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Effect of age on brain oxygenation regulation during changes in position

Rodolfo Gatto [a,*], William Hoffman [b], Chanannait Paisansathan [b], William Mantulin [c], Enrico Gratton [c], Fady T. Charbel [a]

[a] *Department of Neurosurgery, University of Illinois at Chicago, 912 South Wood Street 4th FL, NPI building, Chicago, IL 60612, USA*
[b] *Department of Anesthesiology, University of Illinois at Chicago, IL, USA*
[c] *Laboratory of Fluorescence and Dynamics, University of Illinois at Urbana/Champaign, Urbana, Champaign, IL, USA*

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Abstract

Introduction: Reports indicate that brain regulation of oxygenation is inhibited in patients with low baseline oxyhemoglobin concentrations and that brain oxyhemoglobin concentrations are decreased with aging. The purpose of this study was to determine if regulation of brain oxygenation to changes in blood pressure is inhibited by normal aging.
Methods: Brain oxyhemoglobin (OHb) and deoxyhemoglobin (HHb) concentrations were determined from the forehead using a frequency domain near infrared spectroscopy in 27 healthy volunteers. Subjects were separated into two groups by age (20–39, $n = 16$; 40–60, $n = 11$). Brain hemoglobin and non-invasive blood pressure were measured in (1) supine, (2) sitting, (3) supine and (4) sitting positions with 10-min equilibration intervals between each determination. Statistical differences were determined by two way repeated measures analysis of variance.
Results: Young subjects were 28 ± 5 years (mean $\pm$ S.D.) and older subjects were 48 ± 6 years. In supine position, OHb and HHb were 28.4 ± 8.3 and 15.4 ± 2.4 μmol/L, respectively, in young; 22.4 ± 5.7 and 13.4 ± 2.9 μmol/L, respectively, in older subjects, both $P < 0.05$ between groups. Changing position from supine to sitting decreased OHb 5% and increased HHb 5% with no difference between groups.
Conclusions: There was a small but significant decrease in OHb and an increase in HHb from supine to sitting position, and this effect was similar between young and older subjects. Regulation of brain oxygenation during modest decreases in blood pressure did not change in normal aging to 60 years compared to young adults.

Keywords: Frequency domain near infrared spectroscopy; Brain tissue oxygenation; Sit up test; Age

1. Introduction

Compromised brain hemodynamics due to aging or cerebral ischemia may inhibit brain oxygenation autoregulation during physiological and anesthetic challenges (Burton et al., 2004; Casati et al., 2005). In this setting, modest hypotension or hypocapnia can accentuate brain hypoxic changes (Enlund et al., 1989; Hampson et al., 1990; Torella and McCollum, 2004). However, pathophysiological factors that may magnify this effect are unclear (Artru et al., 1998; Mehagnoul-Schipper et al., 2003). Recent studies suggest that patients with low baseline brain hemoglobin concentrations have a compromised ability to maintain an adequate brain oxygenation state during modest hypotension (Paisansathan et al., in press). This may be related to the finding that aging decreases brain hemoglobin concentrations and the ability to respond to hypercapnic challenges (Gatto et al., in press). The results of these studies suggest that aging may attenuate cerebrovascular responsiveness and brain oxygenation. The purpose of this study was to see if normal aging alters brain oxygen regulation during decreases in blood pressure produced by changing from supine to sitting position.

2. Material and methods

Institutional review was obtained from our institution and informed consent for each volunteers subject. A frequency domain near infrared spectroscopy (FD-NIRS) brain tissue oximeter (Oxiplex TS: ISS Inc., Champaign, IL) was used to measure cerebral tissue oxyhemoglobin (OHb), deoxyhemoglobin (HHb), and to calculate oxygen saturation (SO_2) and total hemoglobin (tHb). SO_2 was calculated as $SO_2 = OHb/(OHb \pm HHb)$ and $tHb = OHb + HHb$ (Gratton et al.,

* Corresponding author. Tel.: +1 312 996 4842; fax: +1 312 996 9018.
E-mail address: rgatto@uic.edu (R. Gatto).

