Research Article

Reliability and reactivity of the prefrontal hemodynamic responses in essential hypertension: a functional near infrared spectroscopy study

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Abstract

Prefrontal (PFC) cerebral vasoreactivity may be altered in hypertension but has not been studied during postural change and carbon dioxide (CO_2) rebreathing. In this study, a dual procedure of 5% CO_2 rebreathing with positional change (standing to supine and reverse) was performed on normotensive (N = 24) and essential hypertensive males (N = 16) (18–55 years) to assess reliability of PFC responses using functional near infrared spectroscopy. The groups (matched on age levels, N = 13) were also compared on their hemodynamic reactivity (change of oxyhemoglobin or total hemoglobin as a function of change in end tidal CO_2). Test–retest reliability within one session and 7 days later was moderate to high (intraclass correlation coefficient = .63–.901) in both normotensive and hypertensive groups for all hemodynamic measures; whereas reliability of reactivity measures for oxyhemoglobin and total hemoglobin was moderate (intraclass correlation coefficient = .68–.762). Functional near infrared spectroscopy–measured PFC hemodynamic responses are highly reproducible in normotensive and adult essential hypertensive males. J Am Soc Hypertens 2015;■(■):1–10. © 2015 American Society of Hypertension. All rights reserved.
Keywords: Carbon dioxide rebreathing; high blood pressure; orthostatic stress; vascular reactivity.

Introduction

A decline in cerebral hemodynamic responsiveness has been associated with reduction in cognitive proficiency and may be an important intermediary in the relationship between hypertension and cognitive impairment.[1,2] Hajjar et al. used magnetic resonance imaging (MRI), to identify impaired vasoreactivity in all the cerebral cortical zones of hypertensives, the frontoparietal region in particular. These findings, however, were among severe hypertensives and may not be applicable to mild-to-moderate (eg, Stage 1) hypertensives.

Two important techniques in measuring cerebral vasoreactivity include Transcranial Doppler sonography[3] and MRI.[1] However, given the reliance of the former technique on middle cerebral artery flow velocity, it might not be the appropriate measure of microvascular changes in cortical parenchyma which is relevant to hypertensive small vessel disease.[2] In the case of MRI, testing is limited to static positions; thus, information related to postural changes (eg, in surgical positioning) and function in general[4] is not available. A potentially more appropriate technique of cortical hemodynamics and vasoreactivity is functional near infrared spectroscopy (fNIRS).

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fNIRS is a neuroimaging technique that has been validated with MRI, positron emission tomography, and other established techniques in the measurement of cerebral hemodynamic responses in a variety of disorders (for review see Ferrari and Quaresima).[5] This noninvasive optical technique measures relative changes in oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) concentration associated with cortical activity and blood flow at the microvascular level. Its main advantage is that it allows real-time, in situ testing in different body positions under varying functional stresses that resemble both clinical and prosaic scenarios. Using the principles of the modified Beer–Lambert Law, this approach measures the absorption changes in near infrared light (700–1300 nm) associated with the hemoglobin chromophore (light absorbing compound) to indirectly monitor changes in O_2Hb and HHb.[6] fNIRS offers biochemically specific information at the microvascular level that allows monitoring of the close association between hemodynamic responses, positional changes, and functional tasks.

Over the past 20 years, test–retest reliability of fNIRS measurements has been established in both healthy and diseased populations under different experimental conditions. Relevant to this study, fNIRS reliability has been established in carbon dioxide (CO_2) rebreathing[7] and positional changes.[8] However, to our knowledge simultaneous testing of these two procedures, CO_2 rebreathing and postural change, has not been performed. Hence, information on the reliability of the known vasoreactive changes that accompany alterations in $PaCO_2$ and body position in a healthy population[3] is not available, never mind for hypertensives. Thus, an important perspective in explaining the relationship between cognition and hypertension, in the form of cerebrovascular responsiveness to positional stress, is unexplored.

The primary purpose of the present study was to examine the test–retest reliability of hemodynamic responses in a group of normotensive and Stage 1 hypertensive participants using fNIRS. The secondary purpose was to compare cerebrovascular reactivity, as determined by hemodynamic responsiveness, between these two groups during CO_2 rebreathing and positional stress. It was hypothesized that (1) the hemodynamic responses of oxygenation (O_2Hb), deoxygenation (HHb), total blood volume changes (total hemoglobin [tHb]), hemoglobin difference (HbDiff), as well as CO_2 reactivity scores for O_2Hb and tHb would be reproducible in the two groups and (2) CO_2 cerebrovascular reactivity scores for O_2Hb and tHb would be significantly impaired in the hypertensives.

Methods and Procedures

Participant Recruitment

Uncomplicated Stage 1 hypertensives and normotensives (18–55 years) were recruited from the city of Edmonton,

Alberta, between January 2012 and April 2013. Recruitment was limited to males because the impact of gender on hemodynamic responses is unclear.[9] Volunteers with nervous system or psychiatric disorders, heart, or kidney ailments were excluded. Smokers and recreational drug users were also excluded. The use of antihypertensive medication did not preclude participation in the study, but blood pressure levels were well controlled for more than 6 months in the hypertensives, as advised by the family physician.

