EXECUTIVE FUNCTION AND INSTRUMENTAL ADL PERFORMANCE IN OLDER ADULTS WITH HEART FAILURE

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by

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Introduction

Heart Failure

HF is a clinical syndrome characterized by the inability of the heart to pump enough blood to meet the metabolic needs of the body (Francis, Wilson Tang, & Sonnenblick, 2004). Depending on the type of HF, patients have either difficulty with ventricular filling (diastolic HF) or with ventricular emptying (systolic HF) (Lejermtel, Sonnenblick, & Frishman, 2004). HF typically develops as a result of the manifestation of predisposing conditions that damage the heart (Hoth, 2010). As many as 75% of patients with HF have hypertension prior to a formal HF diagnosis, however, other common risk factors include diabetes, coronary heart disease, and obesity (Rosamond et al., 2008; Lloyd-Jones et al., 2002). Ultimately, HF results in insufficient blood flow to the tissues of the body (i.e., diminished cardiac output) and reduced endothelial and vascular function (Kubo, Rector, Bank, Williams, & Heifetz, 1991; Treasure et al., 1990; Lip & Gibbs, 1999).

Heart Failure Severity and Symptomatology

HF patients often experience adverse symptomatology and reduced quality of life. Common symptoms among patients with HF include shortness of breath, edema, exercise intolerance, fatigue and weakness, rapid heartbeat, cyanosis (blueness of skin), reduced exercise ability, persistent coughing, fluid retention, lack of appetite, and decreased arousal or alertness (Mayo Clinic, 2011; Hoth, 2010). Many of these symptoms function relative to the severity of HF. Severity of HF is most commonly classified according to the New York Heart Association (NYHA) Guidelines. NYHA is comprised of four classes, including Class I: no symptoms associated with ordinary activity and no limitation of physical activity; Class II: slight limitation of physical activity, though comfortable at rest; Class III: marked limitation of physical activity, but remains comfortable at rest; Class IV: inability to perform physical activity without discomfort and symptoms of cardiac insufficiency or chest pain at rest (American Heart Association, 2011). Other common classifications of HF severity include left ventricular ejection fraction, cardiac index, and cardiac output, all of which use an index of the amount of blood being pumped out of the heart for diagnosis (Mayo clinic, 2011).

Heart Failure Prevalence and Societal Burden

HF affects nearly 6 million Americans in the United States alone and poses as a major public health concern due to increases in the prevalence of its risk factors such as obesity, hypertension, and type 2 diabetes mellitus (Lloyd-Jones et al., 2009; Heidenreich et al., 2011). It is projected that by the year 2030 there will be a 25% increase in the prevalence of HF (Heidenreich et al., 2011). Additionally, nearly 660,000 new cases of HF are diagnosed each year and HF has become the most common reason for re-hospitalization. Indeed, HF accounts for annual direct and indirect costs of approximately $39.2 billion (Jencks, Williams, & Coleman, 2009; American Heart Association, 2010; Rosamond et al., 2008).

The Effects of Heart Failure on Instrumental Activities of Daily Living (ADLs)

An important contributor to poor outcomes in HF patients is difficulty performing self-care behaviors in this population, including reduced instrumental ADL performance. Instrumental ADLs include daily tasks that are required for independent living, including shopping (Norberg, Boman, & Lofgren, 2008), household chores (Sonn & Asberg, 1991), medication management (Richardson, 2003; Roberts, 1999), food preparation, laundry, finances, and transportation

(Lawton & Brody, 1969). Recent work found HF patients reported receiving elevated rates of assistance with laundry, housekeeping, food preparation, shopping, and finance management (Alosco et al., 2012). Consistent with this pattern, Norberg and colleagues (2008) demonstrated 75% of HF patients with NYHA Class I and II are dependent in instrumental ADLs. This same study showed dependence in instrumental ADLs increased to 90% among NYHA III and IV patients. HF patients in this study exhibited particularly high rates of dependence in shopping, transportation, cooking, and cleaning. Notably, HF patients have particular difficulties managing medications. This is unfortunate as decreased ability to manage medications is linked with increased risk of all cause mortality in this population (Fitzgerald et al., 2011), higher risks of disability, re-hospitalization, diminished quality of life and admission to geriatric wards (Jencks et al., 2009; Campbell, Banner, Konick-McMahan, & Naylor, 1998).

Demographic and Medical Predictors of Instrumental ADLs in Heart Failure

Past work has identified several predictors of reduced instrumental ADL performance in HF. Demographic contributors to reduced instrumental ADL ability include older age and being female (Seo, Roberts, Pina, Dolansky, 2008; Whitson et al., 2010). Dyspnea (i.e., shortness of breath), fatigue, and reduced muscle strength have also been documented as medical predictors of impaired instrumental ADL (Seo, Roberts, LaFramboise, Yates, & Yurkovich, 2011). This pattern is not surprising given poor functional and physical capacity associated with HF (Drexler & Coats, 1996**;** MacGowan, Panzak, & Murali, 2001; Varvaro, Sereika, Zullo, & Robertson, 1996; Davie, Francis, Caruana, Sutherland, & McMurray, 1997; Welsh et al., 2002). Increased depressive symptomatology has also been identified as a significant contributor to reduced instrumental ADLs in HF, which is noteworthy given the high rates of depression in this population (Havranek, Ware, & Lowes, 1999; Skotzko et al., 2000; Rutledge, Reis, Linke, Greenberg, & Mills, 2006; Friedman, Lyness, Delavan, Li, & Barker, 2008).

Cognitive Impairment in Heart Failure

Another likely contributor to reduced independence in instrumental ADLs in HF patients is cognitive impairment. Cognitive impairment is common in persons with HF, with prevalence estimates reaching nearly 75% in some studies (Vogels, Scheltens, Schroeder-Tanka, & Weinstein, 2007a). When compared to medical and healthy participants, HF patients exhibit specific impairments in memory, psychomotor speed, and executive function (Pressler et al., 2010a). Moreover, HF is associated with elevated risk for Alzheimer’s disease, vascular dementia, and abnormalities on neuroimaging (Qiu et al., 2006; Acanfora et al., 1996; Almeida et al., 2005; Roman, 2005).

