et al., 2003; Bush & Shin, 2006). The total amount of time to complete the test ranged from 8 to 15 minutes.

The Digit Span Test from the Wechsler battery is a widely used standardized measure of attention, specifically, attentional capacity that is free from distractability (Lezak, Howieson, Bigler, & Tranel, 2012). The test has two parts, digit span forward (DSF) and backward (DSB). The DSF demands low attentional capacity whereas the DSB requires high attentional capacity (Lezak et al., 2012). Participants were instructed to repeat the sequence of numbers that the tester said aloud immediately after the tester finished saying the numbers. The time to finish this test was < 5 minutes. The numbers of digits participants repeated correctly were used for analysis, with higher scores indicating better attention. Test-retest reliability coefficients ranged between .66 and .89 (Lezak et al., 2012). Construct validity was supported by comparing healthy and closed head injury patients (Shum, McFarland, & Bain, 1990).

The Trail Making Test is a standardized measure of attention requiring effective inhibition of competing stimuli to complete the tasks rapidly and accurately (Bowie & Harvey, 2006; Reitan, 1958). The test is mental tracking of a sequence involving more than one stimulus or thought at a time, and flexibility in shifting the course of an ongoing activity. Part A requires participants to connect a series of randomly arrayed, distinct circles numbered 1 to 25 in order as quickly as possible. Part B, the higher demand condition, requires participants to connect a series of 25 circles numbered 1 to 13 randomly intermixed with letters from A to L, alternating between numbers and letters, and proceeding in ascending order. The time to discontinue for each test is 300 seconds (Bowie & Harvey, 2006), and the total time for the Trail Making Test was less than 10 minutes, including instruction. The time to complete including the time for correction of any errors was recorded. A longer completion time represents poorer attention. The reliability of alternate forms of the Trail Making Test was .78 among 15 head injury patients (Franzen, 1996) and .89 and .92 among over 300 healthy adults (Charter, Adkins, Alekoumbides, & Seacat, 1987). Construct validity was supported among healthy adults and patients with closed head injury (Shum et al., 1990). The ability of the test measuring the frontal lobe function was validated by an fMRI study of 12 healthy young adults (Zakzanis, Mraz, & Graham, 2005). Four different forms of the Trail Making Test A were created by moving the numbers forward in the original Trail Making Test A with four different starting points for this study. Test-retest reliability of the 4 different forms of Trail Making A was .86 in 20 HF patients and .84 in 20 healthy adults. The same version of Trail Making Test B was used, and test-retest reliability was .96 in HF and .90 healthy adults in this study.

The Stroop test is involved in selective processing of different visual features on the test (letters and ink colors of words in color) and measures “concentration effectiveness” including the ability to ignore distractions (Lezak et al., 2012; Shum et al., 1990; Stroop, 1935). A computerized Stroop test was programmed for this study, and used 4 colors (red, blue, yellow, and green) and two commands, which were reading letters of color names and their print colors. The color names were not always matched to the print colors. The trials showing color names that have same letters and print colors were called congruent trials, and otherwise the trials were called incongruent trials. Three sessions were provided at each observation, which were reading letters, reading colors, and a combination of reading letters and colors after a cue that tells participants which component of color names they should respond to. In the combination trials, when the commands were switched from word to color, or color to word, those trials were considered switched trials for analysis. When the commands were the same (color to color, or word to word), those were considered non-switching trials. Differences in performance between switched and non-switched trials were used for assessment of attention switching. Each session had 24 trials that were randomly selected from congruent and incongruent trials with a 1:1 ratio. Practice trials were provided, and test performance was examined for error rates and response time. Reliability was satisfactory (Franzen, Tishelman, Sharp, & Friedman, 1987). Construct validity was supported in patients with traumatic brain injury (Ponsford & Kinsella, 1992), and a meta-analysis showed that impaired performance on Stroop test was most common in patients with frontal lobe lesions (Demakis, 2004).

Mood (secondary outcome). The Positive and Negative Affect Schedule (PANAS) scale measures positive and negative affect with 20 items (Watson, Clark, & Tellegen, 1988). It is comprised of two 10-item mood scales of positive mood (interested, excited, strong, enthusiastic, alert, inspired, active determined, attentive, and proud) and negative mood (distressed, upset, guilty, scared, hostile, irritable, ashamed, nervous, jittery, and afraid). Participants were asked to rate to what extent they felt the mood described by the adjectives at that very moment on a 5-point Likert scale that ranges from 1 ("very slightly" or "not at all") to 5 ("extremely"). Possible scores range from 10 to 50 for each of the positive and negative mood scale. For the positive mood scale, the Cronbach's alpha coefficient was 0.86 to 0.90, and 0.84 to 0.87 for the negative mood scale among normative healthy adults (Watson et al., 1988).[71] In 80 chronic HF patients, internal consistency was .86 for the positive mood and .85 for the negative mood scale (Nahlén & Saboonchi, 2010). In this study, the internal consistency Cronbach's alpha for each scale was .82 and .67 in 20 HF and .912 and .55 in 20 healthy adults. Convergent and discriminant validity were supported in non-clinical populations (Watson et al., 1988).

Preferences in interventions. Participants responded to the question "Do you like the picture?" using 1 ("like"), 2 ("neutral"), and 3 ("do not like") to measure preference for each photograph. Total scores ranged from 50 to 150 for each set of intervention. The total scores were transformed from 0 to 100 and reversed, so that higher scores indicated greater preference.

Participant characteristics. Participant demographic, biological, clinical, and cognitive characteristics were obtained at the beginning of the interview and from the medical record in order to describe the sample. It was important to examine characteristics possibly associated with participants' attention and mood. Demographic variables included age, gender, race, ethnicity, years of education, marital status, and employment status.

Biological variables obtained were level of blood pressure, pulse rate, and saturated oxygen (SpO_2). Blood pressure was measured twice by using an aneroid sphygmomanometer following guidelines from American Heart Association at the beginning of each visit (Pickering et al., 2005). SpO_2 was measured by Nonin WristOx® 3100, which monitors proximal saturated oxygen and pulse rate from a finger tip probe every 4 seconds. The data of SpO_2 and pulse rate were stored in the device and downloaded to the computer for analysis.

Clinical characteristics of left ventricular ejection fraction (LVEF), New York Heart Association (NYHA) classes, and brain natriuretic peptide (BNP) levels were collected from medical chart review to describe heart function and severity of the disease only for HF patients. Symptom severity of HF was assessed by a visual analogue scale for common HF symptoms (fatigue, breathless at rest, breathless with activities, swelling, sleep disturbance, and overall effects of the symptoms), PROMIS fatigue short form, and Current Dyspnea Status. The PROMIS fatigue short form has 8 items and responses were reported on a 5-point Likert scal from '1 = not at all/never' to '5 = very much/always'. Possible range of the scale is 8 to 40. Reliability and validity was supported in 48 HF patients (Flynn et al., 2015). Current Dyspnea Status has one question, "How much difficulty are you having in breathing now?", participants were asked to answer on a 5-point Likert scale from '1 = not short of breath' to '5 = very severely short of breath'. The content and predictive validity was supported among 58 HF patients (Weber et al., 2014). The visual analogue scale was administered to healthy participants to compare symptoms and validate differences between the two groups.

Cognitive characteristics were assessed in terms of level of attentional demands related to chronic disease, cognitive activities, activities in nature helping attention restoration, and perceived effectiveness in doing cognitive activities. First, to examine attentional demands, an

11-item questionnaire asking how much mental effort patients needed during self-care activities (e.g., diet, medications, and symptom monitoring) was developed and administered at baseline. A 6-point Likert scale '0 = none' to '5 = very much' was used. Possible scores range from 0 to 55 and higher scores represent greater attentional demands. The internal consistency of the scale was .91 among 22 patients with HF who completed baseline interviews. Second, cognitive activities may have a protective role in cognitive decline, and cognitive decline has been shown to be associated with declined cognitive activity (Rowe & Kahn, 1997; Schinka et al., 2005). The Florida Cognitive Activities Scale was used to describe the frequency, intensity, and duration of 25 common cognitive activities that participants performed (Schinka et al., 2005). Possible scores ranged from 0 to 100, and higher scores mean more frequent cognitive activities with or without more challenging activities (e.g., new and complex activities). Cronbach alpha coefficients were .76 - .77 in 34 HF patients (Pressler et al., 2011). Third, activities that involved interactions in nature during the previous month were assessed to examine the quantity of interactions with nature at baseline (e.g., walking in the park, listening to birds, and tending plants). The 8-item questionnaire was developed based on an intervention protocol developed to improve attention among women with breast cancer (Cimprich & Ronis, 2003). The frequency of each cognitive activity was analyzed. A higher number indicates more frequent nature activities. Fourth, the perceived effectiveness in doing common cognitive activities that require directed attention was examined by the Attentional Function Index (AFI) (Cimprich, 1992; Cimprich, Visovatti, & Ronis, 2011). It consists of 13 items and individuals were asked to answer the question 'how are you doing in each area at the present time' for each item. For this study, the scales were converted from a visual analog scale (100mm) into a numeric rating scale from 0 to 10 because a numeric rating scale is easy to complete and it is easier to score the answers (Hawker, Mian, Kendzerska, & French, 2011). Higher scores indicate better attention. The AFI has three subscales that measure effective action (7 items), attentional lapses (3 items), and interpersonal effectiveness (3 items). Internal consistency reliability has been satisfactory in past studies among 72 undergraduate students (Cronbach alpha = 0.84) (Tennessen & Cimprich, 1995) and 172 women with breast cancer (Cronbach alpha = .92) (Cimprich et al., 2011). Construct validity was supported (Cimprich et al., 2011).

The Mini-Mental Status Examination (MMSE) was administered to determine eligibility. The MMSE scores range from 0 to 30, and higher scores indicate better global cognition. The cut-off score for this study was 24 (22 for patients with less than a 9th grade education) (Folstein et al., 1975; Tombaugh et al., 1996).

Statistical analysis

Descriptive and univariate analyses were computed to describe sample characteristics. Pearson correlations were conducted to examine relationships between sample characteristics and outcome variables before the variables were added to the linear mixed models.

To examine the hypotheses about the efficacy of the NRE intervention in improving attention and mood, linear mixed models were computed. This approach allowed for differing numbers of observations across participants and subject level random effect to account for individual effect (West, Welch, & Galecki, 2014). Separate mixed models were created for attention and mood. Age, education, and order of receiving the NRE intervention (first visit or the second visit) were entered into the models as covariates. Interactions between types of treatment and time (pre and post-test) were entered into the final models. Patients who withdrew were excluded from analyses because most of them were lost to follow-up before the baseline survey. There was missing data on the Stroop test from a healthy participant who refused to perform the Stroop test because of frustration in not remembering computer keys responding to the stimuli. Pairwise comparisons were used for post-hoc analyses.

In addition to independent analyses for each neuropsychological test of attention, sub-domains of attention (interference - directed attention, sustained attention, and attention switching) were analyzed by creating composite z scores. Interference scores reflecting the directed attention function were calculated from the Trail Making Test, MSIT, and Stroop test. The first step of creating composite z scores for directed attention was subtracting differences of error rate z scores between congruent and incongruent trials in MSIT and Stroop test, and then averaging the z scores from the MSIT and Stroop test. The second step was doing the same procedure with response time z scores of the MSIT and Stroop test, and adding differences between the Trail Making Test A and B z scores before averaging it. The final step was averaging composite error rate z scores and composite response time z scores. Sustained attention was calculated by averaging z scores of MSIT and Stroop test congruent trials and Trail Making Test A scores. Attention switching was measured by a Stroop test combination session. Differences in error rates and response time between switched trials (word to color, or color to word) and non-switched trials (word to word, or color to color) were calculated, and average z scores of error rates and response time were used for the linear mixed models. For all composite z scores, scores above zero means better performance than average.

To examine research question 1, which investigates how the individual's preference on each treatment affects the efficacy of the NRE intervention, total preference scores were entered as a covariate into the final linear mixed models and coefficients for the interaction effect between preference and treatment types were estimated for each outcome variables. For research question 2, whether HF patients and healthy adults respond differently to the NRE intervention, data from both groups were added together and the group variable was added to the linear mixed models for the efficacy test. Analyses were performed using IBM SPSS Statistics 21.0. A significance level < .05 was used.

Results

Twenty HF and 20 age- and education-matched healthy participants completed the study (Figure 3.2). Seven HF patients and 1 healthy participant withdrew because of being too busy (n = 3), too sick (n = 2), and for unknown reasons (n = 3). No one was ineligible due to MMSE scores below 24.

Participant characteristics at baseline are presented in Table 3.2. The mean MMSE score was higher in healthy participants (p = .007) than HF patients. Seven HF patients and 1 healthy participant had MMSE scores lower than 27, which indicates possible dementia for college educated older adults (O'Bryant et al., 2008). Biological characteristics and cognitive characteristics were different between HF and health participants at baseline. Patients with HF had lower mean blood pressure, SpO_2, and perceived effectiveness in cognitive activities (AFI) compared to the healthy participants. Time having SpO_2 less than 95% was recorded during the visits. On average, HF patients had four times longer time with SpO_2 < 95% than healthy (8.8 ± 17.1 vs 2.1 ± 4.5 minutes, p = .103), but it did not reach significance on a t-test. Medians of minutes of SpO_2 < 95% was 0.75 and 0.15 among HF and healthy participants, respectively, and Mann-Whitney U test showed significant differences (p = .030). Symptoms related to HF were worse among the HF patients, validating that the two groups of participants are different. No differences were found in demographic characteristics (e.g., age, education, gender, race, marital status, etc.), cognitive activities, activities in nature, and pulse rate between HF and healthy participants.

All HF patients (100%) and 4 healthy participants (18.2%) responded that they had a chronic disease requiring self-care activities. The disease reported from healthy participants included hypothyroidism, hypertension, and back pain. No healthy participants reported that they were receiving help from others for disease-related self-care. Five HF patients reported that they received help from family members or friends to maintain self-care. However, all of the participants having a chronic disease defined themselves as the main person responsible for the self-care activities. From the questionnaire of mental effort that participants needed during self-care activities, healthy participants (4 out of 5) reported that their self-care activities required very little mental effort and were rarely confusing or complex. In contrast, HF patients reported that the HF self-care required somewhat to moderate mental effort on average and bothered them a little bit on a 0 to 5 Likert scale.

