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Cognitive Function in Heart Failure is Associated with Nonsomatic Symptoms of Depression but Not Somatic Symptoms

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Abstract

Background—Patients with heart failure (HF) have high rates of cognitive impairment and depressive symptoms. Depressive symptoms have been associated with greater cognitive impairments in HF; however, it is not known whether particular clusters of depressive symptoms are more detrimental to cognition than others.

Objective—To identify whether somatic and/or nonsomatic depressive symptom clusters were associated with cognitive function in persons with HF.

Methods—Participants were 326 HF patients (40.5% female, 26.7% race-ethnicity, aged 68.6±9.7 years). Depressive symptoms were measured using a depression questionnaire commonly used in medical populations: the Patient Health Questionnaire-9 (PHQ-9). Somatic and Nonsomatic subscale scores were created using previous factor analytic results. A neuropsychological battery tested attention, executive function, and memory. Composites were created using averages of age-adjusted scaled scores. Regressions adjusting for demographic and clinical factors were conducted.

Results—Regressions revealed that PHQ-9 Total was associated with Attention ($\beta=-.14, p=.008$) and Executive Function ($\beta=-.17, p=.001$). When analyzed separately, the Nonsomatic subscale – but not the Somatic symptoms subscale ($p=.092$) – was associated with Attention scores ($\beta=-.15, p=.004$) and Memory ($\beta=-.11, p=.044$). Both Nonsomatic ($\beta=-.18, p<.001$) and Somatic symptoms ($\beta=-.11, p=.048$) were related to Executive Function. When included together, only the

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Nonsomatic symptom cluster was associated with Attention ($\beta=-.15, p=.020$) and Executive Function ($\beta=-.19, p=.003$).

Conclusions—Greater overall depressive symptom severity was associated with poorer performance on multiple cognitive domains, an effect driven primarily by the nonsomatic symptoms of depression.

Clinical Implications—These findings suggest that screening explicitly for nonsomatic depressive symptoms may be warranted and that the mechanisms underlying the depression-cognitive function relationship HF are not solely related to sleep or appetite disturbance. Thus, interventions which target patients' somatic symptoms only (e.g., poor appetite or fatigue) may not yield maximum cognitive benefit compared to a comprehensive treatment which targets depressed mood, anhedonia, and other nonsomatic symptoms.

Keywords

depressive symptoms; cognition; heart failure; neuropsychological testing

Introduction

Patients with heart failure (HF) have been found to have a high prevalence of cognitive impairment (up to 73%).¹⁻³ Sauve and colleagues⁴ report that HF patients have four times greater risk of cognitive impairment compared to matched community controls. These HF-related cognitive deficits have been implicated in poorer HF outcomes, such as impaired self-care, greater disability, and increased mortality among patients with HF.^{5, 6} In addition to prevalent cognitive impairment, individuals with HF have also high rates of depressive symptoms^{7, 8} with 20–50% presenting with elevated depressive symptoms or major depressive disorder.⁹⁻¹² Depressive symptoms are also associated with adverse HF outcomes, including increased hospital readmission rates and decreased survival.^{9, 12, 13} Importantly, evidence indicates that cognitive impairment and depressive symptoms are related in patients with HF.^{14, 15} For example, greater depressive symptoms have been shown to predict poorer cognitive function in persons with HF after controlling for demographic and medical variables.^{14, 15} Pathways linking depression and cognitive function in HF may involve pathological changes in brain structure, function, and/or perfusion, as individuals with HF demonstrate atrophy, white matter hyperintensities, and cerebral hypoperfusions,^{14, 16} all factors that are associated with both impaired cognition¹⁶⁻¹⁸ and elevated depressive symptoms.^{19, 20}

One limitation of the studies examining the link between cognitive impairment and depressive symptoms in HF is that they typically examine depression as a unidimensional construct. However, evidence suggests that depression is comprised of multiple dimensions, including affective, cognitive, behavioral, and somatic symptoms.²¹ Indeed, these symptom clusters have been shown to have differential impact on HF outcomes^{22, 23} as well as other indices of cardiovascular function.²⁴⁻²⁹ For example, some studies found that the somatic symptoms cluster (e.g., sleep disturbance, appetite changes, and low energy) was the strongest predictor across a variety of outcomes,^{22, 25, 29} whereas other studies reported similar results for the nonsomatic symptom clusters (e.g., cognitive, affective, or behavioral

symptoms).^{23, 26–28} For example, Schiffer et al.²² found that individuals with high somatic symptom scores had a greater incidence of mortality than those with low scores (31% vs. 15%; hazard ratio = 2.3). Given these conflicting findings and the paucity of studies examining depressive symptom clusters in HF populations, it is not clear whether specific depressive symptom clusters are most damaging to HF outcomes.³⁰ Additionally, no study to date has specifically examined whether certain depressive symptoms clusters are better predictors of cognitive impairment in HF than are others.

