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Author manuscript *J Clin Nurs*. Author manuscript; available in PMC 2016 September 14.

Published in final edited form as:

J Clin Nurs. 2014 March ; 23(5-6): 829-836. doi:10.1111/jocn.12214.

## Executive Dysfunction is Independently Associated with Reduced Functional Independence in Heart Failure

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## Abstract

**Aims and Objectives**—To examine the independent association between executive function with instrumental activities of daily living and health behaviors in older adults with heart failure.

**Background**—Executive function is an important contributor to functional independence as it consists of cognitive processes needed for decision-making, planning, organizing, and behavioral monitoring. Impairment in this domain is common in heart failure patients and associated with reduced performance of instrumental activities of daily living in many medical and neurological populations. However, the contribution of executive functions to functional independence and healthy lifestyle choices in heart failure patients has not been fully examined.

**Design**—Cross-sectional analyses.

There are no conflicts of interest.

Contributions: Study Design: MA, MBS, NR, RC, LS, JH, JG Data Collection: MA, MBS, JG Manuscript Preparation: MA, MBS, NR, RC, LS, LC, RJ, MD, JH, JR, JG

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**Methods**—175 heart failure patients completed a neuropsychological battery and echocardiogram. Participants also completed the Lawton-Brody instrumental activities of daily living scale and reported current cigarette use.

**Results**—Hierarchical regressions revealed reduced executive function was independently associated with worse instrumental activity of daily living performance with a specific association for decreased ability to manage medications. Partial correlations showed executive dysfunction was associated with current cigarette use.

**Conclusions**—Our findings suggest that executive dysfunction is associated with poorer functional independence and contributes to unhealthy behaviors in heart failure. Future studies should examine whether heart failure patients benefit from formal organization schemae (i.e., pill organizers) to maintain independence.

**Relevance to Clinical Practice**—Screening of executive function in heart failure patients may provide key insight into their ability to perform daily tasks, including management of treatment recommendations.

#### Keywords

Cognition; executive functions; heart failure; instrumental activities of daily living

## **1. INTRODUCTION**

Heart failure (HF) is a highly prevalent condition currently affecting an estimated six million persons in the United States alone, with nearly 600 000 new cases added every year (Roger et al. 2012). HF has become the most common reason for hospital readmissions and is associated with elevated risk for mortality and poor quality of life (Jencks et al. 2009, Bennett et al. 2003, Roger et al. 2004).

Persons with HF exhibit reduced ability to perform key instrumental activities of daily living (IADL). For instance, recent work found HF patients frequently reported receiving assistance with laundry, housekeeping, food preparation, shopping, medication management, driving, and finances (Alosco et al. 2012, Norberg et al. 2008). This pattern is concerning, as reduced functional independence is associated with increased mortality risk (Fitzgerald et al. 2011, Bowling et al. 2012), higher risks of disability, re-hospitalization, diminished quality of life and admission to geriatric wards (Jencks et al. 2009 Campbell et al. 1998, Dee Geest et al. 2003). Predictors of reduced IADL performance in HF include older age, being female (Seo et al. 2008 Whitson et al. 2010), dyspnea, fatigue, reduced muscle strength, and greater depressive symptomatology (Seo et al., 2011, Friedman et al. 2008).

Cognitive dysfunction is another likely contributor to reduced functional independence in HF. Patients with HF are at risk for Alzheimer's disease (Qiu et al. 2006) and cognitive impairment is found in up to 75% of patients (Vogels et al. 2007). Cognitive dysfunction in HF is associated with poor psychosocial outcomes (Pressler et al. 2010a, Kravitz et al. 1993; Mascitelli & Pezzetta 2006, Brega et al. 2008), including elevated risk of mortality (Pressler et al. 2010b). Indeed, poor outcomes in this population may stem from the adverse influence

of cognitive impairment on adherence to important treatment recommendations (i.e., medication schedule) (Hawkins et al. 2012).