Attention and Mood at Baseline

Patients with HF performed worse on three of the attention tests than healthy participants at baseline (Table 3.3): Trail Making Test; MSIT; and Stroop test. On the Digit Span test performance, no statistically significant difference was found between HF and healthy participants, although there was a trend that HF patients had lower scores in Digit Span Backward ($p = .063$). In the analyses of composite z scores for sub-domains of attention, interference and sustained attention, these scores were poorer among HF patients compared with healthy adults ($p = .016$ and $.003$, respectively). Attention switching scores had narrow ranges (2.19 and 2.31, respectively) and were not significantly different between HF and healthy participants ($p = .444$).

In univariate analyses, characteristics that were associated with better attention included female gender, younger age, higher systolic blood pressure, higher mean SpO_2, shorter duration of having SpO_2 lower than 95%, more cognitive activities, and less demands for mental effort. Subjective attention function measured by AFI was associated with objective attention test performance. Education and frequency of activities related to nature were not significantly correlated with attention. The HF characteristics associated with better attention were NYHA class I or II, higher LVEF, and lower level of BNP. In HF, BNP ranged from 6 to 1349 pg/mL, and 7 patients (35%) had BNP levels greater than 400 pg/mL. The patients with higher BNP showed a poorer Trail Making B test scores (141 vs 79, $t = -3.302$, $p = .004$), interference z scores from Trail Making Test (1.3 vs 0.1, $t = -3.115$, $p = .006$), and sustained attention composite scores (3.2 vs 0.1, $t = -5.929$, $p = < .001$). PROMIS Fatigue scores and Current Dyspnea Scale scores were not correlated with attention.

Positive mood scale average scores were 33 among both HF and healthy participants, which indicates a high level of positive mood. Higher level of positive mood was found in HF patients with NYHA class III or IV compared to ones with class I or II (36 vs 29, $p = .032$), but both HF and healthy participants had higher scores on positive mood. Performing more frequent activities requiring cognitive skills was associated with higher levels of positive mood. Demographic and other biological/clinical characteristics did not show any relationships with positive mood. Negative mood scale scores were 12 in HF and 11 in healthy group, which indicates a low level of negative mood. A lower level of negative mood was slightly associated with lower diastolic blood pressure. Participants who reported higher scores on the perceived attention function measure were more likely to have lower levels of negative mood. There were no significant differences in positive and negative mood between HF and healthy participants.

Efficacy on Attention of the NRE intervention

Results from the linear mixed models are presented in Tables 3.4 and 3.5 for HF and healthy participants, respectively. Hypotheses 1 and 3 were rejected. Patients with HF did not show significant time by treatment interaction effects, which indicates that there was no significant improvement in any of the attention measures after the NRE intervention compared to the urban control condition (Table 3.4). There was significant improvement on post-tests with MSIT response time from incongruent trials, MSIT interference scores, Trail Making Test B, Stroop test error rates from incongruent trials, and overall interference scores. However, the improvement was not significantly greater after NRE intervention than after the urban control condition. Age was a significant predictor of Trail Making Tests and sustained attention. Education was only predictive of MSIT error rates from congruent trials. No order effect was found.

Similar to the results in HF patients, healthy participants did not show significant time by treatment interaction effects as well (Table 3.5). Time was significantly predictive of improved attention; in other words, healthy adults had better scores on post-tests compared to pre-tests of MSIT, Stroop test, overall interference z scores, and sustained attention z scores. Significant order effects were found in Stroop test response time from congruent trials and sustained attention z scores. Regardless of the intervention they received, the 2 test scores on their second research visit were better than the ones on the first research visit. Younger age was a significant predictor of better scores on Trail Making Test B, differences between Trail Making Test A and B, and differences between Stroop test switched and non-switched trials' error rates, which means performance decreased with aging, especially when there were conflicts or changes on tasks. Education was not predictive of attention test scores. From post hoc analyses, response time from Stroop congruent trials and non-switching trials, and sustained attention z scores significantly improved after the NRE intervention but not after the urban control condition. There were several test showing improvement after both the NRE and urban control condition that were error rates from MSIT incongruent trials, Stroop test incongruent trials and switching trials, response time from Stroop test incongruent trials and switching trials, and interference z scores. After the urban intervention, z scores for response time differences between Stroop test incongruent and congruent trials showed significant improvement but not after NRE intervention.

Aim 2 : Efficacy on Mood of the NRE intervention

Positive and negative mood status did not significantly change after the NRE intervention compared to the urban control treatment in either the HF group or healthy adults group. In HF, positive mood scale scores changed very slightly after both NRE and urban control condition (Table 3.3). In the mixed model for positive mood, a significant order effect was found, specifically, HF patients expressed more positive mood on their second research visit compared to the first ($p = .021$). The mixed model for negative mood in HF did not show any significant predictors.

In healthy participants, there was a significant treatment effect for positive mood ($p = .006$). The NRE intervention was predictive of a higher positive mood compared to the urban control condition, but no significant treatment by time interaction was found. Post hoc analysis did not show any significant difference between pre- and post-tests after both interventions.

Preference and Responsiveness to the Intervention

The average preference score was significantly higher in the NRE intervention (80.60 ± 16.93) compared to the urban control condition (45.28 ± 17.02) ($p = < .001$). A preference score of 50 indicates neutral feelings about the intervention on average. The preference for each type of intervention did not differ between HF and healthy adults (p = .933). There were 2 outliers: one HF patient reported less favorable responses to nature pictures than other participants, and one healthy adult reported more favorable responses to urban pictures than other participants. The reasons were 'bland nature scenes' and 'reminding the participant the urban scenery where the participant grew up.'

Linear mixed models in a pooled sample with both HF and healthy participants showed that preference was a significant predictor of attention improvement after the NRE intervention (Table 3.6). More specifically, sustained attention significantly improved after the NRE intervention and the higher the preference scores the better attention (post hoc analysis, F = 9.679, p = .002). Preference scores were predictive of positive mood (p = < .001), but there was no time by treatment by preference interaction effect.

Influences of Having HF in Responding to the Intervention

Responsiveness to NRE intervention was significantly different between HF and healthy adults on attention switching (Time x Treat x Group interaction p = .045, Table 3.6). Whereas HF patients showed significantly decreased attention switching after the urban control condition, healthy participants did not have any significant changes after the interventions. Figure 2 shows changes of attention switching in HF and healthy participants separately after the interventions. There were no other differences between HF and healthy participants on the other measures of attention responding to the intervention. No group effects on mood changes after the interventions were found.

Discussion

The purpose of this study was to test the efficacy of NRE intervention on attention and mood in HF patients and age-, education-matched healthy adults. Notwithstanding that the hypotheses on improvement on attention and mood after NRE intervention were only partially accepted from the pooled sample analyses, this study is important for several reasons. First, biological and psychological factors (e.g., SpO_2, mental effort) were found to be associated with poorer attention. Second, to our knowledge, this is one of the few studies focused on specific domains of cognition in HF patients, specifically attention, with comprehensive neuropsychological tests measuring different aspects of attention. Third, we believe it is the first experimental study examining the efficacy of the theory-based NRE intervention in HF patients. Finally, individual preference and having HF were significant to intervention responsiveness.

At baseline, attention was worse in HF patients compared with healthy adults even after age and education were controlled. The findings are consistent with previous studies examining cognitive function in HF (Pressler et al., 2010c; Sauvé et al., 2009; vogels et al., 2007). Patients with HF showed significantly lower systolic and diastolic blood pressure due to medications and had lower average SpO_2 than healthy participants. The lowered blood pressure might negatively influence attention in HF patients (Gottesman et al., 2010). A higher level of BNP was associated with worse attention. That is consistent with previous findings that higher BNP was associated with developing dementia in older adults (Kerola et al., 2010)[81] and HF patients (Van den Hurk et al., 2011).

The NRE was not efficacious in improving attention and mood in both HF patients and healthy adults. There was some significant improvement in attention after the NRE intervention from post hoc analysis. Patients with HF showed improved attention on 1 test and healthy participants showed it on 3 tests. However, the improvement was not found in linear mixed models. As described earlier, the same intervention was tested in young healthy adults and resulted in significant improvement on attention (Berman et al., 2008). The reasons for this difference may be found in research methods (higher number of attention tests, a longer time to complete pre- and post-test, small sample size, limited dose of the intervention, and statistical analysis) and population characteristics (age, having a chronic disease). With aging, when the brain structure and function change, more changes were found in gray matter that may indicate less capacity to improve attention (Rowe & Kahn, 1997). In other studies, the diagnosis of HF was closely related to worsened brain integrity in HF patients compared to healthy adults (Kumar et al., 2011; Pan et al., 2012; woo et al., 2009). A lower capacity of attention or limited attentional resources from these brain changes may not necessarily mean that there is more room for improvement. Instead, the lowered attention might be related to less responsiveness to the intervention due to the worsened brain integrity.

This study not only enrolled older adults with a serious chronic disease, but also administered more attention tests with a longer interview time compared to the previous study by Berman et al (2008). The previous study used 2 tests in young university adults (Berman et al., 2008), whereas this study administered 4 tests with increased complexity compared to those used in the study by Berman et al. Both healthy older adults and HF patients may feel easily fatigued with the same tests and more with increased number of tests. In addition, compared to the short intervention time (7 minutes), the time for completing the attention battery at pre- and post-intervention was longer (25 minutes to 1 hour). The ratio between test and intervention, or the absolute intervention dose might not be adequate to allow the attentional network to rest and thereby restore attention function. The participants might need more time to intervene. Previous studies used nature as an intervention, with intervention doses ranging from 5 minutes to a whole day, but the optimal dose of the interventions was not clear in the literature (Bratman, Hamilton, & Daily, 2012).

Furthermore, the approach to statistical analysis was different in this study than that of previous NRE intervention studies. This study utilized linear mixed models that have strengths in examining time effects and individual characteristics with intervention effects over repeated measures ANOVA or ANCOVA that have been used in previous studies. The significant time and individual effects were prominent in mixed models, and it may indicate that gaps between pre- and post-tests (approximately 30 minutes to 1 hour for each test) was too short increasing practice effects on neuropsychological tests and the small sample size (20 individuals for each group analysis) impacted the study results.

The final mixed models with significant preference and group effects showed a few significant improvements in attention (Table 3.6). Although interference z scores indicating the function of directed attention did not improve, sustained attention significantly improved after the NRE intervention compared to the urban control condition in both groups. Attention switching was better preserved after the urban intervention in healthy adults compared to HF patients. The definition of sustained attention is very similar to the definition of attention that people know without any clarification, which is monitoring stimuli for a prolonged time and maintaining focus. Improved sustained attention may have implications for important aspects of HF self-care because sustained attention is required when the patients listen to their doctors monitoring changes of their HF symptoms and signs. Implications of better attention switching have not been discussed in studies of people with illness. Attention switching is related to their flexibility in responding to input stimuli and changing their behaviors based on the evaluation of the stimuli. Therefore, improved attention switching may provide more capacity enabling people to react to a changing environment or changing threads of thoughts. Interference skills supported by directed attention is more extensively required under the situation having conflicts, and improvement in directed attention was expected after the NRE intervention based on Attention Restoration Theory. Descriptive statistics showed improved directed attention, but this improvement did not reach significance level. An unexpected result found in the Digit Span Forward test was that there was improved performance after the urban control condition compared to the NRE intervention in the pooled sample. The improvement was very small (less than 1 score), but it was statistically significant. A bigger sample size and stronger dose of the intervention would provide more variances on observations and might lead to more accurate results on attention improvement.

The findings on positive influences of preference were interesting. Preference was not significantly correlated with improved attention in a previous study, although the preference on the pictures was greater on nature pictures than urban pictures (Berman et al., 2008). The role of preference was not clearly addressed in Attention Restoration Theory. However, preference may moderate the impact of nature on improved attention. The components of NRE intervention (being away, fascination, extent, and compatibility) were closely related to the favorability of environment (Bratman et al., 2012), and this close relationship may explain how preference was predictive of attention improvement (Bratman et al., 2012). Preferences on natural environment were similar across all participants, but there were 2 outliers. One HF patient reported a less favorable response to nature pictures, and 1 healthy participant reported a more favorable one to urban pictures, compared to other participants. The reasons given were 'bland nature scenes' and 'reminding the participant of the urban scenery where the participant grew up.' This may indicate that individual experience or meaning to individual is important. This study is a feasibility study, and thus, participants had no options choosing the scenes most attractive or preferable to them. Providing more autonomy over intervention content may affect the intervention effects.

Patients with HF, who have received optimized therapies, responded to the interventions differently than did healthy age- and education-matched participants. The possible reasons for this disparity are the following: the attentional demands from self-care activities related to chronic disease in HF patients did not decrease, so HF patients experienced more attentional fatigue and showed little improvement; and lower SpO_2 levels in HF patients still exist and may affect their attention performance. From the baseline analysis of this study, mental effort from self-care activities and oxygen saturation were examined to explain more reasons for worse attention in the HF population, and more perceived mental effort and lower systematic oxygen saturation level were associated with poorer attention in some of the attention tests. This supports both physiological changes and psychological burden from HF that may affect decreased attention. The NRE intervention did not have components reducing either attentional demands or improving oxygenation. In addition, perhaps the NRE intervention cannot work when patients are not adequately oxygenated. These factors may potentially explain the smaller impact of NRE interventions in people with disease, especially cardiovascular disease, and should be considered while designing future studies for attention interventions.

Mood, a secondary outcome of NRE intervention did not change, and it was similar to the study results with the same format of intervention in healthy young adults (Berman et al., 2008). In contrast, NRE interventions with physical activity in a real natural environment (walking in the park vs. walking in downtown area) improved mood among healthy young adults and patients with mood disorder (Berman et al., 2008). Attention Restoration Theory does not describe the relationship between a physical activity component and attention improvement, but nature in reality rather than a virtual environment may intensify the feelings of being away or fascination by embracing multiple sensory stimulations, such as auditory, olfactory, and somatic stimulations. One more consideration with mood is its measurement. Surprisingly, the mood status measure with PANAS did not show significant differences between HF and healthy older adults, despite the fact that HF patients are more likely to have a higher prevalence of negative mood, such as depressive mood and anxiety (MacMahon & Lip, 2002). With the PANAS measuring diverse aspects of mood, the distribution of positive and negative mood did not show normal distributions of observations. Thus, administering different measures of mood status that are focused on a specific mood such as depressive mood may lead to different results. There is also possibility of selection bias that individuals with poor mood less likely to enroll in research studies, while they might have more potential to improve. To examine efficacy of the intervention on mood, more targeted eligibility criteria for HF patients with poor mood might be needed.

