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Focusing neurovisceral integration: Cognition, heart rate variability, and cerebral blood flow

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Abstract

The neurovisceral integration hypothesis suggests in part that cerebral control of autonomic function conveys comparable control of executive function and, hence, correlation among vagally determined high frequency heart rate variability (HF-HRV), executive function, and regional cerebral blood flow (CBF). In 440 middle-aged men and women, resting HF-HRV was related to regional CBF derived from a resting arterial spin-labeled MRI scan and to seven neuropsychological tests of executive function. Despite some intercorrelations, regression modeling failed to support integrated central control of HF-HRV and executive function. Integration between autonomic and cognitive control appears more circumscribed than the general integration suggested by the neurovisceral integration hypothesis.

Descriptors

Neurovisceral integration; Cerebral blood flow; Neuropsychology; Executive function; Heart rate variability

A link between autonomic nervous system function and emotion is generally accepted, whereas links with cognitive function are less well defined. The neurovisceral integration hypothesis introduced by Thayer and Lane (2000, 2009) suggests that both cognitive and emotional functions are regulated by brain systems also involved in the regulation of autonomic function. The linkage with cognitive function is not entirely novel in that early concepts of general arousal (Lindsley, 1951), orienting/alerting (Graham & Clifton, 1966; Lacey & Lacey, 1978; Sokolov, 1990), and the regulation of action (Jennings & van der Molen, 2005) posited specific autonomic changes that were concomitant with particular cognitive functions.

The neurovisceral integration hypothesis extends such views by suggesting a general linkage between executive function and frontal and midbrain areas that regulate the vagal control of

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the heart (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012; Thayer & Brosschot, 2005; Thayer & Lane, 2000, 2009). The hypothesis was first formulated in the context of emotion regulation and dysregulation (Thayer & Lane, 2000). It was proposed that affective regulation required selective attention to motivationally or affectively relevant stimuli and the inhibition of attention to irrelevant stimuli. Furthermore, what made stimuli relevant to the organism could be defined by their impact on the organism's well-being—thus characterizing aspects of selective attention in affective or motivational terms. Therefore, from a neurovisceral perspective, attentional and affective regulation worked together in the process of self-regulation and goal-directed behaviors. Accordingly, most of the initial work bearing on the neurovisceral hypothesis involved viewing attentional and affective regulation as two largely inseparable processes. However, the hypothesis can also be extended to focus on attentional and cognitive processes in the absence of affective dimensions, and this focus characterizes the aims of the present study. Empirically, examination of this aspect of the hypothesis has been based primarily on high frequency heart rate variability (HF-HRV) as reflecting frontal/midbrain vagal control and its relationship to cognitive function. For example, in one such examination of the hypothesis, resting HF-HRV was related to working memory, sustained attention, mental flexibility, and inhibition in a study of naval cadets (Thayer, Hansen, Saus-Rose, & Johnsen, 2009).

Thayer et al. (2012) in a meta-analysis identified brain areas related to autonomic control, specifically cardiac vagal control. They termed these areas as comprising a rostral limbic system. Areas included were the anterior, insular, and orbitofrontal cortices; amygdala; periaqueductal gray; ventral striatum; and autonomic brainstem motor nuclei. They note the concurrence between prior invasive work in animal models and current human neuroimaging findings. Similar areas were identified in another meta-analysis of human studies of brain function that reported relationships between regional brain activity and parasympathetic activity and responses (Beissner, Meissner, Bar, & Napadow, 2013). The relevance of these brain areas to the control of resting HF-HRV was established in analyses of the dataset currently reported on; 8 of 14 areas based on the meta-analyses of vagal reactivity were also significantly related to resting HF-HRV (Allen, Jennings, Thayer, Gianaros, & Manuck, in press. Hence, the brain areas putatively related to vagal control and affective/cognitive regulation are reasonably well specified by the existing literature. The empirical linkage of these areas to measures of HF-HRV and affective/cognitive function, though, has not been well investigated.

A close examination of the relationships between resting HF-HRV and cognitive functions supporting the neurovisceral hypothesis suggest some specificity between HF-HRV and particular cognitive functions. Available results are not uniformly robust and seem to largely suggest relationships with maintaining attention and cognitive inhibition. Relatively early papers from Thayer and coworkers suggested modest relationships between resting HF-HRV and speed and accuracy of response to monitoring tasks, with trends toward stronger relationships when detection of memorized sequences was required (Hansen, Johnsen, & Thayer, 2003). The same set of tests was administered to a demographically similar sample in a subsequent study (Hansen et al., 2009). The results did not replicate directly, except for the strengthening of a trend finding in the initial study for appropriately identifying sequences. The results did show a conceptual replication, but only if performance indices

were globally considered. Low HF-HRV participants performed more slowly than did high HF-HRV participants in the initial study, and they performed more poorly on accuracy indices on similar tasks in the second study (i.e., given differing speed-accuracy tradeoffs between studies, the results can be termed a reasonable replication). In recent work, high and low HF-HRV participants were compared on a task in which learned word pairs were followed by a practice session in which some initial words of a pair were followed by a no-recall cue, while other initial words were to be followed by recall (Gillie, Vasey, & Thayer, 2014). The results showed that participants with higher HF-HRV were more capable of inhibiting their recall—resulting in a greater difference in recall between rehearsed items and items with the inhibit instruction. The overall association between executive function and HF-HRV was questioned recently, however, in a large sample from the MIDUS study (Kimhy et al., 2013). Although correlations were present with an overall executive function score and individual scores related to perceptual-motor speed, working memory, a number series task, and a stop-signal/task switching measure, these were absent when age, gender, and education were accounted for as covariates. Moreover, it is also noteworthy here that smaller-scale studies not specifically addressing the neurovisceral hypothesis have observed a failure for baseline HF-HRV to relate to cognitive performance (Duschek, Muckenthaler, Werner, & Reyes del Paso, 2009; Yasumasu, Reyes del Paso, Takahara, & Nakashima, 2006).