Etiology of Cognitive Impairment in Heart Failure

Past work suggests the etiology of cognitive impairment in patients with HF may be a combination of factors, including reduced cerebral perfusion and pathophysiological effects of medical comorbidity (Vogels et al., 2008; Alosco et al., 2012; Alosco et al., 2012; Knecht et al., 2012; Garcia et al., 2012). However, much work has examined the relationship between cardiac and cognitive function. Specifically, reduced cardiac index and left ventricular ejection fraction among patients with HF have both been shown to be associated with poorer global cognitive function, including impairments on neuropsychological measures of memory and executive function (Hoth, Poppas, Moser, Paul, & Cohen, 2008). Typically, autoregulatory mechanisms of the body maintain cerebral blood flow during brief fluctuations of reduced blood flow; however, in the presence of older age and HF such mechanisms become compromised (Hoth, 2010).

Indeed, reduced cardiac pumping efficiency appears to cause decreased cerebral perfusion potentially resulting in ischemic damage from deprivation of oxygen and nutrients (Hoth, 2010). As such, highly plastic regions of the brain that require copious amounts of oxygen to function at an optimal level are often most vulnerable to damage among patients with HF (Pressler et al., 2010a). Consistent with this notion, most frequently observed cognitive deficits in older adults with HF involve frontal and temporal lobe functioning including attention, executive function, memory and psychomotor speed (Vogels et al., 2007b; Rains, 2002; Pressler et al., 2010a). For instance, one study found patients with low cardiac function performed worse on tasks of sequencing and planning (i.e., executive function) relative to patients with normal cardiac functioning (Jefferson, Poppas, Paul, & Cohen, 2007).

Executive Dysfunction in Heart Failure Patients

Impairments in executive function are particularly prevalent in patients with HF. Executive function consists of operations of the frontal lobe regions of the brain, including planning, organizing, and monitoring behavior (Kalmar, Gaudino, Moore, Halper, & DeLuca, 2008; Ramsden, Kinsella, Ong, & Storey, 2008). As mentioned above, inadequate functioning of the frontal cortex as a result of ischemic damage from cerebral hypoperfusion is common among HF patients (Vogels et al., 2008; Pressler et al., 2010a; Moody, Bell, & Challa, 1990). In turn, it is well established that patients with HF commonly exhibit impairments in executive function (Bauer et al., 2012; Pressler et al., 2010a) and such impairments appear to increase as HF severity increases (van den Hurk et al., 2011; Pressler et al., 2010a). Specific impairments on neuropsychological tests of executive function among HF patients include Trail Making Test B (Pressler et al., 2010a), Digit Span Backward (Pressler, Kim, Riley, Ronis, & Gradus-Pizlo, 2010b), and the Watson Clock Drawing Test (Serber et al., 2008). In fact, up to 20% and 17% of

HF patients demonstrate abnormal performance on Trail Making Test B and the Watson Clock Drawing Test, respectively (Serber et al., 2008).

Neuroimaging Abnormalities of Frontal Brain Regions in Heart Failure

Previous work has also demonstrated abnormal neuroimaging of regions of the brain responsible for executive functions (i.e., frontal lobes) among patients with HF. Specifically, imaging studies have shown HF patients to exhibit reduced gray matter volume, resting cerebral blood flow, and demylination of the frontal and prefrontal areas (Woo, Macey, Fonarow, Hamilton, & Harper, 2003; Woo, Kumar, Macey, Fonarow, & Harper, 2009; Kumar et al., 2011; Caparas et al., 2000). Serber and colleagues (2008) also found HF patients that demonstrated poorer performance on the Trail Making Test B and the Watson Clock Drawing Test also displayed corresponding structural injury of the frontal cortex. In addition to direct injury to the frontal areas of the brain theoretically produced from the pathological effects of HF, the frontal lobes and cognitive abilities associated with the prefrontal cortex are also sensitive to the effects of increasing age (Lowe & Rabbitt, 1997; Cabeza, 2001; Raz & Rodrigue, 2006). This is noteworthy, as HF is most prevalent among persons aged 65 years or older (Roger et al., 2012).

Cognitive Impairment and Psychosocial Consequences in Heart Failure

Cognitive impairment in HF is associated with a number of adverse psychosocial outcomes. Cognitive deficits in patients with HF have been linked with decreased health related quality of life, poor adherence to key treatment recommendations, and increased risk of mortality (Bennett, Cordes, Westmoreland, Castro, & Donnelly, 2000; Bennett & Sauve, 2003; Casey, Hughes, Wachter, Josephson, & Rosneck, 2008; Foster et al., 2011; Pressler et al., 2010b). Perhaps surprising, HF patients also exhibit elevated rates of non-adherence to smoking and alcohol abstinence (19.8% and 40%, respectively) (Kravitz et al., 1993), and such behaviors may be linked with cognitive function (Mascitelli & Pezzetta, 2006).

Cognitive Impairment and Instrumental ADLs in Heart Failure

There is also evidence suggesting cognitive impairment may be associated with decreased ability to perform instrumental ADLs among older adults with HF. For example, a recent study found that reduced performance on the Mini Mental State Examination and Trail Making Test A among patients with HF is associated with reduced ability to independently manage their medication and drive a car (Alosco et al., 2012). Past work theorizes that cognitive dysfunction limits HF patients' ability to perform self-care behaviors through poor decision-making and reasoning processing (Pressler et al., 2010b).

Executive Dysfunction and Psychosocial Consequences

Specific impairments in executive function are likely a significant contributor to reduced psychosocial functioning in patients with HF. For instance, recent work found decreased executive function is a significant predictor of mortality (Pressler et al., 2010b) and is associated with reduced participation in intensity varying activities (Foster et al., 2011) and decreased functional status (Bauer et al., 2012) among HF patients. Indeed, past work among older adult populations also suggests executive function may play a prominent role in the maintenance of quality of life and other psychosocial factors, including basic ADLs (Davies et al., 2010; McAuley et al., 2011; Pohjasvaara et al., 2002).

