HHS Public Access

Author manuscript

Health Psychol. Author manuscript; available in PMC 2016 November 17.

Published in final edited form as:

Health Psychol. 2014 November ; 33(11): 1337–1343. doi:10.1037/hea0000039.

Greater Physical Activity is Associated with Better Cognitive Function in Heart Failure

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Abstract

Objective—Nearly 6 million Americans have heart failure (HF), up to 80% of which exhibit cognitive deficits on testing. Physical inactivity is common in HF, yet little is known about the possible contribution of physical inactivity to cognitive dysfunction in this population.

Methods—Older adults with HF (N=93; M_{age} = 68.5, 33.7% women) completed neuropsychological testing, as well as cardiac and physical activity assessment as part of a larger protocol. Heart failure severity was measured via impedance cardiography. Physical activity was assessed via an Actigraph accelerometer and operationalized using daily step count and time engaged in moderate-vigorous activity (minutes/day).

Results—Linear regression analyses controlling for sex, high blood pressure, diabetes, depressive symptomatology, and HF severity showed that greater physical activity (both step count and minutes spent in moderate-vigorous activity) was associated with better executive function/ attention, processing speed, and scores on a screening measure of cognition.

Conclusions—These findings indicate that physical activity is an independent predictor of cognitive function in persons with HF. Future work is needed to clarify the mechanisms by which physical activity benefits cognitive function in HF and determine whether interventions to promote physical activity can attenuate cognitive decline over time.

Keywords

Cognitive function; Physical activity; Heart failure; Cardiovascular disease; Attention; Executive function; Older adults

Introduction

Nearly 6 million Americans have heart failure (HF) and 670,000 new cases are identified each year (American Heart Association, 2011). Through the increased prevalence of risk factors such as hypertension and type 2 diabetes (Lloyd-Jones et al., 2009; National Heart, Lung, and Blood Institute, 2012), HF is projected to afflict 1 in 5 adults during their lifetime (American Heart Association, 2011; Lloyd-Jones et al., 2009). HF currently accounts for an estimated $17.4 billion in Medicare costs per year (Jencks et al., 2009) and is a leading cause of re-hospitalization (Lloyd-Jones et al., 2009; National Heart, Lung, and Blood Institute, 2012).

In addition to its many medical consequences, HF is also associated with increased risk for neurological disorders such as Alzheimer's disease, stroke, and vascular dementia (Oiu et al., 2006; Roman, 2005; Wang et al., 2003), and cognitive deficits are common prior to the onset of these conditions. For example, studies estimate cognitive impairment affects 30–50% of HF patients, though in some cohorts impairment can occur in up to 80% of (Bennett and Suave, 2003). A growing number of risk factors for cognitive impairment in this population have been identified, including greater HF severity, structural deterioration of the brain, reduced cerebral blood flow, and the presence of medical/psychiatric comorbidities (Bennett et al., 2005; Dimopoulos et al., 2006; Pressler et al., 2010; Roman, 2004; Siachos et al., 2005; Vogels et al., 2007).

Another likely contributor to cognitive impairment in persons with HF is low levels of physical activity. HF patients exhibit low levels of physical activity compared to age-matched controls (He et al., 2001) and the progression of HF is associated with a declining capacity for physical activity (Pina et al., 2003). In turn, greater physical activity levels are associated with better cognitive function in healthy older adults and persons with cardiovascular disease (Colcombe and Kramer, 2003; Gunstad et al., 2005; Smith et al., 2010). Some preliminary evidence for an association between physical activity and cognitive impairment in HF already exists (Alosco et al., 2012). However, no study has examined the contribution of different aspects of physical activity (e.g. frequency, intensity) and cognitive function or utilized a comprehensive neuropsychological test battery. Such findings may provide clearer insight into the importance of physical activity to neurocognitive outcomes in persons with HF and provide key insight into underlying mechanisms. Based on the above, we hypothesized that greater physical activity would be independently associated with better cognitive function in older adults with HF.