Other recent work has shown relationships to measures of attention regulation, but interpretation is limited to some degree as affective stimuli were being evaluated; that is, executive function is confounded with affective processes. An interesting series of studies was completed using emotional faces pictorially presented with veridical (all frequencies) versus only high or low spatial frequency information. High HF-HRV relative to low HF-HRV participants were found to (a) more accurately discriminate between high frequency fearful and neutral faces, but not between low frequency or veridical faces (Park, Van Bavel, Vasey, Egan, & Thayer, 2012); (b) disengage their attention from high frequency fearful faces more successfully, but only when sufficient time preceded the required response (Park, Van Bavel, Vasey, & Thayer, 2013); and (c) disengage more rapidly as well from veridical and low spatial frequency fear faces, again with a relatively long interval between the facial cue and the response cue (Park, Van Bavel, Vasey, & Thayer, 2012). The suggestion that the correlation with HF-HRV is dependent on the presentation timing or other task variables employed is supported in a recent study. In an experiment without spatial frequency manipulation, visual detection with either high or low perceptual load was examined in the presence of a background fearful or neutral face (Park, Vasey, Van Bavel, & Thayer, 2013). Low perceptual load conditions yielded a directional result suggesting faster disengagement from the fearful face in high HF-HRV subjects relative to low HF-HRV subjects, replicating the findings just discussed. With high load, however, high HF-HRV subjects disengaged more slowly from fearful than neural faces (disengaging equally as fast as low HF-HRV subjects from the fearful face). In sum, these later experiments make a strong case for HF-HRV relating to the engagement and disengagement of attention, but the exact task/type of processing required alters relationships. The authors suggest that the results are somewhat consistent with the view that forebrain processes, assumed to be engaged more with high frequency visual stimuli and longer processing intervals, relate most strongly to joint control

of attention and HF-HRV. A direct relationship between change in HF-HRV and change in regional brain function has also been reported, but with an affective task. An association was observed between change in HF-HRV and change in activation of the subgenual anterior cingulate cortex between trial blocks in which words were counted that had either affective or nonaffective meaning (Lane et al., 2013).

Other supportive evidence has come from less typical participant samples. A report in children used a similar task to the complex monitoring tasks of Hansen and colleagues (2003). A significant correlation was observed between HF-HRV and a signal detection measure of accuracy during the initial block of performance (Suess, Porges, & Plude, 1994). A relationship between higher HF-HRV and better resistance to interference on the traditional and an emotional Stroop task was also observed in a sample composed entirely of dental phobics (Johnsen et al., 2003). In panic disorder patients, Stroop performance, Wisconsin card sort, and task-shifting performance were assessed and evaluated relative to HF-HRV (Hovland et al., 2012); significant correlations were found for scores on the Wisconsin card sort and Stroop but not on the task-shifting measures. In normal adults, Mathewson et al. (2010) found a relationship between HF-HRV change and Stroop performance, but only a marginal relationship with baseline HF-HRV. Interpretation of this study is limited by use of an emotion/face version of the Stroop that failed in their study to yield typical interference effects. In a variety of speeded monitoring tasks of varying complexity, Luft, Takase, and Darby (2009) found that greater HF-HRV was related to fewer anticipatory response errors across all tasks. This was a sample of highly fit athletes. In short, the relationship between HF-HRV and executive function has garnered some support, but HF-HRV has not proven to be robustly related to all variants of executive function. However, given the lack of relationship between many putative measures of executive function, this is not entirely unexpected (Duckworth & Kern, 2011). Major differences in participant samples hinder interpretation, as do the variety of dependent measures used to infer relationships. Positive results are suggestive of relationships between HF-HRV and one set of processes relevant to, but not encompassing, executive function: the environmental engagement and disengagement (inhibition) of attention.

The current study provides the opportunity to test one operationalization of the neurovisceral hypothesis. In some sense, the hypothesis is a framework for investigation that can be operationalized in a number of ways. The current data integrates individual differences in resting HF-HRV, resting brain perfusion in areas related to HF-HRV, and executive function measures from neuropsychological testing. Resting HF-HRV is employed because primary support for the neurovisceral hypothesis has been derived from this measure and also because this measure has added importance given its widespread correlation with health/disease (Britton et al., 2007; Gianaros et al., 2014; Kemp, Quintana, Felmingham, Matthews, & Jelinek, 2012). The hypothesis generates predictions that these measures should be intercorrelated, potentially with brain perfusion acting as a concurrent mediator between HF-HRV and executive function. More precisely, HF-HRV should be positively correlated with resting cerebral blood flow (CBF) in each of the regions of interest previously defined as within the rostral limbic system and also positively correlated with performance measures on tests of executive function. Finally, CBF in regions of interest should correlate with performance on tests of executive function and mediate the

relationship between HF-HRV and these test scores. The neurovisceral hypothesis has not been refined sufficiently to make specific predictions about the strength of expected relationships for specific tests of executive function and specific cerebral regions of interest. Thus, in the current work, we examine a range of specific tests of executive function. If relationships are demonstrated in support of the theory, then such support should be tempered by correction for the large number of correlations done with specific tests. Note that the data do not permit testing of whether task-induced changes in HF-HRV or brain perfusion relate to each other or cognitive function as the HF-HRV, brain perfusion, and executive function assessments all took place at different times; such relationships have been reported, for example, relations between HF-HRV change and cognitive function (Mathewson et al., 2010). More generally, the current dataset is not relevant to the claim that affect regulation is related to forebrain areas that also regulate HRV, but only relevant to the hypothesis that executive function without an affective component is related to these fore-brain areas. The value of the current test is enhanced by use of a relatively large sample, measures of brain as well as cardiac and cognitive regulation, and use of a midlife community sample. Relationships are examined between brain regions of interest identified as consistently related to HF-HRV in a meta-analyses and in our data (Beissner et al., 2013), neuropsychological results from tests identified a priori as executive function tests, and HF-HRV derived from a rest period with paced respiration. The sample size is also large enough to see if relationships vary by demographic characteristics (e.g., sex, race/ethnicity). Sex is important given that the predominance of initial support of the hypothesis is in males, while race/ethnicity is of significant interest due to the conclusions of a recent review showing ethnic differences in HRV indices (Hill et al., 2014).

Method

Participants

The present study involved 490 participants (231 male, mean age 42.77 years, *SD* 7.35 years) recruited via a mass mailing to residents of Allegheny County, PA, for participation in the Adult Health and Behavior (AHAB) study (see related reports from this study in Gianaros et al., 2014; Jennings et al., 2013). Based upon laboratory and clinical assessments, participants were excluded if they had any of the following: history of cardiovascular disease/ heart surgery; prior stroke/history of cerebrovascular disease; a neurological disorder, prior convulsions, or a concussion involving a loss of consciousness; chronic kidney/liver disease; cancer; insulin-dependent diabetes/fasting glucose > 126mg/dL; high resting blood pressure (systolic/diastolic ≥ 160/100 mm Hg); use of psychotropic, lipid-lowering, glucocorticoid, or cardiovascular (e.g., antihypertensive) medications; or a DSM-IV diagnosis of schizophrenia or bipolar disorder determined by the Structured Clinical Interview, nonpatient edition (First, Spitzer, Gibbon, & Williams, 1996). The study was approved by the University of Pittsburgh Institutional Review Board, and all participants gave informed consent.