Because the performance of IADLs require higher-order cognitive processes (Kalmar et al. 2008), specific executive functions impairments may play an important role in HF patients' reduced ability to perform IADLs. About 20% of persons with HF exhibit impairments on neuropsychological measures assessing executive function (Serber et al. 2008). Impairments in executive function are linked to poor IADL performance in other neurological populations, (i.e., Alzheimer's disease, multiple sclerosis; Marshall et al. 2011, Razani et al. 2007; Kalmar et al. 2008, Perry & Hodges 1999) independent of problems in memory and global cognition.

In response to these findings, recent work has demonstrated a correlational relationship between poorer executive function and reduced IADL performance in HF—though the effect of important medical and demographic characteristics were not accounted for in these studies (Bauer et al. 2012, Foster et al. 2011). Further, these studies have also not clarified that generalized cognitive decline—rather than specific deficits in executive function—account for this pattern.

The purpose of the current study was to examine the association between executive functions and IADL performance among older adults with HF. We sought to estimate the magnitude of that association while accounting for cognitive function in other domains as well as known demographic and medical contributors. We further examined whether executive dysfunction was associated with unhealthy lifestyle behaviors (i.e., cigarette use).

## 2. METHODS

#### 2.1 Participants

The sample consisted of 179 persons with HF from a large-scale NIH funded research study examining neurocognitive function in older adults with HF. For inclusion, participants must have been between the ages of 50-85 years, English speaking, and had a diagnosis of New York Heart Association (NYHA) HF class II, III, or IV at the time of enrollment. Potential participants were excluded for a history or current diagnosis of a significant neurological disorder (e.g. dementia, stroke), head injury >10 minutes loss of consciousness, severe psychiatric disorder (e.g. schizophrenia, bipolar disorder), substance use/dependence, renal failure, and/or sleep apnea. Participants averaged 68.10 (SD = 10.25) years of age, were 36.3% female, and 80.4% Caucasian, 13.4% African American, and 6.2% other. Examination of participants' medical records indicated that the sample had an average left ventricular ejection fraction of 41.04 (SD = 15.11). See Table 1 for participant demographic and medical characteristics.

#### 2.2 Measures

**Neuropsychological Assessment**—Executive function was assessed using the Frontal Assessment Battery (FAB) and Letter Number Sequencing (LNS). The FAB is comprised of six subtests that assess cognitive operations believed to depend on frontal lobe functioning (Dubois et al. 2000): conceptualization, abstract reasoning, mental flexibility, motor

programming, executive control, resistance to interference, self-regulation, inhibitory control and environmental autonomy (Stuss et al. 1994 Grafman 1994; Luria 1966; Milner & Petrides 1984; Stuss & Benson 1986). It is a brief (less than 10 minutes) test with strong psychometric properties (i.e., Cronbach's alpha = .78 (Gifford & Cummings, 1999), interrater reliability of r = .87 (Dubois et al. 2000), and good concurrent validity with the Wisconsin Card Sorting Test r = .77, and the MATTIS Dementia Rating Scale r = .82 (Dubois et al. 2000). The FAB also demonstrates strong discriminant validity, as prior work has shown it to distinguish between controls and patients with frontal cognitive impairment (Dubois et al. 2000).

Letter Number Sequencing is a measure of working memory that involves listening to an unordered sequence of numbers and letters and responding with ordered numbers and letters. This task has good test-retest reliability of .75 (Wechsler 1997a). Working memory is considered an executive process, as it taps into aspects of executive functions such as cognitive flexibility and manipulation of information (Carpenter et al. 2000; Wechsler 1997a, 1997b). Furthermore, functional neuroimaging findings have also revealed activation of areas common to executive functions during administration of LNS such as the orbitofrontal and the dorsolateral prefrontal cortex (Haut et al. 2000).

Attention/psychomotor speed, memory, and language were also assessed using neuropsychological measures with strong psychometric properties, including digit symbol coding (Smith 1983), Complex Figure Test long delayed recall (Loring et al. 1990), and Animal Fluency (Morris et al. 1989).