A further important facet of this study is that there is no overlap between the intervention and attention measurements. When training interventions have similar features of attention measures, assessment of improved attention because of the training interventions is sometimes hard to distinguish from behavioral training effects on specific skills. The NRE intervention based on Attention Restoration Theory did not have components of attention tests used in this study. Thus, there is chance to mask the intervention effect with training effects of attention skills on top of practice effects from administering same neuropsychological tests multiple times. Moreover, the foundation of NRE intervention is its relaxing quality unlike training. Participants, including HF patients, expressed the view that the intervention was easy and enjoyable enough to do on a daily basis. For patients with HF who have decreased attention, yet have more mentally demanding self-care activities critical to their life, NRE intervention is to comply with.

There are several limitations of the study that should be noted. First, the sample size was small due to the greater heterogeneity of participants for the analysis than estimated during sample size calculation. The sample size was calculated with effect sizes based on differences between the pre- and post-test in the NRE intervention compared to the urban control condition. Although increased variances were added to the sample size calculation, intercepts reflecting individual differences were still predictive of attention in linear mixed models. Second, only one dose of NRE intervention (50 photographs of nature) was provided and examined as a way of improving attention. Multiple doses of the intervention in a longer duration of study were not examined in this study. Knowledge about the optimal dosage of NRE intervention to improve attention and long-term effects does not yet exist.

In conclusion, this study provided preliminary support for the intervention efficacy in improving attention. Healthy adults were better able to maintain their attention switching skills compared to HF patients. This might indicate that improving attention with NRE intervention is possible among patients with chronic disease even after a decrease in attention due to pathophysiological changes. However, the intervention was not efficacious in improving mood. This study addressed the neuropsychological mechanisms of decreased attention in HF and improvements of it, and provided implications for future study designs. Various doses of NRE interventions with a longer period of follow-up in a larger sample size will provide more solid results of the intervention efficacy in HF patients.

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Conflict of Interest

The author has no conflict of interest.

Table 3.1. Elements of Attention Restorative Stimuli: Nature vs Urban Environment

Elements	Nature	Urban
Being away	Often	Less often
Fascination	Soft	Hard
Extended feelings	More	Less
Compatibility	High	Low
Example of pictures		

Table 3.2. Sample Characteristics of Heart Failure and Healthy Participants at Baseline

Characteristic	Total (n = 40)	HF Group (n = 20)	Healthy Group (n = 20)	t or x^2 (p-value)
Age, years, mean ± SD	59.2 ± 12.1	59.5 ± 12.8	58.8 ± 11.6	0.181 (.857)
Education, years, mean ± SD	15.0 ± 2.2	14.8 ± 2.4	15.3 ± 2.0	-0.708 (.483)
MMSE,[a] mean ± SD	28.1 ± 1.7	27.4 ± 1.8	28.8 ± 1.2	32.134 (.007)*
Gender, n (%)				0.100 (1.000)
Men	21 (52.5)	11 (55)	10 (50)	
Women	19 (47.5)	9 (45)	10 (50)	
Race, n (%)				2.590 (.274)
African-American	3 (7.5)	2 (10)	1 (5)	
Asian	2 (5)	2 (10)	0 (0)	
White	35 (87.5)	16 (80)	19 (95)	
Ethnicity, n (%)				0.362 (.834)
Hispanic	2 (5)	1 (5)	1 (5)	
Non-Hispanic	35 (87.5)	17 (85)	18 (90)	
Unknown	3 (7.5)	2 (10)	1 (5)	
Marital status, n (%)				0.107 (1.000)
Married	25 (62.5)	12 (60)	13 (65)	
Not married	15 (37.5)	8 (40)	7 (35)	
Employment, n (%)				3.010 (.222)
Employed	13 (32.5)	4 (20)	9 (45)	
Not employed	4 (10)	2 (10)	2 (10)	
Retired	23 (57.5)	14 (70)	6 (45)	
Handedness, n (%)				1.558 (.407)
Right handed	33 (82.5)	15 (75)	18 (90)	
Left handed	7 (17.5)	5 (25)	2 (10)	
FCAS,[b] total, mean ± SD	47.3 ± 9.8	45.4 ± 10.9	49.2 ± 8.4	-1.249 (.219)
AFI,[c] total, mean ± SD	98.1 ± 20.1	86.5 ± 19.2	109.8 ± 13.3	-4.467 (<.001)*
Effective action	53.1 ± 11.9	40.3 ± 11.0	60.9 ± 6.4	-5.445 (< .001)*
Attentional lapses	22.9 ± 5.5	20.8 ± 6.6	25.0 ± 3.3	-2.954 (.015)*
Interpersonal effectiveness	22.2 ± 6.5	20.4 ± 6.9	23.9 ± 5.7	-1.765 (.086)
Activity in Nature, frequency, mean ± SD	9.2 ± 6.3	10.0 ± 5.9	7.5 ± 5.7	1.364 (.181)
Systolic blood pressure, mmHg, mean ± SD	117.6 ± 14.3	110.9 ± 8.7	124.4 ± 15.7	-3.366 (.002)*
Diastolic blood pressure, mmHg, mean ± SD	70.0 ± 11.6	66.2 ± 9.1	73.8 ± 12.7	-2.192 (.035)*
SpO2,[d] %, mean ± SD†	97.1 ± 1.3	96.6 ± 1.4	97.6 ± 1.0	-2.667 (.011)*
Time having SpO2 lower than 95%, minute, mean ± SD†	5.5 ± 12.8	8.8 ± 17.1	2.1 ± 4.5	1.701 (.103)
Pulse rate, mean ± SD†	73.3 ± 10.9	75.1 ± 13.0	71.6 ± 8.2	1.022 (.313)

Symptoms related to heart failure, (0 to 10, higher is worse), mean ± SD				
Breathlessness at rest	0.6 ± 1.4	1.2 ± 1.8	0 ± 0	2.881 (.010)*
Breathlessness with activity	3.1 ± 2.9	4.5 ± 2.6	1.7 ± 2.6	3.356 (.002)*
Fatigue	2.0 ± 2.6	3.4 ± 2.8	0.5 ± 1.1	4.313 (<.001)*
Daytime sleepiness	2.5 ± 3.9	4.3 ± 3.1	0.7 ± 1.0	5.047 (<.001)*
Overall symptom impact on everyday life	2.6 ± 3.4	4.7 ± 0.4	3.6 ± 1.0	5.092 (<.001)*
LVEF,[e] mean ± SD	-	37.6 ± 15.1	-	-
BNP[f] before enrollment, mean ± SD	-	295.7 ± 336.3	-	-
NYHA[g] class, n (%)	-		-	-
II		9 (45)		
II to III		4 (20)		
III		6 (30)		
IV		1 (5)		
PROMIS[h] Fatigue SF 8a, mean ± SD	-	22.2 ± 8.9	-	-
Current Dyspnea Status, mean ± SD	-	1.4 ± 0.8	-	-

[a]Mini-Mental Status Examination

[b]Florida Cognitive Activities Scale

[c]Attentional Function Index

[d]Peripheral capillary oxygen saturation from pulse oximeter

[e]Left ventricular ejection fraction

[f]Brain natriuretic peptide

[g]New York Heart Association

[h]Patient Reported Outcomes Measurement Information System

†sample size for this analysis, heart failure = 20, healthy adults = 19

*$p < .05$

Table 3.3. Comparisons of Attention and Mood between Heart Failure and Healthy Groups at Baseline (n = 40)

	HF Group (n = 20)	Healthy Group (n = 20)	t	p-value
Attention				
MSIT, error rate (%)				
Congruent	0.7 ± 1.3	0.1 ± 0.2	2.133	.045*
Incongruent	5.7 ± 3.3	4.4 ± 3.7	1.183	.244
Difference (Con - Incon)	5.0 ± 3.3	4.3 ± 3.6	0.632	.531
z-score of the difference	0.1 ± 1.0	-0.1 ± 1.1	0.632	.531
MSIT, response time (ms)				
Congruent	776 ± 135	701 ± 116	1.867	.070
Incongruent	1081 ± 137	977 ± 153	2.245	.029*
Difference (Con - Incon)	305 ± 56	275 ± 67	1.525	.136
z-score of the difference	0.3 ± 0.9	-0.3 ± 1.1	1.525	.136
MSIT, average z-score	0.2 ± 0.8	-0.2 ± 0.9	1.310	.198
Attentional Capacity				
Digit Span Test, score				
Forward	6.75 ± 1.33	6.70 ± 1.46	.113	.910
Backward	4.25 ± 1.25	4.96 ± 1.05	-1.916	.063
Trail Making Test (seconds)				
A (only numbers)	41.06 ± 13.87	26.68 ± 9.84	3.780	.001*
B (number-letter)	100.40 ± 49.45	59.74 ± 20.04	3.408	.002*
Difference (B - A)	59.3 ± 41.9	33.1 ± 21.1	2.506	.018*
Stroop Test, error rate (%)†				
Congruent	2.6 ± 3.5	1.3 ± 3.4	1.191	.241
Incongruent	26.0 ± 16.8	13.0 ± 10.7	2.881	.007*
Difference (Con - Incon)	23.3 ± 15.2	11.7 ± 9.9	2.853	.007*
z-score of the difference	0.4 ± 1.1	-0.4 ± 0.7	2.853	.007*
Stroop Test, response time (ms)†				
Congruent	421 ± 94	295 ± 68	0.513	.611
Incongruent	1646 ± 517	1703 ± 521	-0.348	.730
Difference (Con - Incon)	262 ± 245	380 ± 301	-1.342	.188
z-score of the difference	-0.2 ± 0.9	0.2 ± 1.1	-1.342	.188
Stroop test, average z-score	0.1 ± 0.6	-0.1 ± 0.7	0.965	.341
Directed attention, z-score†	0.64 ± 1.83	-0.73 ± 1.51	2.537	.016*
Sustained attention, z-score†	0.95 ± 2.27	-0.95 ± 1.40	3.179	.003*
Attention switching, z-score†	0.07 ± 0.55	-0.07 ± 0.60	0.773	.444
Mood, PANAS				
Positive mood	33.10 ± 7.72	32.20 ± 8.81	.344	.733
Negative mood	11.70 ± 2.92	11.00 ± 1.59	.941	.353

Note: MSIT = Multi-source Interference Task; Con = congruent trials; Incon = incongruent trials

For attention measures, higher scores indicate worse attention, except for the Digit Span Test

†sample size for this analysis, heart failure = 20, healthy adults = 19

*$p < .05$

Table 3.4. Means, Standard Deviations, and Linear Mixed Models Analysis for Outcome Variables in Heart Failure (n = 20)

	Nature (n = 20)		Urban (n = 20)		Mixed Models Analysis, P Value					
Outcome variables	Pre-test	Post-test	Pre-test	Post-test	Age	Education[a]	Order	Time	Treat	Treat xTime
Attention										
MSIT, error rate (%)										
Congruent	0.56 ± 1.18	1.24 ± 4.42	0.48 ± 0.88	1.08 ± 1.96	.229	.048*	.719	.056	.717	.901
Incongruent	4.79 ± 3.40	4.59 ± 4.42	4.67 ± 2.42	4.27 ± 3.92	.564	.081	.801	.646	.729	.874
Incongruent - congruent (z score)	-0.12 ± 0.92	-0.38 ± 0.82	-0.14 ± 0.77	-0.42 ± 0.82	.834	.423	.519	.122	.859	.917
MSIT, RT (ms)										
Congruent	755 ± 143	737 ± 123	741 ± 116	721 ± 114	.065	.232	.318	.090	.156	.932
Incongruent	1047 ± 150	1019 ± 145	1043 ± 123	1015 ± 128	.074	.117	.380	.042*	.792	.985
Incongruent - congruent (z score)	0.01 ± 0.66	-0.15 ± 0.95	0.19 ± 0.91	0.05 ± 1.05	.800	.298	.955	.222	.114	.928
MSIT, interference (z score)	-0.06 ± 0.66	-0.26 ± 0.62	0.03 ± 0.68	-0.19 ± 0.77	.931	.249	.786	.071	.476	.976
Attentional Capacity										
Digit Span (raw score)										
Forward	6.80 ± 1.44	6.55 ± 1.19	6.70 ± 1.22	6.55 ± 1.15	.452	.264	.368	.279	.785	.785
Backward	4.40 ± 1.54	4.55 ± 1.79	4.30 ± 1.75	4.85 ± 1.42	.720	.130	.341	.115	.649	.364
Trail Making (sec)										
A (only numbers)	41.90 ± 14.87	41.80 ± 21.67	41.92 ± 17.99	44.38 ± 28.18	.020*	.141	.953	.703	.674	.679
B (number-letter)	97.78 ± 47.52	87.37 ± 45.35	98.29 ± 52.80	88.04 ± 44.39	.009*	.051	.897	.019*	.891	.985
B - A	55.88 ± 40.22	45.57 ± 37.34	56.36 ± 43.23	43.65 ± 28.88	.027*	.081	.893	.036*	.894	.823
Stroop, error rate (%)										
Congruent	4.17 ± 8.14	2.5 ± 3.24	3.47 ± 4.84	2.92 ± 3.55	.861	.441	.371	.332	.903	.626
Incongruent	23.61 ± 18.28	18.19 ± 18.30	19.72 ± 15.81	14.31 ± 16.03	.494	.248	.412	.035*	.126	1.000
Incongruent - congruent (z score)	0.13 ± 1.24	-0.14 ± 1.27	-0.10 ± 1.00	-0.45 ± 1.06	.424	.275	.491	.096	.146	.828
Non-switched	10.49 ± 15.69	10.24 ± 14.28	11.12 ± 17.21	8.66 ± 12.78	.685	.114	.255	.582	.846	.653

