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Cybersickness-related changes in brain hemodynamics: A pilot study comparing transcranial Doppler and near-infrared spectroscopy assessments during a virtual ride on a roller coaster

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ABSTRACT

Our aim was to assess cerebral blood flow changes during cybersickness. Transcranial Doppler (TCD) ultrasound and near infrared spectroscopy (NIRS) were used separately in two independent experiments. In both studies, a 15-min virtual roller coaster ride was used as a provocative visual stimulus. Subjective nausea ratings were obtained at 1 min intervals. The TCD study was performed in 14 healthy subjects (8 males and 6 females); in this study we also measured heart rate and arterial pressure. In a separate study a 52-channel NIRS device (Hitachi ETG-4000) was used to monitor activated brain regions by measuring oxy-hemoglobin (HbO_2) concentration in 9 healthy subjects (4 male, 5 females). The TCD study results showed a significant increase in systolic ($+3.8 \pm 1.8$ mm Hg) and diastolic ($+6.7 \pm 1.3$ mm Hg) pressure at the end of the virtual ride (maximum nausea) compared to baseline (no nausea). We also found that middle cerebral artery (MCA) and posterior cerebral artery (PCA) systolic flow velocity decreased significantly at the end of the ride when compared to baseline values. Likewise, the relative systolic and diastolic conductance in the MCA decreased significantly (-0.03 ± 0.02 cm $\times$ s^{-1} $\times$ mm Hg^{-1}, t, $p = 0.0058$ and -0.03 ± 0.01 cm $\times$ s^{-1} $\times$ mm Hg^{-1}, $p = 0.05$, respectively) at maximum nausea when compared to no nausea. Additionally, there was a significant decrease (-0.02 ± 0.01 cm $\times$ s^{-1} $\times$ mm Hg^{-1}, $p = 0.03$) in the relative systolic conductance in the PCA at the end of the ride. Analysis of the NIRS results showed a significant increase in HbO_2 concentration in 15/52 channels in parieto-temporal regions of both hemispheres in participants who experienced motion sickness symptoms during the experiment. This increase in HbO_2 concentration correlated with increasing nausea and motion sickness symptoms. We conclude that cybersickness causes complex changes in cerebral blood flow, with an increase in perfusion in some cortical regions, but with a decrease of global cerebral perfusion.

1. Introduction

Motion sickness (MS) is considered to be a general feeling of discomfort in ordinary routine life but also a major operational hazard for pilots and space agencies. It is currently well accepted that conflicting signals from the spatial orientation senses – visual, vestibular and proprioceptive leads to the development of motion sickness [1]. This sensory conflict which was first described by Irwin [2] and later explained by James [3] in the early 19th century can be a result of single sensory system mismatch such as canal-otolith interaction during Coriolis cross-coupling, or between two or more sensory systems such as visual/vestibular/proprioceptive interference [4]. These early findings suggest that the vestibular system plays a critical role in the pathogenesis of motion sickness [2]. Other research has concluded that subjects with bilateral vestibular deficit are immune to motion sickness [3,5]; hence the vestibular system is indispensable in evolution of motion sickness. One potential cause of neuronal dysfunction responsible for motion sickness is alteration in regional cerebral blood supply; thus a close investigation of vestibular inputs in the regulation of cerebral blood flow is essential for better understanding the underlying mechanisms associated with motion sickness.

A recent study has found that people who suffer from motion sickness during parabolic flight are more likely to have orthostatic intolerance and increased cerebrovascular resistance after flight [6].

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Serrador et al. reported an increase in cerebrovascular resistance and decreases in cerebral flow velocity minutes before any motion sickness symptom was experienced in an experiment where subjects were rotated in a human centrifuge [7]. A study by Heckmann [8] found that caloric vestibular stimulation of the semicircular canals increases blood flow in the basilar artery. A similar study utilizing caloric stimulation reported an increase in the middle cerebral artery (MCA) blood flow while a significant decrease was seen in the flow in the posterior cerebral artery (PCA). These researches suggest that cerebral blood flow (CBF) changes with increasing nausea and motion sickness.

There are several methods to assess CBF; in recent studies a link between the neural metabolism and perfusion in the brain has been demonstrated using devices such as single photon emission computed tomography [9], positron emission tomography [10] and the xenon-133 inhalation technique [11]. Transcranial Doppler (TCD) ultrasound is another method that has been widely used for monitoring cerebral perfusion in stroke [12–14] and trauma [13], for screening brain lesions [15,16], and for other studies focused on haemodynamic changes in the brain during diverse tasks (e.g. cycling, reading, writing or visual stimulation [17,18]). Another technique which is extensively used in observing CBF is near infrared spectroscopy (NIRS). This device uses the basic concept of emission of near-infrared light (NIR) at the surface of the head and detection of reflected light at a distance of a several centimeters to determine hemoglobin concentration in the cerebral cortex. Due to the non-invasive nature and simple application of the NIRS device, this tool has been utilized in various aspects of brain imaging. Some studies have used this tool to monitor brain injury and ischemic regions in the brain looking at regional cerebral blood flow in brain-injured patients [19], others have employed this tool to screen brain activation regions while performing certain mental [20,21] and physical [22,23] tasks. NIRS has been used to closely monitor brain blood flow in other neurogenic diseases such as dementia, Alzheimer's [24], schizophrenia [25] and infant brain studies [26,27]. Several previous studies have shown close correspondence between fMRI and NIRS signals with significant spatial and temporal correlations [28] [29].