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1997). The FD-NIRS monitor utilized multidistance technique and modulated near-infrared light to determine hemoglobin content in brain tissue (μmol/L) (Fantini et al., 1999). Each diode emitted light at wavelengths of 690 or 830 nm. The four source-detector distances of the probe ranged from 1.98 to 4.08 cm. The optical probes were inserted in soft, flexible polyurethane with a dimension of 3 cm × 5 cm. The amount of hemoglobin in the skin and skull was separated and not considered in the brain tissue oxygenation measurements (Toronov et al., 2003).

2.1. Protocol

Continuous measurements of brain oxygenation levels in 27 healthy volunteer subjects were performed. Each patient was initially measured in the supine position. In this study, the probes were placed on the right forehead, 1 cm from midline on each subject. We used this location to avoid the frontal sinus at the topographic distribution between medial cerebral artery and anterior cerebral territory was a watershed sensitive point.

Initially, in supine position, we measured baseline values for 10 min. We asked the subject to sit up with feet down from supine position (head from 0 to 90°) for 10 min, lie down again for 10 min and finally sitting for another 10 min. Systolic, diastolic and mean blood pressure were non-invasively measured with by plethysmographic technique on the right arm of each subject once during each treatment condition at the end of the 10 min equilibration period.

During the sitting positions, the subject was asked to elevate the level of the pressure cuff to the level of the head during pressure measures. Based on this maneuver, blood pressure was related to the level of the brain.

All data are reported as mean ± S.D. Subjects were separated into two groups by age (20–39, $n = 16$; 40–60, $n = 11$). Comparisons between supine and sitting position were performed with repeated measures analysis of variance with Tukey tests for post hoc analysis.

3. Results

Young subjects were 28 ± 5 years (mean ± S.D.) and older subjects were 48 ± 6 years. An example of the change in OHb, HHb tHb and SO_2 during changes in position are shown in Fig. 1. Mean blood pressure changes during changes in position are shown in Fig. 2. There was no difference in blood pressure between groups but there was a significant decrease in blood pressure at the level of the brain when volunteers changed from supine to sitting position. Brain oxygen saturation, also shown in Fig. 2, was not significantly different between age groups but did significantly decrease from supine to sitting position.

OHb effects of changes in position are shown in Fig. 3. There was a significantly lower OHb in older compared to younger volunteers. There was also a significant decrease in OHb from supine to sitting position, but this change was not significantly different between the groups. HHb was also lower in older compared to young subjects during each treatment. HHb increased significantly from supine to sitting position and this change was not different between groups.