Tests and Procedures

All the participants provided written informed consent before testing which was conducted at the Work Physiology Laboratory, Faculty of Rehabilitation Medicine, University of Alberta. Participants were advised to avoid a heavy meal and caffeinated drinks for 2 hours before testing. Each participant arrived 1 hour before test time to complete required forms and to be familiarized with test equipment and procedures. Each participant then provided details of medication and relevant medical history and completed the code for physical activity and the Beck Depression Inventory II. The examiner advised each participant of the right to withdraw from the study at any time without repercussions. Participant height, weight, head circumference, resting heart rate, and blood pressure were then measured using American College of Sports Medicine standard measuring techniques. To examine the intersession reliability of the hemodynamic responses, each participant completed two test sessions 7 days apart. During each test session, the procedures described below were repeated to examine the intrasession reliability of the hemodynamic responses. The experimental procedures were approved by the Health Research Ethics Board of the University of Alberta.

Participant Preparation

fNIRS optodes were attached bilaterally to the participant's forehead just rostral to the supraorbital ridge with an emitter–detector distance of 4.5 cm for each pair. There was a distance of 2–3 cm on either side of midline for each optode pairing, the center of which corresponded to FP1 and FP2 on the 10–20 International Systems. The chest strap to monitor heart rate with a remote device (Polar Global CS100, Finland) was then secured, followed by the blood pressure cuff placed on the left arm of the participant. To monitor end tidal CO_2, participants were attached to a metabolic cart (VMax 20, Sensormedics, USA) by a leak-free mask with a two-way Hans Rudolph valve. All testing was performed by the same investigator and occurred between 12 noon and 6 PM Mountain Standard Time.

Test Protocol

Participants were randomly assigned to a starting position, either standing or supine lying on a plinth (head elevated 10–15° from the horizontal on a firm pillow). Blood pressure was monitored in the starting position using the auscultatory method after a 5-minute rest (three readings 1 minute apart thereafter). fNIRS recording began with baseline, resting in the starting position for 2 minutes, and continued throughout testing. After baseline, the participant was asked to breathe for 30–90 seconds from a black 5L anesthetic bag containing 5% CO_2 and balance N_2 via the Hans Rudolph valve attached to the metabolic cart. The duration of rebreathing was chosen to correspond with the time that increase in cerebral blood flow would be detectable and time to reach steady state $PaCO_2$[10] without participant discomfort. The participant was then moved from the original starting position to a new position of either supine lying or standing. This change in position took 15–20 seconds, and the participant remained in the new position for a further 3 minutes. The 3-minute timeframe was identical to the established physiological test for position change in orthostatic evaluation.[11] End tidal CO_2 was monitored during this period by the metabolic cart; blood pressure at the left arm was remeasured at the end of the trial (similar to pretrial). This procedure was repeated in the same session after 5 minutes of rest with mask removed. Finally, the entire procedure was repeated in a second session 7 days later. See Figure 1 for the test protocol.

Cardiorespiratory Measurements

The VMax 20 machine was calibrated before each test according to the manufacturer's specifications. The oxygen and CO_2 analyzers were calibrated using precision medical gases (4% CO_2, 16% O_2, balance N_2; and 0% CO_2, 26% O_2, balance N_2). The pneumotach was calibrated for volume using a 3L syringe. Metabolic measurements were recorded in the breath by breath mode throughout each test session simultaneously with the fNIRS measurements.

fNIRS Measurements and Data Analysis

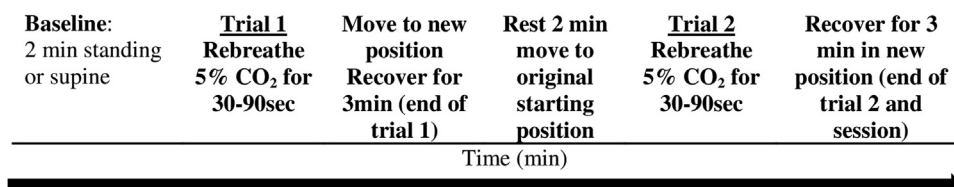O_2Hb, tHb, HHb, and $HbDiff$ changes were monitored simultaneously from the left and right prefrontal (PFC) lobes using a continuous wave dual channel fNIRS machine (Artinis Oxymon Mk III, the Netherlands) with wavelength of 760 and 850 nm. These hemodynamic responses were calculated from changes in optical density at the two wavelengths with the application of the principles of the modified Beer–Lambert law using the manufacturer supplied software. The emitter–detector distance of 4.5 cm corresponded to fNIRS penetration depth sufficient to reflect changes in prefrontal cortical gray matter.[12] fNIRS sampling from both the left and right prefrontal lobes was conducted at 10 Hz, and predetermined events were inserted in the fNIRS output for subsequent analysis. A moving average of five samples per second was applied to the output to smooth the traces of the four hemodynamic variables. Delta values (peak minus baseline) were obtained from the output trace and calculated for each variable. The peak used was that identified in the second (new) position (standing or supine lying for 3 minutes) after rebreathing. Peak was identified by a colleague who was unfamiliar with the objectives of the study. Delta values for end tidal CO_2 were calculated as follows: peak end tidal CO_2 in the new position after rebreathing CO_2 minus (−) resting end tidal CO_2 during baseline in the starting position. The use of delta values for hemodynamic measures in this experiment was consistent with the practice for continuous wave fNIRS measurement.[6]

Calculation of CO_2 Reactivity

The reactivity of hemodynamic responses to the hypercapnic challenge and postural change was calculated as the relative change from baseline in the values of O_2Hb and tHb (delta values) per increase in end tidal CO_2. This approach to calculating CO_2 reactivity is consistent with the research of Hajjar et al[1] who used blood flow as a function of end tidal CO_2 in calculating cerebral vasoreactivity.