Activities of Daily Living—The self-report version of the Lawton Brody Activities of Daily Living Scale was used to assess the participant's performance of IADLs. Clinical assessment of ADLs provides information regarding functional independence (Norberg et al. 2008). IADLs include complex activities such as transportation, traveling, management of finances, telephone use, meal preparation, housekeeping, laundry, shopping, and medication maintenance. IADL scores range from 0 to 16 with higher scores reflecting greater functional independence (Lawton & Brody 1969). Any response that indicated receiving assistance was deemed impaired on that activity. The Lawton Brody IADL scale demonstrates strong inter-rater reliability (r=.85), and concurrent validity with other measures of functional status that assess physical health, orientation and memory, behavioral and social adjustment, and ADLs (Graf 2008).

**Cigarette Use**—HF participants were also administered a brief questionnaire that assessed current cigarette use. Specifically, participants were asked to indicate the total amount of cigarettes they currently smoke per week.

**Demographic and Medical History**—Demographic and medical characteristics were ascertained through participant self-report and medical record review.

#### 2.3 Procedures

The local Institutional Review Board (IRB) approved the study procedures and all participants provided written informed consent prior to study enrollment. Participants

completed baseline demographic, medical and psychosocial self-report measures, including IADL function. A medical chart review for each participant was then completed. A brief neuropsychological examination was conducted on all HF participants to assess functioning in multiple domains of cognition, including executive function.

## 2.4 Statistical Analyses

To facilitate clinical interpretation and maintain directionality within scales all raw scores of the neuropsychological measures were transformed to T-scores (a distribution with a mean of 50, and a standard deviation of 10) using existing normative data correcting for age. A composite score was computed for executive function that consisted of the mean of the T-scores for the FAB and LNS. Consistent with clinical interpretation, impairment in these domains for the current study was defined as a T-score of 1.5 standard deviations below the mean (t < 35). It is a commonly used cutoff for the clinical identification and diagnosis of cognitive impairment (Peterson et al., 1999).

Multiple linear hierarchical regression analyses were conducted to examine the independent association between executive function and IADLs. Total IADL composite score served as the dependent variable. Demographic and medical variables were entered into block 1, including age, gender (1 = male; 2 = female), education, LVEF, depressive symptomatology (as assessed by the BDI-II), and diagnostic history of hypertension and diabetes (1 = positive history; 0 = negative history). These medical and demographic variables were included as covariates due to their known influence on cognitive function and self-care behaviors. Digit symbol coding, Complex Figure Test long delayed recall, and Animals Fluency Test were entered into block 2. Finally, executive function was entered into block 3 to determine its incremental predictive validity beyond medical, demographic characteristics, and functioning in other cognitive domains. Partial correlations adjusting for the aforementioned demographic, medical, and cognitive variables were then computed to examine the independent relationship between executive function, performance in specific IADLs and self-reported cigarette use.

## 3. RESULTS

#### IADL and Cognitive Test Performance

HF patients in the current study frequently reported receiving assistance with everyday tasks, as the sample averaged 13.53 (SD = 2.87) on the IADL scale. Specifically, 27.4% reported receiving assistance with shopping, 31.9% with food preparation, 39.1% with housekeeping, and 39.6% with laundry. Of particular interest, 7.8% reported receiving assistance with driving, 5.6% with medication management, and 11.2% with financial matters. See Table 2 for details.

Impairments on neuropsychological tests were also prevalent in the current sample. Consistent with clinical convention for cognitive impairment (i.e. T < 35), 29.6% of the sample scored below that cutoff on the FAB. Impairments on LNS were less common (5.6%). Refer to Table 3 for cognitive test performance in the current sample.

#### **Executive Function and IADLs**

A multiple linear hierarchical regression analysis found being male ( $\beta = .29$ , p < .001), a positive history of diabetes ( $\beta = -.19$ , p = .01), and increased scores on the BDI-II ( $\beta = -.15$ , p = .04) was associated with poorer total IADL performance. After adjusting for medical and demographic characteristics, test performance on neuropsychological measures assessing attention/psychomotor speed, memory, and language was not associated with IADLs (p > .05). However, in the final block, executive function score demonstrated incremental predictive validity for total IADLs beyond medical and demographic factors and independent of functioning in other cognitive domains ( $\beta = .24$ , p = .01). Better performance on executive function tests was associated with better IADL. See Table 4 for a full summary of hierarchical regression analyses.