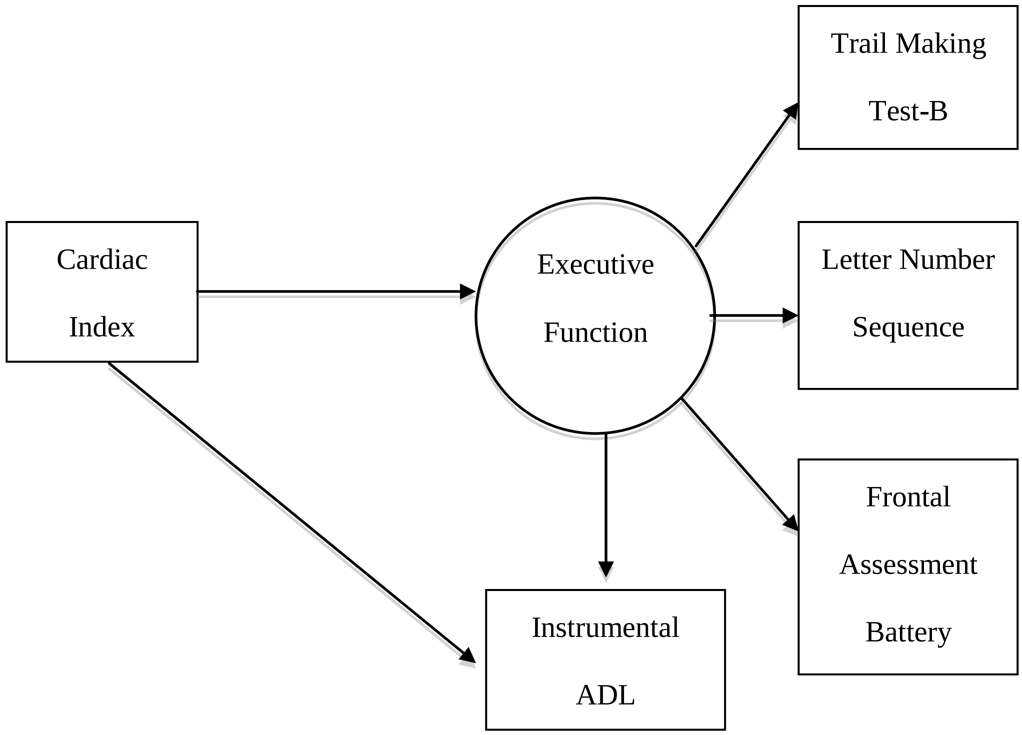
The Role of Executive Function in the Performance of Instrumental ADLs

Due to the higher-order cognitive processes needed to maintain functional independence, it seems likely that impairments in executive function may best account for HF patients reduced ability to perform instrumental ADLs. Consistent with this notion, regions of the brain essential for instrumental ADL performance (i.e., frontal and temporal functioning) are frequently damaged in this population due to reduced oxygenation (Vogels et al., 2007a; 2007b; Vogels et al., 2008; Rains, 2002, Pressler et al., 2010a; Pressler et al., 2010b). In fact, executive performance has been linked with self-reported instrumental ADLs among persons with a history of cardiovascular disease (Jefferson, Paul, Ozonoff, & Cohen, 2006). The effect of executive function on instrumental ADL performance also appears to be evident within healthy aging. For example, executive function was shown to mediate the relationship between other neuropsychological domains and daily functioning among a sample of aging healthy elderly (Bryant et al., 2011). In other samples of healthy older adults, changes in executive function over time and performance on neuropsychological tests of executive function were also shown to significantly predict instrumental ADLs (Royall, Palmar, Chiodo, & Polk, 2004; Bell-McGinty et al., 2002). Finally, the negative impact of executive dysfunction on a patient's capacity to perform instrumental ADLs has been well documented among other medical populations including Alzheimer's disease and multiple sclerosis (Razani et al., 2007; Kalmar et al., 2008; Perry & Hodges, 1999). For example, one study found that when compared to typical Alzheimer's disease patients, Alzheimer patients with frontal involvement were more likely to exhibit worse ADL performance (Back-Madruga et al., 2002). Similarly, impaired executive function was also associated with poorer instrumental ADL performance among a sample of psychiatric patients (Gildengers et al., 2007).

In response to these findings, increasing awareness of the importance of executive functioning in maintaining functional independence has led to recent explorations of the correlational relationship between executive function and functional ability in HF persons (Bauer et al., 2011; Foster et al., 2011). However, these prior studies do not examine potential mechanisms of the association between executive function and instrumental ADL performance. Furthermore, these past studies did not comprehensively evaluate executive function with multiple neuropsychological measures. In-turn, relatively little is known about the relationship between executive function and instrumental ADL performance among HF patients.

The current study proposed a literature-derived model that examined the association between HF severity (as assessed by cardiac index), executive function and instrumental ADLs. Specifically, the model states that executive function mediates the relationship between HF severity and instrumental ADL performance. Refer to Figure 1 for a detailed depiction of the proposed model. The current study also sought to examine the relationship between executive function and psychosocial outcomes. It was expected that decreased performance on neuropsychological tests of executive function would be associated with poorer psychosocial functioning.

Figure 1. Executive Function Mediates the Relationship Between Heart Failure Severity and Instrumental ADL Performance



Method

Participants

The current sample consisted of 159 persons with HF from an ongoing large-scale NIH funded research study examining the cognitive benefits of cardiac rehabilitation (CR) in HF patients. Retrospective observational analyses were conducted on these first 159 consecutive cases that completed baseline assessment. After screening for missing data the sample size was reduced to 120. Participants eliminated were not significantly different from the remaining sample in terms of age ($t(157) = -.31$, $p = .76$), gender (χ^2 (1, $N = 159$) = .08, $p = .77$), education ($t(157) = -1.19$, $p = .24$), estimated premorbid intelligence ($t(156) = -.64$, $p = .52$), HF severity (as assessed by cardiac index) (t (157) = 1.62, $p = .11$), instrumental ADL performance ($t(153) = -1.65$, $p = .10$), systolic blood pressure ($t(157) = -.42$, $p = .68$), diastolic blood pressure ($t(157) = .30$, $p = .76$), or in terms of diagnostic history of depression (χ^2 (1, $N = 159$) = .1.72, $p = .19$) diabetes (χ^2 (1, $N = 159$) = .58, $p = .45$), myocardial infarction (χ^2 (1, $N = 159$) = .92, $p = .34$), or elevated total cholesterol (χ^2 (1, $N = 159$) = .1.59, $p = .21$).

