Published in final edited form as:
J Int Neuropsychol Soc. 2009 January ; 15(1): 137–141. doi:10.1017/S1355617708090073.

Sustained attention is associated with left ventricular ejection fraction in older adults with heart disease

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Abstract

Poor cardiac pumping efficiency has shown to lead to cognitive impairments in patients with cardiovascular disease (CVD). The current study examined the relationship between left ventricular ejection fraction and sustained attention and inhibitory processes measured by the Adaptive Rate Continuous Performance Task and the Go/No-go test. Participants were 67 older outpatients (age 68.5 ± 7.4) with a range of CVD. Associations between cognition and ejection fraction were examined *via* linear regression analysis. Results were consistent with the hypothesis that lower ejection fraction is significantly associated with decrements in sustained attention and vigilance. Overall, the results provide support for the hypothesis that a change in cardiac pumping leads to decrements in some aspects of attention; however, inhibitory processes are relatively spared.

Keywords

Cardiovascular disease; Ejection fraction; Sustained attention; Vigilance; ARCPT; Go/No-go

INTRODUCTION

With a longer life expectancy, the prevalence and incidence of cardiovascular disease (CVD) among the elderly have increased substantially (Futterman & Lemberg, 2000). Historically, clinical research has focused on the effects of chronic CVD on cognition due to either specific vascular risk factors (e.g., hypertension) or the subsequent effects of cardiac procedures [e.g., coronary artery bypass grafting (CABG)]. Although clinicians generally recognize that elderly patients with chronic CVD often become frail and experience significant functional problems (Landi et al., 2001), reductions in function may be misattributed to either general aging or specific risk factors and not related to reductions in overall cardiac performance. There is now

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evidence that CVD is associated with cognitive decline even in the absence of clinical stroke (Paul et al., 2005). Rather, diminished systemic perfusion from cardiac pump function and/or peripheral vascular dysfunction increases the likelihood of cerebrovascular-associated brain disturbances (Kalaria, 2003) and circulatory insufficiency, which leads to inadequate cerebral perfusion and cerebral hypoxia, differentially affects discrete brain regions (i.e., predominant patterns of white matter lesions in the frontal, occipital lobes and in the periventricular regions in severe anoxic state; Ammermann et al., 2007).

Although the sequelae of hypoxemia or anoxia are complex and diverse in regard to cerebral functioning (see Caine & Watson, 2000, for review), reduced localized cerebral blood flow has been found in individuals diagnosed with heart failure (i.e., posterior cortical areas; Alves et al., 2005) and a history of cardiac arrest (i.e., frontal hypoperfusion; Roine et al., 1991), and those exhibiting neuropsychological complications related to CABG (i.e., frontal and left parietal hypoperfusion; Degirmenci et al., 1998). These cortical areas in particular have been linked to the attention network (Toro et al., 2008). Hypoperfusion to these areas may result in a variety of cerebral insults from diffuse changes in white matter (O'Sullivan et al., 2002) to subcortical atrophy (Appelman et al., 2008), either of which could contribute to reductions in cognitive functioning. Although changes in cognitive functioning are a common part of normal aging (Brickman et al., 2007), interpretations of results from studies reporting more global dysfunction are complicated by the demand of underlying attentional processes on other cognitive domains (e.g., memory). Our prior research with cardiac outpatients supports this observation by demonstrating that attention and executive deficits adversely impact significant learning impairment and functional outcome (Jefferson et al., 2006).

The objective of the current study was to focus on various measures of attention since associated brain regions may be particularly sensitive to reductions in cerebral blood flow. The outpatients in the current study represent a heterogeneous group with a wide variability in cardiac functioning. We hypothesized that among older adults with CVD, diminished ejection fraction would be associated with reductions in various forms of attention.