Switched	12.75 ± 14.99	7.16 ± 8.71	9.63 ± 13.80	6.55 ± 8.19	.993	.188	.376	.067	.425	.590
Switched - non-switched	2.26 ± 9.12	-3.08 ± 10.25	-1.49 ± 13.96	-2.11 ± 8.08	.449	.177	.297	.190	.539	.298
Stroop, RT (ms)										
Congruent	1432 ± 476	1352 ± 338	1285 ± 304	1281 ± 296	.367	.978	.534	.429	.043*	.476
Incongruent	1641 ± 541	1616 ± 513	1598 ± 353	1659 ± 387	.103	.701	.869	.797	.999	.554
Incongruent - congruent (z score)	-0.40 ± 0.87	-0.20 ± 1.30	-0.02 ± 0.68	0.21 ± 0.76	.122	.524	.500	.199	.023*	.911
Non-switched	1485 ± 405	1370 ± 416	1509 ± 519	1492 ± 447	.134	.475	.874	.359	.310	.492
Switched	1619 ± 693	1654 ± 547	1373 ± 376	1475 ± 464	.248	.513	.709	.520	.047*	.750
Switched - non-switched	134 ± 468	284 ± 462	-136 ± 341	-18 ± 418	.571	.932	.732	.171	.004*	.869
Stroop, interference (z score)	-0.14 ± 0.71	-0.17 ± 1.03	-0.06 ± 0.65	-0.12 ± 0.77	.127	.222	.889	.748	.644	.940
Composite z scores of attention										
Overall interference	0.08 ± 1.96	-0.45 ± 2.25	0.25 ± 1.74	-0.37 ± 1.68	.079	.079	.823	.024*	.619	.849
Sustained attention	1.17 ± 2.60	1.09 ± 3.34	0.77 ± 2.27	1.10 ± 1.68	.039*	.064	.704	.713	.571	.575
Attention switching	0.11 ± 0.45	0.06 ± 0.60	-0.25 ± 0.68	-0.18 ± 0.50	.716	.248	.587	.938	.016*	.636
Mood, PANAS (raw score)										
Positive mood	30.1 ± 7.9	30.6 ± 10.5	31.9 ± 7.3	30.5 ± 8.2	.866	.306	.021*	.727	.521	.497
Negative mood	11.9 ± 4.1	11.7 ± 4.3	11.6 ± 3.2	10.5 ± 1.8	.409	.689	.105	.322	.254	.492

RT = response time

* $p < .05$

Table 3.5. Means, Standard Deviations, and Linear Mixed Models Analysis for Outcome Variables in Healthy Adults (n = 20)

	Nature (n = 20)		Urban (n = 20)		Mixed Models Analysis, P Value					
Outcome variables	Pre-test	Post-test	Pre-test	Post-test	Age	Education[a]	Order	Time	Treat	Treat xTime
Attention										
MSIT, error rate (%)										
Congruent	0.36 ± 1.60	0.00 ± 0.00	0.05 ± 0.24	0.05 ± 0.21	.613	.852	.285	.331	.491	.337
Incongruent	4.13 ± 4.00	1.77 ± 1.99	3.67 ± 3.93	2.13 ± 2.20	.756	.255	.983	<.001*	.922	.420
Incongruent - congruent (z score)	-0.25 ± 0.97	-0.83 ± 0.57	-0.30 ± 1.11	-0.74 ± 0.64	.803	.230	.869	<.001*	.872	.628
MSIT, RT (ms)										
Congruent	661 ± 93	629 ± 79	662 ± 122	636 ± 127	.218	.408	.199	.026*	.729	.807
Incongruent	921 ± 148	890 ± 129	921 ± 152	886 ± 154	.553	.181	.701	.040*	.891	.895
Incongruent - congruent (z score)	-0.48 ± 1.26	-0.47 ± 1.29	-0.50 ± 0.99	-0.66 ± 0.85	.564	.079	.259	.577	.444	.545
MSIT, interference (z score)	-0.37 ± 0.98	-0.65 ± 0.89	-0.40 ± 0.86	-0.70 ± 0.61	.805	.099	.431	.004*	.678	.938
Attentional Capacity										
Digit Span (raw score)										
Forward	6.85 ± 1.18	6.90 ± 1.41	6.80 ± 1.15	7.25 ± 1.21	.428	.273	.183	.218	.458	.324
Backward	5.05 ± 0.95	5.40 ± 1.57	4.55 ± 0.89	5.00 ± 1.45	.738	.343	.097	.096	.062	.833
Trail Making (sec)										
A (only numbers)	27.44 ± 9.67	24.68 ± 6.92	25.03 ± 7.28	24.95 ± 7.57	.052	.411	.806	.219	.352	.246
B (number-letter)	58.10 ± 22.37	53.03 ± 22.32	56.88 ± 20.66	55.25 ± 21.84	.006*	.560	.612	.225	.856	.533
B - A	30.66 ± 21.85	28.35 ± 18.60	31.86 ± 18.22	30.30 ± 19.70	.019*	.777	.650	.511	.593	.899
Stroop, error rate (%)										
Congruent	0.29 ± 0.88	1.17 ± 2.67	1.17 ± 3.38	0.44 ± 1.04	.956	.207	.067	.883	.883	.110
Incongruent	11.70 ± 9.82	4.24 ± 4.38	10.82 ± 10.47	5.70 ± 7.26	.266	.397	.665	<.001*	.831	.394
Incongruent - congruent (z score)	-0.45 ± 0.70	-1.04 ± 0.21	-0.57 ± 0.67	-0.89 ± 0.50	.207	.479	.915	<.001*	.872	.151
Non-switched	8.89 ± 16.40	4.01 ± 5.93	6.76 ± 10.33	4.54 ± 7.42	.126	.727	.477	.091	.698	.520
Switched	6.04 ± 7.13	1.05 ± 3.15	5.88 ± 10.56	1.40 ± 4.35	.917	.568	.219	.001*	.945	.848

Switched - non-switched	-2.85 ± 15.37	-2.96 ± 4.46	-0.88 ± 7.95	-3.14 ± 6.62	.031*	.969	.872	.563	.660	.598
Stroop, RT (ms)										
Congruent	1282 ± 300	1178 ± 275	1242 ± 332	1180 ± 352	.474	.798	.013*	.013*	.567	.531
Incongruent	1630 ± 510	1445 ± 467	1595 ± 522	1407 ± 423	.293	.930	.202	.001*	.480	.976
Incongruent - congruent (z score)	0.11 ± 1.05	-0.19 ± 0.94	0.12 ± 0.91	-0.33 ± 0.70	.196	.635	.574	.008*	.629	.560
Non-switched	1578 ± 479	1333 ± 540	1408 ± 441	1341 ± 484	.473	.743	.081	.016*	.201	.158
Switched	1547 ± 515	1311 ± 410	1515 ± 536	1283 ± 417	.313	.927	.114	.001*	.648	.977
Switched - non-switched	-30.36 ± 513	-22 ± 248	108 ± 306	-58 ± 246	.662	.479	.646	.271	.476	.221
Stroop, interference (z score)	-0.17 ± 0.74	-0.62 ± 0.51	-0.23 ± 0.69	-0.61 ± 0.55	.164	.544	.723	<.001*	.775	.726
Composite z scores of attention										
Overall interference	-1.00 ± 1.66	-1.80 ± 1.31	-1.13 ± 1.44	-1.79 ± 1.11	.317	.428	.553	<.001*	.709	.673
Sustained attention	-1.09 ± 1.30	-1.64 ± 1.11	-1.37 ± 1.53	-1.72 ± 1.19	.088	.778	.043*	.005*	.228	.527
Attention switching	-0.25 ± 0.69	-0.17 ± 0.40	-0.01 ± 0.42	-0.21 ± 0.51	.189	.578	.384	.545	.314	.170
Mood, PANAS (raw score)										
Positive mood	33.20 ± 8.29	32.80 ± 9.53	31.55 ± 9.34	30.00 ± 9.69	.248	.103	.115	.219	.006*	.466
Negative mood	11.40 ± 1.93	11.15 ± 1.73	10.95 ± 1.67	11.40 ± 2.35	.095	.114	.181	.781	.781	.332

RT = response time

* p < .05

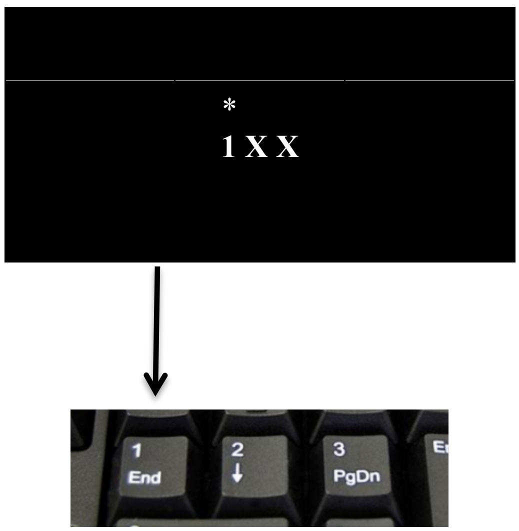
Table 3.6. Linear Mixed Models Analysis: Tests of Research Questions on Influence of Having Heart Failure and Preference for the Pictures (n = 40)

	Intercept	Age	Education[a]	Order	Time	Treat	Group	Treat xTime	Treat x Time x Group	Preference	Treat x Preference	Time x Treat x Preference
Attention												
MSIT, average z score (incongruent-congruent)	.528	.591	.612	.332	.613	.005*	.044*	.957	.713	.550	.001*	.236
Trail Making Test A	.215	.001*	.101	.345	.462	.124	<.001*	.133	.710	.905	.090	.400
Trail Making Test B	.310	<.001*	.044*	.435	.769	.493	<.001*	.595	.571	.346	.288	.608
Stroop, average z score (incongruent-congruent)	.234	.020*	.148	.630	.076	.169	.200	.686	.142	.306	.278	.508
Attentional Capacity												
Digit Span Forward	<.001*	.306	.788	.801	.049*	.329	.461	.021*	.358	.028*	.074	.054
Digit Span Backward	.014*	.384	.460	.788	.279	.947	.246	.326	.501	.042*	.572	.475
Composite z scores of attention												
Overall interference	.217	.032*	.315	.366	.898	.058	.012*	.693	.886	.811	.036*	.627
Sustained attention	.510	.001*	.075	.988	.016*	.625	<.001*	.001*	.344	.185	.862	.006*
Attention switching	.498	.043*	.549	.282	.214	.337	.219	.531	.045*	.380	.110	.386
Mood, PANAS												
Positive mood	.220	.470	.078	.002*	.194	.162	.749	.732	.460	<.001*	.756	.401

	Negative mood	<.001*	.337	.991	.051	.717	.345	.764	.785	.473	.108	.833	.852

* p < .05

Figure 3.1. Examples of Congruent and Incongruent Trials in the Multi-source Interference Task



A. A congruent trial: the target number is matched to the location of the number. Congruent trials always have 2 letters of X and only 1 number, '1' in this case.

B. An incongruent trial: the target number is not matched to its location in the number key. In this example, target number '1' is in the middle, but a participant is required to press the most left key. Incongruent trials have only numbers.

Figure 3.2. CONSORT Flow Diagram of the Study

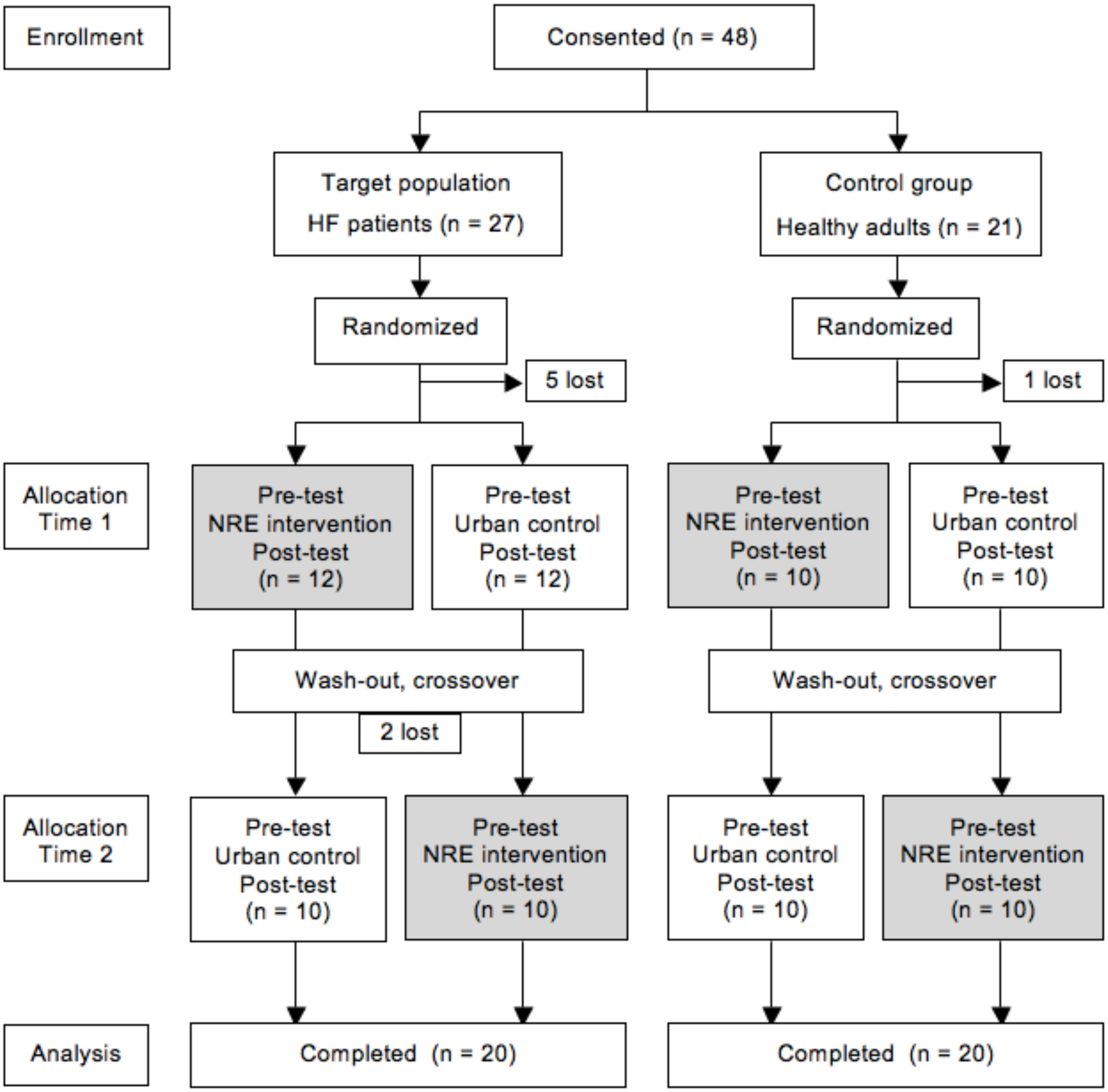
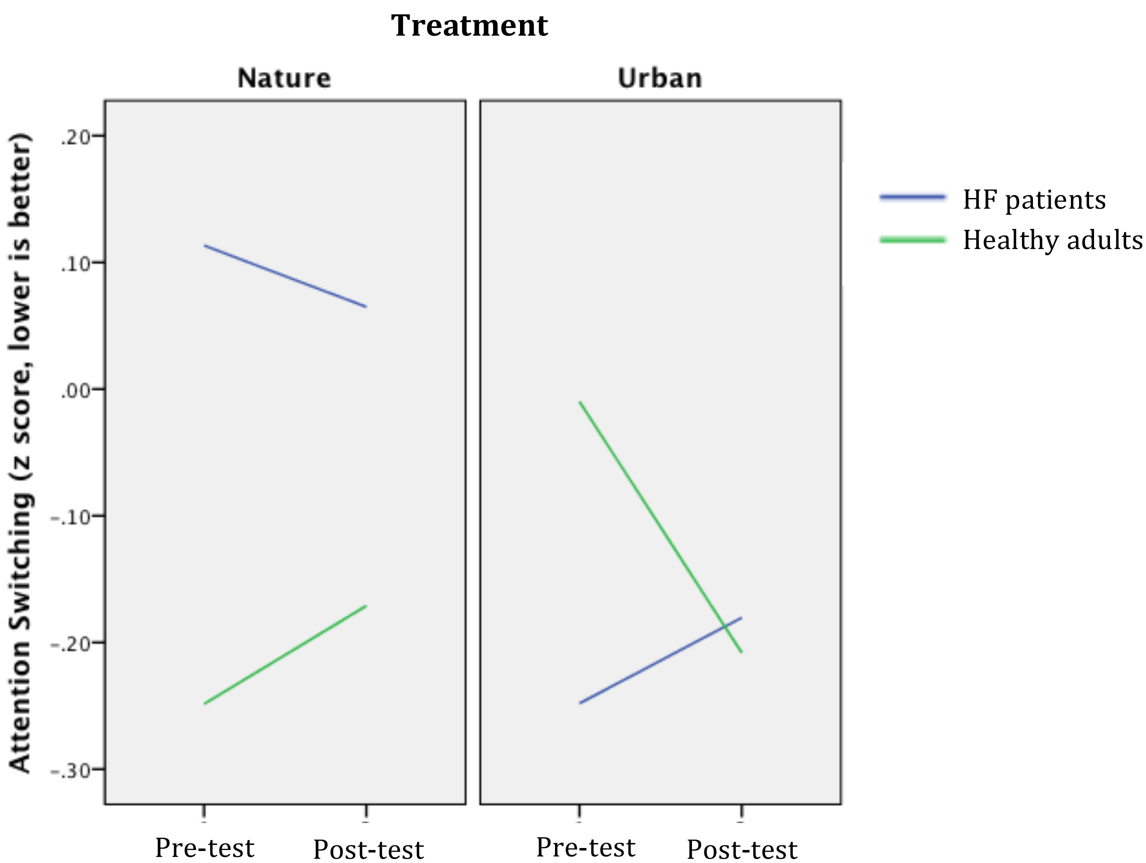