The number of participants available for analyzing the three limbs of the neurovisceral hypothesis varied. We retained all participants available for testing each limb. Participant loss was due to technical errors or participant refusal (e.g., claustrophobia during MRI).

Available n = 440 for relating HRV and neuropsychological function, 432 for relating HRV and cerebral blood flow, and 413 for relating neuropsychological function and cerebral blood flow. Demographic characteristics of the 413 participants were compared to the 77 participants not having both neuropsychological and cerebral blood flow data to determine potential sampling bias. Differences assessed by t tests and differences in proportion failed to show any statistically significant results.

HRV Protocol and Assessment

HRV was derived from a continuous recording of a two-lead electrocardiogram (ECG) attached bilaterally to the wrists throughout a 5-min period of paced respiration (11 breaths/minute; ≈ 0.18Hz). Pilot observations suggested that 11 breaths/minute was a comfortable rate for most people. Participants were instructed to breathe naturally in response to two auditory tones signaling them to inhale and exhale. Respiration was monitored using a thoracic strain gauge. During the paced respiration, participants were seated and asked to remain stationary in a temperature-controlled recording chamber to control for the effects of individual differences in breathing frequency and movement on HRV (Berntson et al., 1997). A 5-min period of ECG data collection with unpaced breathing was also available, but results using HRV values from this assessment were essentially the same as the results reported (paced and unpaced Ln HF-HRV were correlated r = .84). The natural log of the measure was used to correct for the skewness of the raw measure.

The ECG was collected in the morning, and participants were asked to not drink caffeine for 4 h, avoid alcohol or exercise for 12 h, and abstain from over-the-counter medications for 24 h. ECG signals were digitized at a sampling rate of 1000 Hz (LabView acquisition software, National Instruments Corporation, Austin, TX). An interbeat-interval time series was derived from the ECG, corrected for artifacts in the R-wave detection process, and the band-limited variance within the HF (0.12–0.40 Hz) was extracted using PhysioScripts (Christie & Gianaros, 2013). HRV assessment was done within an average of 2 weeks of brain imaging.

MRI Acquisition

The brain images were collected on a 3T Trio TIM whole-body scanner (Siemens, Erlangen, Germany) using a 12-channel phase-arrayed head coil. Supine subjects in the scanner bore viewed screen images on a small mirror opposite their eyes that reflected a computer-controlled screen placed outside of the scanner bore. Resting perfusion images were acquired with a pulsed arterial spin-labeling (PASL) sequence. Interleaved perfusion images with and without arterial spin labeling were obtained over a 5-min, 28-s period using gradient-echo echo-planar imaging (EPI). The PASL sequence employed a modified version of the flow-sensitive alternating inversion recovery method (Kim, 1995), specifically applying a saturation pulse 700 ms after an inversion pulse. To reduce transit artifact, a 1,000-ms delay separated the end of the labeling pulse and the time of image acquisition. Resting perfusion image acquisition parameters were field of view (FOV) = 240 × 240 mm, matrix = 64 × 64, repetition time (TR) = 4,000 ms, echo time (TE) = 18 ms, and flip angle (FA) = 90°. Twenty-one slices (5 mm thick, 1-mm gap) were acquired sequentially in an inferior-to-superior direction, yielding 80 total perfusion images (40 labeled, 40 unlabeled, 2

initial discarded images allowing for magnetic equilibration), and the acquisition time of each slice was 45 ms. A 24-s equilibrium magnetization of brain (two sets of 21 slices; TR = 8,000 ms; all other parameters are described as above) provided two images for CBF baseline quantification.

fMRI Preprocessing

Resting perfusion images were preprocessed with computational routines implemented in Statistical Parametric Mapping software (SPM8; Wellcome Trust Centre for Neuroimaging, London, UK). For preprocessing, a magnetization prepared rapid gradient echo (MPRAGE) structural scan was segmented into gray and white images. Resting perfusion images were realigned to the first image of the series, and one averaged baseline image was then calculated from the two realigned images for later use of CBF imaging reconstruction. Each individual's gray image realigned was coregistered to the respective mean perfusion image. The 80 realigned perfusion images and one averaged baseline image were then smoothed with a 12-mm full-width at half-maximum (FWHM) isotropic Gaussian kernel. CBF imaging reconstruction was followed. The realigned and smoothed 40 labeled and 40 unlabeled perfusion images were submitted to pairwise subtraction (e.g., the even-numbered unlabeled/control image is subtracted from odd-numbered labeled image). Subtraction images were converted to an absolute CBF image series using a validated algorithm (Wang et al., 2003). This perfusion series was then averaged, generating for each individual a single resting voxelwise CBF image and a global CBF value, both in units of mL/100g/min. After the perfusion reconstruction step, each individual's mean CBF images and structural gray image were then spatially normalized to the International Consortium for Brain Mapping 152 template (Montreal Neurological Institute; MNI) of gray image with voxel size of 3 × 3 × 3mm to preserve concentration of the image using trilinear interpolation method. A normalized mean CBF image was then generated for each participant.

Regions of Interest

Regions of interest (henceforth, ROIs) were selected from two meta-analytic reviews. The center point of each ROI was drawn from the reviews and a 10-mm radius spherical shape (i.e., a uniform diameter of 20 mm) was drawn around the center point and ASL flow values extracted. The first review related HF-HRV indices to brain areas and observed five areas with consistent associations (Thayer et al., 2012). An additional set of nine ROIs were drawn from the regions relating brain areas to parasympathetic function in a separate review (Beissner et al., 2013). These areas overlapped to a significant degree with the ROIs drawn from the Thayer et al. meta-analysis but were centered somewhat differently and included added areas. The ROIs, their abbreviations, and their location are shown in Table 1.