METHOD

Participants

Participants consisted of 76 older adults recruited from the outpatient cardiology offices affiliated with the Rhode Island Hospital and the Miriam Hospital in Providence, Rhode Island. The majority of the participants were identified from patients undergoing noninvasive cardiovascular assessment for coronary heart disease at the Rhode Island Hospital Heart Failure Clinic. Participants were native English speakers with normal or corrected hearing and vision at the time of testing. In addition to an extensive medical history interview and medical chart review, patients were assessed for signs of stroke or other neurological abnormalities by a cardiologist (AP). Participants were excluded from the study if they had a history of stroke, a moderate or severe traumatic brain injury (with loss of consciousness), or any other documented significant neurological disease (e.g., dementia, multiple sclerosis). In addition, participants were administered a comprehensive neuropsychological battery and were excluded if they demonstrated any focal determents on formal testing. Any questionable cases were discussed between one of the primary cardiologists on this study (AP) and a board-certified neuropsychologist (RAC). Additional exclusion criteria included a diagnosed current psychiatric illness and history of substance abuse with subsequent hospitalization. Table 1 lists the clinical characteristics of the sample.

All participants scored below the cutoff for clinically significant depression (<10) on the Beck Depression Inventory (Beck & Steer, 1993) and were nondemented (Dementia Rating Scale >124), indicating intact global cognitive functioning according to published norms (Mattis, 1988). Institutional IRB approval was granted, and informed consent was obtained from all participants prior to testing. Participants were compensated $50 each.

Echocardiogram

Participants were asked to refrain from taking vasoactive medications (e.g., calcium channel blockers, ACE inhibitors, and beta blockers), drinking caffeinated beverages, exercising, or smoking for 6 hr before the vascular assessment. Furthermore, all participants fasted for 6 hr prior to their cardiac assessment. Prior to testing, patients remained supine for 15 min in a quiet room.

A complete, transthoracic echocardiogram was obtained from each participant according to the American Society of Echocardiography guidelines. Although many different indices can be derived from the echocardiogram results, our primary interest for this research was to examine left ventricular ejection fraction. Ejection fraction is a general measure of how well the heart is pumping, specifically the performance of the left ventricle (LV). The LV end-diastolic and end-systolic volumes (LVEDV and LVESV, respectively) were calculated, and ejection fraction is a product of the following formula: (LVEDV – LVESV)/LVEDV. Reference ranges have been previously published; typically values >0.55 are considered normal, 0.45–0.55 mildly abnormal, 0.30–0.44 moderately abnormal, and <0.30 severely abnormal (Lang et al., 2005).

Neurocognitive Assessment

All participants completed a standardized neuropsychological assessment by trained research assistants under the supervision of a licensed clinical neuropsychologist (RAC). Results of assessments of other cognitive domains have been reported previously (Paul et al., 2005).

Adaptive Rate Continuous Performance Test—This computerized test is a modification of the standardized Continuous Performance Test (Rosvold et al., 1956), which is used to measure vigilance and sustained attention. The Adaptive Rate Continuous Performance Test (ARCPT) requires identification of target stimuli in specific combinations (i.e., the letter "A" followed by the letter "X"). Trials are presented in 10 blocks of 100 trials. A series of letters is presented on a computer monitor for a 100-ms duration each. A total of 60 targets are presented (A–X), comprising 15% of the total stimuli. Targets are grouped into 10 blocks containing six targets per block for subsequent scoring, though participants are unaware of these blocks, as stimulus presentation is continuous once the task begins. When the target appears on the screen, the participant is instructed to press the spacebar on a computer keyboard. The ARCPT differs from the conventional CPT in that the interstimulus interval (ISI) varies across blocks of trials as a function of the participant's performance. A unique aspect of the ARCPT is this adaptive rate. The ISI, which is initially set at 60 ms, decreases by 4 ms after each correct response and increases by 4 ms after each error. The ISI settles at a final ISI, which reflects the minimum ISI at which participants can maintain 80% accuracy.

Sustained attention indices derived from the ARCPT are measures of accuracy of target detection, including misses and false-positive errors, from which discrimination ability (d') and response bias (β) are derived. An additional two indices provide measures of the consistency of attention over time, an Inconsistency Index, which measures variability over the 10 blocks of the ARCPT, and Vigilance Decrement, which measures the decline in overall performance across the duration of the test. Also, a measure of speed of processing is based on the ISI occurring by the end of the test (Final ISI), which represents the fastest sustained stimulus presentation rate that the patient was able to achieve. In total, six separate ARCPT indices were examined in the current study (i.e., Vigilance Decrement, response bias, Final ISI, discrimination, inconsistency, and false-positive response). The ARCPT has shown to be a highly reliable and valid measure. Based on the normative data, the group as a whole was more variable on the Inconsistency Index, although not impaired. Vigilance Decrement was reflected a normal rate of speed; however, the total ISI was slower. Accuracy was well above chance (Cohen & Gunstad, 2008).