Addressing this limitation can help to determine the relative importance of depressive symptom clusters in predicting cognitive impairment in HF and could have significant scientific and clinical implications. First, identifying which clusters are the most detrimental to cognitive function in HF patients could help to identify the mechanisms underlying the relationship between depression and cognitive impairment in HF. Second, systematically targeting the most harmful clusters and their mechanisms could result in more effective HF treatment strategies, which adequately address depression and cognitive deficits. Accordingly, the primary objective of this study was to compare the relative importance of somatic and nonsomatic depressive symptom clusters in predicting cognitive function in a large sample of patients with HF.

Method

Participants of the Heart Failure Adherence, Behavior, and Cognition Study (Heart ABC)

The sample was 326 persons with HF enrolled in the larger, ongoing Heart ABC study.³¹ Study eligibility requirements were as follows: (1) Aged 50–85 years at enrollment, (2) Documented systolic HF diagnosis within 36 months of study enrollment, (2) physician-documented New York Heart Association class II or III 3 months duration at the time of study enrollment, (3) No cardiac surgery within last 3 months, (4) No history of neurological disorder or injury (e.g., Alzheimer’s disease, dementia, stroke, seizures), (5) No history of moderate or severe head injury, (6) No past or current history of psychotic disorders, bipolar disorder, learning disorder, developmental disability, renal failure requiring dialysis, or untreated sleep apnea, (7) No current substance abuse or within the past 5 years, and (8) No current use of home tele-health monitoring program for HF. Participants with complete data on the measures of depressive symptoms and cognitive function were selected.

Measures

Depressive Symptoms—Depressive symptoms were assessed using the Patient Health Questionnaire-9 (PHQ-9).³² The PHQ-9 consists of 9 items assessing the following symptoms of depression: (1) anhedonia, (2) depressed mood, (3) sleep difficulties, (4) fatigue, (5) appetite changes, (6) poor self-esteem, (7) concentration problems, (8) psychomotor retardation/agitation, and (9) suicidal ideation. Items are rated 0=*not at all*, 1=*several days*, 2=*more than half the days*, and 3=*nearly every day*. We calculated the PHQ-9 Total (sum of all items; range: 0–27) and two subscale scores based on previous factor analytic results in patient populations.^{33, 34} The PHQ-9 Somatic subscale was computed by summing the sleep disturbance, fatigue, and appetite changes items (Items 3–5; range: 0–9), and the PHQ-9 Nonsomatic subscale was computed by summing the remaining

six items (Items 1–2 and 6–9; range: 0–18). Higher total and subscale scores indicate more severe symptom levels with the following clinical cut-offs for the total score: No depression: 0–4; Mild depression: 5–9; Moderate depression: 10–14, and Moderately Severe-to-Severe depression: 15 or greater. The PHQ-9 has demonstrated good reliability and validity.³² Cronbach's α was .84 for the PHQ-9 Total, .80 for the Somatic subscale, and .71 for the Nonsomatic subscale. The subscales were strongly correlated at $r(326) = .63, p < .001$.

Cognitive Function—Cognitive function across multiple domains was assessed using a comprehensive neuropsychological test battery, comprised of tests with strong psychometric properties. These tests were selected because they comprise the gold standard assessment of neuropsychological functioning across a variety of cognitive domains and ensured that our assessment of cognitive functioning was comprehensive and accurate. Several tests for each domain were selected to maximize our assessment of each neuropsychological construct by utilizing unique assessment techniques. The three cognitive domains were the following:

1. *Attention*: The capacity to attend to and process information was measured by four tests. First, for both the Stoop Word and Stroop Color subtests, participants read lists of colored words as quickly as possible.³⁵ Next, for Trail Making Test A, patients connect 25 numbers in ascending order, as quickly and accurately as possible, and are timed.³⁶ Last, for Letter-Number Sequencing, patients are asked to repeat a series of letters and numbers in a specific order.³⁷
2. *Executive function*: The capacity to problem-solve, plan, inhibit, and reason was assessed using three tests. First, for the Stroop Color-Word subtest, participants are asked to identify the ink color (e.g., red ink) of a written list of color words (e.g., “blue”) as quickly as possible.³⁵ Second, for the Trail Making Test B, patients connect 25 alternating numbers and letters in ascending order and are timed.³⁶ Third, for the Frontal Assessment Battery (FAB), participants complete six subtests, including conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy.³⁸
3. *Memory*: The capacity to retain and recall verbal information was measured using the Rey Auditory Verbal Learning Test Learning Over Time, True Hits, Short Delay, and Long Delay scores.³⁹ For this test, participants are read a 15-item word list five times and are asked to repeat as many words as they can remember each time. After the fifth trial, participants are read an interference list and then asked to recall words from the original list. They are also asked to recall the original words after a 20-minute delay.

Covariates—The following variables were included as covariates/potential confounders of any observed relationship between cognitive function and depression: gender (0 = male, 1 = female), race-ethnicity (0=white, 1= non-white), education level (1 = 8th grade or less, 2 = 9–11th grade, 3 = high school, 4 = technical or trade school, 5 = some college, 6 = bachelor's degree, 7 = master's degree), socioeconomic status (SES), Charlson Comorbidity Index (CCI) score⁴⁰, and baseline self-reported HF severity. SES was estimated using subjects' zip code.⁴¹ The SES score was calculated as a z-score using indicators of income and education for each zip code⁴¹ with zero as the sample mean and higher scores indicating

higher socioeconomic status. The CCI is a summary score of comorbid medical conditions (e.g., diabetes, peripheral vascular disease, myocardial infarction, etcetera).⁴⁰ Baseline self-reported heart failure severity was assessed by asking participants' questions about their current symptoms/limitations. An example item is: *Do you markedly reduce physical activity due to tiredness, heart fluttering, shortness of breath, anginal pain?* Based on their responses, we assigned them to the corresponding NYHA class, ranging from Class I (Mild) and Class II – (Mild) to Class III (Moderate) and Class IV (Severe).⁴² Thus, we categorized some patients' HF severity as class I or IV based on their current self-reported symptoms/limitations at the time of their baseline assessment despite our aforementioned inclusion criteria of physician-documented NYHA class II or III at the time of enrollment. We also assessed participants' body mass index using measured height and weight and their ejection fraction from their medical record.

Procedure

All patients enrolled in Heart ABC³¹ were recruited from inpatient and/or outpatient cardiology practices in northeast Ohio and gave their written, informed consent to participate. All procedures were approved by the Institutional Review Boards of Kent State University, Summa Health Systems, Inc., and Case Western Research University and were completed in accordance with the Helsinki Declaration. After recruitment and written consent, a trained, qualified research assistant conducted the series of self-report questionnaires and neuropsychological testing for the baseline line visit either at the medical center or at the patient's home. All research assistants (5 at each site) were trained to perform standardized test administration of the neuropsychological tests by a research coordinator supervised by a licensed clinical neuropsychologist (J.G.). Research coordinators conducted quarterly evaluations of research assistants to ensure standardization of test administration. Inter-rater reliability was assessed and determined to be satisfactory (90.3% concordance).

Data Analyses

Raw neuropsychological test scores were converted to age-adjusted scaled scores using normative data for each test ($M = 10$, $SD = 3$). To facilitate interpretation, the scaled scores for each test were then converted to T-scores ($M = 50$, $SD = 10$). The T-scores for the tests in each domain were then averaged to create a composite score for that domain: attention, executive function, and memory (e.g., the T-scores for the Stroop Color-Word, Trails B, and FAB tests were averaged together to create the Executive Function composite score). T-scores ≤ 35 are indicative of cognitive impairment. To examine the relationship between depressive symptoms and cognitive function, a series of linear regressions was conducted. Each analysis was conducted with the Attention, Executive Function, or Memory composite score as the dependent variable in separate regressions, and the following covariates were always included on Step 1: gender, race-ethnicity, education level, SES, CCI score, and NYHA HF severity. Two primary types of regressions were run: independent-entry and simultaneous-entry. For independent-entry models, either the PHQ-9 Total, the Somatic subscale, or the Nonsomatic subscale was entered alone on Step 2. In the simultaneous-entry models, the Somatic and Nonsomatic subscales were entered together on Step 2 in order to determine whether the depressive symptom clusters had unique effects on the cognitive

variables. If the continuous PHQ-9 Total score was related to a cognitive variable in the regression models, an analysis of covariance (ANCOVA) was run to compare the variable across the PHQ-9 severity categories, adjusting for the same covariates as the regression models. All data analyses were conducted using IBM SPSS version 20.0 statistical software.