Executive Function

A battery of neuropsychological tests was administered during one session of the overall study. The battery required approximately 1 h. Tests of executive function were selected a priori for analyses. Planning-related executive functions were not well represented, but measures available provided a reasonable assessment of working memory and interference control (Miyake & Friedman, 2012; Miyake, Friedman, Emerson, Witzki, & Howerter, 2000). The following measures were used:

- Wechsler Memory Scale (WMS) II supplemental subtests—spatial span backward raw score (SP-BACK; Wechsler & Stone, 1973). This test is designed as a spatial analogue of the digit memory span test and requires the reverse ordering from memory of the sequence of spatially arrayed blocks touched by the tester. The test assessed working memory in that the sequence must be remembered and also reordered.
- WMS III Primary Subtests—digit span raw score (DGT-BACK; Wechsler & Stone, 1973). This test requires the reproduction of digit sequences but in reverse order of that presented. This test assesses working memory in that digits must be retained as well as reordered.
- Four-Word Memory Test—15-s., correct (4WRD-STM; Morrow & Ryan, 2002). This test presents four words to retain and then interference due to backwards counting is required over the 15-s retention interval. This test assesses memory combined with interference control.
- Digit Vigilance Time (in seconds) Page 1 (DIGVIG1; Lewis, 1995). Higher scores correspond to lower performance. This test requires the rapid scanning of a page of numbers crossing out only the number designated as the target. This tests perceptual-motor speed in combination with a minimal working memory load.
- Digit Vigilance Time (in seconds) Page 2 (DIGVIG2; Lewis, 1995). Higher scores correspond to lower performance. This is the second page of the test that may reflect fatigue as well as the basic skill.
- Trails B Time (in seconds) (TRAILS B; Reitan, 1958; Spreen & Strauss, 1998). Higher scores correspond to lower performance. This task requires the timed connection of numbers and letters in sequence within a spatial display (e.g., 1 to a, 2 to b). This tests the use of working memory of well-learned sequences, transformation of these to an output order, and perceptual-motor speed.
- Stroop Interference Score (STRP-INT; Golden, 1978). Higher scores correspond to better resistance to interference. This creates a resistance to interference score based on the speed of reading color names and color patches relative to the speed of reading out the color of printed color names.

Statistical Approach

The neurovisceral integration hypothesis suggests relationships between variables that are not stipulated to be specific to gender or ethnicity. Given this, Pearson product moment correlations between the measures reflecting elements of the theory were initially computed over the whole sample. These were then examined separately by sex and race. The influence of sex was examined given that important supportive data for the theory were from male, Caucasian European participants (Hansen et al., 2003, 2009). Similarly, race was examined due to differences in HF-HRV (Hill et al., 2014) and the prior supportive data largely from Caucasian Europeans. Bivariate correlations supportive of relationships anticipated by the neurovisceral integration hypothesis could then be examined to see if suitable for possible testing using mediation analyses. No significant differences in correlation between sexes

were observed. An exploratory examination of race, however, suggested differential effects, which are reported. One-tailed significance tests were justified when correlations replicated the brain area to HF-HRV relationships identified by meta-analysis (Thayer et al., 2012). When directionality was not predicted, two-tailed significance tests ($p < .05$) were applied.

The critical mediation of the HF-HRV relationship by activity in related brain regions was tested in a multiple regression analysis. Neuropsychological tests showing a bivariate relationship with Ln HF-HRV were the dependent variable. In Step 1 of the multiple regression, Ln HF-HRV was the sole predictor. In Step 2, blood flow in a brain region was added. The presence of possible mediation was tested by the presence of a significant change in the beta weight from Step 1 for Ln HF-HRV. Although the neurovisceral hypothesis does not specify any dependency on age, years of schooling, smoking history, depression, or body mass index, these variables were also tested in regression models to test if they altered the HF-HRV to cognition relationships and to test if they magnified or suppressed the interrelationships of HF-HRV, cognition, and brain region.

Results

Participant Characteristics

Table 2 shows the demographic characteristics of the participants as well as mean values for cerebral blood flows, HF-HRV, and executive function scores. The proportion of males in the sample was .47, current tobacco users .14, and those of Caucasian ethnicity .83. Characteristics for the African-American participants are presented separately; among African Americans, the proportion male was .33 and the proportion of those using tobacco . 24. Numbers of subjects are those having data for the relation of neuropsychological function and HRV. Numbers for other analyses are noted in subsequent tables.

Cerebral Blood Flow and HF-HRV

Correlations between individual differences in resting HF-HRV and the selected regions of interest were statistically significant when CBF values were used directly for global blood flow and all ROIs. High correlations ($r = .8$ or better) between global and regional flows, however, suggested that regional ROIs should be expressed as proportional to global CBF (i.e., ROI CBF/global CBF). Allen et al. (in press) discusses the global/regional flow relationships in this sample; the regional flows analyzed were less than mean total CBF in eight areas, but greater in two. Table 3 presents the correlations for global CBF and the proportional ROI measures. The correlations differ in sign between global and proportional flows with subcortical areas as well as the temporal pole and supra and angular gyri areas showing significant negative correlations. African Americans fail to show a positive correlation between global CBF and HF-HRV, but do show significant negative relationships for the cortical regions that differ from the correlations for Caucasian Americans for three of the ROIs (see Allen et al., in press, for further information of African American–Caucasian relationships between CBF and HF-HRV).

Differences between correlations for the African and Caucasian American samples were tested after an r to z transform. Correlations were significantly different (at least $p < .05$) for

global CBF, dorsal anterior cingulate (dACC), rostral medial frontal gyrus (MFG), and ventral anterior cingulate (vACC). For Caucasian Americans, high HF-HRV was related to greater global CBF. For African Americans, high HF-HRV was related to lower CBF for the two ACC and MFG areas.

Correlations Between Executive Functions and Regional CBF

Correlations between measures of executive function and CBF overall and in ROIs were largely absent. Table 4 presents descriptive data for the performance on the executive function tests. A number of correlations with CBF were nominally significant despite the overall appearance of absence of relationships. In the overall sample, the digits backward results showed negative correlations with both HF-HRV and rostral MFG CBF, while the Stroop interference scores showed a similar negative correlation with both HF-HRV and putamen (PUT) CBF. In these regions, greater CBF is related to poorer performance on the executive function measure. Appendix Table A1 shows these results for the overall sample and then separately by ethnic/racial group. For Caucasians, the digits backward negative correlation with HF-HRV was significant, and a relationship between trails B and global CBF emerged relating greater CBF with faster performance on trails B. The relationship with the Stroop interference score was not significant in Caucasian Americans. This relationship was greater in African Americans, but not significant. African Americans showed correlations between the dorsal posterior cingulate (dPCC) ROI for backwards memory span, digits backward, and four-word memory.