Statistical Analysis

Normality of the data was initially examined using the Shapiro–Wilks test. Independent t tests were used to compare the mean characteristics of the normotensive and hypertensive participants. To examine the differences and interaction between the repeated trials and side of the PFC in the hypertensive and normotensive groups, a three-way (Group × Side × Trial) repeated-measures analysis of

Baseline: 2 min standing or supine	**Trial 1** Rebreathe 5% CO_2 for 30-90sec	**Move to new position** Recover for 3min (end of trial 1)	**Rest 2 min** move to original starting position	**Trial 2** Rebreathe 5% CO_2 for 30-90sec	**Recover for 3 min** in new position (end of trial 2 and session)

Time (min)
⟶

Figure 1. The procedure describes trial–retrial reliability testing of normotensive and hypertensive participants during carbon dioxide (CO_2) rebreathing and postural change.

covariance was performed for each of the four hemodynamic changes (O_2Hb, tHb, HHb, and HbDiff). To address concerns on scalp to cortex distance biasing fNIRS measurements, head circumference was used as a covariate for all comparisons between the groups. Test–retest reliability was calculated for all four hemodynamic variables in the groups using the two-way mixed intraclass correlation coefficient (ICC). This reliability was examined between the two trials in one session and between the two sessions using mean values for each trial. Bland–Altman analyses were performed using the MedCalc software (MedCalc version 13.1, Belgium) to verify the agreement of the hemodynamic responses in the trials. This procedure is a plot of the differences between two trials against their averages. A horizontal line represents the mean difference; and the limits of agreement are defined as the mean difference ±1.96 standard deviation either side of the line.[13] Data points outside the limits of agreement on these plots were considered as outliers. Common variance and derived regression equations were obtained from Pearson correlations between the two trials within the session.

To compare hemodynamic reactivity between the groups, 13 hypertensives were first matched on age levels with 13 normotensives from the original sample, as advocated by Green and Salkind.[14] ICCs of the reactivity scores of both groups were then calculated for the O_2Hb and tHb variables. Thereafter, a repeated-measures multivariate analysis of covariance (MANCOVA) (head circumference included as a covariate) was performed to compare the two groups with the dependent variables of CO_2 reactivity calculated for O_2Hb and tHb. "F" ratios were adjusted using the Greenhouse–Geisser procedure, and the Bonferroni correction was applied to control type 1 error. Statistical significance was established at α level of 0.05. Statistical analyses were completed with the Statistical Package for the Social Sciences, version 21 (SPSS, Inc, Chicago, USA).

Results

Participant Characteristics

Twenty-four normotensive and 16 Stage 1 hypertensive males participated in this study. All participants were fluent in the English language and conversant in at least one other language. They were right hand dominant except for two normotensives and one hypertensive and were all employed in white collar occupations. There were no known comorbidities among the hypertensives. See Table 1 for a summary of salient participant characteristics.

After matching on age levels, there was no significant difference between the groups on BMI, head circumference, years of formal education, and Beck Depression Inventory II scores. However, resting systolic and diastolic blood pressure were significantly higher in the hypertensive group ($P < .05$). The period from the initial hypertension diagnosis to testing ranged from 1 to 20 years (mean 5.53 ± 5.59). Four hypertensive participants were taking calcium channel blockers, and five were on angiotensin receptor blockers. (Three of these were not included in the matching.) Four other participants were being treated with a combination of medication including angiotensin-converting enzyme inhibitors and diuretics. Three other hypertensives were not medicated, but medically monitored while advised to alter lifestyle (diet and weight loss). The hypertensive group was evenly split on the usual time of day for taking the medication—morning or evening.

Hemodynamic Trends During CO_2 Rebreathing and Positional Change in Hypertensives and Normotensives

Traces of the hemodynamic trends in the two conditions, (1) standing–supine lying and (2) supine lying–standing, are represented for both groups in Figure 2.

The trends were similar for both groups with higher concentrations noted for the normotensives, although it should be cautioned that comparing traces across groups may not be accurate in fNIRS measurement.[6] During baseline, the trace exhibited a stable and uniform pattern with minimal change in O_2Hb, tHb, HbDiff, and HHb. During CO_2 rebreathing, fNIRS trace concentrations of the first three variables systematically increased during the 30–90 seconds and peaked in the supine lying–standing condition immediately before the participant being moved to standing. After standing, there was a sharp decline in the first three

Table 1
Participant characteristics for reliability study of normotensive and hypertensive males (mean $\pm$ SD)

Group	Age	Body Mass Index	Code of Physical Activity	Years of Formal Education	Resting Systolic BP (mm Hg)	Resting Diastolic BP	Resting Heart Rate (bpm)
Normo (N = 24)	36.46 ± 9.01	27.84 ± 4.30	5.46 ± 1.45	16.23 ± 1.96	116.69 ± 11.6	78.15 ± 6.6	69.85 ± 8.9
Hyper (N = 16)	40.23 ± 10.51	29.77 ± 4.84	4.69 ± 2.53	17.54 ± 2.60	127.15 ± 8.12*	83.54 ± 6.17†	72 ± 11.18

