Reseach Article *10.2478/gsr-2016-0007*

Monitoring Tissue Oxygen Saturation in Microgravity on Parabolic Flights

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ABSTRACT

Future spacecraft and crew habitats are anticipated to use a moderately hypobaric and hypoxic cabin atmosphere to reduce the risk of decompression sickness associated with extravehicular activity. This has raised concerns about potential hypoxia-mediated adverse effects on astronauts. Noninvasive technology for measuring tissue oxygen saturation (StO_2) has been developed for clinical use and may be helpful in monitoring oxygenation during spaceflight. We conducted a technical evaluation of a handheld StO_2 monitor during a series of parabolic flights, and then undertook a preliminary analysis of the data obtained during the flights from six individuals. The StO_2 monitor operated normally in all gravity conditions. There was considerable variability in StO_2 between and within individuals. Overall, transition to microgravity was associated with a small decrease in StO_2 of 1.1±0.3%. This evaluation has established the basic function of this technology in microgravity and demonstrates the potential for exploring its use in space.

Key words: StO_2; Hypoxia; Hypobaric Cabin; Weightlessness; Zero *g*; Suborbital Spaceflight

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INTRODUCTION

Near-infrared spectroscopy provides a non-invasive means of measuring tissue oxygenation, exploiting the characteristic light absorption properties of oxygenated and deoxygenated hemoglobin in the near-infrared wavelength range to determine tissue oxygen saturation (StO_2). Monitors typically measure oxygen saturation across a muscle tissue field containing both arterial and venous blood, such as the thenar eminence of the hand. In clinical practice, StO_2 has mainly been developed as an indicator of peripheral tissue perfusion in critically ill patients, as StO_2 is lowered when perfusion is reduced in association with, for example, major hemorrhage or sepsis (Duret et al., 2015; Neto et al., 2014). A fall in StO_2 can also be caused by a reduction in oxygen delivery to the tissues when blood oxygen content is reduced, such as at high altitude or when gas exchange is impaired in the lungs (Martin et al., 2009; Sandfeld et al., 2013).

Due to the shape of the hemoglobin-oxygen dissociation curve, a moderate fall in arterial

partial pressure of oxygen from normal levels would be expected to cause a greater reduction in StO_2 than in arterial oxygen saturation measured by pulse oximetry (SpO_2), and may therefore provide a means of detecting more subtle changes in oxygenation. A handheld StO_2 monitor has recently been developed for portable use, introducing the potential to measure StO_2 noninvasively in challenging environments such as space. StO_2 monitoring could be investigated for its utility in various clinical scenarios in space, and could also be explored as a means of monitoring potential effects of the spaceflight environment on oxygenation.

In the future this could include the effects of moderately reduced cabin pressure with consequently reduced oxygen levels, which NASA and others have proposed for the design of future spacecraft and crew habitats (Bacal et al., 2008; Norcross et al., 2013; Scheuring et al., 2008). Such an atmosphere would expose astronauts to a mildly hypoxic environment comparable to a commercial aircraft cabin, which is known to stimulate classic physiological responses, such as ventilatory acclimatisation (Fatemian et al., 2001), erythropoietin secretion (Gunga et al., 1996), and hypoxic pulmonary vasoconstriction (Smith et al., 2013; Smith et al., 2012; Turner et al., 2015). This design approach would have the benefit of making extravehicular activity safer and easier with respect to the risk of decompression sickness and associated denitrogenation protocols, as well as other potential advantages including reduced risk of fire, decreased structural strength and weight requirements, reduced requirement for stored or generated oxygen, and even a speculative effect as a countermeasure against spaceflight anemia (Bacal et al., 2008; Buckey, 2006; Scheuring et al., 2008). However, the wider health and performance implications of this environment require careful consideration, including the scope for physiological interaction between hypoxia, hypobaria, and hypogravity, which has yet to be investigated (Norcross et al., 2013). Measurements of StO_2 could be a useful adjunct in this setting, and we aimed to evaluate portable StO_2 monitoring technology with a view to future use in space using parabolic aircraft flights to assess its function in microgravity.

MATERIALS AND METHODS

Personnel

Six members of the research team participated in the study, five men and one woman (mean [± SD] age 33±4 yr). All personnel were in good health and provided written informed consent. The study was approved by the Oxford Tropical Research Ethics Committee and by the NASA Institutional Review Board, and was conducted in accordance with the Declaration of Helsinki.