Results

Participants

Participants were predominantly older (age = 68.6, $SD = 9.7$), white (73.3%), male (59.5%), and had at least a high school diploma (88.3%) (See Table 1). On average, overall depressive symptom severity was subclinical (PHQ-9 < 5), but the standard deviation was adequate, indicating considerable individual differences in severity (PHQ-9 Total $M = 4.6$, $SD = 4.9$). Additionally, the sample had a wide range of depressive symptom severity levels, including 27.9% Mild ($n = 91$), 7.4% Moderate ($n = 24$), and 5.8% Moderately Severe-to-Severe ($n = 19$). Bivariate correlations between the PHQ-9 Total score and covariates indicates that PHQ-9 was associated with age ($r(326) = -.13$, $p = .02$), gender ($r(326) = .13$, $p = .02$), race-ethnicity ($r(326) = .12$, $p = .03$), SES ($r(326) = -.19$, $p = .001$), education level ($r(326) = -.18$, $p = .001$), and self-reported HF severity ($r(326) = .37$, $p < .001$). At the group level, participants had average performance in Attention ($M = 44.3$), Executive Function ($M = 45.9$), and Memory ($M = 47.9$) (See Table 1). Participants exhibited the following percentages of cognitive impairment (defined as T-score ≤ 35) on the composite domains: 12% for Attention, 11% for Executive Function, and 6.1% for Memory.

Demographic and Clinical Factors Associated with Cognitive Function

Regressions revealed that the following covariates were significantly associated with Attention: gender ($\beta = .18$, $p = .001$), race-ethnicity ($\beta = -.24$, $p < .001$), education level ($\beta = .30$, $p < .001$), and SES ($\beta = .12$, $p = .029$). Together, all covariates accounted for 22.5% of the variance in Attention ($p < .001$). A similar pattern was found for Executive Function with all the covariates accounting for 24.2% of the variance ($p < .001$) and significant associations observed with gender ($\beta = .15$, $p = .004$), race-ethnicity ($\beta = -.26$, $p < .001$), and education level ($\beta = .35$, $p < .001$). The covariates accounted for 18.3% of the variance in Memory ($p < .001$) with gender ($\beta = .43$, $p < .001$), race-ethnicity ($\beta = -.13$, $p = .020$), and education level ($\beta = .14$, $p = .013$) reaching significance. With the exception of SES and Attention, SES, medical comorbidity, and HF severity were not significantly related to any cognitive variables (all $ps \geq .09$).

Depressive Symptoms Clusters Associated with Cognitive Function

Independent-entry regression analyses adjusting for all demographic and medical covariates revealed that the PHQ-9 Total was associated with Attention ($p = .008$) and Executive Function scores ($p = .001$) (see Table 2) and accounted for an additional 2% and 3% of the variance, respectively. A trend was detected between the PHQ-9 Total score and Memory ($p = .067$) (see Table 2) and accounted for an additional 1% of the variance. Given that the PHQ-9 Total was negatively associated with Attention and Executive Function, we ran an ANCOVA to determine whether attention (Figure 1) and executive function (Figure 2) differed across the PHQ-9 severity categories. The ANCOVA omnibus test showed a trend

for attention, $F(3, 311) = 2.13, p = .096$ and was significant for executive function, $F(3, 311) = 4.60, p = .004$.

Independent-entry analyses for the Somatic and Nonsomatic symptoms subscales indicated that the Nonsomatic subscale ($p = .004$) – but not the Somatic symptoms subscale ($p = .092$) – was associated with Attention scores (see Table 2). A similar pattern emerged for Memory, with the Nonsomatic subscale ($p = .044$) significantly related to Memory but no relationship detected between Somatic symptoms ($p = .259$) (see Table 2). Both the Nonsomatic ($p < .001$) and Somatic symptoms ($p = .048$) predicted Executive Function.