DBP, diastolic blood pressure; hyper, hypertensive; normo, normotensive; SBP, systolic blood pressure; SD, standard deviation.
Code for physical activity, out of 7, 1 indicates very sedentary and 7 indicates very high level activity (as per Ross and Jackson, 1990).
* Significant at $P = .013$ (hypertensive with higher resting SBP).
† Significant at $P = .042$ (hypertensive with higher resting DBP).
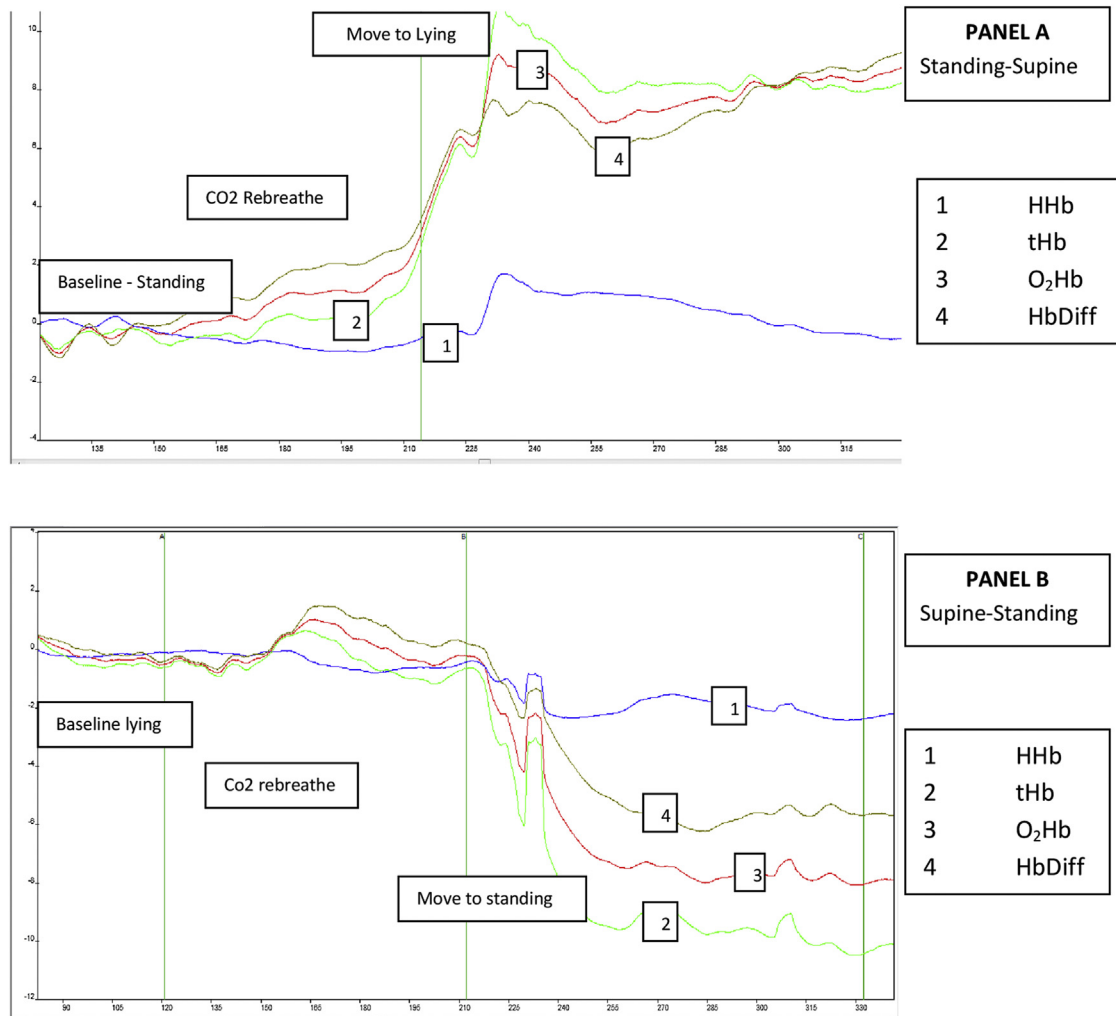
Figure 2. This is a representative trace of near infrared spectroscopy hemodynamic response over the prefrontal lobes during carbon dioxide (CO_2) rebreathing and postural change in a hypertensive participant. (A) Normotensive. (B) Hypertensive. HbDiff, hemoglobin difference; HHb, deoxyhemoglobin; O_2Hb, oxyhemoglobin; tHb, total hemoglobin.

variables (O_2Hb, tHb, and HbDiff) toward baseline. HHb remained relatively unchanged in the rebreathing procedure and across both positions. During the standing–supine lying condition, the initial trend during baseline and CO_2 rebreathing was similar to the other condition. However, when moved to supine lying, there was a sharp systematic increase in O_2Hb, tHb, and HbDiff. These variables remained elevated for more than the 3 minutes of supine lying while trending toward the baseline. In both conditions and groups, there was a trend for O_2Hb and tHb to parallel each other in the trace.

Similar to the hemodynamic responses, the end tidal CO_2 rose during the rebreathing and continued to increase until peak in the standing–supine lying condition for a further 110 seconds in the normotensives and 156 seconds in the hypertensives. In the supine lying–standing condition, end tidal CO_2 continued to rise until peak for a further 102 seconds in the normotensives and a further 135 seconds in the hypertensives after rebreathing termination. In both conditions, end tidal CO_2 returned to baseline within 3 minutes in the two groups. A comparison of the times to achieve peak end tidal CO_2 and peak O_2Hb in both conditions across the groups are demonstrated in Figure 3.