Participants were recruited from Summa Health System in Akron, Ohio, a mid-size, Mid-western city in Northeast Ohio. Summa Health System is a network of teaching, and medical school affiliated hospitals. Participants reflect the HF population receiving treatment at this facility in terms of age, gender, race, ethnicity, and socioeconomic status. Consent from the participants to examine their medical records was obtained upon enrollment, and inclusion/exclusion of participants was based on a thorough medical history review conducted by research team members, including a licensed neuropsychologist.

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 if their medical status, based on self-report and corroborated by medical record review, indicated 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. Examination of participant's medical records was also conducted to characterize the sample in terms of medical comorbidities and demographics. Participants averaged 67.71 ± 9.17 years of age, were 33.3% female, and 84.2% Caucasian, 8.3% African American, and 7.5% other. See Table 1 for participant demographic characteristics.

Table 1. Demographic Characteristics of 120 Older Adults with Heart Failure.

Demographic Characteristics	
Age, mean (SD)	67.71(9.17)
Gender (% Women)	33.3
Race (% Caucasian)	84.2
Education, mean (SD)	13.55(2.43)
AMNART	110.77(13.80)
Medical Characteristics	
Cardiac Index, mean (SD)	2.73(1.03)
Diabetes (% yes)	37.5
Myocardial Infarction (% yes)	57.5
Systolic Blood Pressure, mean (SD)	115.33(16.16)
Diastolic Blood Pressure, mean (SD)	64.69(9.29)
Elevated Total Cholesterol (% yes)	67.5
Depression (% yes)	22.5

AMNART = American National Adult Reading Test

Measures

Heart Failure Severity. Cardiac Output (CO) from a seated resting baseline was calculated for each patient to estimate preservation of cardiac function. Impedance cardiography signals were recorded via a Hutcheson Impedance Cardiograph (Model HIC-3000, Bio-Impedance Technology, Chapel Hill, NC) using a tetrapolar band-electrode configuration. The electrocardiogram (ECG) was recorded from the Hutcheson Impedance Cardiograph using disposable ECG electrodes. The basal thoracic impedance (Zo), the first derivative of the pulsatile impedance (dZ/dt) and the ECG waveforms were processed using specialized ensemble-averaging software (COP, BIT Inc., Chapel Hill, NC), which was used to derive stroke volume using the Kubicek equation. Following instrumentation, impedance cardiographic signals were recorded for seven 40-second periods during a 10-minute resting baseline. Finally, all CO measurements were divided by body surface area (BSA), yielding cardiac index. See Table 1.

Blood pressure was measured seven times during the 10 minute resting baseline using an automated oscillometric BP device (Accutor Plus Oscillometric BP Monitor, Datascope Corp, Mahwah, NH) providing systolic, diastolic, and mean arterial pressures. Initiating the blood pressure reading triggered a concurrent 40-second impedance cardiography measure. A composite consisting of the average systolic and diastolic blood pressure across the seven trials was computed.

Activities of Daily Living. The self-report Lawton Brody Activities of Daily Living Scale was used to assess the participant's performance of instrumental and basic ADLs. Clinical assessment of activities of daily living (ADLs) provides information regarding functional independence (Norberg et al., 2008). Basic ADLs include feeding, dressing, grooming, bathing, toileting, and ambulation. Instrumental ADLs include complex activities such as transportation, traveling, management of finances, telephone use, meal preparation, housekeeping, laundry, shopping, and medication maintenance. Basic ADL scores range from 0 to 12 and instrumental ADL 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 Instrumental ADL 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)**.**

Quality of Life. The Short Form-12 Quality of Life Measure (SF-12) (Ware, Kosinski, & Keller, 1996) measures health-related quality of life. The two primary composite scores, Physical Composite Score (PCS; physical functioning, role-physical, bodily pain, and general health) and Mental Composite Scale (MCS; vitality, social functioning, role-emotional, and mental health) were used in the analyses. Both subscales of the SF-12 have been shown to demonstrate strong test-retest reliability (r = .89 for PCS and r = .76 for MCS) (Ware et al., 1996). This measure has also been shown to demonstrate strong psychometric properties (i.e., reliability and validity) in HF populations (Bennett & Sauve, 2003).

Substance Use. HF participants were also administered a brief questionnaire that assesses current use of alcohol and cigarettes. Specifically, participants are asked to indicate the total amount of cigarettes they currently smoke per week and how many days in the past 30 days they had at least one alcoholic beverage.

Executive Function. Executive function was assessed using Trail Making Test B, Frontal Assessment Battery (FAB), and Letter Number Sequencing (LNS). Trail Making Test B asks individuals to quickly connect alternating numbers and letters (Reitan & Wolfson, 1993). Test completion time is a widely used measure of executive function, with strong psychometric properties (e.g. test-retest reliability up to $r = 0.89$) (Spreen & Strauss, 1991; Dikmen, Heaton, Grant, & Temkin, 1999). Longer time of completion is indicative of worse performance. Trail Making Test B is a valid measure of executive function for the purposes of this study as it has previously been shown to predict instrumental ADLs in community dwelling and cognitively impaired older adults (Cahn-Weiner, Boyle, & Malloy, 2002; Baum, Edwards, Yonan, & Storandt, 1996).

The FAB is comprised of six subtests that assess frontal lobe functioning (Dubois, Slachevsky, Litvan, & Pillon, 2000), specifically, conceptualization, abstract reasoning, mental flexibility, motor programming, executive control, resistance to interference, self-regulation, inhibitory control and environmental autonomy (Stuss, Eskes, & Foster, 1994; Grafman, 1994; Luria, 1966; Milner & Petrides, 1984; Stuss et al., 1986). It is a brief (less than 10 minutes) test with strong psychometric properties (i.e., Cronbach's alpha = .78 (Gifford & Cummings, 1999), inter-rater reliability of $r = .87$ (Dubois et al., 2000), and ideal 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 verbally ordering numbers and letters that are orally presented in an unordered sequence. This task has excellent psychometric properties, with 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, Just, & Reichle, 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 lobes and the dorsolateral prefrontal cortex (Haut, Kuwabara, Leach, & Arias, 2000).