When the Somatic and Nonsomatic symptoms were included in the simultaneous-entry model to determine their unique effects on cognitive function, only the Nonsomatic symptom cluster remained associated with Attention ($p = .020$) and Executive Function ($p = .003$). The relationship between Nonsomatic symptoms and Memory was reduced to a trend ($p = .096$). The Somatic symptom cluster was not related to any cognitive variables in the simultaneous-entry models (all $ps > .312$). Thus, the relationship observed between the PHQ-9 Total and cognitive variables was largely due to the Nonsomatic subscale.

Of note, we conducted a sensitivity analysis in which we added participants' ejection fraction percentages and body mass index as covariates in Step 1 of the models but the pattern of results remained unchanged (data not shown; available upon request). Given the strong correlation between the Somatic and Nonsomatic subscales, we also checked the collinearity statistics for each simultaneous-entry regression. The tolerance and variance inflation factor scores were all $.83$ and 1.21 , respectively, indicating that multicollinearity was not an issue in the analyses.

Discussion

In a large sample of patients with HF, we found that greater overall depressive symptom severity predicted poorer attention and executive function with a trending effect for poorer memory function. The observed effects of depressive symptom severity on multiple cognition domains were driven primarily by the nonsomatic symptoms of depression and not the somatic symptoms. These findings indicate that the physical symptoms of depression, such as fatigue and appetite disturbance, may not be as strongly implicated in depression-related cognitive deficits in HF, whereas cognitive, affective, and behavioral symptoms, such as poor self-esteem, anhedonia, and psychomotor slowing, may play a larger role in cognitive performance.

Our findings are consistent with investigations documenting a relationship between greater overall depressive symptom severity and cognitive impairment in persons with HF. For example, Garcia et al.¹⁵ found that greater depressive symptom severity was associated with poorer performance across multiple cognitive domains, including attention, executive function, psychomotor speed, and language. Our study extends this work by suggesting that the effects may have been driven by the nonsomatic symptoms of depression. To our knowledge, our study is the first to examine specific depressive symptoms clusters as predictors of cognitive function in a HF sample. Two studies of older adults^{43, 44} also

suggest that nonsomatic symptoms of depression (e.g., dysphoria, meaninglessness, apathy) predict neuropsychological functioning, but these studies did not directly examine persons with HF or adjust for somatic symptoms of depression. Studies that have directly investigated somatic versus nonsomatic depressive symptom clusters in persons with HF did not examine cognitive function as the outcome but instead focused on physical outcomes, such as cardiac event-free survival, all-cause mortality, and/or health status^{22, 23}. The results of these studies are mixed, with some indicating that somatic symptoms are more health toxic²² while others suggest that nonsomatic symptoms are better predictors of poor health outcomes²³.

Several factors may explain why the nonsomatic scores were better predictors of cognitive function in our study as well as clarify the discrepant results across studies. First, the somatic items on measures like the PHQ-9 may be measuring HF severity level instead of true depressive symptoms in persons with HF, as previously suggested by Lee and colleagues.²³ For instance, in our sample, the correlation of HF severity level with somatic symptoms was stronger than with nonsomatic symptoms ($r = .38$ vs. $.30$, respectively). Additionally, the somatic subscale predicted attention when entered into a model without covariates, an effect that was eliminated only after including HF severity (results not shown; available upon request). The stronger association between somatic depressive symptoms and health status may explain why the somatic subscale is often found to be the better predictor in previous studies which have examined physical outcomes, such as cardiac event-free survival, all-cause mortality, and/or health status^{22, 45}, rather than the cognitive outcomes that were analyzed in our study. Future studies would benefit from examining both cognitive and physical HF outcomes and their relationship with specific depressive symptoms clusters.

Next, differences in the measurement of depressive symptoms might have contributed to our results. For instance, the use of the PHQ-9 versus other symptom measures of depression (e.g., the Beck Depression Inventory; BDI) can impact which items/symptoms are represented on the somatic vs. nonsomatic subscales as well as the number of items and corresponding variability. The study with findings consistent with ours (i.e., nonsomatic symptoms predicted cardiac event-free survival in HF patients)²³ also utilized the PHQ-9 and equivalent subscale computations. The fewer number of items on the Somatic subscale (3-items) compared to the Nonsomatic subscale (6-items) of the PHQ-9 may yield less variability in scores, which, in turn, may contribute to the failure to detect an association between the Somatic subscale and outcomes. In contrast, the study that showed that somatic symptoms were better predictors of mortality used the BDI,²² which contains a different representation of depressive symptoms than the PHQ-9 (e.g., greater number of somatic than nonsomatic items). Furthermore, the somatic subscale of the BDI was calculated using items that were included in our nonsomatic subscale (e.g., psychomotor changes). These differences highlight the importance of clearly describing how symptom clusters are calculated within and across studies.