Go/No-go Test—This test of response competition and inhibition is an adaptation of the standard Go/No-go paradigm (Lezak, 1995). Briefly, the examiner shows a sequence of finger extensions on his or her right hand (either index finger only or index and middle fingers together) with a 1-s interval between stimuli. Participants are instructed to show their index finger of their dominant hand if they were presented with a two-finger demonstration and not show any fingers if presented with only one finger from the examiner. This portion of the task followed a standard contrasting motor paradigm in which participants were instructed to show one finger if they saw two examiner fingers and two fingers if they saw one examiner finger. Therefore, a prepotent response was established to respond with a two-finger response in the subsequent No-go condition. A random sequence of 40 stimuli was presented with half of the stimuli being the No-go (i.e., showing a two-finger response). The number of commission errors was recorded (i.e., responding to "No-go" stimuli) as well as total number of errors including perseveration and failure to respond to "Go" stimuli (Table 2).

Echocardiograms were completed between 2 and 4 weeks after the completion of the neuropsychological battery.

Data Analysis

Descriptive statistics were performed to characterize the sample with respect to demographic and clinical characteristics, ejection fraction, and neurocognitive performance. Pearson's correlations between sex and age were used to investigate the relationship of these *a priori* factors to ejection fraction and ARCPT variables, the respective dependent and independent variables in the primary model. Last, multiple regression analyses were performed using SPSS 13.0 (SPSS Inc., Chicago, IL) to examine the association between ejection fraction and attention performance, which was entered in one step.

RESULTS

Independent *t*-test analysis was performed on all the clinical characteristics (i.e., CABG, stenting, angioplasty, CAD, arrhythmia, heart failure) and ejection fraction. Individuals with heart failure diagnosed by their cardiologist, which by definition is a result of reduced cardiac output, had significantly lower ejection fractions than participants without heart failure (mean heart failure group = 0.5182 ± 0.120 *vs.* non-heart failure = 0.60832 ± 0.110, $p = .011$). In addition, bivariate correlations between ejection fraction and sex and age were not significant. However, significant relationships with neurocognitive measures were observed. Increased age was related to worse ARCPT discrimination ($r = -.316$, $p = .005$) and longer finial ISI ($r = .232$, $p = .044$). Men made more Go/No-go errors than women ($r = -.275$, $p = .016$).

Since neither age nor sex was significantly associated with ejection fraction, the final regression analysis consisted only of the neuropsychological variables. The six ARCPT indices and Go/No-go errors were independent measures entered in one step with ejection fraction entered as the dependent measure. Three of the six ARCPT variables were significant predictors of ejection fraction (vigilance: $\beta = -.32$, $p = .012$; discrimination: $\beta = -.42$, $p = .039$; and false-positive errors: $\beta = -.51$, $p = .045$). This model accounted for 20.5% of the total variance [$F(7, 60) = 2.21$, $p = .046$, $r = .453$]. No association emerged for the Go/No-go test.

DISCUSSION

The present study assessed the relationship between ejection fraction and sustained attention and disinhibition among an older adult cohort with stable cardiovascular insufficiencies. Consistent with our *a priori* hypotheses, ejection fraction was associated with impairments with specific aspects of attention, specifically continuous vigilance and discriminability; patients with lower cardiac pumping efficiency had difficulty on measures of sustained attention. Ejection fraction was not associated with one of the measures of disinhibition, the Go/No-go test, perhaps demonstrating specificity for certain attentional-based processes.