Premorbid Intelligence. The American National Adult Reading Test (AMNART) was used to assess premorbid intellectual function. The AMNART asks individuals to read a list of irregularly pronounced words. The AMNART is a reliable estimate of intelligence in medical populations (Blair & Spreen, 1989; Friend & Grattan, 1998; Uttl, 2002).

Demographic and Medical History. Demographic characteristics and medical history were collected through a medical record review and through self-report. The self-report medical history questionnaire has been used in past studies of cognition in persons with cardiovascular disease and was used to assess medical and psychiatric history, including topics such as neurological conditions, head injury, renal problems, learning disorders, and developmental disorders. Further, medical records were obtained and reviewed at each assessment time point to ensure eligibility and to corroborate self-reported information regarding current medical status, cardiac conditions, and comorbid medical conditions. Information obtained from medical record review took precedence in the case of a discrepancy between self-reported medical status and the record review. See Table 1 for medical characteristics of the sample.

Procedure

The local Institutional Review Board (IRB) approved the study procedures and all participants provided written informed consent prior to study enrollment. Data were stored and analyzed at Kent State University. Specifically, participants completed baseline demographic, medical and psychosocial self-report measures, including ADL function. A medical chart review for each participant was then completed. As a means to quantify HF severity, all participants completed baseline impedance cardiography administered by a trained research assistant. A brief neuropsychological examination was conducted on all HF participants, including TMTB, FAB, and LNS, to assess executive function.

Statistical Analyses Part I

To facilitate clinical interpretation and avoid undue discrepancy among scales all raw scores of the neuropsychological measures assessing executive function 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. 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 ($t < 35$) (Putzke et al., 2000).

The current study intended to use Structural Equation Modeling (SEM) using EQS 6.1 software (Hu & Bentler, 2006) to test the hypothesized meditational model depicted in Figure 1. SEM is advantageous as it allows the testing of all of the components of the theoretical network in Figure 1 while simultaneously modeling measurement error. For the proposed model, cardiac index was represented as an observed exogenous variable and total score on the instrumental ADL scale served as the observed endogenous variable. Executive function represented the mediator variable and was a latent variable with three indicators, including TMTB, FAB, and

LNS. SEM is used to depict a causal model of correlations and covariances among a set of exogenous and endogenous variables. In turn, an innate assumption of SEM mediation analyses entails the significant correlation between the exogenous, mediator, and endogenous variables. Thus, a bivariate correlation matrix was initially performed to determine the presence of possible mediation.

Results Part I

HF Severity and Cognitive Impairment

The current sample of older adults with HF demonstrated an average cardiac index that fell within normal levels of cardiac index during impedance cardiography (M = 2.73, SD = 1.03). Consistent with clinical convention, a T-score cutoff of 35 (i.e., 1.5 SD below the mean) was used to define cognitive impairment within the sample. Impairment on tests of executive function was prevalent in the sample. Specifically, 26.7% exhibited clinically meaningful impairments on the FAB and 17.5% did so on the TMT-B. Few participants exhibited impairment on LNS (i.e., 4.2%). See Table 2 for raw and T-score means and standard deviations of the executive function measures.

Table 2. Descriptive statistics of Neuropsychological Test Performance (*N* = 120)

	Raw Test Performance, mean (SD)	***T*-score,** mean (SD)	***% T-score < 35***
Executive Function Measures			
TMTB (seconds)	127.15(79.25)	43.74(17.99)	18.3
FAB	15.75(2.66)	41.96(23.79)	26.7
LNS	9.05(2.67)	51.52(9.27)	4.2

TMTB = Trail Making Test B; FAB = Frontal Assessment Battery; LNS = Letter Number Sequencing

Reported ADL function

HF patients in the current study frequently reported receiving assistance with everyday tasks, as the sample averaged 13.68 ± 2.96 on the instrumental ADL scale. Specifically, 25.0% reported receiving assistance with shopping, 28.3% with food preparation, 34.2% with housekeeping, and 38.3% with laundry. Of particular interest, 5.6% reported receiving assistance with driving, 5.8% with medication management, and 10.8% with financial matters. See Table 3.

Table 3. Instrumental Activities of Daily Living Performance among the Current Sample of Older Adults with HF (N = 120)

Instrumental ADL	**% Needing Assistance**
Telephone Use	1.6
Shopping	25.0
Food Preparation	28.3
Housekeeping	34.2
Laundry	38.3
Transportation	5.8
Medication Management	5.8
Finances	10.8
Instrumental ADL, mean (SD)	13.68 (2.96)

ADL = Activities of Daily Living

Missing Data and Univariate Normality

All variables were examined for missing data and for violations in univariate and multivariate normality. Cases with missing data were dealt with using listwise deletion reducing the sample size from 159 to 120. As noted in 2.1 Participants, those eliminated were not significantly different from the remaining sample on key variables.

Histograms and examination of variable z-scores was conducted to identify outliers disrupting univariate normality. TMTB and the FAB violated univariate normality presenting with elevated skewness and kurtosis values (skewness TMTB = -2.34, kurtosis TMTB= 6.42; skewness FAB = -2.01, kurtosis FAB = 5.38). TMTB had a total of 6 outliers and the FAB had a total for 4 outliers, as defined by data >2.5 SD from the mean. Histograms also revealed non-normal distributions for TMTB and the FAB. To preserve power the outliers were not eliminated from analyses, rather data for TMTB and the FAB was transformed by calculating the square of each value. Negative values and negatively skewed distribution of these variables made a square transformation appropriate (Field, 2009). It was also important to retain the outliers in the analyses, as these values are representative of the clinical population being sampled from (i.e., person's with increased HF severity are likely to have scores on TMTB and the FAB outside of the normal distribution). After data transformation of these variables, histograms and skewness and kurtosis values revealed a normal distribution. The remaining variables in the analyses were univariate normal.