Method

Participants

Older adults with HF were recruited from the outpatient cardiology clinic at Summa Akron City Hospital. Study participants were consecutively enrolled in a longitudinal study examining the neuropsychological aspects of HF. Strict inclusion/exclusion criteria were chosen for entry into the parent study to maximize generalizability to other samples and to capture the independent contribution of HF on cognitive function. Thus, participants of the current study met all criteria for parent study entry. For inclusion, participants had to be 50–

85 years of age, English-speaking, have a documented history of HF, and be stable on heart failure medications. Participants with a history of neurological disorder (e.g., stroke, Alzheimer's disease), significant psychiatric conditions (e.g., schizophrenia), developmental disability, or cardiac surgery within four weeks of study entry were excluded. A total of 159 study participants were enrolled in this aspect of the study. Participants were then excluded due to incomplete actigraphy data due to mechanical issues (N = 65) or missing BDI-II scores (N = 1), reducing the sample size to 93 (M_{age} = 68.48, ± 9.48; 33.7% women). Key medical and demographic variables were examined to ensure data was not systematically missing; T-tests revealed no significant difference ($p > .05$) existed between groups in terms of cardiac output, cognitive scores, or BDI scores. See Table 1 for demographic and clinical characteristics.

Measures

Neuropsychological test battery—Participants attended study appointments in an office setting at the recruiting hospital and completed a battery of well-established measures, including:

Global cognitive functioning

Modified Mini Mental Status Examination (3MS): This brief screening is comprised of several short tasks, including orientation, similarities, animal fluency, learning and recall of a short list of target words, and a copy of a geometric figure. The 3MS has been found to be reliable (alpha = 0.87) and valid screening measure of global cognition in both typically aging individuals and disease groups (McDowell et al., 1997).

Attention/executive function

Letter Number Sequencing (LNS): This measure of working memory asks participants to listen to strings of numbers and letters of increasing length and order them according to predetermined rules. Letter number sequencing is a subtest of the standardized WAIS intelligence instrument, which is very well validated across ages and disease groups (Wechsler, 2008).

Digit Symbol Coding: This task of psychomotor speed and complex attention asks participants to transcribe a geometric shape to its corresponding number. Digit Symbol Coding is also a subtest of the standardized WAIS intelligence instrument, which is very well validated across ages and disease groups (Wechsler, 2008).

Trail Making Test A and B (TMT-A, TMT-B): On Trail Making Test A task, participants connect a series of 25 numbered dots in ascending order as quickly as they can (e.g. 1–2–3, etc.). Trail Making Test B adds a set-shifting component and requires participants to alternate between numbers and letters in ascending order (e.g. 1-A–2-B, etc.). Trailmaking Test A and B have excellent reliability and validity and have been utilized extensively across samples, including among patients with cerebrovascular disease (Borstein, 1985).

Stroop Color Word Test: This test measures selective attention and cognitive inhibition. Participants first read columns of words spelling out colors printed in black ink (word

subtest), then identify the color of the ink in which a series of X's is printed (color subtest) and finally indicate the ink color of a word (which spells out a color), ignoring the verbal content (color-word subtest). An interference score was calculated based on word and color subtest performances to determine expected performance on the color-word subtest and compared the score to actual color-word test performance. The Stroop Test has been studied in healthy older adult populations as well as among patients with cognitive dysfunction and other medical conditions (Uttl and Graf, 1997).

Psychomotor Speed

To examine the association of physical activity with cognitive tasks containing a speeded component, several indices from above were used to generate an index of psychomotor speed, specifically: Trail Making Test A, Trail Making Test B, and Stroop Color Word Test.

Memory

California Verbal Learning Test-Second Edition (CVLT): Individuals are asked to learn, recall, and recognize a 16-item word list. Indices of Short Delay Free Recall, Long Delay Free Recall, and Recognition are generated. The CVLT has been examined in older adults (Paolo et al., 1997) with and without cognitive impairment as well as other disease groups. It shows adequate reliability (alpha = .84) and validity, and is a commonly utilized test of memory and learning.