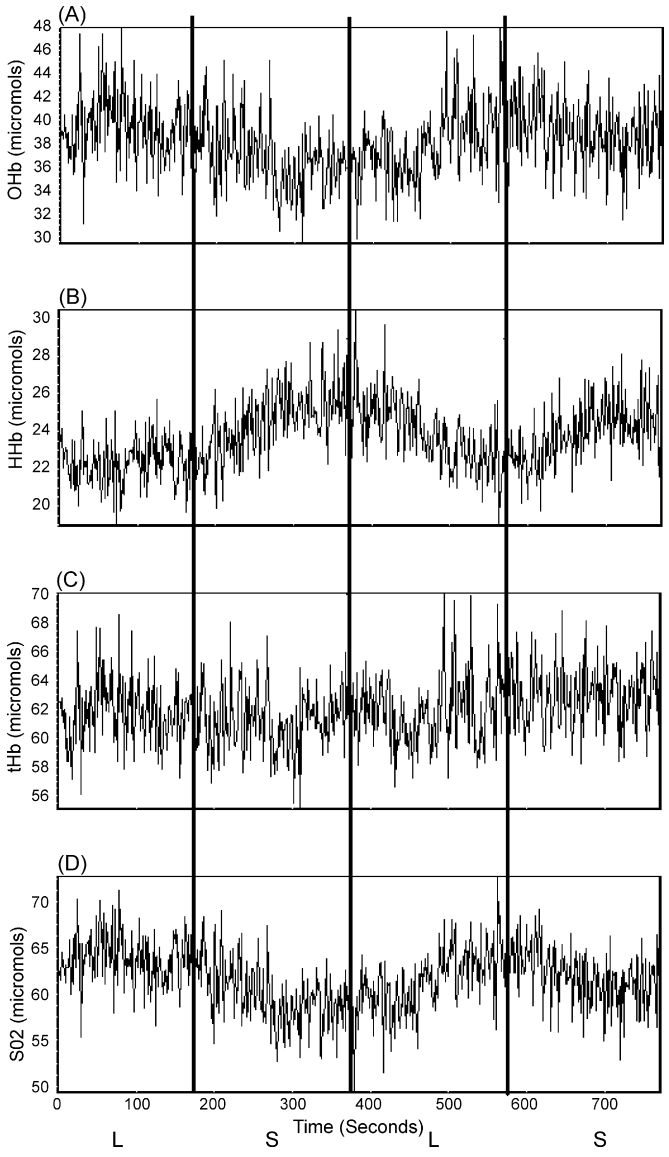

Fig. 1. Real time, right frontal brain tissue measurements of oxyhemoglobin (A), deoxyhemoglobin (B), total hemoglobin (C), oxygenation index (D) during lying position (L) and sitting up position (S) in a young healthy volunteer.

Total hemoglobin changes are shown in Fig. 4. Total hemoglobin was lower in old compared to young subjects during all treatment conditions, but there was no change in tHb in either group during change in position from supine to sitting.

4. Discussion

These results show that normal aging with a range of 40–60 years produced a decrease in OHb and HHb measured in frontal cortex compared to subjects 20–39 years. During changes in position from supine to sitting, blood pressure, brain oxygen saturation and OHb decreased and HHb increased, with no difference in the response between the groups. These data indicate that under baseline conditions, normal aging produced a significant decrease in brain hemoglobin concentration and maintained brain oxygen saturation constant. During modest decreases in

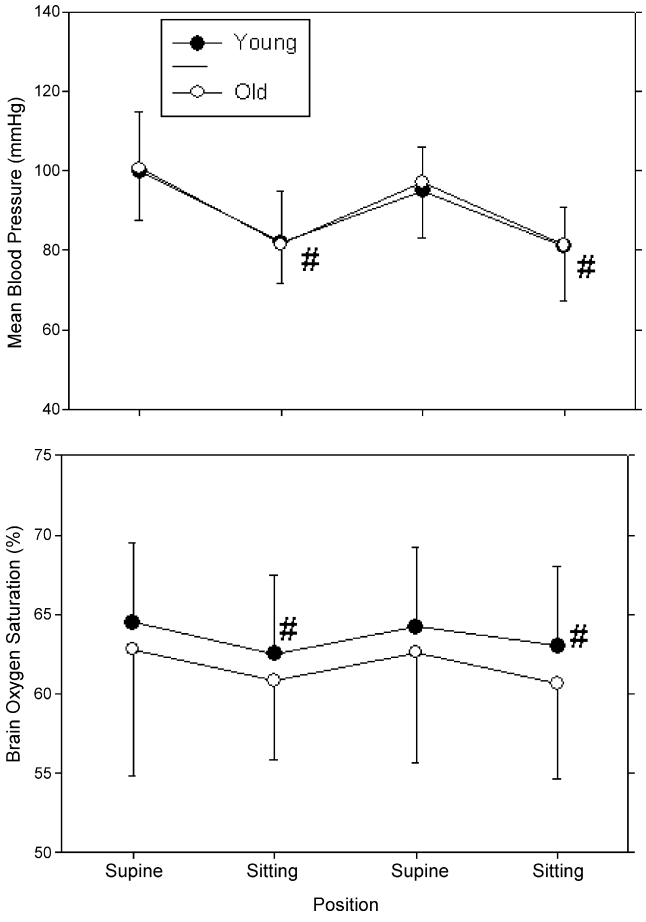

Fig. 2. Mean arterial pressure and brain oxygen saturation in 16 young and 11 older subjects in supine and sitting position. Mean ± S.D. $^{\#}P < 0.05$ sitting compared to previous supine position in both groups. There were no differences between groups in blood pressure or brain oxygen saturation or the change related to a change in position.