Figure 3.3. Attention Switching Responsiveness to Each Intervention between Heart Failure and Healthy Group



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Chapter 4

Validating Use of the Multi-Source Interference Task in Patients with Heart Failure

Abstract

Background: The Multi-source Interference Task (MSIT) is a computerized neuropsychological test designed to examine the function of the dorsal cingulate cortex that is the center of interference. Interference skills supported by directed attention are important to maintaining goals in daily activities including self-care for heart failure (HF). Directed attention is often impaired in patients with HF; however, to our knowledge, the MSIT has not been used in HF.

Objective: The purpose of the study was to examine construct validity of the MSIT in HF patients.

Methods: The MSIT was validated in data obtained from a cognitive intervention study among 22 HF patients. Descriptive statistics were used to examine interference effects. Construct validity was evaluated using correlations between the MSIT and two other measures of attention: **2** Trail Making and Stroop Test. Additional analyses were conducted between the MSIT and Attentional Function Index, which is a measure of perceived effectiveness of attention, and a questionnaire for attentional demands.

Results: Interference effects were found to be significant in the MSIT error rates and response time, and these were consistent with the significant interference effects from Trail Making and Stroop Tests. Overall interference z scores of MSIT were not correlated to Trail Making A and B, Stroop Test interference scores, and attentional demands, but were correlated with perceived attention function measured by Attenional Function Index. The MSIT scores showed significant correlations with other objective and subjective measures of attention.

Discussion: Construct validity of the MSIT was supported in part among patients with HF. The MSIT is sensitive in detecting interference effects, and HF patients showed worse interference skills compared to healthy adults. However, the small sample size limits the generalizability of the results. Future studies need to include measures of interference as well as measures of simple attention skills maintaining focus.

Keywords: attention; heart failure; psychometrics

Introduction

Attention is important in daily living in initiating and maintaining activities to achieve goals because, without attention, nothing can be sensed and stored in memory nor can a memory be built (James, 1890; Kaplan & Berman, 2010). Attention is particularly necessary for people with chronic disease so that they can learn self-care regimens to treat the disease and continue the activities as scheduled, such as taking medications on time and seeing their doctors. However, a paradox exists whereby attention is more likely to be impaired when the demands for attention on processing information increase (Hammar, Lund, & Hugdahl, 2003) because attentional resources are finite (Kahneman, 1973). It is known that patients with heart failure (HF) have a higher risk of cognitive impairment and vascular dementia (Cohen & Gunstad, 2010), and attention impairment has been found in 15% to 27.4% (Jung et al., 2015b) as one of the most impaired cognitive domains in HF (Bauer, Johnson, & Pozehl, 2011; Pressler, 2008). Attention impairment has had a serious impact on HF patients, resulting in, for example, lower adherence to the HF self-care regimen, leading to more frequent re-hospitalizations and higher mortality rates (Cameron et al., 2010; Dickson, Tkacs, & Riegel, 2008). Despite the serious impact of attention impairment on healthcare outcomes of HF, there are few studies focusing on attention.

Attention is a complex concept often viewed as a set of processes (James, 1890; Mirsky et al., 1991), and thus, measures of attention should be relevant to the attention constructs impaired in a specific population or disease (Kindlon, 1998). Directed attention is an effortful attention that regulates focus by ignoring distractions that interfere with one's focus of attention (James, 1890), and it is especially important in managing chronic disease effectively. This aspect of attention is not just about HF patients maintaining their focus on a task or an object, but is more about following instructions or trains of thought when there is interference in which the stimuli are in conflict with one another. Proactive interference refers to “difficulty in learning new information because of already existing information” (American Psychological Association, n.d.), and it recruits directed attention to resolve the interference (Berman, Jonides, & Lewis, 2009; Kaplan & Berman, 2010; Weissman, Mangun, & Woldorff, 2002). Directed attention is a resource common to many cognitive and self-regulatory behaviors, as directed attention is devoted to interfering information, there will be less directed attention resources available to help maintain current focus of attention (Kaplan & Berman, 2010).

Ineffective inhibition of directed attention is related to more negative interference effects, such as more errors on performance and slower responses (Kaplan & Berman, 2010). The brain areas involved in attention-based processes during interference include dorsal cingulate cortex (Nee, Jonides, & Berman, 2007). Ineffective function of this region, or attention-based information processing for interference, leads to larger interference effects in behaviors, for example, slower response time and higher error rates.

As a measure of directed attention during interference, the Multi-source Interference Task (MSIT) was developed by Bush and colleagues (2003). It is a computerized neuropsychological test that was originally designed to examine the function of the dorsal anterior cingulate cortex, which is critical to directed attention, by asking an individual to report the number which is different from the others among 3 displayed numbers: 1, 2, and 3. To examine interference effect, the test uses two different types of trials, congruent and incongruent. Congruent trials are trials that do not have interference and have a target number that is always matched in its position (e.g., 1XX, X2X, or XX3) with two letters of X. In contrast, incongruent trials are trials that have an interference component and a target number is never matched with its position (e.g., 212, 233, or 332) (Bush et al., 2003). To calculate the interference effect, which reflects directed attention function, subtracting methods from scores of incongruent trials to scores of congruent trials are computed. In most cases, performance on incongruent trials is slower and less accurate compared to the one in congruent trials. Differences between incongruent and congruent trials that are larger than usual indicate lower directed attention. The content validity of MSIT has been supported in healthy young adults with functional brain imaging technique (Bush et al., 2003; Bush & Shin, 2006). Initial validation of the MSIT was conducted among 8 healthy young adults and the results showed that the MSIT produced reliable activation the dorsal anterior cingulate cortex measured by a functional magnetic resonance (fMRI) imaging. In addition, the activation of the brain area was associated with longer reaction time and increased error rates compared to the congruent trials. Bush and Shin (2006) tested the MSIT among 25 healthy adults during a fMRI, and showed similar results to their previous validation.

The MSIT has 3 strengths as a measure of attention. First, the test is not sensitive to literacy because it uses only Arabic numbers. Second, there is less chance of observer bias than is the case with traditional paper-pencil based neuropsychological tests because the test is computerized so that influence from testers is smaller. Third, the test is a game-like format and enjoyable rather than frustrating or embarrassing to participants. Despite the strengths of the MSIT and validated ability to examine interference effect and directed attention, it has not been used in studies among patients with HF before this study. In addition, behavioral impact of ineffective directed attention has been examined in the laboratory setting with brain imaging techniques, but it has not been linked to their behavioral effectiveness in everyday activities. Therefore, the aim of this study was to examine validity of the MSIT in HF patients. Hypotheses were: 1) performance on the MSIT incongruent trials is worse than performance on the MSIT congruent trials, with higher error rates and longer response times; 2) performance on the MSIT is correlated with two other interference tests: Stroop test (incongruent trials - congruent trials) and Trail Making Test (Part B - Part A); and 3) MSIT performance in HF is significantly decreased compared to healthy adults. Research questions were proposed on relationships between ineffective inhibition of attention from the MSIT and perceived attention function, and between the MSIT performance and perceived mental effort.

Methods

Data used were from a randomized crossover study designed to improve attention by using a cognitive intervention in HF obtained between April 2014 and May 2015 (Jung et al., 2015a). The cognitive intervention was based on the Attention Restoration Theory and involved watching a series of slides with nature photographs in 7 minutes. The active control condition was involved watching slides with urban environment photographs in 7 minutes. Inclusion criteria for HF participants were: adults; diagnosed with HF; and able to read and hear the English language. Inclusion criteria for healthy adults were the same except for the diagnosis of HF. Exclusion criteria for both groups were: attention deficits disorder, dementia, stroke history, major neurological and psychiatric disorder; not-corrected vision; color blindness; and a Mini-Mental State Exam (MMSE) score < 24 in order to screen possible dementia (cutoff point of 22 for participants with less than 9th grade education). The study was approved by an Institutional Review Board, and written informed consents were obtained from all participants before their participation.

Sample

Baseline data from 22 HF patients that were collected before the patients received any cognitive intervention were used. From the same study, data from 20 age- and education-matched healthy adults were used as a comparison. The participants were recruited at an outpatient clinic in a tertiary hospital and the online recruitment site linked to the hospital (https://umclinicalstudies.org/).

Measures

Four attention measures including the MSIT were administered in the original intervention study, and only MSIT, Trail Making Test, and Stroop test were included for the validity evaluation because these three tests measure interference while 4th test, the Digit Span Test, does not.

Multi-Source Interference Task. This computerized neuropsychological test was designed to measure function of the dorsal anterior cingulate cortex that supports directed attention function. Participants were instructed to report the number that is different from the others among three numbers displayed on the computer screen, which is the target number, as quickly as possible. The number keys '1, 2, and 3' on the laptop keypads were used and participants were asked to use their index, middle, and ring fingers to respond. A total of 192 trials (8 sessions, 24 trials/session) were administered to each participant based on the protocol developed by Bush and Shin (2006). Practice sessions (24 trials per practice session) were provided while participants were comfortable doing the actual test sessions. Error rates and response times were recorded by the types of test, which were congruent and incongruent trials (Figure 4.1). If a participant could not respond to a trial within 2 seconds, that trial was excluded from the response time analysis to obtain more accurate data. To calculate interference scores, subtraction of congruent trials test scores from incongruent trials were computed. To examine the overall level of the interference effect, z scores with the mean scores of the pooled sample (HF and healthy) were computed separately for error rate and response time, and then those two z scores were averaged for each participant. Higher z scores indicate bigger interference effect, which means worse interference skills.

Trail Making Test. This test was designed to measure attention and mental tracking, and was comprised of two parts (Bowie & Harvey, 2006; Reitan, 1958). Part A has 25 numbered circles, and participants were asked to connect the circles in order as quickly as possible. Part B has 25 circles with numbers (1 to 13) and letters (A to L), and participants were asked to connect the circles by alternating between numbers and letters in ascending order as quickly as possible. Time to complete, including the time for correction of any errors, was recorded. Longer completion time means poorer attention. Test-retest reliability for Part A ranged from very low ($r = .36$) to very high ($r = 94$) based on population characteristics, and Part B has been found above .65 (Lezak et al., 2012). Construct validity was supported among people with closed head injury and healthy adults (Shum, McFarland, & Bain, 1990). The test was validated in a fMRI study among 12 healthy adults that showing the activation of the frontal lobe was associated with difference performance scores between Trail Making A and B (Zakzanis, Mraz, &Graham, 2005).

Stroop Test. Stroop test was designed to measure inhibition function of attention and a well-validated measure of interference (Lezak et al., 2012). In this study, the Stroop test was programmed for computer use with E-Prime® 2.0 software (Psychology Software Tools, Inc). As with the paper version of the Stroop test, the test used 4 colors (red, blue, yellow, and green) and had two commands; reading letters of color names or their print colors. When the color names are not matched to the print colors, the trials are called incongruent and require interference skills. A total of 72 trials in three sessions were administered to each participant in this study (Dixit et al.; 2012; Hermens & Walker, 2012). Practice trials (20 trials per practice session) were provided while participants were comfortable doing the actual Stroop test.