Lastly, our finding that nonsomatic symptoms instead of somatic symptoms were associated with cognitive function may be explained by the differential association of these symptom clusters with specific brain regions and/or function. For example, a study using resting state fMRI data examined somatic (e.g., sleep disturbance, weight loss) and nonsomatic (e.g.,

hopelessness, cognitive problems) depressive symptoms in patients with major depressive disorder. The authors found that more nonsomatic symptoms than somatic symptoms were associated with abnormal brain activity across a variety of brain regions, such as the orbitofrontal cortex, cingulate cortex, and insula. Importantly, these frontal, limbic, and insular regions are closely implicated in attention, executive function, and/or memory⁴⁶⁻⁴⁹. A related line of evidence indicates that cerebral hypoperfusion, a documented concomitant of HF⁵⁰, is related to nonsomatic depressive symptoms in the same or closely related brain regions (e.g., cingulate cortex, dorsolateral prefrontal cortex, medial prefrontal cortex)⁵¹. Such findings emphasize the need for studies that use advanced neuroimaging techniques to determine how depressive symptom clusters may be differentially associated with brain changes in HF.

Several limitations of our study should be noted. First, we were not able to use the aforementioned neuroimaging techniques and, consequently, cannot elucidate the anatomic correlates of our findings and verify that the depressive symptoms clusters were differentially associated with brain structure or function. Second, our study was cross-sectional, so we are unable to determine whether depressive symptoms promote cognitive impairment or vice versa. Third, the PHQ-9 was our single measure of depressive symptoms. Use of multiple measures (e.g., the BDI and/or CES-D) may provide more comprehensive information about the depressive symptoms clusters and their associations with cognitive function. Fourth, detailed information regarding participants medication use (e.g., duration and dose of antidepressants) was not collected and such information may be important given that some antidepressants have been shown to affect cognitive function.⁵² Lastly, use of a comprehensive neuropsychological battery to assess cognitive impairment is a strength of our study design, but we also recognize that such a time-intensive assessment would not be feasible for most clinical settings. Given that the PHQ-9 is fast and easy to administer, we suggest that providers could use the PHQ-9 in conjunction with a shorter cognitive screening test (e.g., the Montreal Cognitive Assessment; MOCA) in order to determine whether referral for more extensive neuropsychological testing is warranted.

Despite these limitations, our study has several potential implications. First, the findings suggest that persons with HF who have elevated nonsomatic symptoms are at risk for poorer cognitive function, which may impact their ability to adhere to the complex HF treatment regimen, given evidence that cognitive deficits and greater depressive symptoms predict poorer HF outcomes.^{5, 6, 9, 13} Thus, if our findings are replicated, screening explicitly for nonsomatic depressive symptoms may be warranted. Next, our findings imply that the mechanisms underlying the depression-cognitive function relationship in HF are not solely related to sleep or appetite disturbance. Thus, interventions which may primarily target patients' somatic symptoms (e.g., fatigue medications like modafinil⁵³ or appetite-stimulants like mirtazapine⁵⁴) may not yield maximum cognitive benefit compared to a comprehensive treatment which targets depressed mood, anhedonia, and other nonsomatic symptoms. Examples of interventions which can target both somatic and nonsomatic symptoms include cognitive behavioral therapies (CBT)⁵⁵ and exercise.⁵⁶ The impact of depression treatments on cognitive function in patients with HF is not yet known; however, exercise training is a promising treatment for both depression^{57, 58} and cognition.^{59, 60} Such possibilities should

be fully explored in prospective, controlled trials of depression interventions and cognition in HF.

In brief summary, our study sought to compare the relative importance of somatic and nonsomatic depressive symptom clusters in predicting cognitive function in a sample of patients with HF. We found that overall depressive symptom severity was associated with poorer performance on multiple cognition domains, an effect driven primarily by the nonsomatic symptoms of depression. Our results suggest that future research is needed to determine how depressive symptoms clusters may be differentially associated with brain changes in HF. Such findings may clarify the pathways from depression to poorer cognitive function in persons with HF and inform the development of effective depression interventions, which may ultimately improve cognitive function in this population.