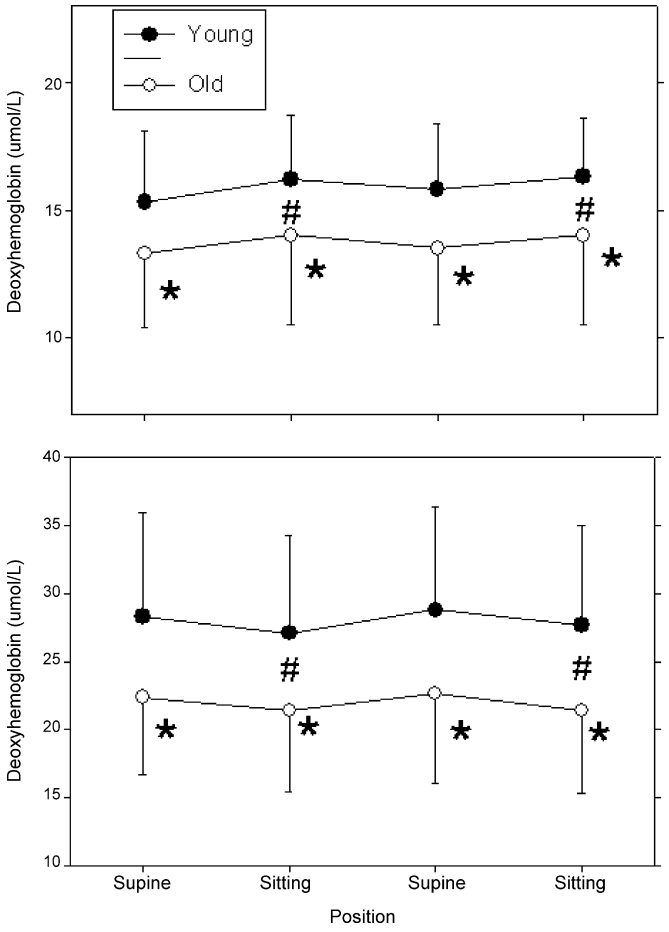

Fig. 3. Brain oxyhemoglobin and deoxyhemoglobin concentrations in supine and sitting position in 16 young and 11 older subjects. Mean ± S.D. $^{*}P < 0.05$ old compared to young, $^{\#}P < 0.05$ sitting compared to previous supine position in both groups with difference in the response between groups.

blood pressure, there was no difference in the ability to regulate brain oxygenation in older subjects. Other studies conclude that regulation of brain oxygenation is significantly compromised when blood pressure is decreased during anesthesia in elderly patients or patients with low baseline OHb and HHb concentrations associated with cerebral pathology (Casati et al., 2005; Paisansathan et al., in press). Our data indicate that normal aging to 60 years does not alter brain oxygen regulation even though OHb and HHb are decreased.

Using tilt test, contradictory findings using continuous near infrared spectroscopy were reported. (Kurihara et al., 2003) studied brain oxygenation in five healthy subjects during head up tilting. They found a significant decrease in tissue SO_2 and OHb between the subjects during the head up position, but no changes in HHb were seen during these challenges. Decreases in OHb and SO_2 and an increase in HHb were described during head up tilt by Krakow et al. (2000). Nevertheless, this group was not able to correlate these findings with MABP or a decrement in cerebral blood flow measured with transcranial Doppler.

In this study, we evaluated a basic autoregulatory test (sit up test) to induce hemodynamic changes using FD-NIRS technology. We observed that sit up position was associated with