Paced HF-HRV and Executive Function

The only measure of executive function related to HF-HRV in the entire sample was the Stroop interference score (bivariate correlation, $r = .13$, $n = 440$, $p < .01$). Correlations with the other neuropsychological tests were $r = .05$ or less. Among Caucasians ($n = 363$), greater HF-HRV was related to better performance on three tests of executive function: digits backward ($r = 2.12$, $p < .05$), trails B ($r = 2.12$, $p < .05$), and Stroop interference ($r = .19$, $p < .01$). No correlations were observed among African Americans, although a correlation of $r = .21$ with trails B (opposite in sign from Caucasian sample) was observed but not significant due to the sample size ($n = 70$).

Assessment of Shared and Independent Relationships to Executive Function

Regression analyses were used to model the joint contribution of HF-HRV and CBF to measures of executive function. These analyses were done solely on the Caucasian subsample due to the lack of relationships observed in the African American subsample. For executive function measures showing significant correlations, the relationship between HF-HRV and the measure was first modeled. A brain CBF area showing significant correlations was then added to the model. Both HF-HRV and CBF relationships were expected to retain their relationship if each independently related to executive function. If the relationship of HRV to executive function was dependent on its relation to brain CBF, then the strength of relationship of HRV to executive function would be expected to decrease. Table 5 shows the results of these analyses. HF-HRV is combined sequentially with overall CBF, parahippocampal gyrus (pHIP), PUT, amygdala (AMY), dPCC, HIP, superior temporal

gyrus (STG1), and STG2 CBF as independent variables in multiple regression. Trails B, digits backward, and Stroop interferences scores were modeled as separate dependent variables. The results uniformly show independent contributions of HRV and CBF.

The further analysis of participant characteristics checked to see if these altered any of the key relationships in the regression analyses. The influence of age, gender, body mass index, education, depression, and tobacco use were examined. Inclusion of these factors failed to uncover any mutual influence of Ln HF and brain area on the neuropsychological scores; that is, relative relationships presented in Table 5 were unaffected. As might be expected, race, age, and education did relate significantly to trails B performance; race and age related significantly to both digits backward and Stroop interference performance.

Discussion

Our test of one operationalization of the neurovisceral hypothesis found specific supportive relationships, an absence of strong, general support for the hypothesis, and a number of important unanticipated relationships. Among Caucasian Americans, CBF in areas related to HF-HRV largely replicated the results of meta-analyses showing specific brain areas related to HF-HRV (see also Allen et al., in press). Importantly, overall CBF was related to HF-HRV and normalizing the specific ROI measures for overall CBF reduced correlations; correlations became significantly negative for a number of areas—predominantly subcortical areas. Prior work has not to our knowledge examined mean global CBF. Our results did replicate the prior associations between areas and HF-HRV (parasympathetic function), but we found that CBF in these regions was strongly related to global CBF. Furthermore, the direction and amplitude of the correlations were very similar between the global CBF to HF-HRV correlation and that to each of the region-specific flows. In short, the associations reported in the meta-analyses may be due to global CBF, and different relationships might emerge when flows are corrected for global CBF. Indeed, this is what we observed (see further development of brain/vagal function relationships in Allen et al., in press). Note that correction for global mean CBF will necessarily induce some negative correlations among regional CBFs (Murphy, Birn, & Bandettini, 2013; Murphy, Birn, Handwerker, Jones, & Bandettini, 2009). Though the implication of this for relationships to a third variable, such as HRV, is unclear, some caution in interpretation is warranted. Caucasians, but not African Americans, did demonstrate a small number of correlations between specific executive functions and either CBF or HF-HRV. Given the breadth of the neurovisceral hypothesis, these findings question the predictions deriving from the hypothesis as much as they support them. Considering the number of correlations computed, significant correlations must be taken as guides to further exploration rather than as confirmatory findings. They offer the promise, however, of narrowing the hypothesis to more clearly capture any shared regulation of visceral and cognitive function. After a brief consideration of the African American results, our findings will be discussed specifically for the Caucasians in the sample given the differences observed between ethnic groups in the relationships of HF-HRV.

African Americans

Clear, but unexpected, differences in relationship between HF-HRV, brain blood flow, and neuropsychological tests were found between African and Caucasian American participants. Global CBF was unrelated to HF-HRV among African Americans, but normalized CBF in two regions of the anterior cingulate cortex as well as the medial prefrontal cortex were negatively related to blood flow (i.e., relatively more blood flow in these regions was related to lower resting HF-HRV). Although limited by sample size, correlations between CBF and neuropsychological tests were absent, dissimilar to correlations of Caucasian Americans, and trended toward better performance relating to less CBF. Similarly, correlations between resting HF-HRV and neuropsychological tests were absent/minimal, dissimilar to correlations of Caucasian Americans, and trended toward better performance relating to less HF-HRV. In a number of cases, correlations were significantly different between African and Caucasian Americans. These ethnic differences are potentially important and should certainly be investigated further. For the current focus, however, it is clear that we have failed to demonstrate neurovisceral integration within African Americans, as executive function was unrelated or inappropriately related to both relevant CBF and HF-HRV. This conclusion must be circumscribed. It is limited by the somewhat small number of African Americans and the focus on resting HRV, resting CBF, and a limited number of tests of executive function. Furthermore, given that despite greater cardiovascular disease risk African Americans generally have higher HF-HRV than Causcasian Americans, the present findings may provide valuable information about this conundrum (Hill et al., 2014). Relationships that were observed between HF-HRV and CBF among African Americans are discussed further in a companion report (Allen et al., in press).

Caucasian Americans

A number of pairwise relationships were consistent with the neurovisceral hypothesis, but the results failed to show the conceptually critical evidence of integrating central regulation with both HF-HRV and executive function. Mean global CBF was positively related to HF-HRV, and the majority of regional flows were related negatively to HF-HRV (when regional CBF was normalized by global CBF). Global CBF was related to better performance on one executive function test, trails B. HF-HRV was related to better performance on three tests of executive function: trails B, digits backward, and Stroop interference. Interestingly, the magnitude and pattern of these correlations was similar to those found prior to demographic corrections in the MIDUS sample (Kimhy et al., 2013). As such, the validity of these correlations is strengthened despite the fact that within our dataset these correlations could readily be interpreted as due to chance given the number of correlations computed. The neurovisceral hypothesis would, however, require that the relation between HF-HRV and the tests of executive function be significantly reduced when global or regional flow related to HF-HRV was covaried. Covarying these flow values, however, results in essentially no change in the relationships of HF-HRV.