Findings from neuroimaging studies provide one possible explanation as to why some, but not all, attention measures were related to ejection fraction. Research using the Continuous Performance Test has found widespread neuronal activation patterns in prefrontal and frontal cortex (Adler et al., 2001). It is possible that discriminability and subsequent false-positive errors are associated with error monitoring and error processing systems in the brain. These two systems only partially overlap with brain regions engaged in inhibitory control and response competition. Gehring and Knight (2000) reported that the lateral prefrontal cortex interacts directly with the anterior cingulate in monitoring behavior and guiding compensatory systems. In addition, the neural correlates of vigilance and sustained attention have also been largely localized to include the right prefrontal as well as the parietal lobe and thalamus (Sarter et al., 2001). These anterior structures are potentially vulnerable to systemic reductions in blood flow due to both their overall mass and their contiguous circuits with subcortical structures (Cummings, 1993), many of which are susceptible to alteration in blood flow (Moody et al., 1990). An alternative explanation is that these processes, and thus subsequent error monitoring, are more sensitive to cognitive impairments associated with reduced systemic perfusion.

Our findings expand the existing literature by illustrating the association between a direct measure of cardiac pumping efficiency and different elements of attention in a cohort that presents unique issues associated with neurovascular aging (Tao et al., 2004). However, there are several limitations that must be considered. Most participants were well educated and identified themselves as whites of European descent; therefore, we are unable to determine if results generalize to other ethnic groups. Although extensive medical background was taken and participants with a clinical history of stroke were excluded, there remains the possibility that the participants in this study had experienced underlying silent infarcts that were not clinically identifiable. Whereas changes in large vessel functioning usually become acutely obvious, alterations to smaller vessels may occur without detection and lead to substantial changes in cognitive functioning in apparently neurologically intact older adults (Enzinger et al., 2007). In addition, this study was aimed at studying ejection fraction as a mechanism of cardiovascular functioning, and a measure of cerebral perfusion was not included. Ultimately, it will be important to examine how cardiac function relates to cerebral profusion *via* other neuroimaging measures such as Arterial Spin Labeling (Liu & Brown, 2007).

In conclusion, there is considerable value in the study of cognitive function in relationship to cardiac dysfunction associated with CVD. Consideration of reduced cognitive capacity related to neuronal changes stemming from CVD is essential as the population of elderly with CVD increases. Since most CVD patients have a mixture of risk factors, studying patients encompassing a broad range of cardiovascular dysfunction through the simultaneous measurement of cardiovascular, peripheral vascular, and cerebrovascular function will likely facilitate the detection of cognitive effects associated with a poor systemic vasculature.

ACKNOWLEDGMENTS

This work was supported by National Institute of Health grants AG017975 (RAC), AG026850 (KFH), HL074568 (JJG), HD043444 (ALJ), and AG020498 (BAJ, APH).

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Table 1

Clinical characteristics of sample

	Mean	*SD*	Range	%
Male				55
Female				45
Age	68.5	7.37	56–85	
Education	14.26	2.80	8–20	
Caucasian				89.8
African American				8.5
Other				1.7
Coronary artery disease				35.6
CABG				30.3
Angioplasty				28.3
Heart failure				24.2
Stenting				19.0
Cardiac arrhythmia				16.7

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Table 2

Neuropsychological functioning of sample

Measure	**Mean**	***SD***	**Range**
MMSE total	28.78	1.318	25–30
DRS total	137.80	3.78	126–144
DRS subtests			
Attention	35.91	1.34	31–37
I/P	35.91	1.83	29–37
Construction	5.55	0.89	3–6
Conceptualization	36.50	2.16	31–39
Memory	24.00	1.51	18–25
ARCPT discrimination (d')	2.43	0.61	0.24–3.66
ARCPT bias (β)	0.63	0.30	−0.13 to 1.0
ARCPT inconsistency	8.71	3.77	3.0–20.0
ARCPT vigilance	0.05	0.05	−0.06 to 0.29
ARCPT final ISI	95.91	62.96	28.1–397.6
ARCPT false-positive errors	2.96	3.89	0.0–25.0
Go/No-go errors	1.04	1.29	0.0–1.0

Note. MMSE = Mini-Mental Status Examination; DRS = Mattis Dementia Rating Scale; I/P = initiation/perseveration (Folstein et al., 1975).