Analysis procedures were the same as those used with MSIT, which calculating differences between congruent and incongruent trials' error rates and response times and then averaging z scores of error rate and response time difference to calculate overall interference effects. Construct validity was supported in patients with traumatic brain injury, (Ponsford & Kinsella, 1992). The Stroop test was sensitive to frontal lobe damage (Demakis, 2004).

Attentional Function Index (AFI). The AFI is a 13-item self-reported questionnaire measuring effectiveness of directed attention (Cimprich, 1990; Cimprich, Visovatti, & Ronis, 2011). Participants were asked to answer each question about perceived effectiveness in doing common cognitive activities that require directed attention, and responded from 0 to 10 for each item. Higher scores indicate better perceived attention. There are three subscales: effective action (7 items), attentional lapses (3 items), and interpersonal effectiveness (3 items). Construct validity was supported in 172 women with breast cancer (Cimprich, Visovatti, & Ronis, 2011). Reliability was satisfactory in the same breast cancer patients (Cronbach's alpha = .92). In the current sample of 22 HF patients and 20 healthy adults (mean age = 59 years), Cronbach's alphas were .81 and .90, respectively. This subjective measure of directed attention was administered to examine how the interference effect measured by the MSIT was associated with ineffective inhibition participants perceived in everyday activities.

Mental Effort. A 11-item self-report questionnaire was developed by the authors to assess the level of mental effort for their self-care activities necessary to managing chronic disease. Seven items were related to how much mental effort was needed for specific self-care activities (e.g., medications, diet, doctor's appointment, and symptoms of the disease), and three questions were about patients' evaluation of their self-care regimen in terms of how complex, confusing, and burdensome they were. Possible scores range from 0 to 55, with higher scores indicating greater mental effort. The internal consistency reliability of the scale was .91 among 22 patients with HF.

Statistical Analysis

All analyses were completed using IBM SPSS 21. Descriptive statistics were used to present sample characteristics. Construct validity was assessed by correlation analyses and contact analysis (t-tests) (Campbell & Fiske, 1959; Westen & Rosenthal, 2003). Convergent validity was tested with Pearson correlations of MSIT with Trail Making Test and Stroop Test that are theoretically consistent measurements with MSIT. A correlation between .30 and .50 was considered "medium" and >.50 was considered "large" (Cohen, 1988). Discriminant validity was assessed by independent t-tests between HF patients and healthy adults. The significance level was set at $p < .05$.

Results

Sample Characteristics

The mean age of HF patients was 58.9 years, and the years of education completed was14.6 years on average. There were more men than women (n = 13 vs. 9), and more non-Hispanic White patients (73%). The mean LVEF was 38% and the mean BNP level was 273pg/ml. One showed NYHA class IV symptoms and others had class II (n = 9) and III (n = 12 including the number of patients who showed symptoms between II and III). Healthy participants' characteristics were similar to the HF group, except for the Mini-Mental Status Examination (MMSE) and AFI (Table 4.1). Patients with HF had lower MMSE (27.4 vs 28.8) and AFI scores than healthy participants (84.6 vs 109.8).

Construct Validity

Hypothesis I was supported in that performance on incongruent trails of MSIT was worse than congruent trials. Patients with HF showed significantly better performance in both error rates (5.4%, t = -7.327, p < .001) and response time (308 ms, t = -26.607, p = < .001) during congruent trials compared to incongruent trials (interference condition) (Table 4.2). In healthy participants, the interference effects (worse performance in incongruent trials) were significant in error rates (3.5%, t = -5.294, p < .001) as well as response times (36ms, t = -18.413, p < .001).

The interference effects were similar in other attention measures. In details, Stroop test results were worse in incongruent trials in both error rates (t = - 6.999, p < .001) and response time (t = - 5.117, p < .001) compared to congruent trials. Trail Making B scores were worse than Trail Making A (t = - 6.939, p < .001). Thus, interference effects remained significant across the measures.

Hypothesis II was partially supported. Although MSIT overall interference scores were not significantly correlated with Stroop overall interference scores, significant correlation was found between MSIT error rates in congruent trials and Stroop response time z scores (r = -.478, p = .025 in Table 4.3), Correlations between MSIT and Trail Making interference scores were not significant. However, raw score analyses showed significant correlations between MSIT response time in both incongruent and congruent trials and Trail Making A and B (r = .431 - .521, Table 4.3).

Hypothesis III was partially supported. Overall interference scores from MSIT were not significantly worse in HF patients compared to age- and education-matched healthy adults. Similarly, Stroop test interference scores did not differ by groups. Only Trail Making interference scores showed significant differences between groups (t = 32.274, p = .010, Table 4.2).

Raw score analyses of the MSIT and Stroop test, which separates interference effects on error rates and response time, showed significant difference between HF and healthy adults. The MSIT error rates in congruent trials were higher in the HF group than healthy group (0.65% vs 0.05%, $p = .032$), and MSIT response time in incongruent trials were longer in HF group compared to healthy group (1077ms vs 701ms, $p = .029$). In contrast, Stroop response time in incongruent trials did not differ significantly, but error rates in incongruent trials were higher in the HF group than healthy group (26% vs 13%, $p = .007$). Accordingly, z scores of difference between the trial types were higher in HF ($p = .006$), which indicates a worse level of interference skills reflected in increased errors and slower response time.

Research Questions

Correlations between MSIT interference scores and AFI total scores were significant in that the worse interference skills in MSIT, the worse perceived attention function ($r = -.500$, $p = .018$). The relationship was more prominent in response time of MSIT ($r = -.445$, $p = .038$). Among subscales of AFI, effective action and attentional lapses in daily activities were moderately associated with MSIT interference scores at $p = .1$ level. However, interpersonal effectiveness was not ($r = -.316$, $p = .152$). All HF patients reported that they have a chronic disease requiring mental effort, and so did 4 out of 20 healthy adults. From the Mann-Whitney analysis, the amount of mental effort required for their self-care activities did not differ between those two groups (median = 7 in HF and 6 in healthy group). In HF patients, correlations between MSIT interference scores and mental effort were not significant.

Discussion

Construct validity of MSIT in examining directed attention in HF patients was examined and partially supported in this study. Among patients with HF, interference effects in MSIT were significant (hypothesis I) which indicates the MSIT is a valid measure of effectiveness of directed attention supporting interference skills. The MSIT interference scores produced similar results with the two other well-validated measures of directed attention, the Trail Making Test and Stroop Test supporting convergent validity of MSIT (hypothesis II). However, discriminant validity of MSIT overall interference scores in detecting differences between HF and healthy participants was not supported, and only raw scores of MSIT were supported (hypothesis III). It indicates that the overall interference scores of MSIT may not be a sensitive measure of detecting differences between HF patients, but Trail Making Test is. Among 3 tests used in this study, only Trail Making Test interference score was able to detect differences between the two groups' directed attention.

Raw scores of MSIT appeared to be more sensitive than overall z scores of MSIT (average z scores of error rate and response time interference scores) during the construct validity testing, especially response time scores. The reason may stem from the nature of MSIT commands. Participants were asked to respond to the target number as quickly as possible, but accuracy was emphasized more than speed as their goal. This may result in similar error rates but different response time in MSIT. The speed and error rate tradeoffs were found in the Attention Network Test as well, which is one of the foundations of MSIT and uses flankers instead of numbers (McLeod et al., 2010). Thus, when the scores from error rates and response time were averaged, the significant differences may disappear. Another supporting result for this tradeoff is that MSIT response time was more sensitive than overall interference scores to detecting differences between HF and healthy participants and had moderate to strong correlations with Trail Making Test scores. Separate analysis of MSIT response time and error rate also revealed significant relationships with age and education. In details, the MSIT response time had significant correlations with age and education had a significant relationship with the error rates (Table 4.3). The relationships are consistent with the finding in Trail Making Test and Stroop Test.

Directed attention measured by MSIT interference scores had a medium size correlation with perceived attentional function measured by AFI (research question 1), and the result was consistent with its conceptual relationship. Similar to the MSIT sensitivity to the group differences, the interference score from MSIT response time was correlated with the perceived attention function but not correlated to interference scores from error rate differences. All HF patients perceived that their chronic disease required extra mental effort to learn and follow the self-care activities. However, the amount of mental effort that HF patients perceived was “a little” on average in this study, and correlations with MSIT interference scores were not significant (research question 2).

However, the support for construct validity is limited by several factors. First, the small sample limits generalizing the results. Second, MSIT is little influenced by participants’ literacy, but might be more influenced by computer literacy. All HF patients in this study completed MSIT successfully, but using this computerized test in different populations may produce confounding effects in examining interference skills. Third, the command of MSIT, which asked participants to respond to the target numbers within 2 seconds, may affect the results because the trials that participants were unable to answer in 2 seconds were excluded from the analysis. Different MSIT commands allowing more time for responses may lead to different results.

In conclusion, there was a preliminary evidence of validating use of MSIT in HF patients to examine directed attention from interference skills. In the real world, there are always multiple stimuli that compete with important information or cognitive processes, and directed attention plays an important role in those situations. Thus, not only Trail Making A, which has been the most frequently used in HF (Bauer et al., 2010; Jung et al., 2015b), but also measures examining directed attention such as MSIT should be included in future studies.

Table 4.1. Descriptive Statistics of Sample Characteristics

Characteristic	Total (n = 42)	HF Group (n = 22)	Healthy Group (n = 20)	t or x^2 (p-value)
Age, years, mean ± SD	58.9 ± 11.9	58.9 ± 12.5	58.8 ± 11.6	0.029 (.977)
Education, years, mean ± SD	14.9 ± 2.2	14.6 ± 2.4	15.3 ± 2.0	-1.022 (.313)
MMSE, mean ± SD	28.1 ± 1.7	27.4 ± 1.9	28.8 ± 1.2	-2.904 (.006)*
Gender, n (%)				.349 (.757)
Men	21 (52.5)	13 (59)	10 (50)	
Women	19 (47.5)	9 (41)	10 (50)	
Race, n (%)				4.171 (.244)
African-American	4 (10)	3 (14)	1 (5)	
Asian	2 (5)	2 (9)	0 (0)	
White	35 (83)	16 (73)	19 (95)	
More than one race	1 (2)	1 (4)	0 (0)	
Ethnicity, n (%)				.266 (.876)
Hispanic	2 (5)	1 (5)	1 (5)	
Non-Hispanic	37 (88)	19 (86)	18 (90)	
Unknown	3 (7)	2 (9)	1 (5)	
Marital status, n (%)				.155 (.758)
Married	26 (62)	13 (59)	13 (65)	
Not married	16 (38)	9 (41)	7 (35)	
Employment, n (%)				3.536 (.171)
Employed	13 (31)	4 (18)	9 (45)	
Not employed	5 (12)	3 (14)	2 (10)	
Retired	24 (57)	15 (68)	6 (45)	
Handedness, n (%)				2.027 (.243)
Right handed	34 (81)	16 (73)	18 (90)	
Left handed	8 (19)	6 (27)	2 (10)	
AFI, total, mean ± SD	96.6 ± 21.1	84.6 ± 19.9	109.8 ± 13.3	-4.864 (< .001)*
Effective action	52.2 ± 13.1	44.3 ± 12.6	60.9 ± 6.4	-5.460 (< .001)*
Attentional lapses	22.7 ± 5.9	20.6 ± 7.0	25.0 ± 3.3	-2.614 (.014)*
Interpersonal effectiveness	21.7 ± 6.9	19.7 ± 7.3	23.9 ± 5.7	-2.082 (.044)*
Number of people having chronic disease requiring mental efforts, n (%)	26 (62)	22 (100)	4 (20)	28.431 (< .001)*
Mental effort, mean ± SD (range)	9.81 ± 10.27	10.68 ±10.88 (0 - 39)	5.00 ± 3.56 (0 - 8)	33.500 (.471)
LVEF, mean ± SD	-	37.6 ± 14.5	-	-
BNP before enrollment, mean ± SD	-	273.0 ± 328.3	-	-
NYHA[g] class, n (%)	-		-	-
II		9 (41)		
II to III		4 (18)		
III		8 (36)		
IV		1 (5)		

Note. * $p < .05$. AFI = Attentional Function Index. BNP = brain natriuretic peptide. HF = heart failure. LVEF = left ventricular ejection fraction. MMSE = Mini-Mental Status Examination. NYHA class = New York Heart Association classification.

Table 4.2. Descriptive Statistics of Attention Measures

Attention Measures	HF Group (n = 22)	Healthy Group (n = 20)	t	p-value
MSIT, error rate (%)				
Congruent	0.65 ± 1.21	0.05 ± 0.24	2.279	.032*
Incongruent	6.04 ± 3.41	4.36 ± 3.72	1.527	.135
z-score of the difference	0.14 ± 0.97	-0.16 ± 1.03	0.985	.331
MSIT, response time (ms)				
Congruent	769 ± 130	701 ± 116	1.785	.082
Incongruent	1077 ± 132	977 ± 153	2.268	.029*
z-score of the difference	0.24 ± 0.87	-0.27 ± 1.08	1.684	.100
MSIT, interference z-score	0.19 ± 0.77	-0.21 ± 0.85	1.310	.198
Trail Making Test (seconds)				
A (only numbers)	40.92 ± 13.40	26.68 ± 9.84	3.780	.001*
B (number-letter)	100.70 ± 47.24	59.74 ± 20.04	3.408	.002*
Difference (B - A)	59.77 ± 40.40	33.05 ± 21.09	2.506	.018*
Trail Making, interference z-score	0.36 ± 1.15	-0.40 ± 0.60	32.274	.010*
Stroop Test, error rate (%)†				
Congruent	2.65 ± 3.48	1.32 ± 3.39	1.241	.222
Incongruent	26.26 ± 17.63	13.01 ± 10.72	2.881	.007*
z-score of the difference	0.38 ± 1.09	-0.44 ± 0.68	2.951	.006*
Stroop Test, response time (ms)†				
Congruent	1365 ± 407	1325 ± 295	0.372	.712
Incongruent	1622 ± 498	1703 ± 521	-0.509	.614
z-score of the difference	-0.21 ± 0.87	0.24 ± 1.11	-1.466	.151
Stroop test, interference z-score	0.08 ± 0.59	-0.10 ± 0.75	0.880	.384

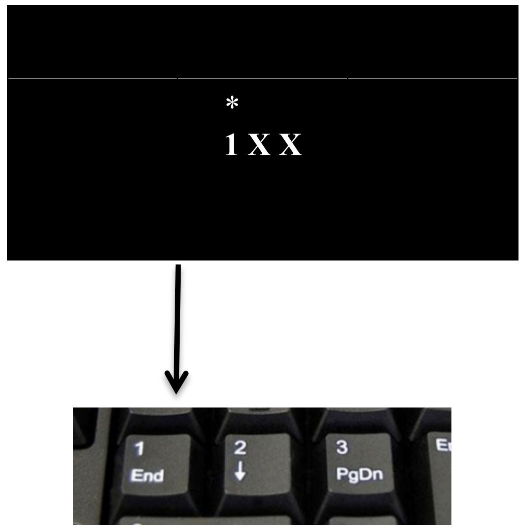
Note. * $p < .05$. HF = heart failure. MSIT = Multi-Source Interference Task.