The replication of regional CBF relationships with HF-HRV, though useful, was tempered by complexities not foreshadowed in the Thayer et al. (2012) review. Importantly, our CBF data were from a resting scan and assessed by a quantitative measure of CBF. The literature comparisons reviewed in Thayer et al. (2012) were of three sorts: overall activation in

response to a task, regions relatively more active with affective relative to cognitive/motor task, and regions relatively more active with cognitive/motor task relative to affective task. It is important, and perhaps surprising, that areas identified by correlation between activated CBF and HF-HRV also showed a relationship when resting/nonactivated regional CBF and HF-HRV were related. Global CBF was not analyzed in the meta-analysis, but was as strongly related to HF-HRV as any of the specific areas in our data. As noted above, these observations raise the issue of whether task-related comparisons used in the meta-analysis might not be specific to either task or brain area, but be relationships due to a relation of global CBF and degree of HF-HRV present before the task even began. We attempted to assess specific relations by normalizing regional CBFs with global CBF. This resulted in significant inverse relationships in the majority of the midbrain ROIs examined. This suggests for Caucasian (but not African) Americans that the midbrain areas exert an inhibitory “fine-tuning” of the overall excitatory relationship between global CBF and HF-HRV (Murphy et al., 2009, 2013). Further assessment of these novel relationships and the African American results goes beyond the current focus, but is available in Allen et al. (in press).

The expectation of the neurovisceral integration hypothesis that HF-HRV would relate to executive function may be less novel than the integration with brain—namely, that regional CBF underlying resting HF-HRV would also indicate areas regulating executive function (i.e., active task performance). Surprisingly, little research has related resting regional cerebral blood flow to individual differences in neuropsychological performance in healthy adults, though some work has examined global blood flow (MacInnes et al., 1984; Rabbit et al., 2007). In our results, a correlation relating greater global CBF and better trails B performance was supportive of the hypothesis. Trails B requires the sequencing of numbers and the alphabet in order to connect points rapidly that alternate between numbers and letters, “connect the dots” sequencing 1,a,2,b,3,c.… Thus, this task has components of working memory, sequencing, and a perceptual-motor speed demand. Negative correlations between a test of working memory, digits backward, and the medial PFC and control of interference and right and left insula could also be interpreted as supportive. Note, though, that inhibition or deactivation of these areas related to better performance. This direction of relationship is the opposite of the relationship of these areas with HF-HRV when areas are uncorrected for global CBF, but consistent with the relationship of one of the areas (left anterior insula [AIns]) once corrected. Interestingly, relatively better performance on each of these executive functions tests also was related to greater HF-HRV, as was performance on digits backward and the Stroop task. Despite concerns with directionality differences between the relevant pairs of correlations, these correlations were the strongest affirmation of the neurovisceral integration hypothesis. The hypothesis, however, has as its key element the integrated control of HF-HRV and executive function, and regression models were consistent with independent rather than integrated control when all variables suggestive of support of the hypothesis were analyzed.

Evaluating the Neurovisceral Hypothesis

The current results directly question one aspect of the neurovisceral integration hypothesis. Neural areas inferred to control vagal modulation of heart rate during rest do not also

routinely regulate executive function. The current results show that individual differences in CBF in brain areas related to vagal control are unrelated to individual differences in the same areas related to executive function. There are limitations to our study that should be considered. The HF-HRV data were not collected concurrently with the brain scan data, although they were collected during resting conditions comparable to those in the studies reporting HRV correlations with cognition. Ideally, HF-HRV would have been collected both inside of the scanner concurrently with brain scanning and outside of the scanner. This would have allowed us to verify that HF-HRV at rest is a trait characteristic and not one unduly influenced by state during testing in our results. Similarly, another limitation is that the tests of executive function also were not performed simultaneously with either the HRV or neuroimaging assessments. In addition, few associations were found between the neuropsychologically based executive function tests and CBF, further limiting the ability to fully test the neurovisceral hypothesis. Finally, menstrual phase data were not available for normally cycling women (26% of sample) participating in the study. We should also note again that we did not test all possible executive functions.

We emphasize that our findings are limited to questioning only one aspect of the neurovisceral integration hypothesis. The important and central aspect of the neurovisceral hypothesis is that the areas related to vagal control also relate to the executive control functions active during emotion regulation. The current results can be seen as questioning this only if one assumes that the functions required during emotion regulation are exactly those required during working memory, sequencing, and interference control with the nonaffective content used in neuropsychological tests. Even if this were true, it seems likely that there might be individual differences in the degree to which these executive functions are engaged during affect regulation that are quite disparate from differences those individuals would show engaging these functions during strictly cognitive functioning. In short, our results suggest that the neurovisceral hypothesis requires greater definition of the conditions/ contexts in which vagal and executive function regulation may employ shared processes/regional brain activation.

Neurovisceral Integration in Context of Vagal-Cognitive Relationships

The neurovisceral integration hypothesis emphasizes the central control that permits rapid adaptability of the individual within the environment; “thus, because of these reciprocally interconnected neural structures that allow the prefrontal cortex to exert an inhibitory influence on subcortical structures, the organism is able to respond to demands from the environment, and organize their behavior effectively” (Thayer et al., 2009). Within this general framework, a number of conceptual approaches have linked autonomic and cognitive/behavioral function. General arousal theory suggested that variation in brain stem activation (similarly cited in the neurovisceral view) concurrently altered motivation, attention, and sympathetic activation/vagal withdrawal (e.g., Lindsley, 1951). Psychological activation/arousal is still commonly accepted to speed heart rate, and faster heart rate is related to less HF-HRV (Billman, 2013). Building on orienting reflex views of Sokolov (1990), Graham and Clifton (1966) established that orienting toward an environmental event elicited a brief, vagal slowing of heart rate potentially facilitating attention. Lacey and Lacey (1974) similarly suggested that brief cardiac deceleration indicated “openness to the