Physical activity

Physical activity was assessed by the Actigraph GTIM accelerometer (Abel et al., 2008). Participants were instructed in how to wear the accelerometer (over the right hip, affixed to an elastic belt, preferably worn under their waistbands) and provided with a set of instructions for wear over a 7-day period. A valid day of wear was considered greater than or equal to 10 hours of wear per day and the activity data was restricted to participants with at least 3 valid days of accelerometer wear. Average daily step count was utilized as the primary independent variable in statistical analyses. To further explore physical activity intensity within older adults with HF, daily minutes of moderate to vigorous intensity activity was utilized as a secondary independent variable.

HF Severity

HF severity was assessed in two ways. It was first characterized descriptively by NYHA classification (see Table 1) through detailed medical record review at the time of recruitment into the study. However, given the potential concerns regarding this clinical index, HF severity was also directly operationalized as resting cardiac output (i.e. Abudiab et al., 2013), measured by impedance cardiography using the Hutcheson Impedance Cardiograph model 3000, which is built to FDA standards with a clinical-grade ECG. Impedance cardiographer records changes in thoracic impedance via a tetrapolar electrode system, together with a standard ECG (Sherwood et al., 1997). The Kubicek equation was used to derive stroke volume from impedance signals recorded using the standard tetrapolar band electrode configuration (Sherwood et al., 1997).

Depressive Symptoms

Due to the high rates of comorbidity between heart failure and depression (Thomas et al., 2008) and depression's independent impact on cognitive functioning in this population (Foster et al., 2011), depressive symptoms were entered as a covariate in the current analyses. Individuals completed the Beck Depression Inventory-II (BDI-II), a 21-item self-report measure to evaluate the presence and severity of depression. This measure has good psychometric properties and is commonly used among persons with medical conditions (Amau et al., 2001). BDI-II scores range from 0 to 63, with higher scores indicative of greater symptomatology.

Procedures

The local Institutional Review Board (IRB) at both Kent State University and Summa Health System approved the study procedures and all participants provided written informed consent prior to study enrollment. During a single assessment visit at a laboratory in an outpatient clinical setting, participants completed demographic and psychosocial self-report measures and neuropsychological test battery. They were then instrumented with the accelerometers as described above. Accelerometers were later returned by mail.

Analyses

Raw scores from each cognitive test were converted to standardized T scores using published normative data. All T scores were adjusted for age and for the CVLT, age and sex. Composite scores were then calculated for the attention/executive, memory, and processing speed domains. Only global cognitive function, measured by the 3MS instead of a mean standard score, retained its raw scoring. Separate hierarchical regression analyses were conducted for each cognitive domain. Sex, heart failure severity (assessed as cardiac output), history of hypertension and type 2 diabetes mellitus (1 = positive history, 0 = negative history), and depressive symptomatology (as assessed by the BDI-II) were entered in the first block of each model. Average daily step count was entered into the second block of the model. This analysis was repeated using moderate to vigorous intensity activity (minutes/day) in the second block of the model. Separate hierarchical regression analyses were again conducted for each cognitive domain and covariates were retained to promote interpretability.

Post-hoc analyses were conducted to specifically examine the impact of fatigue on this relationship. The previous regression analysis was repeated with the original covariates in the first block, followed by two fatigue-related items from the BDI-II (Item 15 assessing loss of energy and item 20 assessing tiredness or fatigue) in the second block, and step count in the third block. These analyses were conducted for each cognitive domain.

Results

Low Levels of Physical Activity in HF

On average, the participants wore the accelerometer for 826 +/− 83 minutes per day and exhibited low levels of physical activity, averaging just 3501.00 +/− 2314.94 steps per day.

Based on daily step counts, 46.3% participants were categorized as sedentary, 27.4% limited physical activity, and just 26.3% as physically active. Consistent with this pattern, patients spent a large portion of time being sedentary (587 +/− 75 min/day). These low levels of physical activity are common in heart failure populations (Schnell-Hoehn, Naimark, & Tate, 2009; van der Wal et al., 2006).