Equipment

The technology under evaluation was the InSpectra StO_2 Spot Check (model 300) (Hutchinson Technology Inc., Hutchinson, MN, USA). This is a commercial off-the-shelf monitor that weighs 400 g and is powered by a rechargeable battery. The reusable sensor is designed to be clipped to the thenar eminence of the hand, and thenar StO_2 was the main measure of interest in this study. The sensor has also been used on the medial plantar surface of the foot, although this may be less reliable (Van Haren et al., 2013). Real-time StO_2 is measured continuously and the display value is updated every two seconds.

Protocol

This work was undertaken at Ellington Field, Houston, Texas, as part of a parabolic flight campaign through the NASA Flight Opportunities Program. There were four 0 *g* parabolic flights on a modified Boeing 727 aircraft, with three personnel on each flight, and all flights followed the same profile. There were 40 parabolic trajectories per flight, with a short period of level flight in between each bracket of 10 parabolas. Each parabola provided approximately 17 seconds of microgravity during freefall, when the gravitoinertial acceleration was 0 *g*, in between periods of modest hypergravity of up to approximately 1.8 *g* (Karmali and Shelhamer, 2008). The cabin pressure altitude was maintained constant at 5,600 ft (1,700 m) throughout the parabolas. On a small number of parabolas the *g* profile or cabin pressure altitude varied from these values, such as with early pullout from the final parabola of a bracket, and these were excluded from the evaluation.

Measurements

Study personnel formally evaluated the monitor technology and performed StO_2 measurements on each other, and pulse oximetry was used to measure SpO_2 and heart rate (WristOx$_2$ 3150, Nonin Medical Inc., Plymouth, MN, USA). On each flight, three 10-parabola brackets were dedicated to recording measurements from each of the three study personnel in turn, with one individual as the test subject and the other two recording measurements during each bracket. Measurements were made in this way on 120 parabolas across the four flights. The fourth 10-parabola bracket on each flight was used for technical evaluation of other aspects of the monitor's function, including powering on/off, self-test function, and ease of use while free-floating. When performing measurements, StO_2 monitors and pulse oximeters were attached continuously at the hand and foot over the 10-parabola bracket, and each variable was recorded simultaneously at the end of each microgravity and hypergravity phase. Hands and feet were kept warm to avoid possible effects of peripheral vasoconstriction. Parabolic measurements were made in the supine position, which during microgravity meant floating horizontally above the aircraft floor, and were compared with supine measurements at 1 *g* performed pre-flight and in-flight (during level flight prior to the parabolas).

Statistical Analysis

Although primarily a technical evaluation, unique StO_2 data were obtained in the course of this evaluation, and in order to take full advantage of this opportunity we conducted a preliminary analysis of the effect of dynamic transition from ~1.8 *g* to 0 *g* using Student's two-tailed *t*-test for paired samples. Measurements from all four flights were used in the analysis. Values of $P<0.05$ were considered statistically significant, and data are reported as mean ± SEM.

RESULTS

The StO_2 monitor technology functioned normally in all gravity conditions, including powering on/off and performing its self-test function. The monitor was generally easy to use in microgravity, and this was aided by tethering it to the body. The 1-meter cable length was appropriate for use in weightless conditions and the visual display was easy to read. The monitor provided thenar StO_2 measurements appropriately during parabolas, which are shown in Figure 1. For each person, StO_2 is reported from an average of 17 parabolas, and there was considerable variability between and within individuals (Figure 1).