However, the inherent limitation of these screening methods when used in conjunction with physical motion sickness provocation – motion artifacts and other major technical restrictions- have constrained the application of these technologies in assessing CBF during motion sickness. To overcome this limitation, in this study we have adopted a standardized virtual reality (VR) provocation method to elicit motion sickness. Although motion sickness is characterized by a physical sensation of motion, exposure to VR provokes similar symptoms to motion sickness. This is caused by the feeling of movement in a virtual environment while being stationary. Cybersickness is relatively common, and most people feel some level of sickness during a provocative VR experience. A study on cybersickness symptoms discovered that 80% of subjects experienced symptoms of cybersickness in the first 10 min of their VR exposure [30]. In our previous studies where we used a simulated ride in a rollercoaster, with vigorous linear and angular accelerations, we found that all participants developed some level of nausea and/or other motion sickness symptoms during this provocative exposure [31,32]. Some of the most common symptoms related to cybersickness were nausea, dizziness and disorientation that are similar to "classical" motion sickness symptoms.

The objective of this study was to examine temporal changes in cerebral blood flow in subjects who experience nausea during visually induced motion sickness. TCD and NIRS were used to study the changes in global and local CBF, respectively. To our knowledge these techniques have not been used to investigate brain hemodynamics during cybersickness. We hypothesized that blood flow would decrease in subjects who experience cybersickness symptoms. We also expected to see an increase in Posterior Cerebral Artery (PCA) blood flow due to activation of the visual cortex in response to visual provocation. We also anticipated that NIRS results would be consistent with TCD data, and will demonstrate a decrease in cortical blood flow in subjects who develop motion sickness.

2. Methods

2.1. Participants

This study was conducted in two groups of young healthy subject with the approval of the Newcastle University Humans Research Ethics Committee. The exclusion criteria were history of vertigo, vestibular dysfunction or neurological disorders as well as ortostatic intolerance. All subjects verbally confirmed that they are healthy and not using any medication. Cerebral blood flow velocity was measured by trans-cranial Doppler (TCD) ultrasound in 14 volunteers (8 males and 6 females, average age 28 ± 7.0 y.o. range 19–48 y.o.). Cortical blood flow was measured by functional near-infrared spectroscopy (fNIRS) in another group of 9 volunteers (4 male, 5 female, average age 33.3 ± 5.4 y.o., range 26–42 y.o.)). All participants were exposed to visual provocations leading to motion sickness (visually-induced motion sickness, VIMS). All participants gave informed written consent and completed a Motion Sickness Susceptibility Questionnaire [33] before the experiment started.

2.2. Cerebral blood flow recordings

In the TCD monitoring experiment, after fitting a head-mounted VR display (Oculus Rift DK2, Oculus VR, USA), the 2 MHz TCD probes were placed bilaterally on the head and adjusted to obtain optimal flow signals from the MCA on one side and from the PCA on another side. The probes were connected to the TCD ultrasound device (DWL, Germany) that has a 100 Hz sampling rate.

The other group of participants were fitted with a skullcap containing 52-channel fiberoptic probes. We used an optical topography system (ETG-4000, Hitachi Medical Corporation, Japan) for the NIRS measurements. Designed for comfort and flexibility, the skullcap holds the sensors and detectors in place and secures the probes in precise locations around the subjects' head. The light source optical fiber tips are "sprung", ensuring continual scalp contact for accurate readings. This device uses continuous laser diodes with two wavelengths, 695 and 830 nm, as light sources; the transmitted light signal is sampled every 100 ms.

2.3. Experimental setup, data collection and analysis

Before virtual ride commencement, a baseline 5-min recording was performed. During this period, a neutral static image was presented on the rift display. Subsequently, a simulated Helix rollercoaster ride (Helix, Archivision, Netherlands) was activated. The ride lasted for 15 min or until a subject decided to stop due to discomfort, whichever occurred first. During the experiment, subjective nausea ratings were assessed every minute using 10-point scale from zero (no nausea) to nine (just about to vomit). All recordings continued for 5 min after the ride termination. In the TCD study we also assessed heart rate (HR), systolic (SAP) and diastolic (DAP) arterial pressure at the beginning and then every 2 min in the experiment using a cardiovascular profiling instrument PulseWave CR2000 (Hypertension Diagnosis, USA).

In the TCD experiment, systolic and diastolic TCD data were transferred into the Lab Chart 8.0 software (AD Instruments, Sydney, Australia) for analysis. As all participants terminated the ride at different times from the onset, overall averaging for their flow traces was not possible; thus, for comparison we selected two data points: "Baseline" (an average of the 2nd and 4th min of control period) and "End Ride" data from the last minute of the ride. Relative conductances of the MCA (C_{MCA}) and PCA (C_{PCA}) were computed according to the formula: $C_{MCA} = V_{MCA}/AP$ and $C_{PCA} = V_{PCA}/AP$, where V represents blood flow velocity in cm/s. Flow data values for these calculations