Cognitive Impairment is Prevalent in HF

Cognitive impairment was prevalent in the sample, with many participants exhibiting clinically meaningful levels of impairment (i.e. T-scores <35; Heaton et al., 2004). For example, 28.4% showed significant impairment on the 3MS, a measure of global cognitive functioning.

Reduced Physical Activity Predicts Poorer Cognitive Function in HF

Correlation analyses revealed physical activity (i.e. daily step count) was associated with performance on multiple cognitive tasks (see Table 2). To clarify these univariate findings, a series of regressions were conducted to investigate whether physical activity indices independently predict cognitive function in older adults with HF. After controlling for sex, cardiac output, hypertension, type 2 diabetes, and BDI-II scores, average daily step count independently predicted global cognitive function ($F(6,91) = 2.538$, $\Delta R^2 = .070$, $p = .026$), attention/executive function ($F(6,91) = 5.243$, $\Delta R^2 = .072$, $p < .001$), and processing speed ($F(6,91) = 5.069$, $\Delta R^2 = .041$, $p = .032$). In each case, lower levels of physical activity were associated with poorer test performance. No such relationship emerged for memory tests ($F(6,91) = 0.518$, $\Delta R^2 = .014$, $p = .793$). See Table 3.

The relationship between step count and global cognition ($F(6,91) = 2.392$, $\Delta R^2 = .059$, $p = .019$), attention/executive function ($F(6,91) = 2.809$, $\Delta R^2 = .070$, $p = .006$), and processing speed ($F(6,91) = 2.111$, $\Delta R^2 = .040$, $p = .038$) remained significant after adjusting for fatigue as measured by items from the BDI-II. Step count did not significantly predict memory after adjusting for fatigue ($F(6,91) = 1.008$, $\Delta R^2 = .012$, $p = .316$).

Differential Effects of Activity Intensity and Cognitive Function

Correlation analyses revealed physical activity (i.e. duration of moderate-vigorous intensity activity) was also associated with several cognitive tasks (see Table 2). After adjusting for demographic and medical variables linear regression revealed minutes spent in moderate-vigorous intensity activity independently predicted global cognitive function ($F(6,91) = 2.266$, $\Delta R^2 = .056$, $p = .022$), attention/executive function ($F(6,91) = 5.535$, $\Delta R^2 = .083$, $p < .001$), and processing speed ($F(6,91) = 5.069$, $\Delta R^2 = .041$, $p = .032$) . In each case, lower levels of physical activity were associated with poorer test performance. No such relationship emerged for memory tests ($F(6,91) = 0.622$, $\Delta R^2 = .020$, $p = .183$). See Table 4.

Discussion

Consistent with past studies, low levels of physical activity and cognitive dysfunction was common in this sample of HF patients. Physical inactivity is a known contributor to poor outcomes in this population, including increased mortality risk and reduced quality of life

(Dickstein et al., 2008). The current study extends these findings and suggests that low levels of physical activity are also independently associated with poorer cognitive function in older adults with HF.

The current findings indicate that both low levels of daily physical activity (i.e. low step count) and less time spent at an elevated activity level (i.e. low minutes/day in moderate-vigorous intensity activity) are associated with reduced cognitive function, even after controlling for HF severity. A likely explanation for these findings is that physical activity increases cardiorespiratory fitness, which has been linked to better cognitive function in HF (Angevaren et al., 2008). In turn, greater physical fitness is associated with many physiological benefits that preserve cognition, including better endothelial and improved cardiac output (Davison et al., 2010; Jefferson, 2010). Participation in daily physical activity may also lead to improvements in cerebral perfusion (Rogers, Meyer, and Mortel, 1990), which is noteworthy as reduced cerebral blood flow and subsequent ischemia has been theorized to underlie cognitive deficits in HF (Jefferson et al., 2007). Prospective studies are needed to further elucidate the mechanisms by which physical activity may provide neuroprotective benefits in HF patients, particularly as it relates to increased cardiorespiratory fitness.