Bivariate Correlation Matrix

Preliminary bivariate correlations were conducted to examine the relationship between measures of executive function (FAB, TMTB, LNS), cardiac index, and total instrumental ADLs. Contrary to expectations, cardiac index was not significantly related with the FAB, TMTB, LNS, or total instrumental ADLs. The FAB was significantly associated with instrumental ADL performance ($p < .05$). See Table 4. Given that cardiac index was not associated with measures of executive function or total instrumental ADLs, SEM examining the meditation of executive function between the relationship of cardiac index and total instrumental ADL was not conducted.

Table 4. Bivariate Correlation Matrix

	CI	TMTB	FAB	LNS
CI	--	--	--	--
TMTB	-.09	--	--	--
FAB	.13	.34**	--	--
LNS	.05	.54**	.39**	--
IADL	-.05	.05	.19*	.14

Note. CI = Cardiac Index; TMTB = Trail Making Test B; FAB = Frontal Assessment Battery; LNS = Letter Number Sequencing; IADL = Instrumental Activities of Daily Living

*$p < .05$; **$p < .01$

Statistical Analyses Part II

In the absence of a correlation between cardiac index and cognitive function, a series of post hoc analyses were conducted to investigate the relationship between executive function and instrumental ADLs. First, multiple linear hierarchical regression analyses were conducted to examine the independent association between executive function and instrumental ADLs. Total instrumental ADL composite score served as the dependent variable. Age, gender (1 = male; 0 = female), estimated premorbid intelligence (as assessed by the AMNART), cardiac index, systolic and diastolic blood pressure, and diagnostic history of diabetes, elevated total cholesterol, myocardial infarction, and depression were entered into the first block (1 = positive diagnostic history; 0 = negative diagnostic history). These medical and demographic variables were included as covariates due to their known influence on cognitive function and self-care behaviors. Executive function consisted of an average composite of T-scores for TMTB, FAB, and LNS and was entered into the second block of the model. Bivariate correlations were also conducted to clarify the relationship between executive function and specific instrumental ADLs. Finally, a series of partial correlations were performed to examine the relationship between executive function with quality of life, basic ADL performance, and alcohol and cigarette use.

Results Part II

Hierarchical Regression Analyses Examining Executive Function and Total Instrumental ADL

Assumptions associated with linear regression were conducted. Examination of the normal P-P plot revealed that actual data of residual values near the mean of the distribution increased more than would be expected for a normal distribution, though generally the distribution did not greatly deviate from normality. Additionally, scatter plot of residuals versus predicted values did not reveal significant violations of homoscedasticity. Cook's distance was examined to assess multivariate normality and the overall influence of cases on the model. Cook's distance ranged from .00 to .08 suggesting no issues with multivariate outliers, as a Cook's distance greater than 1 has been indicated as an established cutoff for the presence of outliers (Field, 2009).

A multiple linear hierarchical regression analysis adjusting for medical and demographic characteristics was then conducted to examine the relationship between executive function and total instrumental ADL. The model examining demographic and medical factors was significantly associated with executive function ($F(10, 109) = 1.94$, $R^2 = .15$, $p = .047$). Specifically, worse total instrumental ADL performance was associated with being male ($\beta = -.29$, $p < .01$) and a positive diagnostic history of diabetes ($\beta = -.20$, $p < .05$). After adjusting for medical and demographic characteristics, a trend emerged for the association between executive function and total instrumental ADL ($\Delta F(1,108) = 2.94$, $\Delta R^2 = .02$, $p = .089$). Greater executive function was associated with increased instrumental ADL performance ($\beta = .18$). See Table 5 for a full summary of hierarchical regression analyses.

Table 5. Association of Executive Function with Instrumental Activities of Daily Living in Older Adults with Heart Failure (*N* = 120): A summary of hierarchical regressions.

	Instrumental ADL *β*(*SE b*)
Block 1	
Age	.02(.03)
Gender	-.29(.60)**
AMNART	.03(.02)
Cardiac Index	-.04(.27)
Systolic	-.08(.03)
Diastolic	.19(.04)
Diabetes	1.20(.58)*
Myocardial Infarction	-.09(.56)
Elevated Cholesterol	.07(.59)
Depression	-.01(.68)
R^2	.15
F	1.94*
Block 2	
EF	.18(.00)
R^2	.17
F for ΔR^2	2.94 (p = .089)

Abbreviations: *β* – standardized regression coefficients, SE – standard error; EF = Executive Function

Bivariate correlations revealed that reduced executive function was significantly associated with reduced independence for driving ability ($r(120) = .22$, $p = .02$). Marginal significance emerged for shopping ($r(120) = .18$, $p = .05$), and a trend for finances (r(120) = .15, $p = .09$). See Table 6.

Table 6. Bivariate Correlations Between Executive Function and Instrumental ADLs (*N*= 120)

Instrumental ADLS	*Executive Function*	*P*
Telephone	.05	.56
Shopping	.18	.05
Food Preparation	.06	.50
Housekeeping	.15	.10
Laundry	.06	.49
Transportation	.22	.02
Medications	.09	.36
Finances	.15	.09

Executive Function and Psychosocial Outcomes

Many participants reported current alcohol and cigarette use, as the sample averaged 3.47 (SD = 7.36) alcoholic beverages in the past month and 6.28 (SD = 25.98) cigarettes per week. In terms of basic ADL tasks, HF participants most commonly indicated receiving assistance with physical ambulation (i.e., 21.7%). See Table 7 for psychosocial descriptives.

Table 7. Psychosocial Characteristics of 120 Older Adults with Heart Failure.