environment" while acceleration indicated rejection of the environment and likely cognitive elaboration. A series of studies by van der Molen and Jennings, however, resulted in the view that brief event-related heart rate changes were a function of a particular executive function, the selection of action, rather than being due to sensory enhancement or direction of attention (Jennings & van der Molen, 2005). Namely, cardiac deceleration was related to the inhibition of action while acceleration occurred when an action was chosen (with the degree of deceleration related to the degree of inhibition and the degree of acceleration related to the metabolic demands of the action chosen). Transient decreases in HF-HRV are also known to occur when events require attention (Porges, Arnold, & Forbes, 1973). In his polyvagal theory, Porges relates HF-HRV to environmental transactions as well as to social and affective factors that are central to the neurovisceral view (Porges, 2011). Individual differences in resting HF-HRV are also known to relate to individual differences in these situationally evoked vagal changes in heart rate that are emphasized by a number of the above authors (Porges & Coles, 1982). These concepts all share with the concept of neurovisceral integration the postulate that vagal changes covary with and likely are induced by cognitive processes related to sensation or action. They differ in the degree to which basic and/or executive functions are seen as integrated with vagal function. They also differ in suggesting process- or state-specific relationships rather than the individual difference perspective of neurovisceral integration based on resting vagal function. Two important observations relate most directly to the current results. First, we tested a trait or individual difference aspect of the neurovisceral hypothesis. Our measures of HRV assumed that this was a stable trait of the individual, and we collected both this and brain activation data under similar state/resting conditions. We did not assess measures of HRV or brain region during an activated state. Second, it is noteworthy that most concepts relate heart rate changes to either sensory orienting or the regulation of action, (i.e., two forms of attention), and that the support for HF-HRV/cognitive linkage within the neurovisceral hypothesis is preponderantly from tasks requiring attentive observation combined with working memory. In short, a conceptual and empirical basis exists to suggest that the neurovisceral hypothesis may apply to state- and process-specific relationships (and that any trait or individual differences relationships may be explained by the state/ process relationships). In this context, a report may be significant of correlations between change in HF-HRV and change in cingulate activation with shifts in attentional focus to and from affective content (Lane et al., 2013). Alternatively, in the context of affective regulation, individual differences in resting variability may be more predictive than differences in response. These possibilities require investigation. Such investigation should also consider the role of sympathetic nervous system activation, which may support the maintenance of an attentive state and cognitive "work" exclusive of processing related to vagal function.

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Appendix 1

Table A1

Resting Cerebral Blood Flow Related to Neuropsychological Tests of Executive Function

Entire sample (*n* = 413)							
	SP-BACK	**DGT-BACK**	**4WRD-STM**	**DGTVIG1**	**DGTVIG2**	**TRAILS B**	**STRP-INT**
Global CBF	−.05	−.06	.02	−.05	−.06	−.04	.01
pHIP	−.01	−.00	−.03	−.01	.05	.03	−.08
PUT	−.03	−.05	−.10	.02	.06	.03	−0.11*
pACC	.04	−.02	.05	.00	.04	.00	−.03
MFG	−.02	−.11*	.02	−.02	−.02	.01	−.04
sACC	−.05	−.03	.03	.06	.05	.01	.01
AMY	.01	.06	−.04	−.02	.01	−.04	−.09
lIns	.06	.07	.00	.03	.09	−.03	−.06
rIns	.02	.07	−.02	−.03	.01	.00	−.11*
Cere	.00	.05	−.04	−.02	.03	−.02	.03

Entire sample (*n* = 413)							
	SP-BACK	**DGT-BACK**	**4WRD-STM**	**DGTVIG1**	**DGTVIG2**	**TRAILS B**	**STRP-INT**
HIP	−.01	.04	.01	.01	.00	.06	−.06
STG1	.01	.03	−.06	.01	−.01	−.03	−.04
dPCC	−.05	−.05	−.07	.02	.00	.10	−.05
PcG	−.01	.10*	−.02	−.01	−.01	−.04	−.00
STG2	−.04	−.05	−.08	−.02	−.04	.01	−.12*
Caucasian Americans (*n* = 344)							
	SP-BACK	DGT-BACK	4WRD_STM	DGTVIG1	DGTVIG2	TRAILS B	STRP-INT
Global CBF	−.04	−.07	.02	−.04	−.08	−.13	.01
pHIP	.02	.03	−.03	.03	.06	−.03	−.04
PUT	−.00	−.01	−.09	.08	.07	−.03	−.09
pACC	.04	−.04	.06	.02	.06	−.02	−.03
Rostral MFG	−.02	−.13	.03	−.04	−.01	−.01	−.02
sACC	−.03	−.01	.06	.02	.04	−.04	.05
AMY	.04	.11	−.02	−.00	.02	−.06	−.04
lIns	.02	.07	−.01	.08	.08	−.03	−.12
rIns	−.01	.09	−.04	.00	.01	−.03	−.16
Cere	−.01	.02	−.07	−.02	.01	.03	.01
HIP	.02	.07	.04	.00	−.00	.03	−.04
STG1	.04	.05	−.03	.02	−.00	−.03	−.02
dPCC	−.00	−.01	−.03	−.02	−.02	.08	−.04
PcG	−.00	.09	−.03	.04	.01	−.04	−.01
STG2	−.03	−.05	−.07	−.00	−.04	−.02	−.10
African Americans (*n* = 63)							
	SP-BACK	DGT-BACK	4WRD_STM	DGTVIG1	DGTVIG2	TRAILS B	STRP-INT
Global CBF	−.06	.06	.08	−.05	.06	.16	.09
pHIP	.04	.02	.05	−.10	.04	−.01	−.16
PUT	.02	.03	.02	−.18	.02	.03	−.09
pACC	.06	.09	.05	−.04	−.07	.06	−.03
Rostral MFG	−.02	−.04	.01	.03	.06	.08	−.11
sACC	−.13	.07	−.04	.17	.12	.11	−.12
AMY	.11	.02	.08	−.08	−.00	−.14	−.16
lIns	.16	.12	.08	−.14	.09	−.01	.08
rAins	.17	.08	.08	−.08	.02	.02	.12
Cere	.01	.24	.06	−.06	.08	−.19	.05
HIP	.01	.10	−.02	.03	.05	.03	−.04
STG1	.02	−.00	−.19	.01	−.01	0.10	−.10
dPCC	−.31	−.28	−.29	.09	.07	.21	−.10
PcG	.08	.15	.03	−.14	−.11	−.05	−.01

Entire sample (*n* = 413)							
	SP-BACK	**DGT-BACK**	**4WRD-STM**	**DGTVIG1**	**DGTVIG2**	**TRAILS B**	**STRP-INT**
STG2	.10	.11	.04	−.07	.07	−.05	−.13

Note. SPN-BACK = backwards spatial memory span; DGT-BACK = digits backward memory span; 4WRD_STM = number correct at 15-s recall in four-word short-term memory test; DGTVIG1 = vigilance score from first set of digits; DGTVIG2 = vigilance score from second set of digits; Trails B5 time score from Trails B completion; STRP-INT = Stroop interference score—positive is less interference. See Table1 for brain area abbreviations. Regional ROIs are normalized by expressing them as a proportion of global CBF.