Active HF patients demonstrated better cognitive function relative to their sedentary peers, who constituted nearly 50% of HF patients of this sample. This pattern is alarming, as physical activity and structured exercise training are strongly recommended in persons with HF in order to improve quality of life, exercise capacity, and reduce mortality and hospitalization rates (Davies et al., 2010; Dickstein et al., 2008; Flynn, Pina, and Whellan, 2009). If confirmed, programs such as cardiac rehabilitation may help HF patients maintain their functional independence through associated cognitive benefits that in HF are linked to treatment adherence and ability to perform important daily tasks (Alosco et al., 2012). Along with other factors such as deficits in perceived social support and self-efficacy (Tierney et al., 2011), cognitive impairment may contribute to reduced adherence to exercise training programs (Conraads et al., 2012) which impose complex demands such as symptom monitoring and following dietary restrictions (Cameron, 2001). Indeed, recent work shows that greater executive deficits were associated with poorer outcomes in cardiac rehabilitation patients (Kakos et al., 2010). Prospective studies are needed to determine the exact role of cognitive function in the completion of exercise training programs and the potential benefits of physical activity on maintaining functional independence in HF patients.

The current study found a relationship between physical activity and cognition in HF within several cognitive domains, including attention/executive function, processing speed, and global cognitive functioning. However, this relationship was not found for memory function. Though the mechanisms for neurocognitive outcomes in HF remain incompletely understood, one explanation for these findings likely involves the sensitivity of impairments to frontal systems function in HF patients. Frontal brain regions, which largely mediate performance on tasks of executive function, processing speed, and attention, are particularly vulnerable to reduced cerebral blood flow (Sabayan et al., 2012). Thus, greater physical activity may translate to improved cerebral blood flow and the frontal lobes may benefit most from these changes (Rogers, Meyer, and Mortel, 1990). Future studies using advanced

neuroimaging to directly quantify cerebral perfusion would clarify this possibility and provide key insight into whether increased physical fitness leads to improved cerebral perfusion and subsequent cognitive benefits (Jefferson et al., 2007; Rogers, Meyer, Mortel, 1990).

The current study emphasizes the hypothesis that physical activity level will physiologically influence the brain and cognitive functioning. However, we acknowledge that this relationship may actually be circular, with more cognitively intact patients engaging in better health habits such as being more adherent, attending doctor's appointments, and intentionally including exercise as a part of their daily routine. Further research, especially prospective studies, should be conducted to clarify the directionality of this relationship.

The generalizability of the current findings is limited in several ways. First, our sample of heart failure patients was fairly homogenous, with the majority of patients in the early stages of heart failure (87% NYHA Class II) and no participants were wheelchair bound. We would expect samples with more severe heart failure and more limited mobility to demonstrate even greater impairment compared to the current study. Similarly, recent research suggests a growing number of factors may contribute to cognitive function in HF that were not available for statistical adjustment in the current study, including fatigue, socioeconomic status, and estimated IQ. The cross sectional approach also limits opportunity for determining the role of physical activity in attenuating cognitive decline in this population. Interestingly, recent evidence among elderly patients demonstrates that higher level of daily physical activity is associated with decreased risk for Alzheimer's disease (Buchman et al., 2012) and a similar benefit may emerge in this high risk population. Finally, though the current work employed well-established neuropsychological measures to investigate this relationship, future work should employ a combination of widely-used clinical measures (as utilized in the current study) in addition to more specific measures of specific abilities (e.g. various aspects of memory, psychomotor speed, etc.). Such instruments may provide further insight into the mechanisms by which physical activity benefits cognitive function in persons with HF.

In summary, the current study demonstrates that higher levels of daily physical activity are independently associated with better cognitive performance in older adults with HF. Prospective studies are needed to clarify the mechanisms linking physical activity and cognitive function in persons with HF and whether interventions to increase activity levels might improve cognitive function in this population.