Reliability of Hemodynamic Responses in Normotensive and Hypertensive Participants

There was no significant interaction or group differences on the three-way repeated-measures analysis of covariance (Group × Side × Trial) for any of the hemodynamic responses, and the use of head circumference as a covariate did not affect the results. With no significant
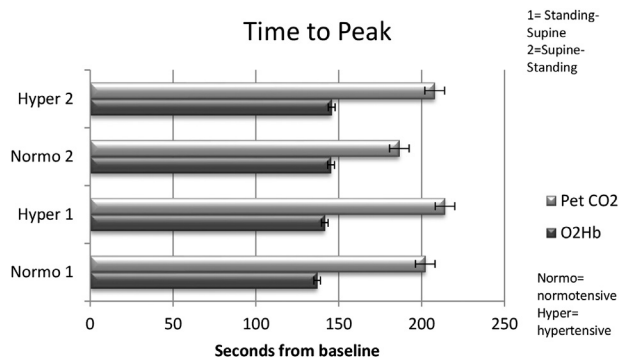
Figure 3. Figure represents a comparison of time recorded in seconds to achieve peak end tidal carbon dioxide (CO_2) and oxyhemoglobin change in normotensive and hypertensive participants.

interaction (Group × Side × Trial) or main effect of side, both sides were pooled thus doubling the number of sample measurements. The trial–retrial and intersession ICCs for the four hemodynamic variables in the two body positions with right and left sides pooled are reported in Table 2.

The trial–retrial ICC for O_2Hb in the normotensive group ranged from 0.630 ($P = .018$) to 0.901 ($P < .000$) in the supine lying–standing condition. In the hypertensive group, trial–retrial ICC in O_2Hb ranged from 0 .627 ($P = .044$) to 0.823 ($P < .000$) across the two conditions.

The trial–retrial ICC in the normotensive for tHb ranged from 0.646 ($P = .014$) to 0.806 ($P < .000$) across both conditions. In the hypertensive group, the ranges for tHb were from 0.610 ($P = .051$) to 0.900 ($P < .000$) across both conditions. For the HHb and HbDiff variables, as noted in Table 2, all ICCs within each group were moderate to high with α levels <.05.

Bland–Altman plots for O_2Hb and tHb in normotensive and hypertensive groups are illustrated in Figure 4A, 4B.

For both groups, the data points in the plots clustered around the horizontal line of mean difference and no systematic bias was evident. In the normotensive group, there was one outlier above and below the 95% confidence interval for tHb during standing–supine lying. In the hypertensive group, there were no outliers for O_2Hb in standing–supine lying. All the other plots were characterized by a single outlier across all conditions in both hypertensive and normotensive groups. The removal of the outliers did not affect the significance level of any of the ICCs.

ICCs of reactivity scores in the normotensive group, as calculated using the O_2Hb and tHb variables, were higher in the standing–supine lying trial–retrial with ranges of 0.68 ($P = .003$) to 0.762 ($P = .000$). The trial–retrial ICC for the normotensive in the supine lying–standing condition ranged from 0.438 to 0.520 ($P = .059$). For the hypertensive group, ICCs across both conditions and variables ranged from 0.643 ($P = .037$) to 0.870 ($P < .000$).

Comparison of Reactivity Measures for O_2Hb and Total Hemoglobin Between Normotensive and Hypertensive Groups

Figure 5A, 5B illustrates the trends in cerebrovascular reactivity in both groups. The hemodynamic reactivity measures, for O_2Hb and tHb, as compared on the repeated-measures MANCOVA, showed a nonsignificant higher normotensive score for both positions ($P > .05$).

Discussion

The association of hypertension with alteration in cerebrovascular reserve and consequent impairment in cognitive function[1] demands reproducible measurement techniques to chart disease impact and changes over time. The main findings of this study were (1) the test–retest and intersession reliability of the hemodynamic responses is moderate to high in both normotensive and hypertensive participants and (2) similarly, test–retest of CO_2 reactivity scores were moderate in both groups, and there were no significant differences between the two groups for the CO_2 reactivity measures during postural changes. The physiological and clinical implications of these findings, discussed below, hinge on the reproducibility of fNIRS-measured prefrontal hemodynamic responses.

Reliability of Hemodynamic Responses in Normotensives and Hypertensives

To our knowledge, this is the first study to demonstrate the reproducibility of fNIRS-measured PFC hemodynamic responses in hypertensives. These findings not only establish the usefulness of fNIRS as a technique in assessing the disease, but in part also address the current shortfall in cortical hemodynamic information related to hypertension. This is an important development if the functional limitations resulting from hypertension are to be reliably measured as a prelude to guiding appropriate therapies. Importantly, this study focussed on relatively young men with controlled and uncomplicated Stage 1 hypertension and was designed to present stresses on the cerebral circulation that would identify changes in hemodynamic responsiveness relevant to function. The robustness and flexibility of fNIRS in accommodating these test situations makes the measurement technique ideally suited to functional brain testing of hypertensives. With confidence in the reproducibility of these measures, innovative approaches to testing will enhance the complexity of testing scenarios, further elaborating information on hypertensive brain function.