Quality of Life	
SF-12 PCS, mean (SD)	44.39(8.69)
SF-12 MCS, mean (SD)	51.39(10.77)
Substance Use	
Total Number of Alcoholic Drinks*	3.47(7.36)
Total Number of Cigarettes**	6.28(25.983)
Basic ADLS	
	% Needing Assistance
Toileting	4.2
Feeding	0.8
Dressing	4.2
Grooming	4.2
Physical Ambulatoin	21.7
Bathing	2.5
Basic ADL, mean (SD)	11.63(.80)

*= Number of alcoholic beverages in the past month; ** = Number of cigarettes per week;

ADL = Activities of Daily Living

A series of partial correlations adjusting for age, gender, estimated premorbid intelligence, cardiac index, systolic and diastolic blood pressure, and diagnostic history of diabetes, myocardial infarction, elevated total cholesterol and depression were performed to examine the association of executive function with quality of life, basic ADLs, and alcohol and cigarette use. Reduced executive function was associated with poorer physical quality of life ($r(108) = .24$, $p = .03$), mental quality of life ($r(108) = .28$, $p = .003$), and decreased basic ADL performance ($r(108) = .21$, $p = .03$). No such pattern emerged between executive function and alcohol consumption in the past month ($r(108) = -.16$, $p = .10$) or with current cigarette smoking ($r(108) = -.05$, $p = .62$).

Discussion

Consistent with previous work, impairments on neuropsychological tests of executive function and instrumental ADL performance were common in the current sample of older adults with HF. Based on previous literature, we hypothesized that executive function would mediate the relationship between HF severity and instrumental ADLs. Although our findings did not support out hypothesis, our results do suggest a possible link between executive function and both instrumental ADL performance and important psychosocial outcomes. Several aspects of our findings deserve brief discussion.

Contrary to expectations, cardiac index was not associated with executive function in the current sample of HF patients. While theories postulate reduced cardiac functioning leads to cognitive impairment through cerebral hypoperfusion, empirical studies are inconsistent in showing this relationship (Alves et al., 2005; Alves & Busatto, 2006; Vogels et al., 2008). For example, improvements in cognitive function and cerebral blood flow following heart transplantation supports the influence of cardiac function on cognition (Deshields, McDonough, Mannen, & Miller, 1996; Massaro, Dutra, Almeida, Diniz, & Malheiros, 2006). Additionally, past studies have also shown indices of cardiac functioning, including cardiac index, to be associated with reduced executive functioning in persons with HF (Hoth et al., 2008; Hoth et al., 2010). However, other studies have found no association or a non-linear relationship between cardiac and cognitive function (Jefferson et al., 2011; Putzke et al., 2000). Surprisingly, Vogels and colleagues (2008) failed to find an association between cerebral blood flow velocity and cognitive function among HF patients, suggesting the pathophysiological effects of HF (i.e., cerebral blood flow) is influenced by other factors (i.e., medical comorbidity). Based on the above, it is clear that future work is needed to clarify the association between measures of cardiac perfusion and cognitive function in HF patients.

There are several potential explanations for these mixed findings. First, the current sample demonstrated relatively preserved rates of cardiac functioning and recent work suggests there may be a potential threshold effect occurring in which cardiac function must fall below a certain L/min to produce neuropathological effects (Jefferson et al., 2011). For instance, Jefferson and colleagues (2011) found a U-shaped association between ejection fraction and cognitive function. Their findings showed that only individuals in the lowest LVEF quintile exhibited significantly reduced neuropsychological test performance, possibly a result of cerebral hypoperfusion. Conversely, persons in the highest LVEF quintile also demonstrated cognitive dysfunction. However, it is unclear how cardiac function altars cognitive functioning and future studies are needed to elucidate the underlying mechanisms between cardiac and brain function.

Moreover, while common theories of cognitive impairment in HF include reduced cardiac functioning resulting in decreased cerebral perfusion (Hoth, 2010), medical comorbidity may also be another potential etiological factor for reduced cognitive function in this population. For example, cardiovascular disease risk factors such as hypertension and diabetes contribute to the development of HF and have been linked with cognitive impairment independent of HF (Braunstein et al., 2003; Roger et al., 2012; Alosco et al., 2012; Alosco et al., 2012). Additionally, hypertension and diabetes are also associated with cerebral microvascular and macrovascular damage (i.e., reduced endothelial functioning, white matter hyperintensities) and hypertension has also been linked with disruptions in cerebral perfusion (Maggi et al., 2009; Legato et al., 2006; Perlmuter, Hakami, & Hodgson-Harrington, 1984; Cannata, Alberoni, Franceschi, & Mariani, 2002; Gunstad; Stanek, Szabo, & Kakos, 2010; Waldstein, Manuck, Ryan, & Muldoon, 1991; Waldstein & Katzel, 2001). Other factors also not accounted for in the current study such as metabolic abnormalities (i.e., low serum, anemia), psychiatric comorbidity and/or social support may also contribute to cognitive impairment in patients with HF (Zuccala et al., 2005; Wolfe, Worrall-Carter, Foister, Keks, & Howe, 2006). Thus, while the current study targeted reduced cardiac index as the potential etiology of executive dysfunction, future work should examine interrelationships between medical comorbidity, executive function, and instrumental ADLs.

There are several methodological limitations of the current study that may also offer explanation for the non-significant associations between HF severity with executive function and instrumental ADLs. First, the study consisted of cross-sectional data and prospective studies are needed to examine the type of relationship (i.e., linear or non-linear) between cardiac index and executive function and the subsequent effects on instrumental ADL performance. Another possible explanation for the inconsistent findings may be the influence of HF duration. Presumably, longer duration of reduced cardiac index would produce greater neuropathological damage and ultimately cognitive impairment. Unfortunately, the current study did not assess duration of disease among the participants. Although unlikely given the patient population utilized for recruitment, it is possible that HF severity was not associated with executive function because participants were recently diagnosed. Prospective studies would provide key insight into the relationship between HF duration and executive function. Similarly, future work should examine the etiological underpinnings of cognitive impairment using neuroimaging and advanced assessments of cerebral blood flow (i.e., functional magnetic resonance imaging). For instance, the current study and much of past studies do not directly assess cerebral perfusion using measures such as positron emission tomography. Future studies using this technique would help clarify the role of cerebral perfusion on brain functioning in HF patients as well as its relationship to cardiac functioning.

