

Greater Variability of Cerebral Vascular Autoregulation in Traumatic Brain Injury During a Working Memory Task

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INTRODUCTION

- The objective of this study was to investigate the cerebral vascular autoregulation (CVA) process in adults with moderate to severe traumatic brain injuries (TBIs) or multiple sclerosis in comparison to healthy adults during the N-back task.
- Functional Near Infrared Spectroscopy (fNIRS; see Figure 1) was used to detect the levels of oxyhemoglobin (Hb_{oxy}), deoxyhemoglobin (Hb_{deoxy}), and total hemoglobin ($Hb_{total} = Hb_{oxy} + Hb_{deoxy}$).
- The N-back paradigm used here considers 4 levels of working memory cognitive load ("0-back," "1-back," "2-back," and "3-back"; see Figure 2).
- The relationship between the level of working memory load and concentrations and spatial distributions of Hb_{oxy} and Hb_{deoxy} was explored.
- A novel type of data analysis was used, based on simple relational operations applied to the Hb_{oxy} and Hb_{deoxy} levels, that correspond to different states in a CVA cycle (see Figure 3).

Figure 2

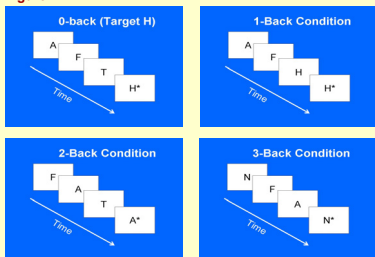


Figure 1



Hb State	State 1	State 2	State 3	State 4	State 5	State 6
Hb_{oxy}	-	-	-	+	+	+
Hb_{deoxy}	-	+	+	+	-	-
Hb_{total}	-	-	+	+	+	-

Figure 3

	Balanced	Uncompensated O ₂ deficit	Compensated O ₂ deficit	Balanced	Uncompensated O ₂ excess	Compensated O ₂ excess
State 1	+	-	-	+	-	-
State 2	-	+	-	-	-	-
State 3	-	-	+	-	-	-
State 4	-	-	-	+	-	-
State 5	-	-	-	-	+	-
State 6	-	-	-	-	-	+

METHODS

- Participants
 - Sub-groups
 - Healthy control (HC) subjects ($N_1 = 10$)
 - Traumatic brain injury (TBI) subjects ($N_2 = 6$)
 - Multiple sclerosis (MS) subjects ($N_3 = 4$)
 - Inclusion Criteria:
 - Between the ages of 18-55 years old.
 - No history of alcohol or drug abuse
 - No history of Psychiatric Disorder
 - Right Hand Dominant
 - No Neurological Disorder in the HC group
 - No other Neurological Disorder in the clinical groups.
- Behavioral task (N-Back test)
 - Consonant letters were presented every three seconds, auditorially, in 24-second epochs.
 - Four Conditions (0-back, 1-back, 2-back, 3-back).
 - Each condition presented (sequence randomized), 3 times.
- Apparatus
 - Multi-channel continuous wave near infrared imager (NIRx Medical Technologies).
 - 30 source and 30 detector optodes (900 channels).
 - Simultaneous dual-wavelength measurement with near infrared light (760nm and 830nm).
 - Optodes placed on forehead 10% above nasion in a 10 cm by 3 cm rectangle configuration (Figure 1).
- Data analysis
 - Optical data low-pass filtered and normalized to a resting-baseline mean value.
 - Images of ΔHb_{oxy} and ΔHb_{deoxy} concentrations computed by using a first-order perturbation algorithm.^{1,2}
 - $\Delta Hb_{oxy} = Hb_{oxy} - Hb_{oxy, baseline}$, $\Delta Hb_{deoxy} = Hb_{deoxy} - Hb_{deoxy, baseline}$.
 - Six vascular autoregulatory states are defined, as shown in Figure 3, according to the algebraic signs of ΔHb_{oxy} , ΔHb_{deoxy} , and their sum $\Delta Hb_{total} = \Delta Hb_{oxy} + \Delta Hb_{deoxy}$.
 - Each relational category reasonably corresponds to a different underlying state of oxygen supply/demand balance or imbalance.
- Time fraction analysis:
 - Autoregulatory state calculation (Figure 3) allows us to compute not only the state-dependent ΔHb_{oxy} and ΔHb_{deoxy} concentrations, but also:
 - The percentage of image pixels that are in each state, at any time frame.
 - The percentage of overall time that each pixel spends in any of the six states.

RESULTS

- Inspection of images of ΔHb_{oxy} vs. time reveals consistent, repeatable trends in the supply of oxygen to the prefrontal cortex during N-Back task runs (Figure 4).
- Direction of the trend is a function of task difficulty: Hb_{oxy} level declines during the least challenging task (0-Back), and increases most markedly during the most difficult (3-Back).
- Oppositely directed trend is seen in ΔHb_{deoxy} vs. time data (not shown).