* $p < .05$.

Table 1

ROIs Analyzed

	MNI coordinates		
Area/region of interest	***x***	***y***	***z***
Parahippocampal gyrus (pHIP) (left)	−24	0	−12
Putamen (PUT) (left)	−26	−8	−2
Dorsal anterior cingulate (dACC) (right)	2	46	6
Ventral anterior cingulate (vACC) (right)	2	22	−2
Medial frontal gyrus (MFG) (right)	10	54	18
Amygdala (AMY) (left)	−20	−6	−18
Insula (lIns) (left, dorsorostral)	−40	0	12
Insula (rIns) (right, dorsorostral)	40	2	12
Cerebellar declive (cere) (left)	−10	−62	−20
Hippocampus (HIP) (right, ventral)	30	−22	−16
Superior temporal gyrus (STG1) (right)	50	−24	2
Dorsal posterior cingulate (dPCC) (left/right)	−6	−44	34
Precentral gyrus (PcG) (left)	−56	6	8
Superior temporal gyrus (STG2) (right)	44	−38	14

Note. HRV-related areas from Thayer etal. (first 5 rows) and parasympathetic areas from Beissner etal. (final 9 rows). MNI = Montreal Neurological Institute.

Table 2

Participant Characteristics (n = 440) with Separate Characteristics for the African Americans within the Sample (n = 70)

	Total sample (*n* = 440)				African Americans (*n* = 70)			
Variable	**Mean**	**Min**	**Max**	***SD***	**Mean**	**Min**	**Max**	***SD***
Age (years)	43.0	30.0	54.0	7.3	44.5	30.0	54.0	7.0
Body mass index (kg/m^2)	26.9	17.5	49.6	5.2	29.2	18.8	45.1	5.8
Systolic blood pressure (mmHg)	114.9	89.0	151.0	11.2	119.3	91.0	147.0	10.4
Diastolic blood pressure (mmHg)	72.3	45.0	99.0	8.2	74.8	58.0	97.0	7.4
Years of school	16.9	9.0	24.0	2.8	15.3	9.0	24.0	2.6
Verbal intelligence estimate (IQ)[a]	111.1	65.0	142.0	12.3	99.3	65.0	130.0	12.8
Performance intelligence estimate (IQ)[a]	111.7	67.0	139.0	12.9	98.9	67.0	129.0	13.3
Ln HF-HRV	6.1	1.8	9.4	1.4	6.3	1.8	9.4	1.5
Respiratory frequency (Hz)	0.22	0.18	0.37	0.05	0.23	0.18	0.34	0.04
Global cerebral blood flow (ml/100 ml/min)	57.9	33.0	100.8	10.4	58.8	35.2	94.1	10.8

N = 430 for all sample participants with both HF-HRV and neuropsychological data.

N = 70 for participants of African American ethnicity with both HF-HRV and neuropsychological data.

N = 432 for cerebral blood flow in the entire sample.

N = 63 for cerebral blood flow in the African American sample.

Note. Caucasian and African American groups differed significantly by *t* test on all variables except LnHF-HRV, respiratory frequency, and global cerebral blood flow. IQ = derived intelligence quotient.

[a]Intelligence estimate was derived from overall testing with the Wechsler Adult Intelligence Scale.

Table 3

Bivariate Correlations Between HF-HRV and Regional Cerebral Blood Flow

LnHF	CBF	pHIP	Put	dACC	MFG	vACC	AMY	lIns	rIns	Cere	HIP	STG1	dPCC	PcG	STG2
All	.15**	−.12*	−.14**	−.04	−.02	.03	−.12*	−.15**	−.10*	.01	−.12**	−.13**	.05	−.03	−.18**
Cau	.22**	−.12*	−.14**	.05	.04	.08	−.11*	−.13*	.07	.00	−.14**	−.15**	.00	−.04	−.20**
AA	−.08	−.18	−.16	−.34**	−.25*	−.26*	−.20	−.19	−.16	−.04	−.12	−.13	.03	−.03	−.13

n = 362 for Caucasian Americans.

n = 63 for African Americans.

n = 432 for the entire sample.

Note. Correlations are presented separately for the entire sample (All). As the brain areas for the entire sample were based on prior directional associations, one-tailed significance testing was applied. Two-tailed significance is reported for the separate Caucasian and African American samples. ROI values are scaled as a proportion of global CBF. Prior to scaling, correlations with ROIs were similar to those for global CBF (i.e., for all subjects, HF was related .09 to pHIP, .07 to posterior PUT, .12 to dACC, .13 to rostral MFG, .15 to sACC. Cau = Caucasian; AA = African American; Ln HF = log HF-HRV; CBF = global cerebral blood flow. See Table 2 for ROI abbreviations.

* $p < .05$ (one-tailed only for All).

** $p < .01$.

Table 4

Performance on Neuropsychological Tests of Executive Function (n = 440)

	Mean	Minimum	Maximum	*SD*
SP-BACK	7.7	2	12	1.7
DGT-BACK	7.8	2	14	2.5
4WRD STM	11.7	1	20	3.9
DIGVIG1	177.5	100	513	42.9
DIGVIG2	181.5	104	540	43.6
TRAILS B	53.4	25	200	20.7
STRP-INT	0.67	219	23	7.44

Note. SP-BACK = backward spatial memory span; DGT-BACK = digits backward span; 4WRD STM = four-word short-term memory; DIG-VIG = digit vigilance for page 1 and below page 2; STRP-INT = Stroop interference score (less interference positive). See text for further detail.

Table 5

Assessment of Joint Influence of HRV and Resting Global and Regional CBF on Cognitive Scores

	Trails B	Digits backward	Stroop interference
Ln HF	−.15	.10[a]	.17
Ln HF with CBF	−.13	.12	.18
Ln HF with pHIP	−.15	.11	.17
Ln HF with PUT	−.15	.10[a]	.16
Ln HF with AMY	−.14	.12	.17
Ln HF with dPCC	−.15	.12	.16
Ln HF with HIP	−.13	.12	.17
Ln HF with STG1	−.14	.11	.18
Ln HF with STG2	−.15	.10[a]	.17

Note. Standardized beta weights from analyses adding CBF variables to HF (Caucasians $n = 337$).

[a] $p = .06$. All other beta values are significant at $p < .05$ or better. No beta value for LnHF was significantly altered by the addition of CBF measures.