To clarify this finding, partial correlations adjusting for medical and demographic characteristics and functioning in other cognitive domains revealed that poorer executive function was associated with reduced independence in food preparation (r(167) = .16, p = .03), housekeeping (r(167) = .16, p = .04), laundry (r(167) = .24, p < .01), and marginal significance for medication management (r(167) = .15, p = .05). See Table 5.

#### **Executive Function and Cigarette Use**

Many participants reported current cigarette use, as the sample averaged 3.84 (SD = 18.67) cigarettes per week. A series of partial correlations adjusting for age, sex, education, LVEF, depressive symptomatology, diagnostic history of hypertension and diabetes, and performance on digit symbol coding, complex figure test delayed recall, and Animal Fluency was performed to examine the association between executive function and cigarette use. Reduced executive function was associated with greater number of cigarettes smoked in the past week (r(167) = -.20, p = .01)

## 4. DISCUSSION

Consistent with past work, reduced IADL performance and executive dysfunction was prevalent in this sample of HF patients. Although past work has shown a correlational relationship between executive function and IADLs in HF, this is the first study to demonstrate that executive function rather than generalized cognitive function is instrumental for functional independence in HF. Several aspects of these findings warrant brief discussion.

The current findings suggest that specific impairments in executive function are independent contributors to HF patients' inability to perform key IADLs. These findings are consistent with past work among patients with Alzheimer's disease (Marshall et al. 2011). It is noteworthy that executive dysfunction was associated with poorer medication management in the sample, as medication non-adherence has recently been linked with increased mortality risk in HF (Fitzgerald et al. 2011). Indeed, many IADLs consist of behaviors similar to those required for adherence to important HF treatment recommendations (i.e., dietary restriction, medication management) (Fitzgerald et al. 2011, Evangelista et al. 2001; Ni et al., 1999). Executive functions are required for successful self-management (Riegel &

Dickson 2008), as they consist of cognitive processes needed for decision-making, planning, organizing, and behavioral monitoring (Kalmar et al. 2008, Ramsden et al. 2008). These cognitive operations depend on intact function of prefrontal cortical regions, and neuropathological injury to these regions is well documented in HF patients (Woo et al. 2003, 2009, Kumar et al. 2011, Caparas et al. 2000; Serber et al. 2008, Vogels et al. 2007). Future studies should examine whether technological devices that externalize and promote executive function (e.g. smart phones) can help patients compensate for their cognitive deficits and improve outcomes in this population.

The current findings also suggest that poorer executive function may play a key role in HF patients' unhealthy health habits such as cigarette smoking. It is surprising that HF patients exhibit elevated rates of non-adherence to smoking (i.e., 19.8%) (Kravitz et al. 1993) given the consequences associated with this behavior. Although the relationship between executive function and cigarette use may be reciprocal, it is also possible that HF patients with cognitive impairment fail to refrain from use due to poor insight or reasoning skills. For instance, deficits in executive function predict substance use in other populations (Nigg et al. 2006). Similarly, cognitive impairment contributes to poor adherence to key treatment recommendations in HF patients (Hawkins et al. 2012). Longitudinal studies are needed to further clarify the relationship and directionality of relationships between cognitive function and substance use in HF patients.

The current findings are limited in several ways. First, future studies should examine the relation between objective and self-reported assessments of IADLs within a HF population, as the current literature mostly relies on self-reports. Second, the current study was based on cross-sectional design and longitudinal studies are needed to examine whether and how individual differences in changes in executive functions and affect IADL performance. Future studies should also clarify the role of gender in ADL function in this population. For instance, the current study found that being male was associated with worse IADL performance. Although this may indicate impairment, it may also be a cumulative index of lifelong behaviors (i.e., some older adult males may be less likely to prepare meals or do laundry in the past and their current inability to do so does not reflect decline in skills). Prospective studies are also encouraged that examine the etiological underpinnings of cognitive impairment using neuroimaging, particularly as it relates to IADL performance.