Table 4.3. Correlations between the Multi-Source Interference Task and Other Attention Measures in Heart Failure Patients (n = 22)

	MSIT Congruent Trials		MSIT Incongruent Trials		MSIT, Incongruent - Congruent, z score		
	Error Rate	Response Time	Error Rate	Response Time	Error Rate	Response Time	Overall Interference
Trail Making A	.255	.431*	-.214	.473*	-.301	.119	-.123
	(.255)	(.045)	(.340)	(.026)	(.173)	(.597)	(.585)
Trail Making B	.283	.463*	.179	.521*	.077	.162	.141
	(.202)	(.303)	(.426)	(.013)	(.734)	(.472)	(.531)
Trail Making B - A, z score	.246	.398	.280	.452*	.190	.150	.206
	(.269)	(.067)	(.207)	(.035)	(.398)	(.507)	(.358)
Stroop, error rate z score	.139	.325	.206	.389	.155	.170	.195
	(.536)	(.140)	(.357)	(.074)	(.492)	(.450)	(.384)
Stroop, response time z score	-.478*	-.102	-.327	-.121	-.155	-.052	-.129
	(.025)	(.653)	(.137)	(.591)	(.490)	(.817)	(.569)
Stroop overall interference z score	-.224	.227	-.051	.271	.029	.119	.086
	(.317)	(.311)	(.823)	(.222)	(.899)	(.598)	(.703)
AFI total score	-.082	.045	-.421	-.137	-.387	-.445*	-.500*
	(.716)	(.841)	(.051)	(.543)	(.075)	(.038)	(.018)
AFI, effective action	-.181	.034	-.392	-.102	-.324	-.332	-.395
	(.421)	(.881)	(.071)	(.651)	(.142)	(.132)	(.069)
AFI, attentional lapse	-.049	-.070	-.265	-.230	-.244	-.395	-.381
	(.828)	(.755)	(.234)	(.302)	(.273)	(.069)	(.081)
AFI, interpersonal effectiveness	.134	.133	-.217	.024	-.262	-.262	-.316
	(.551)	(.555)	(.332)	(.915)	(.239)	(.239)	(.152)
Mental effort total score	.253	.188	.077	.292	-.013	.262	.141
	(.256)	(.102)	(.735)	(.188)	(.953)	(.239)	(.532)
Age	.056	.639*	-.089	.569*	-.108	-.145	-.151
	(.797)	(.001)	(.695)	(.006)	(.632)	(.519)	(.501)
Education	-.491*	.175	-.141	.054	.034	-.291	-.144
	(.020)	(.435)	(.532)	(.812)	(,881)	(.190)	(.522)
LVEF	.158	-.149	-.208	-.232	-.261	-.210	-.286
	(.483)	(.507)	(.352)	(.298)	(.240)	(.349)	(.197)

Note. * $p < .05$. AFI = Attentional Function Index. BNP = brain natriuretic peptide. HF = heart failure. LVEF = left ventricular ejection fraction. MSIT = Multi-Source Interference Task.

Figure 4.1. Examples of Congruent and Incongruent Trials in the Multi-source Interference Task



A. A congruent trial: the target number is located in the same position with the number key on the computer keyboard. Congruent trials always have 2 letters of X and only 1 number, ‘1’ in this case.

B. An incongruent trial: the target number is located in a different position with the number key on the computer keyboard. In this example, target number ‘1’ is in the middle, but a participant is required to press the most left key. Incongruent trials have only numbers.

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Chapter 5

Summary and Conclusions

Heart failure (HF) is a prevalent syndrome affecting 5.1 million people and living with HF is challenging because dysfunction of the heart affects all organs of the body. Insufficient blood supply to the brain has shown negative influences in brain function, and cognitive impairment evaluated with valid, reliable neuropsychological tests was found in 23% to 50% of HF patients (Pressler, 2008). The most impaired cognitive domains in HF include memory, executive function, and attention. Attention is particular concern because it is critical to performing everyday activities (Kaplan, 2001). Attention, in an everyday term is simple and often called concentration and surveillance. The concept of attention, however, is complex in that it is associated with diverse aspects of information processing such as directing focus of the mind into specific stimuli and maintaining or switching the focus.

Despite the complexity of attention, specific aspects of attention that are affected by HF have not been examined and remain unclear. To our knowledge, there is no study that directly targeted improving attention in HF patients. Therefore, the primary purposes of this dissertation were to review existing literature on impaired attention in HF and to improve attention by using a natural restorative environment intervention. Improvement in mood was examined as a secondary outcome of the intervention. Additionally, the validity of the Multi-source Interference Task was examined in patients with heart failure.

As shown in Chapter 2, the results of literature review on attention in HF indicated that approximately 1 in 4 patients with HF experience impaired attention, and HF patients' attention was poorer than healthy adults and other medically ill individuals without HF. However, the conceptual definition of attention and attention impairment in each study was not clearly provided, and the lack of theoretical/conceptual definitions of attention made it difficult to examine different aspects of attention that is impaired in HF (e.g., directed attention, selective attention, attention span). In order to examine the aspects of attention without conceptual definition in the literature, this study reviewed attention measures and found that directed and sustained attention were commonly impaired in HF patients. Directed attention—called voluntary attention—is required in a situation where a person tries to focus on a task or stimulus that is not particularly interesting. Sustained attention involves focusing on a stimulus for a prolonged period of time. Sustained and directed attention are important factors of everyday activities including learning, and the result that poorer attention was associated with poorer self-care adherence in HF from this literature review supported that attention is critical to learning and/or maintaining self-care activities for HF. Despite the importance of impaired attention, little effort has been made to improve the impaired attention in HF from the literature review. Only two medical intervention studies, which targeted increasing cardiac output, resulted in improved attention secondary to the increased blood supply, but the medical treatment is not available for all HF patients with attention impairment. As indicated in Chapter 2, research on underlying factors of impaired cognition including attention has been more focused on pathophysiological factors HF condition (e.g., lowered cerebral blood flow, microembolism in the brain) but not psychological factors such as increased demand for attention.

The amount of demand for attention, specifically directed attention, is a key component of the Attention Restoration Theory that addresses how attention is fatigued and restored. Attention Restoration Theory asserts that when the demand is greater than one's capacity, directed attention function decreases, but when directed attention is rested from reduced or no attentional demand, directed attention function can be restored (Kaplan, 1995/2001). As a way to rest directed attention, more use of involuntary attention is suggested, and nature is considered to be a good source for resting directed attention by reducing demands for directed attention in the theory. Although Attention Restoration Theory does not provide information about how directed attention can be improved in chronically ill patients with brain structural changes, investigators have examined efficacy of natural restorative environment interventions based on Attention Restoration Theory in chronically ill populations (e.g., breast cancer patients, children with attention deficit hyperactivity disorder, patients with major depressive disorder) and found positive results (Berman et al., 2012; Cimprich & Ronis, 2003; Faber Taylor & Kuo, 2009). There is an intervention that was already developed and tested for efficacy in healthy young adults (Berman et al., 2008). The intervention involved showing a series of slides on nature photographs, and the active control condition involved showing a series of slides on urban environment photographs. The present study was designed to examine efficacy of the natural restorative environment intervention in HF.

As indicated in Chapter 3, a randomized crossover study was conducted to improve attention and mood by using the natural restorative environment intervention among 20 HF patients and 20 age- and education-matched healthy adults. Hypotheses were 1) HF patients have greater improvement in attention after NRE intervention compared to the urban control condition; 2) HF patients have greater improvement in mood after NRE intervention compared to the urban control condition; 3) healthy participants have greater improvement in attention after NRE intervention compared to the urban control condition; and 4) healthy participants have greater improvement in mood after NRE intervention compared to the urban control condition. Linear mixed models in separate analysis of each group (20 HF and 20 healthy) did not show significant improvement in neither attention nor mood after the NRE intervention compared to the active control condition. There was a tendency for attention improvement on the measures of directed, sustained attention, and attention switching to be larger than the improvement after the control condition in HF patients, but statistical significance was not found. The linear mixed models showed that individual characteristics had a more significant impact on attention than the intervention in this small sample. These results suggest that a larger sample size is needed to test the intervention efficacy in HF and healthy older adults due to the heterogeneity, and furthermore, longitudinal study designs are necessary to examine attention.

Although the hypotheses were not supported from the separate group analysis of linear mixed models, the pooled sample analysis with all HF and healthy participants (n = 40), indicated that sustained attention significantly improved after the brief intervention (50 nature photographs for 7 minutes) compared to the control condition (50 urban environment photographs for 7 minutes). This preliminary positive finding on attention improvement is consistent with the Attention Restoration Theory and supports that the theory is relevant to HF patients and older adults. Attention Restoration Theory defines attention as *directed* and *involuntary*, sustained attention can fall into the definition of directed attention because James defined directed attention as effortful attention (James, 1890). Although the study used different measures of directed and sustained attention and only found significant improvement in sustained attention, sustained attention measures require mental effort to complete the tests, indicating that directed attention is involved. In this sense, this result is consistent with the theory. If the efficacy is more firmly established, the natural restorative intervention may provide possible strategies that nurses can teach HF patients when attention decreases are noticed in these patients. The intervention takes not much time, requires minimal physical effort, low cost, and is enjoyable. Thus, the intervention has the potential to be widely disseminated.

Attention switching was preserved in healthy adults after the control condition, but HF patients' attention switching performance decreased after the control condition. The different responses to the control condition may indicate that HF patients are more susceptible to the increased demand of directed attention from the control condition, and the increased susceptibility may be because HF patients had poorer attention at baseline that means less available attentional resources.

Another reason for different responses in attention switching may be inadequate oxygen supply in HF patients. Level of oxygen saturation measured during the research visits showed that HF patients had lower average oxygen saturation compared to healthy participants. This lower oxygen saturation in HF patients may be a significant barrier to improving attention from the intervention.

In addition to the oxygen saturation, increased mental effort from self-care activities for chronic diseases was reported in HF patients compared to healthy adults. The natural restorative environmental intervention provided an opportunity to rest directed attention during the time of intervention, but was not designed to reduce the higher level of mental effort in HF. This may affect the responsiveness to the intervention. Given the results that HF patients' attention switching can be more easily fatigued in combination with their lower oxygen saturation and greater mental effort, HF patients may need more frequent natural restorative environmental intervention—as if frequent charges are needed for small batteries with excessive use.

In contrast to the positive results on attention from the intervention, mood did not improve in both HF and healthy participants after the intervention compared to the control condition. As mentioned in Chapter 3, there are three possible reasons of insignificant changes of positive and negative mood. First, mood measured by the Positive and Negative Affect Schedule had ceiling and floor effects, and the measure might not be the best tool to assess intervention responses in HF patients. Second, the mode of the intervention may affect mood improvement. Previous studies showed mood improvement involved in walking in the park (Berman et al., 2008; Berman et al., 2012) that increased interactions with nature in reality rather than interactions with nature in virtual environment as the present study involved. Not only visual but also other senses used in walking in the park might provide more opportunity to improve mood. Third, selection bias that might have been occurred during enrollment may result in less variability of mood changes. Enrolling HF patients with poor mood and delivering the intervention to the patients may change the results.

The Multi-source Interference Task (MSIT) is a computerized neuropsychological test that was administered to assess directed attention involved in interference situations. Interference can occur in which incoming information and earlier information are in conflict with each other (Berman, Jonides, & Lewis, 2009; Kaplan & Berman, 2010). Interference situations make it harder for an individual to keep focused on the original tasks, and it recruits directed attention to resolve the interference situation. The MSIT has not been used in HF patients before this study, and the test needed to be validated in HF. The construct validity of MSIT was supported by the baseline data of the present study and is described in Chapter 4. Construct validity analyses showed that HF patients (n = 22) performed worse in interference situations with competing stimuli than non-interference situations, and this finding is consistent with the finding of interference effect in healthy young adults (Bush et al., 2003; Bush & Shin, 2006). Correlation analyses to confirm content validity of MSIT detecting directed attention showed that better MSIT performance in terms of error rates and response time was moderately associated with better Trail Making Test A and B performance that is a traditional and well-validated measure of directed attention. Directed attention from overall MSIT interference scores had a positive relationship with perceived effectiveness of directed attention measured by the Attentional Function Index as well. However, correlations between average interference scores from MSIT and the average interference scores from the Trail Making Test and Stroop Test were not significant. The possible reason why separate analyses of error rates and response time of MSIT interference scores showed different results from MSIT average interferences scores is the nature of MSIT command. The MSIT asks participants to respond to the target as quickly as possible, but not sacrificing accuracy. Due to the command, response time and error rate can tradeoff, leading to disappearance of significant directed attention effects while averaging response time and error rate for the overall interference scores. These findings provide preliminary support for using MSIT as a valid measure of directed attention in HF population. However, separate analyses for error rate and response time are needed with overall interference scores to assess directed attention more comprehensively.

Taken together, the findings of this study address gaps in the literature on attention impairment in HF, and provide a possible solution to attention impairment. The simple natural restorative environmental intervention can improve HF patients' attention that required to complete goal-directed tasks effectively. Initial content validity of MSIT was supported in HF patients.