Although not statistically significant, the current study indicates a possible relationship between executive function and instrumental ADLs. Reduced ability to perform instrumental ADLs has been linked with re-hospitalization and admissions to geriatric wards (Moser & Worster, 2000; Krumholz et al., 1998; Jaarsma, Halfens, Huijer Abus Saad, 1996). Many instrumental ADLs 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, Berg, Dracup, 2001). Higher-order mental abilities such as executive function are required for successful self-management (Riegal & Dickson, 2008). Indeed, past work has shown reduced executive functioning to be associated with poor treatment adherence (i.e., medication management) among patients with diabetes mellitus and hyperlipidemia (Stilley, Bender, Dunbar-Jacob, Sereika, & Ryan, 2010). Executive functions of the brain consist of advanced cognitive processes, including planning, organizing, and monitoring behavior (Kalmar et al., 2008; Ramsden et al., 2008). Frontal brain regions, which mediate these mental abilities, are particularly vulnerable to damage among HF patients as a result of ischemia, infarction, and hypoxemia (Woo et al., 2003). These pathological changes may place HF patients at risk for poor adherence and ability to perform self-care behaviors, due to their need to adapt to multiple lifestyle changes and the complex medication regimen, including the ability to schedule, plan and perform multiple tasks simultaneously (Burra et al., 2007; Lezak, 1995; Stilley et al., 2010). Future studies are needed to further examine the link between executive function and instrumental ADL performance.

Interestingly, the current study found specific associations between executive function and reported driving ability. Such findings suggest that HF patients may be considered an at-risk population for driving impairment. For instance, impairments in executive function have been shown to be important contributors to driving ability in other populations (i.e., Alzheimer's disease and mild cognitive impairment) (Adler & Kuskowski, 2003; Daigneault, Joly, & Frigon, 2002). Consistent with this pattern, elderly drivers with mild to moderate dementia are up to 8X greater risk of crashing than non-demented elderly (Retchin & Hilner, 1994). Indeed, on-road driving abilities require complex cognitive abilities (i.e., executive function) such as decision-making and awareness of driving environment (Duchek et al., 2003), and reduced abilities in such areas has been linked with poor driving ability (McKnight & McKnight, 1999; Petridou & Moustaki, 2000; Reger, Welsh, Watson, Cholerton, Baker, & Craft, 2004). Findings from this study and previous work from our lab demonstrating the link between cognitive function and reduced self-reported driving ability suggests the need for driving performance to be further studied in this population (Alosco et al., 2012). Specifically, studies should examine driving in patients with HF using objective measures such as drive simulation or on-road testing.

Consistent with past work, our results demonstrated a significant association between reduced executive function with decreased quality of life and poor basic ADL performance. Recent work has shown executive dysfunction predicts mortality in patients with HF (Pressler et al., 2010b). It is plausible that the association between poor quality of life and increased risk of mortality with executive function may be related to the above discussion (i.e., inability to adhere to treatment recommendations and/or monitor symptoms) (Bennett et al., 1998; Murray et al., 2007; Jurgens, Hoke, Byrnes, & Riegel, 2009). Additionally, the association between executive function and basic ADL performance in the current study is consistent with past work among other medical populations (Pohjasvaara et al., 2002). Interestingly, a recent study found HF to be a significant contributor to decreased basic ADL performance over time (Daniel, Timothy, Wanzhu, & Douglas, 2012). The current study also suggests executive dysfunction may play a role in decreased basic ADL performance in HF and prospective studies are needed to validate our results. Lastly, our findings and others indicate that smoking and alcohol consumption is common in this population. Although contrary to the current study, there is reason to expect that such behaviors contribute to poor cognitive function (Mascitelli & Pezzetta, 2006). Cognitive function and smoking and alcohol use may also be a bi-directional relationship, as it is also possible that HF patients with cognitive impairment may fail to refrain from use due to poor insight and/or reasoning. The lack of association between alcohol and smoking use and cognitive function in the current study may be related to methodological limitations. For example, the current study assessed these behaviors through self-report. It is possible that participants significantly under estimated their reported levels of use, as HF patients self-report of adherence to recommendations may be favorably skewed due to patients' tendency to please their clinicians (Adams, Soumerai, Lomas, & Ross-Degnan, 1999). Additionally, the current study also examined current alcohol and smoking status and past work indicates lifetime use may be a better predictor of cognitive impairment (Stewart, Deary, Fowkes, & Price, 2006). Similarly, other medical factors seemingly caused by alcohol and smoking use (i.e., artherosclerosis) may mediate the relationship between consumption and cognitive function (Howard et al., 1998; O'Brien et al., 2003). Longitudinal studies are needed to further clarify the relationship and directionality between cognitive function and substance use in HF patients.

Limitations of the current study deserve further mention. Instrumental ADLs and psychosocial outcomes were assessed using self-report instruments. The use of self-report in a population with possible cognitive deficits may confound the reliability and validity of participant responses. Future studies should examine objective and informant assessments of instrumental ADLs and quality of life within a HF population, as the current literature mostly consists of self-report. Objective approaches are of particular need in this population, as persons with cognitive dysfunction tend to underreport their impairment (Leicht, Berwig, Gertz, 2010; Starkstein et al., 1993). Future studies should also clarify the role of gender on ADL function in this population.

For instance, the current study found that being male was associated with worse instrumental ADL performance. While this may be indicative of impairment, this may also be an artifact of lifelong behaviors (i.e., males may be less likely to prepare meals or do laundry). Furthermore, our sample was relatively homogenous in race and gender and future work that examines cognitive function and treatment adherence in larger more diverse samples of HF persons would increase the external validity of our findings. Finally, the present study did not have a control group for comparison on key variables, including neuropsychological test performance and instrumental ADL performance. Although previous work has shown HF patients to perform worse on cognitive tests relative to control (Pressler et al., 2010a), future work should also utilize a control group with HF patients to validate our findings regarding a possible link between executive dysfunction and poorer instrumental ADL performance and psychosocial functioning.

In summary, the current study does not support executive function as a mediator of the relationship between cardiac index and instrumental ADLs. However, our findings do show preliminary evidence of an association between executive function and instrumental ADLs in this population. The current study further suggests that executive dysfunction in HF may be a significant contributor to poor psychosocial outcomes. 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.

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