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Table 1

Demographic and Medical Characteristics of 93 Older Adults with HF

Characteristics	
Demographic Characteristics	
Age[a] (years)	68.48 (9.48)
Education[a] (years)	13.35 (2.36)
Gender (% women)	33.7
Race (% Caucasian)	86.8
Medical Characteristics	
Hypertension	66.3
Diabetes	26.3
NYHA classification (% Class II)	87
(% Class III)	12
(% Class IV)	1
Test performance[a]	
Depression (BDI-II)	7.82(8.52)
Global Cognitive Functioning (3MS)	93.05(5.50)
Executive Functioning/Attention Composite[b]	
Trails A *	50.60(9.74)
Trails B *	44.30(17.92)
Digit Span	47.92(8.60)
Letter Number Sequencing	51.32(9.35)
Stroop Color Word Test *	44.79(10.60)
Memory Composite[b]	
CVLT Short Delay Free Recall	48.26(10.81)
CVLT Long Delay Free Recall	48.05(10.90)
CVLT Recognition	45.63(12.42)

[a] = mean (standard deviation),

[b] = T scores, mean (standard deviations),

* = task included in Processing Speed Composite

Table 2

Univariate Correlations between Cognitive Tests and Physical Activity

Cognitive Measures	Average Daily Step Count		Moderate-Vigorous Physical Activity (minutes/day)	
	r	*p*	*r*	*p*
Stroop Color Word Test	.39	<0.001	.32	0.002
CVLT Short Delay	.17	0.12	.17	0.10
CVLT Long Delay	.12	0.12	.18	0.08
CVLT Recognition	−.09	0.20	−.10	0.37
Trails A	.17	0.05	.19	0.07
Trails B	.27	0.003	.22	0.04
Digit Span	.36	<0.0001	.32	0.002
Letter Number Sequencing	.32	0.001	.28	0.008
3MS	.33	0.001	.27	0.009

Table 3

Daily Step Count Predicts Cognitive Function in 93 Older Adults with HF

	Global Cognitive Function			Executive Function/Attention			Memory			Processing Speed		
Variable	**B**	**SE B**	**β**	**B**	**SE B**	**β**	**B**	**SE B**	**β**	**B**	**SE B**	**β**
Step 1												
Sex	−.22	1.22	−.02	−.37	1.75	−.02	−.07	1.98	−.00	.42	6.38	.01
High Blood Pressure	−1.61	1.18	−.14	−3.41	1.70	−.19*	−.68	1.92	−.04	−12.8	6.20	−.20*
Diabetes	−1.27	1.30	−.10	−2.08	1.87	−.10	1.61	2.11	.08	−7.12	6.82	−.10
Depression	−.05	.07	−.07	−.27	.10	−.26*	−.08	.12	−.08	−1.22	.37	−.32*
HF severity (Cardiac Output)	.02	.03	.08	.02	.04	.04	−.01	.05	−.01	.023	.16	.014
Step 2												
Average Daily Step Count	.001	.000	.28**	.001	.000	.29**	.00	.00	.12	.003	.001	.22*

* = p<.05,

** = p<.01

Table 4

Differential Effects of Moderate-Vigorous Intensity Activity and Cognitive Function in Older Adults with HF

	Global Cognitive Function			Executive Function/Attention			Memory			Processing Speed		
Variable	**B**	**SE B**	**β**	**B**	**SE B**	**β**	**B**	**SE B**	**β**	**B**	**SE B**	**β**
Step 1												
Sex	.02	1.22	.00	−.01	1.73	.00	.08	1.96	.00	1.38	6.27	.02
High Blood Pressure	−1.98	1.18	−.17	−.40	1.67	−.22*	−.92	1.90	−.05	−14.4	6.08	−.22*
Diabetes	−1.16	1.32	−.09	−1.80	1.86	−.09	1.76	2.11	.09	−6.15	6.76	−.09
Depression	−.09	.07	−.13	−.33	.10	−.32*	−.11	.11	−.11	−1.38	.35	−.37**
HF severity (Cardiac Output)	.03	.03	.10	.03	.04	.06	.00	.05	−.01	.04	.15	.02
Step 2												
Moderate-Vigorous Physical Activity	.03	.01	.24*	.06	.02	.29**	.03	.02	.14	.20	.07	.25**

* = p<.05,

** = p<.01