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Summary and Implications

What's New?

- Depressive symptoms are associated with poorer cognitive function in patients with heart failure (HF), and this effect on cognition is driven primarily by the nonsomatic symptoms of depression.
- These findings suggest that screening explicitly for nonsomatic depressive symptoms in patients with HF may be warranted.
- Interventions which target HF patients' somatic symptoms only (e.g., poor appetite or fatigue) may not yield maximum cognitive benefit compared to a comprehensive treatment which targets depressed mood, anhedonia, and other nonsomatic symptoms.

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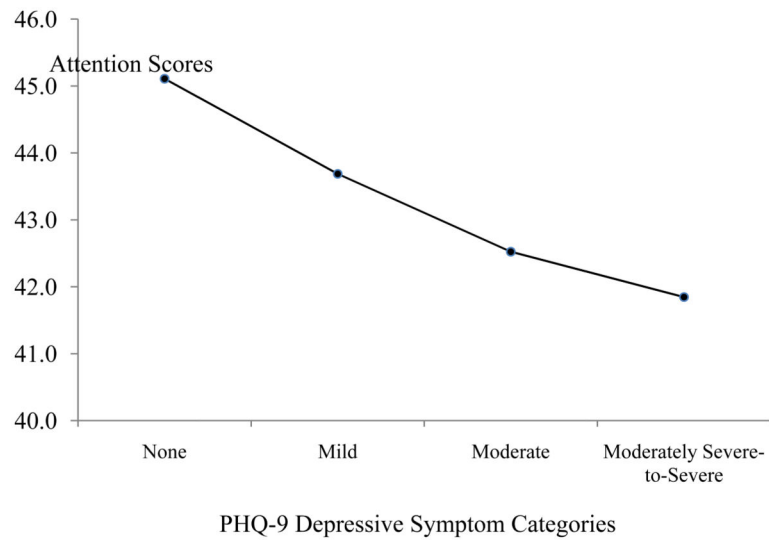


Figure 1.

Average Attention Scores across PHQ-9 Depressive Symptom Categories. *Note.* None = PHQ-9 score 0–4. Mild = PHQ-9 score 5–9. Moderate: PHQ-9 score = 10–14. Moderately Severe-to-Severe: PHQ-9 score: 15 or greater. Covariates appearing in the model were: gender, race-ethnicity, SES, education level, Charlson score, and HF severity level.