Strengths

This is, to our knowledge, the first study that reviewed domain specific cognitive impairment, namely attention, in HF patients and provided an intervention targeting attention. The findings of this study contribute to the current scientific body of knowledge about impaired attention in HF in several ways. First, the findings of the systematic literature review and analysis supported the view that impaired attention is common problem in heart failure and that there is a need to improve attention because impaired attention affects HF patients' self-care activities for managing heart function. Second, not only pathophysiological factors but also psychological factors of impaired attention were examined. Increased demands of directed attention from the self-care activities for HF was reported for the first time, supporting mechanisms of attention impairment in this population. Third, the preliminary results of improved attention after the natural restorative environment intervention may indicate that impaired attention in HF is not a permanent condition but is reversible. Fourth, the intervention was enjoyable and broadly applicable with little burden on the level of physical function as well as efficacious in improving attention. The basis of the intervention is resting directed attention in an aesthetically pleasing natural environment, and it requires a very short period of time and little physical strength. These characteristics may facilitate generalization of the intervention. Fifth, this is the first study that used and validated the Multi-source Interference Task in HF patients. The test is less complex than the Stroop test, and it is easier to create different formats of the test compared to the Trail Making Test. Thus, the test might be the one sensitive and valid measure of directed attention that can be used for multiple observations in longitudinal studies without frustrating participants due to complexity.

Limitations

Despite the strengths noted above, this study was limited in some respects. First, the literature reviewed for impaired attention only included the studies using neuropsychological tests and excluded brain imaging studies that did not administer neuropsychological tests. As a result of these inclusion and exclusion criteria, the relationship between impaired attention and structural changes of the brain in the HF patients was not reported. Second, although the sample size of this intervention study was calculated by power analysis, there were more variances from individuals than expected. The third limitation is that information on which level of attention is good enough for HF self-care activities is not available. The relationship between improved attention and improvement in self-care activities was not examined in this study. Fourth, the natural restorative environment intervention of this study used only one sensory mode, which is visual. Last limitation is that the optimal dose of the intervention and its long-term effects are unclear. With the attainment of this information, the natural restorative environment intervention may help prevent or delay vascular dementia in HF patients.

Implications for Nursing Practice

Nurses educate patients and patients' family all the time and often encounter patients who complaint about their decreased cognitive function. A recent report from American Heart Association about transition care from hospital to home addressed that insufficient education and lower awareness about the disease care in HF patients impede successful transitions (Albert et al., 2015). Nurses intuitively know about decreased attention in HF patients and put more effort to deliver the educations more effectively by modifying content (e.g., using plain words suitable to everyone with any education level, cartoons) and mode (e.g., video, one-on-one education) (Jovicic, Holroyd-Leduc, & Straus, 2006). However, little effort has been made to improve attention and prevent attention impairment among HF patients. The present study provides preliminary evidence that there is an intervention that nurses may be able to suggest to HF patients to improve the patients' attention. In addition, the study proposes that ongoing monitoring would be needed because attention is not static but dynamic, and especially in HF, attention is likely to be more susceptible to the task requires more attentional demands such as multitasking.

Implications for Future Studies

Future studies on a larger scale providing knowledge about the optimal intervention dosage and mode to improve attention are needed. In detail, future studies should be designed to contain a larger sample size due to the strong effect of individual random effects which was found in this study. Effects of varying intervention doses in a longer follow-up period should be examined in the relationship with the amount of attention improvement and sustainability of the improvement. The present study administered the intervention only one-time, and more cumulative or frequent intervention administration may have bigger impact on attention improvement. In addition, diverse formats of the natural restorative environment intervention based on individual's preference will be needed. Providing choices on the intervention formats or contents may increase participants' engagement in the intervention. Comparison of the natural restorative environment intervention efficacy with other cognitive intervention such as cognitive training will be needed. Moreover, combined effect of different types of cognitive intervention or other enhancements should be examined. Determining the onset of impaired attention and the best time to approach HF patients to improve attention should also be explored.

More importantly, future studies should examine the impact of improved attention on self-care adherence including medication compliance and other related healthcare outcomes such as mortality and health-related quality of life.

Conclusions

In conclusion, attention—which is known to be commonly impaired in patients with HF—improved with simple restoring activities. A natural restorative environment intervention based on Attention Restoration Theory was efficacious in improving attention. The intervention has the potential to be generalized because it is easy, safe, and requires little physical effort. Considering that patients with HF are frequently limited in their physical function due to cardiac dysfunction, this intervention could possibly be widely disseminated if the intervention efficacy increases. The Multi-source Interference Task can be administered in longitudinal studies as a sensitive and valid measure of directed attention. This study provides evidence that impaired attention in HF can improve and may delay more serious cognitive impairment such as vascular dementia.

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Appendix

Appendix A. Correlations between Participant Characteristics and Attention and Mood at Baseline (n = 40)

	MMSE	Digit Span For-ward	Digit Span Back-ward	Trail Making A	Trail Making B	MSIT z score	Stroop z score	Interference	Sustanined attention	Attention switching	Positive mood	Negative mood
Age	-.201	-.072	-.183	.245	.539**	-.105	.312	.360*	.321*	-.195	-.056	.021
Education	.216	.025	.087	-.190	-.123	.113	-.019	.011	-.190	-.260	.219	.010
SBP	.138	-.237	.084	-.257	-.137	-.107	-.044	-.120	-.272	-.322*	-.291	.219
DBP	.053	-.007	.236	-.186	-.193	-.147	-.147	-.196	-.243	-.190	-.229	.314*
Mean SpO2	.290	-.139	.145	-.168	-.455**	-.245	-.170	-.433**	-.250	.093	.195	-.186
SpO2<95% (minutes)	-.231	.067	-.140	.169	.426**	.212	.127	.387*	.205	-.142	-.242	.002
AFI	.156	.206	.207	-.407**	-.454**	-.439**	-.308	-.529**	-.315	.028	-.104	-.396*
FCAS	.027	-.127	.110	-.433**	-.109	.057	-.071	.021	-.300	-.066	.497**	.062
Nature activity	-.331*	.183	.075	.039	.198	-.083	.051	.104	.073	.078	.215	.036
HF Symptoms	-.309	-.064	-.209	.335*	.307	.098	.182	.247	.280	-.088	.010	.454**
Mental effort	.023	.078	-.229	.410**	.263	.191	.179	.252	.331*	.173	-.029	.183
LVEF†	-.167	.193	.249	-.242	-.513*	-.297	-.490*	-.614*	-.297	.177	-.221	.145
BNP†	-.059	-.215	-.336	.437	.579**	.101	.364	.502*	.434	-.108	.071	-.187
Fatigue†	.177	.120	.297	-.111	-.299	-.136	.104	-.230	-.182	-.257	.054	.421
CDS†	-.046	.105	.112	-.169	-.016	.023	-.132	-.007	-.043	.078	.020	.225

Note: AFI = Attentional Function Index; BNP = brain natriuretic peptide; CDS = Current Dyspnea Status; DBP = diastolic blood pressure; FCAS = Florida Cognitive Activities Scale; LVEF = Left ventricular ejection fraction; MMSE = Mini-Mental Status Examination; NYHA = New York Heart Association; SBP = systolic blood pressure; SpO2 = Peripheral capillary oxygen saturation from pulse oximeter

†sample size for this analysis, n = 20, only HF participants

Appendix B. Means and Standard Deviations of Outcome Variables (n = 40)

	HF Group (n = 20)				Healthy Group (n = 20)			
	Nature (n = 20)		Urban (n = 20)		Nature (n = 20)		Urban (n = 20)	
Outcome variables	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test	Pre-test	Post-test
Attention								
MSIT, error rate (%)								
Congruent	0.56 ± 1.18	1.24 ± 4.42	0.48 ± 0.88	1.08 ± 1.96	0.36 ± 1.60	0.00 ± 0.00	0.05 ± 0.24	0.05 ± 0.21
Incongruent	4.79 ± 3.40	4.59 ± 4.42	4.67 ± 2.42	4.27 ± 3.92	4.13 ± 4.00	1.77 ± 1.99	3.67 ± 3.93	2.13 ± 2.20
z score, error difference (Incongruent - congruent)	-0.12 ± 0.92	-0.38 ± 0.82	-0.14 ± 0.77	-0.42 ± 0.82	-0.25 ± 0.97	-0.83 ± 0.57	-0.30 ± 1.11	-0.74 ± 0.64
MSIT, response time (ms)								
Congruent	755 ± 143	737 ± 123	741 ± 116	721 ± 114	661 ± 93	629 ± 79	662 ± 122	636 ± 127
Incongruent	1047 ± 150	1019 ± 145	1043 ± 123	1015 ± 128	921 ± 148	890 ± 129	921 ± 152	886 ± 154
z score, response time difference (Incongruent - congruent)	0.01 ± 0.66	-0.15 ± 0.95	0.19 ± 0.91	0.05 ± 1.05	-0.48 ± 1.26	-0.47 ± 1.29	-0.50 ± 0.99	-0.66 ± 0.85
MSIT average z score	-0.06 ± 0.66	-0.26 ± 0.62	0.03 ± 0.68	-0.19 ± 0.77	-0.37 ± 0.98	-0.65 ± 0.89	-0.40 ± 0.86	-0.70 ± 0.61
Digit Span Test, score								
Forward	6.80 ± 1.44	6.55 ± 1.19	6.70 ± 1.22	6.55 ± 1.15	6.85 ± 1.18	6.90 ± 1.41	6.80 ± 1.15	7.25 ± 1.21
Backward	4.40 ± 1.54	4.55 ± 1.79	4.30 ± 1.75	4.85 ± 1.42	5.05 ± 0.95	5.40 ± 1.57	4.55 ± 0.89	5.00 ± 1.45
Trail Making Test (sec)								
A (only numbers)	41.90 ± 14.87	41.80 ± 21.67	41.92 ± 17.99	44.38 ± 28.18	27.44 ± 9.67	24.68 ± 6.92	25.03 ± 7.28	24.95 ± 7.57
B (number-letter)	97.78 ± 47.52	87.37 ± 45.35	98.29 ± 52.80	88.04 ± 44.39	58.10 ± 22.37	53.03 ± 22.32	56.88 ± 20.66	55.25 ± 21.84
B - A	55.88 ± 40.22	45.57 ± 37.34	56.36 ± 43.23	43.65 ± 28.88	30.66 ± 21.85	28.35 ± 18.60	31.86 ± 18.22	30.30 ± 19.70
Stroop Test, accuracy (%)								
Congruent	4.17 ± 8.14	2.5 ± 3.24	3.47 ± 4.84	2.92 ± 3.55	0.29 ± 0.88	1.17 ± 2.67	1.17 ± 3.38	0.44 ± 1.04
Incongruent	23.61 ± 18.28	18.19 ± 18.30	19.72 ± 15.81	14.31 ± 16.03	11.70 ± 9.82	4.24 ± 4.38	10.82 ± 10.47	5.70 ± 7.26
z score (Incongruent - congruent)	0.13 ± 1.24	-0.14 ± 1.27	-0.10 ± 1.00	-0.45 ± 1.06	-0.45 ± 0.70	-1.04 ± 0.21	-0.57 ± 0.67	-0.89 ± 0.50
Stroop Test, response time (ms)								

Congruent	1432 ± 476	1352 ± 338	1285 ± 304	1281 ± 296	1282 ± 300	1178 ± 275	1242 ± 332	1180 ± 352
Incongruent	1641 ± 541	1616 ± 513	1598 ± 353	1659 ± 387	1630 ± 510	1445 ± 467	1595 ± 522	1407 ± 423
z score (Incongruent - congruent)	-0.40 ± 0.87	-0.20 ± 1.30	-0.02 ± 0.68	0.21 ± 0.76	0.11 ± 1.05	-0.19 ± 0.94	0.12 ± 0.91	-0.33 ± 0.70
Stroop average z score	-0.14 ± 0.71	-0.17 ± 1.03	-0.06 ± 0.65	-0.12 ± 0.77	-0.17 ± 0.74	-0.62 ± 0.51	-0.23 ± 0.69	-0.61 ± 0.55
Stroop, error rate (%) for non-switching trials	10.49 ± 15.69	10.24 ± 14.28	11.12 ± 17.21	8.66 ± 12.78	8.89 ± 16.40	4.01 ± 5.93	6.76 ± 10.33	4.54 ± 7.42
Stroop, error rate (%) for switching trials	12.75 ± 14.99	7.16 ± 8.71	9.63 ± 13.80	6.55 ± 8.19	6.04 ± 7.13	1.05 ± 3.15	5.88 ± 10.56	1.40 ± 4.35
Error rate difference (switching - non-switching)	2.26 ± 9.12	-3.08 ± 10.25	-1.49 ± 13.96	-2.11 ± 8.08	-2.85 ± 15.37	-2.96 ± 4.46	-0.88 ± 7.95	-3.14 ± 6.62
Stroop, response time (ms) for non-switching trials	1485 ± 405	1370 ± 416	1509 ± 519	1492 ± 447	1578 ± 479	1333 ± 540	1408 ± 441	1341 ± 484
Stroop, response time (ms) for switching trials	1619 ± 693	1654 ± 547	1373 ± 376	1475 ± 464	1547 ± 515	1311 ± 410	1515 ± 536	1283 ± 417
Response time difference (switching - non-switching)	134 ± 468	284 ± 462	-136 ± 341	-18 ± 418	-30.36 ± 513	-22 ± 248	108 ± 306	-58 ± 246
Attention interference, z score	0.08 ± 1.96	-0.45 ± 2.25	0.25 ± 1.74	-0.37 ± 1.68	-1.00 ± 1.66	-1.80 ± 1.31	-1.13 ± 1.44	-1.79 ± 1.11
Sustained attention, z score	1.17 ± 2.60	1.09 ± 3.34	0.77 ± 2.27	1.10 ± 1.68	-1.09 ± 1.30	-1.64 ± 1.11	-1.37 ± 1.53	-1.72 ± 1.19
Attention switching, z score	0.11 ± 0.45	0.06 ± 0.60	-0.25 ± 0.68	-0.18 ± 0.50	-0.25 ± 0.69	-0.17 ± 0.40	-0.01 ± 0.42	-0.21 ± 0.51
Mood, PANAS								
Positive mood	30.1 ± 7.9	30.6 ± 10.5	31.9 ± 7.3	30.5 ± 8.2	33.20 ± 8.29	32.80 ± 9.53	31.55 ± 9.34	30.00 ± 9.69
Negative mood	11.9 ± 4.1	11.7 ± 4.3	11.6 ± 3.2	10.5 ± 1.8	11.40 ± 1.93	11.15 ± 1.73	1.95 ± 1.67	11.40 ± 2.35

Linear mixed models on each outcome variable for comparing pre and post-test changes between the treatments with age, education, and the order of intervention received (for practice effect) covariates. Random effects for individuals were incorporated in the models.