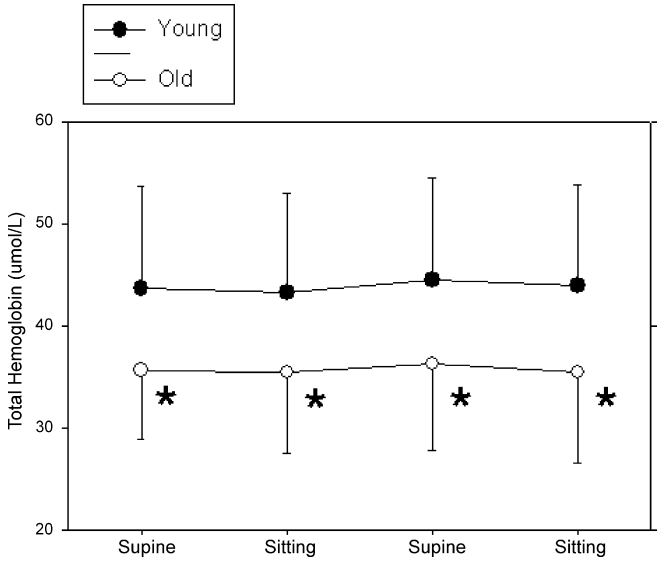

Fig. 4. Total hemoglobin in supine and sitting position in young and old subjects. Mean + S.D. $^{*}P < 0.05$ old compared to young. Data show that young and old values were significantly different but there were no significant changes with changes in position.

a decrease in MABP at the level of the brain and a significant decrease in OHb and an increase in HHb. On the other hand, it is not likely the changes in brain oxygenation with position were clinically significant. During these position changes, cerebral oxygen consumption and cerebral blood flow do not change (Krakow et al., 2000). The decrease in OHb is probably due to a decrease in arterial blood volume related to the 20% decrease in cerebral perfusion pressure. The concomitant increase in HHb represents an increase in cerebral venous volume, which maintained total hemoglobin and cerebral blood volume constant. These results indicate that small but significant shifts in OHb and HHb occur in conjunction with cerebral autoregulation, which maintain cerebral blood volume and intracranial pressure constant.

Even though the autoregulatory effects of sit up position likely represent a small shift from brain arterial to venous volume in healthy volunteers, these changes may be magnified in patients with cerebral pathology. Increased intracranial pressure related to brain tumors or attenuated autoregulation related to chronic cerebral ischemia may magnify or nullify shifts in cerebral hemodynamics. This may be of value to identify the nature and severity of cerebrovascular dysregulation that may occur in specific brain disease states. The ability to measure absolute OHb and HHb concentrations with FD-NIRS may provide valuable information in determining the nature of cerebral pathology.

Aging is one factor that may be related to loss of cerebral oxygen regulation. OHb is decreased as a function of age and this is related to an attenuated increase in OHb during hypercapnia (Gatto et al., in press). Other studies show that patients with compromised baseline OHb are at higher risk to develop brain hypoxia during modest decrease in blood pressure associated with anesthesia (Paisansathan et al., in press). These results suggest that decreased baseline OHb may be related to postural or anesthesia related brain oxygen desaturation that occurs with aging, and this may produce neuronal dysfunction (Casati et al., 2005). Although age was not a significant indicator in the development of brain oxygen desaturation in this study, reduced brain hemoglobin reserve may be a risk factor. On the other hand, the results of this study indicate that normal aging does not impair the ability to regulate brain oxygen during modest decreases in blood pressure.

One of the drawbacks with the technique employed was the limited cardiovascular information that we could get with the instrumentation. A real-time continuous non-invasive blood pressure status could give us valuable information on dynamic regulation of brain hemodynamics that may provide more information than steady state measures of brain hemoglobin and blood pressure measured here. This may help us understand the dynamic physiological mechanism behind this functional test. It is clear that continuous measures using FD-NIRS technology used here can provide this dynamic information. Future studies of this method should include similar dynamic measures of blood pressure to evaluate dynamic brain oxygen regulation.

It is possible that decreased blood hemoglobin concentration in the aged may produce a decrease in brain hemoglobin concentration. However, based on a report that there is no change in hematocrit in normal aging (Feher et al., 2007), we conclude that the decrease in brain total hemoglobin is due to a decrease in brain vascular blood volume rather than hematocrit.

In conclusion, these data show that baseline OHb and HHb decreased with normal aging (40–60 years) but brain oxygen saturation was similar compared to young subjects. A change in position from supine to sitting produced a significant decrease in blood pressure at the level of the brain and concomitant decreases in OHb and increases in HHb that were not different between the age groups. The brain regulatory changes in OHb and HHb were clinically insignificant, and they probably represent a shift from brain arterial to venous blood in order to maintain brain blood volume and intracranial pressure constant. Decreases in baseline OHb and HHb do not alter normal brain oxygen regulation but they may be a risk factor for clinically significant dysregulation that occurs in the elderly and in patients with cerebral pathology.

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