Unique Test Approach

The use of postural changes combined with the known vasodilator of cerebral circulation, CO_2, provided a unique

Table 2
Test–retest reliability (ICC) of hemodynamic responses during CO_2 rebreathing and positional change in normotensive and hypertensive participants

Group (N = Sample Measurements With Both Sides Pooled)	Position	Trial 1 vs. Trial 2		Session 1 vs. Session 2
		Session1	*Session 2*	
Oxyhemoglobin				
Normotensive				
N = 26	Standing–supine	.857**	.855**	.814**
N = 20	Supine–standing	.630*	.901**	.724**
Hypertensive				
N = 14	Standing–supine	.711*	.627*	697*
N = 18	Supine–standing	.762**	.823**	.560*
Total hemoglobin				
Normotensive				
N = 26	Standing–supine	.806**	.670**	.863**
N = 20	Supine–standing	.646*	.690**	.913*
Hypertensive				
N = 14	Standing–supine	.744**	.610*	.493
N = 18	Supine–standing	.787**	.900**	.690*
Deoxyhemoglobin				
Normotensive				
N = 26	Standing–supine	.862**	.631**	.665**
N = 20	Supine–standing	.780**	.654*	.779**
Hypertensive				
N = 14	Standing–supine	.727*	.780**	.798**
N = 18	Supine–standing	.882**	.644*	.899**
Hemoglobin difference				
Normotensive				
N = 26	Standing–supine	.933**	.504*	.702**
N = 20	Supine–standing	.770**	.744**	.675**
Hypertensive				
N = 14	Standing–supine	.826**	.811**	.652*
N = 18	Supine–standing	.824**	.704**	.685*

*$P < .05$; **$P < .01$.

approach to stressing the cerebrovascular reserve. Bright et al[15] demonstrated that in a "predilated" state of the cerebral circulation, such as after experimental hypercapnia, the vasoconstrictive reactivity to hypocapnia is enhanced throughout the gray matter. These researchers stated that a higher vasodilation in the baseline state is known to naturally occur in some cerebrovascular diseases such as forms of stroke, and as suggested by Veglio et al,[2] in hypertension as well. Bright et al postulated that an enhanced vasoconstrictive tendency in the cerebral cortex that is seen in these patients is the result of the resting "predilated" state in their cerebral vasculature. The approach in the present study used the aforementioned experimentally induced predilated state with CO_2 rebreathing. The reliability of the hemodynamic responses using fNIRS as demonstrated in this approach may provoke further novel strategies to testing, predicated on the reactivity of the microvascular cerebral circulation.

Hemodynamic Reactivity and Implications

The secondary hypothesis of this study postulated an impaired hemodynamic reactivity in the hypertensive group. Statistical significance for this assertion was not achieved. However, there was a trend for decreased reactivity in the hypertensives for both test position changes and most remarkably with regard to tHb. The nonsignificant findings are possibly the result of a large age range in the groups, protracted time since the initial hypertension diagnosis, and more importantly, Stage 1 hypertensives may in fact have less impairment in reactivity than do severe hypertensives as reported by Hajjar et al.[1] Nevertheless, the identified trends in this study, suggesting impaired cerebral vasoreactivity, appear to support the prior research findings in severe hypertensives. Additionally, in the hypertensives, there was a tendency for longer time to peak for both O_2Hb and tHb responses. This was also the case for time to peak
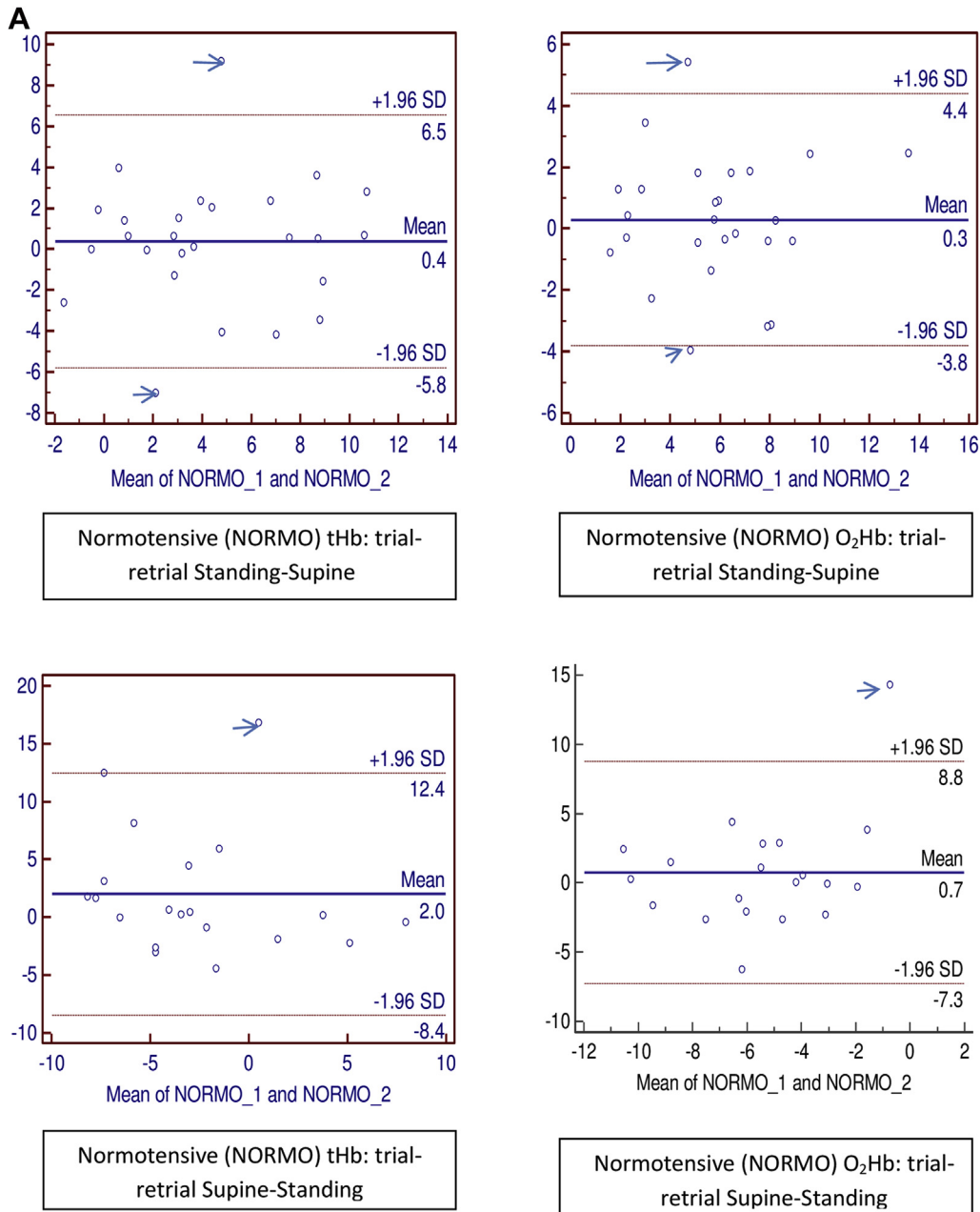
Figure 4. (A) and (B) Figures represent Bland–Altman plots of oxyhemoglobin and total hemoglobin concentration change during trial–retrial carbon dioxide (CO_2) rebreathing and postural change of normotensive and hypertensive participants. (Outliers are identified by arrows.) O_2Hb, oxyhemoglobin; SD, standard deviation; tHb, total hemoglobin.