## CONCLUSIONS AND CLINICAL RELEVANCE

In summary, the current study shows that specific deficits in executive function are associated with poorer IADL performance and may contribute to unhealthy lifestyle choices in HF persons. Such findings have important clinical implications and suggest screening of executive function could provide key insight into functional ability in this population. Future work is needed to elucidate the mechanisms that produce cognitive impairment in this population and the subsequent difficulties in performing self-care behaviors that is frequently observed among HF patients.

## Acknowledgments

This work was supported by National Institutes of Health (NIH) [grant numbers DK075119,HL089311, R37 AG011230 to NR].

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Demographic, Medical, and Psychosocial Characteristics of 179 Older Adults with Heart Failure

Demographic Characteristics			
Age, mean (SD)	68.09(10.25)		
Gender (% Women)	36.3		
Race (% Caucasian)	80.4		
Education, mean (SD)	13.33(2.90)		
Medical Characteristics			
LVEF, mean (SD)	41.04(15.11)		
Hypertension (% yes)	70.4		
Diabetes (% yes)	37.4		
BDI-II	7.94(7.39)		
Cigarette Use			
*	2 94(19 67)		

Cigarettes, mean(SD) \* 3.84(18.67)

Abbreviations-LVEF = Left Ventricular Ejection Fraction; BDI-II = Beck Depression Inventory-II

\* = Number of cigarettes per week

Instrumental Activities of Daily Living Performance among Older Adults with HF (N= 179)

Instrumental ADL	% Needing Assistance
Telephone Use	1.7
Shopping	27.4
Food Preparation	31.9
Housekeeping	39.1
Laundry	39.6
Transportation	7.8
Medication Management	5.6
Finances	11.2
Instrumental ADL, mean (SD)	13.53 (2.87)

ADL = Activities of Daily Living

Descriptive statistics of Neuropsychological Test Performance (N= 179)

	Raw Test Performance, mean (SD)	T-score, mean (SD)	% T-scores < 35*
Executive Function Measures			
FAB	15.46(2.62)	41.15(22.98)	29.6
LNS	8.75(2.49)	50.25(9.21)	5.6
Attention/Psychomotor Speed			
Digit Symbol Coding	49.24(14.65)	47.02(9.43)	10.6
Memory			
CFT Long Delayed Recall	13.03(6.16)	49.63(8.96)	8.9
Language			
Animal Fluency	19.06(4.91)	53.89(11.02)	3.4

Note. FAB = Frontal Assessment Battery; LNS = Letter Number Sequencing; CFT = Complex Figure Test

\* A T-score < 35 is reflective of impairment.

Association of Executive Function with Instrumental Activities of Daily Living in Older Adults with Heart Failure (N= 179): A summary of hierarchical regressions.

	Instrumental ADL
Variable	$\boldsymbol{\beta}(SE b)$
Block 1	
Age	12(.02)
Sex	.29(.44) **
Education	.03(.07)
LVEF	.10(.01)
HTN	01(.46)
Diabetes	18(.43)*
BDI-II	15(.03)*
$R^2$	.15
F	4.23**
Block 2	
CFT	02(.03)
Animal	.02(.02)
Digits	.06(.03)
$R^2$	.15
$F$ for $\mathbb{R}^2$	.26
Block 3	
EF	.24(.02)*
$R^2$	.19
<i>F</i> for $\mathbb{R}^2$	7 .03 *

Note.

Abbreviations:  $\beta$  – standardized regression coefficients, SE – standard error; LVEF = Left Ventricular Ejection Fraction; HTN = Hypertension; BDI-II = Beck Depression Inventory-II; CFT = Complex Figure Test Long Delayed Recall; Digits = Digit Symbol Coding; EF = Executive Function

\* p<.05;

\*\* p<.01

Partial Correlations Between Executive Function and Instrumental ADLs (N=179)

Instrumental ADLS	Executive Function	Р
Telephone	.07	.35
Shopping	.06	.45
Food Preparation	.16	.03
Housekeeping	.16	.04
Laundry	.24	.002
Transportation	05	.54
Medications	.15	.05
Finances	.04	.63

Note. Adjusted for age, sex, education, left ventricular ejection fraction, Beck Depression Inventory-II, diagnostic history of hypertension and diabetes, and cognitive test performance on digit symbol coding, Complex Figure Test long delayed recall, and animal fluency.