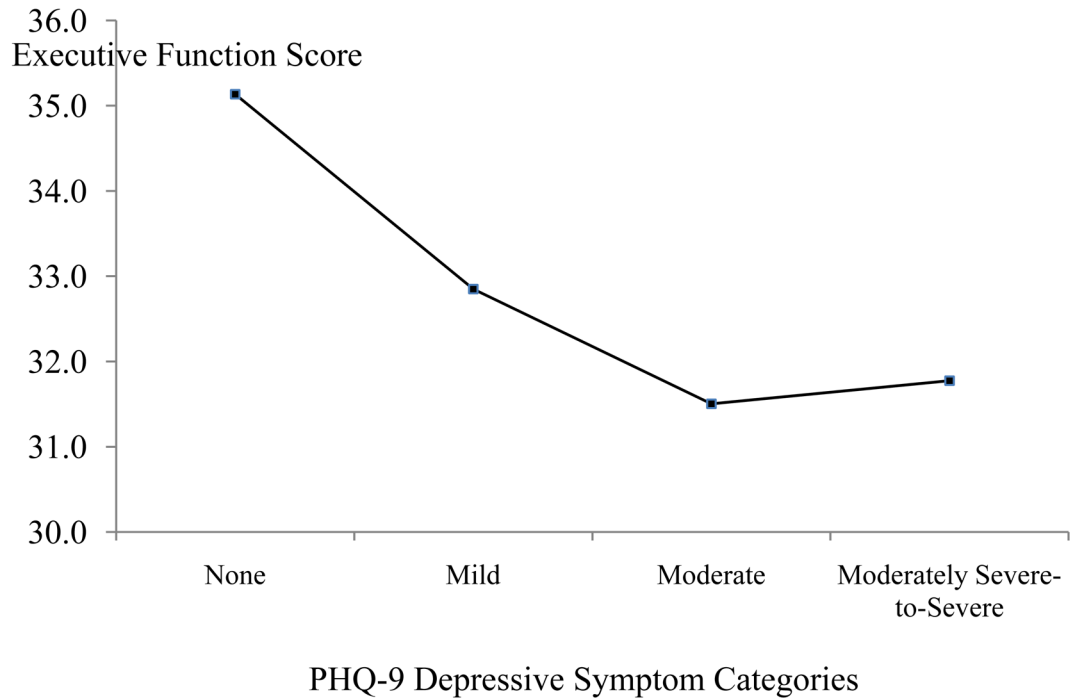


Figure 2. Average Executive Function Scores across PHQ-9 Depressive Symptom Categories. *Note.* None = PHQ-9 score 0–4. Mild = PHQ-9 score 5–9. Moderate: PHQ-9 score = 10–14. Moderately Severe-to-Severe: PHQ-9 score: 15 or greater. Covariates appearing in the model were: gender, race-ethnicity, SES, education level, Charlson score, and HF severity level.

Table 1Characteristics of Participants ($N = 326$)

	<i>M(SD) or N(%)</i>
<i>Demographic and Clinical Factors</i>	
Age	68.6(9.7)
Female	132(40.5)
Non-white ^a	87(26.7)
Education Level	
8 th Grade or Less	8(2.5)
9–11 th Grade	30(9.2)
High School	94(28.8)
Technical or Trade School	36(11.0)
Some College	86(26.4)
Bachelor's Degree	41(12.6)
Master's Degree	31(9.5)
SES Score	.08(4.2)
Body mass index (kg/m ²)	30.3(6.7)
Charlson Comorbidity Index ^b	3.3(1.7)
Ejection Fraction	29.3(8.4)
Self-reported HF Severity at Baseline (NYHA)	
Class I	31(9.5)
Class II	74(22.7)
Class III	205(62.9)
Class IV	16(4.9)
Patient Health Questionnaire-9	
Total	4.6(4.9)
Somatic	2.5(2.3)
Nonsomatic	2.1(3.1)
Cognitive Variable Scores	
Attention Composite Score	44.3(7.5)
Stroop Word	42.8(9.3)
Stroop Color	45.1(9.6)
Trails A	42.4(10.3)
Letter-Number Sequencing	47.0(10.4)
Executive Function Composite Score	45.9(8.1)
Stroop Color-Word	45.1(10.1)
Trails B	41.6(12.0)
Frontal Assessment Battery	51.0(8.2)
Memory Composite Score	47.9(7.8)
Learning Over Time	49.5(10.7)
True Hits	49.1(9.1)
Short Delay	45.6(10.9)

	<i>M(SD) or N(%)</i>
Long Delay	47.3(9.4)

Note. SES = socioeconomic status. NYHA = New York Heart Association. HF = heart failure. Means and standard deviations are presented for continuous variables. Sample size and percentages are presented for categorical variables.

^aOf the non-white participants, 97% identified as African American.

^bMost common comorbidities reported on the Charlson and % of participants: myocardial infarction (50.3%), diabetes (44.5%), and chronic obstructive pulmonary disease; COPD (26.7%).

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Table 2
 Regressions of Depressive Symptom Clusters Predicting Domains of Cognitive Function (N= 326)

Model Entry	Attention			Executive Function			Memory				
	R ²	β	p	R ²	β	p	R ²	β	p		
Independent ^d											
PHQ-9 Total	.24	-.14	.008*	.27	.03	-.17	.001*	.19	.01	-.10	.067 [†]
Somatic	.23	-.09	.092	.25	.01	-.11	.048*	.19	.00	-.06	.259
Non-somatic	.25	-.15	.004*	.27	.03	-.18	.000*	.19	.01	-.11	.044*
Simultaneous ^b	.25	.02		.27	.03			.19	.01		
Somatic		.00	.995		.01	.907				.01	.943
Non-somatic		-.15	.020*		-.19	.003*				-.11	.096

Note. Covariates included in all models were gender, minority status, education level, socioeconomic status, Charlson score, and NYHA heart failure severity class. All covariates were included on Step 1 of each model.

^aThe PHQ-9, Somatic Subscale, or Non-somatic Subscale was entered on Step 2 of three separate models.

^bThe Somatic and Non-somatic subscales were entered together on Step 2 of the same model.

* Significant at $p < .05$

[†] Significant at $p < .07$