end tidal CO_2. These changes may be indicative of impairment in hypertensive cerebrovascular responsiveness which may be consistent with stiffness in vessels and a blunted nitric oxide response.[2]
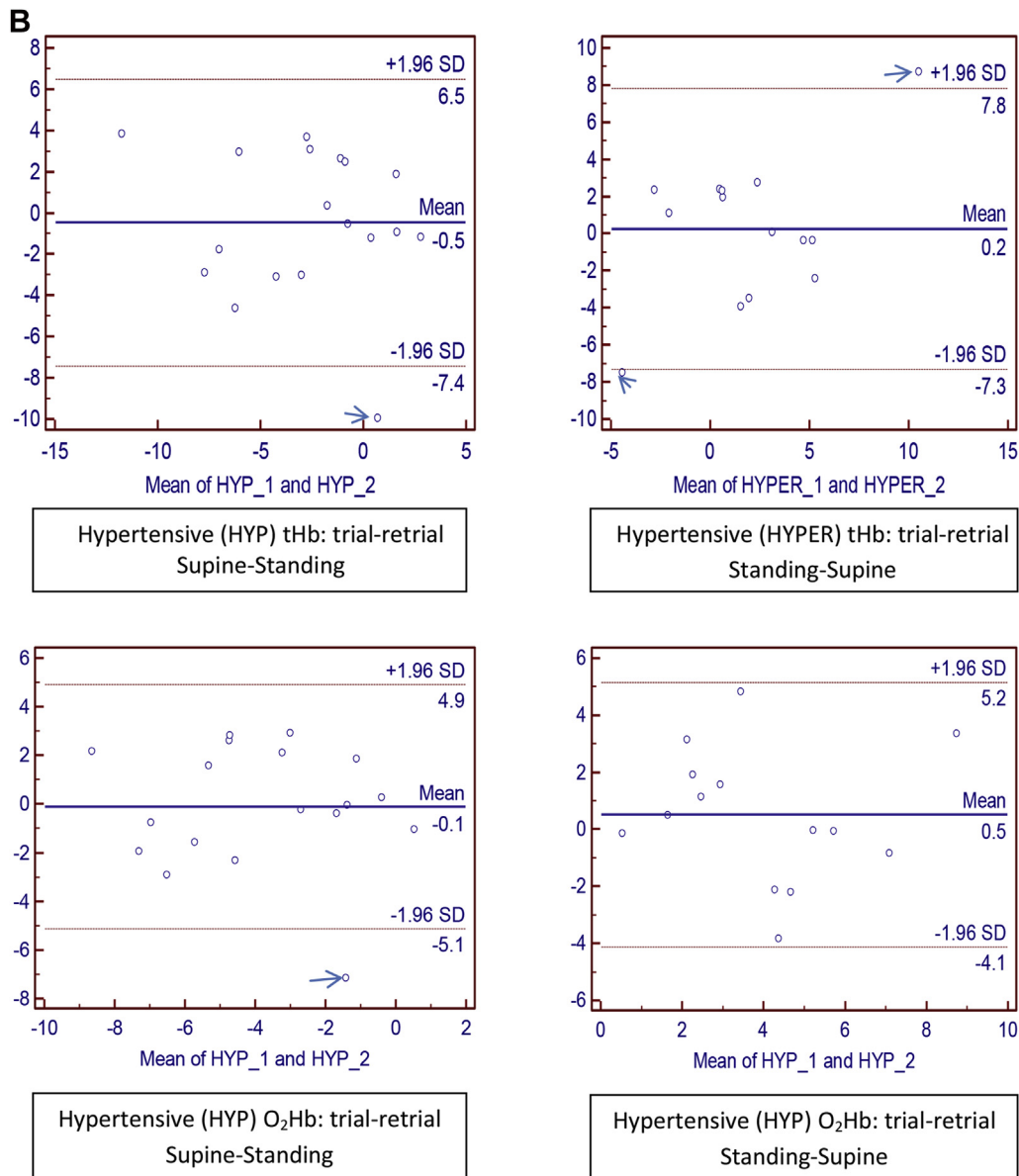
Given that the life period of the present study participants (18–55 years) is arguably the age of greatest productivity, any health deficits may be that much more socially significant. Hence, highly reproducible measurements are critical in making claims regarding the functional impact of the disease. Nevertheless, present