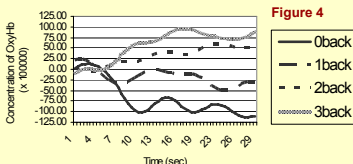
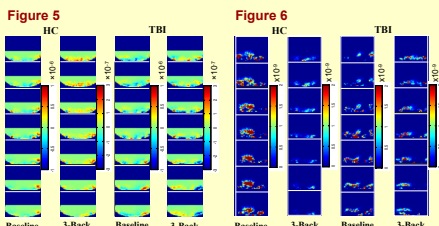


Figure 4



- Images of ΔHb_{oxy} show that there is spatial heterogeneity (i.e., image contrast) in the hemoglobin states, but not necessarily of a magnitude that facilitates interpretation (Figure 5). Likewise for ΔHb_{deoxy} images (not shown).
- Greater image contrast is seen in the spatial maps of only one CVA state's (i.e., state 5) contribution to the overall ΔHb_{oxy} concentration (Figure 6).

- Time fraction analysis:
 - Time intervals compared are for the subject at rest, and while performing the 3-Back task.
 - Spatial distributions of the six CVA state residence-time percentages (Figure 7):
 - One representative participant from each of the three groups.
 - All subjects show preponderance of states 4 and 5 (i.e., increased blood volume) while the subject performs 3-Back task.
 - Healthy control subject has a preponderance of voxels in state 1 (balanced) during resting baseline.
 - Other controls also show predominantly the balanced states (not shown), either primarily state 1, primarily state 4, or a mixture of both.
 - TBI subject has significant percentages of states 1 through 4.
 - MS subject has similar time-fraction spatial distributions for both the resting and 3-Back periods.
 - Percentage of time spent in each CVA state (Figure 8, Figure 9):
 - Group means and standard deviations, for each state and for baseline and 3-Back time intervals, are shown in Fig. 8.
 - Only states 5 and 6 (oxygen excess) show statistically significant inter-group differences.
 - Only HC group shows a significant difference between baseline and 3-Back intervals, for state 5.
 - Impact of performing the task is lower for the other groups.
 - Quantification of statistically significant differences summarized in Fig. 9.
- Co-registration of functional and anatomical images:
 - Volume used for image reconstruction was derived from a 3D structural MRI of an adult human head. Thus it is straightforward to overlay any optical image parameter onto the anatomy, without any need for a warping algorithm.
 - Image co-registration facilitates interpretation of optical feature information
 - Comparing the HC and TBI participants, it is seen that different regions of frontal cortex show increased ΔHb_{oxy} (i.e., union of states 5 and 6) while the 3-Back task is performed (Figure 10).

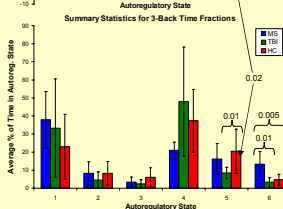
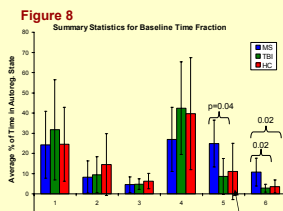
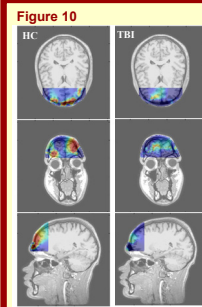
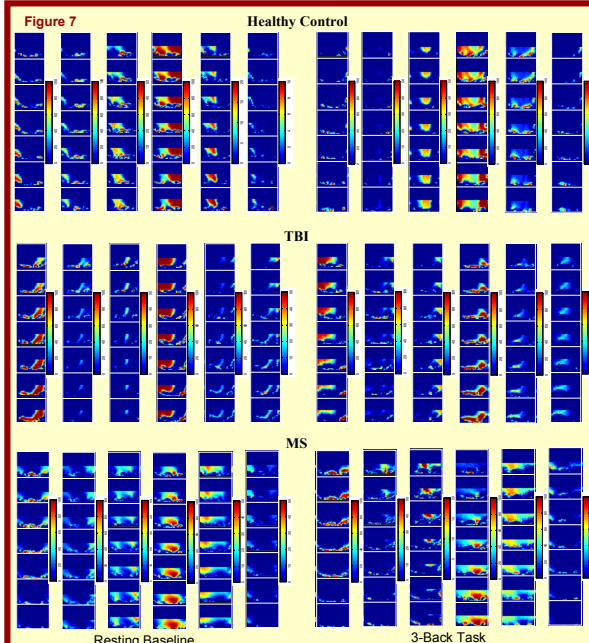
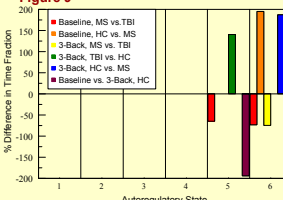


Figure 9



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CONCLUSIONS

- CVA state analysis, especially when residence-time percentages are considered, reveal statistically significant differences between all pairs of subject groups.
 - The noted differences are found only in the oxygen-excess component (states 5 and 6) of the overall hemoglobin signal
- Healthy control group also exhibits a significant task-induced change in average time fraction for state 5, and the other groups do not.
- States 5 and 6 constitute only a fraction of the integrated Hb_{oxy} response.
 - Consequently, the effects noted above are too small to show up as statistically significant differences in the integrated signal.
 - Only by resolving the latter into CVA states are the effects revealed.
- Phenomena noted here are consistent with known physiological manifestations of TBI and MS.

ACKNOWLEDGMENTS

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