interpretations should be tempered by the limitations of this investigation.

Limitations of the Study

The testing of cerebrovascular reactivity was limited by low statistical power in the present study. Given the demonstrated trends and the importance of CO_2 reactivity as a measure of cerebrovascular reserve, further testing is warranted with a larger sample. In this regard, more attention

Hypertensive (HYP) tHb: trial-retrial
Supine-Standing

Hypertensive (HYPER) tHb: trial-retrial
Standing-Supine

Hypertensive (HYP) O_2Hb: trial-retrial
Supine-Standing

Hypertensive (HYP) O_2Hb: trial-retrial
Standing-Supine

Figure 4. (*continued*).

should be paid to the length of time since diagnosis. The wide range used in this study, 1–20 years, was a poorly explained variable in the impact of vessel changes that parallel duration of the disease.[2] Measurement of ischemic changes in the PFC with MRI would strengthen this part of the study. Medication use may also affect vessel reactivity and should be controlled, where ethically feasible, in a subsequent experiment.

The device used was a continuous wave fNIRS machine which does not determine path length of light in the illuminated tissue. Hence, absolute hemodynamic values could not be used in the analysis; and the delta values, as used in the analysis of the present study, limit the ability to use findings. A time-resolved or frequency-resolved device would provide path-length information that permits use of absolute

hemodynamic measures. This would provide unambiguous interpretation of the hemodynamic response impact in hypertension with more ready translation of findings into patient care.

Finally, confounding signals may arise from scalp circulation and arterial blood pressure thus obscuring PFC activation. The magnitude of these effects is unknown in this study and requires being accounted for in a future examination of the subject.

Conclusions

In the present study, the robustness and versatility of fNIRS was demonstrated with strong reliability estimates of hemodynamic responses in a dual procedure of
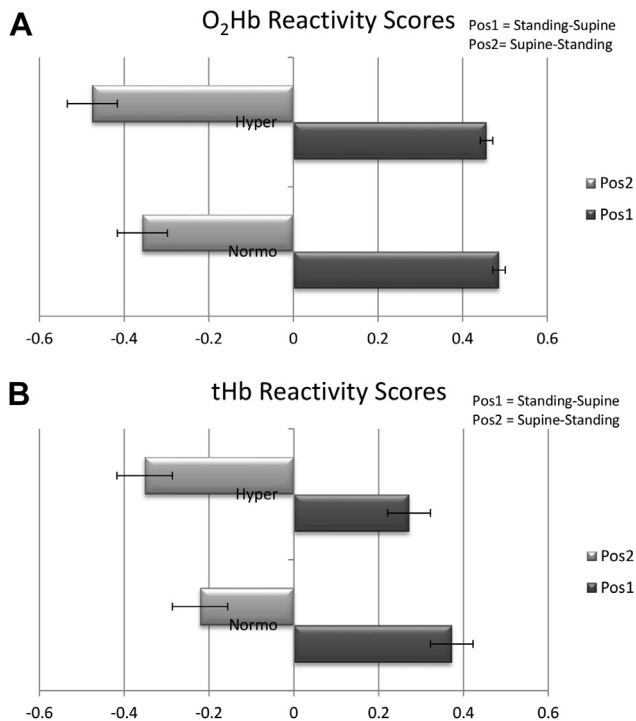
Figure 5. (A) and (B) These figures show reactivity score trends (change in end tidal carbon dioxide per change in hemodynamic measures) averaged across trials for normotensive and hypertensive participants. O_2Hb, oxyhemoglobin; SD, standard deviation; tHb, total hemoglobin; Normo, normotensive; Hyper, hypertensive.

simultaneous CO_2 rebreathing and positional change in both normotensive and Stage 1 hypertensive male participants. Cerebrovascular reactivity in hypertensives, increasingly associated with cerebrovascular accidents and likely altered cognitive performance, was not significantly different from normotensives in this study. However, given the noted trends in vasoreactivity in this group of Stage 1 hypertensives and that identified in severe hypertensives, further research is warranted to control for vasoreactivity as a variable across levels of hypertension. The findings of the present study support the use of fNIRS as a highly reproducible neuroimaging technique that will promote understanding of cerebral hemodynamic responses under meaningful functional stresses.

Acknowledgments

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