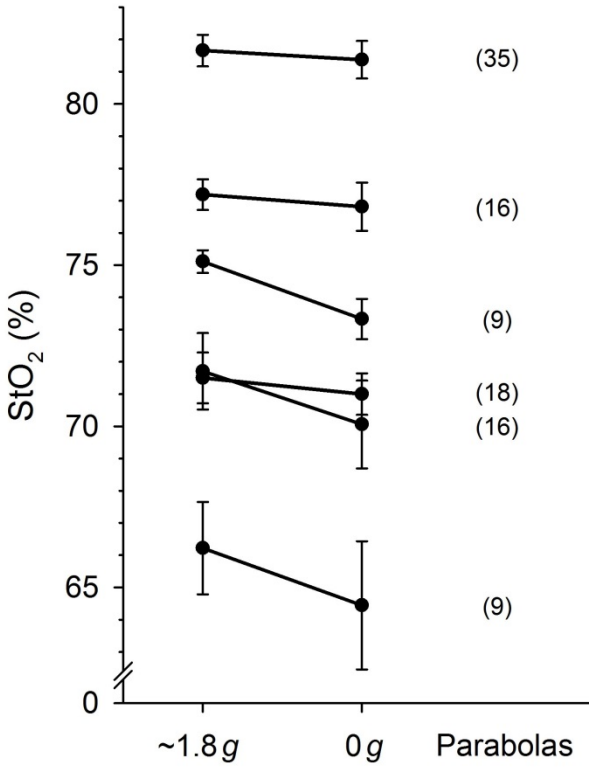

Figure 1. Tissue oxygen saturation (StO_2) in individuals during parabolas. Thenar StO_2 is shown for each of the six members of the research team. The number of parabolas on which each individual's measurements were obtained is also shown. Data are mean ± SEM.

Baseline arterial oxygen saturation measured pre-flight was normal (SpO_2 97±0.5%). Baseline StO_2 (80±2%) was also within the wide normal range of approximately 70-85% that has been reported in the literature. Due to the mildly hypoxic cabin pressure altitude, arterial oxygenation was lowered in-flight (SpO_2 93±0.7%; unchanged with microgravity [P=0.3]), and thenar StO_2 was likewise affected by cabin pressure in-flight (74±3%) and is depicted in Figure 2. Transition to microgravity was associated with a small decrease in StO_2 of

1.1±0.3% (P=0.017), as shown in Figure 2. The StO_2 monitor is designed to be used on the hand and is not intended for use on the foot, and we found that StO_2 values at the foot were well below the physiological range both in 1 *g* (55±5% pre-flight) and in flight (50±3% during both ~1.8 *g* and 0 *g*). Heart rate did not change significantly during the parabolas (63±7 bpm; P=0.14).

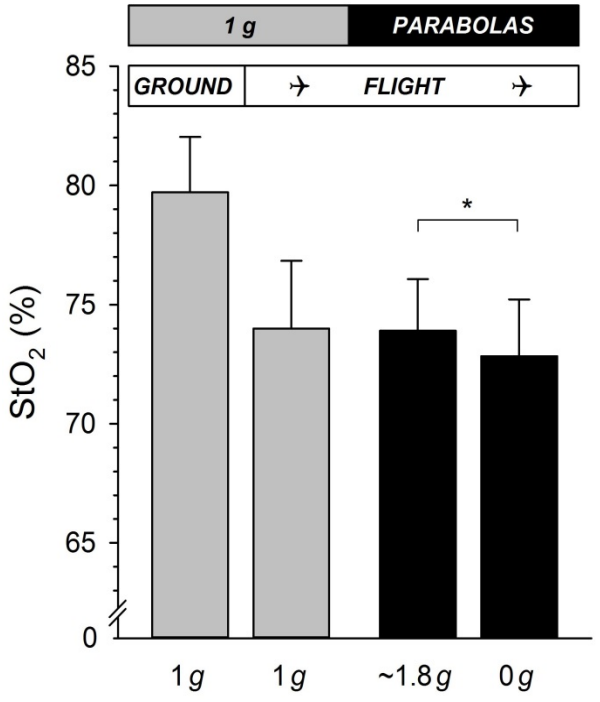

Figure 2. Tissue oxygen saturation (StO_2) during parabolic flights. Thenar StO_2 is shown (mean ± SEM). In-flight measurements were made at a constant cabin pressure altitude of 5,600 ft (1,700 m). Pre-flight and in-flight data recorded at 1 *g* are shown in grey, and microgravity/hypergravity data during parabolas are shown in black. The asterisk denotes a statistically significant change in StO_2 upon transition from hypergravity to microgravity.

DISCUSSION

This evaluation has established that the InSpectra StO_2 monitoring technology operates normally in microgravity. However we observed considerable inter-individual and intra-individual variability in StO_2 values, which is consistent with previous terrestrial studies and is one reason why StO_2 monitoring remains largely a research tool and has yet to be taken up widely in mainstream clinical practice (Lipcsey et al., 2012; Van Haren et al., 2013). It has been suggested that, in addition to possible limitations of the technology itself, various physiological factors could contribute to this variability, including tissue thickness and composition, fluid status, blood viscosity, and temperature-related changes in perfusion. Age did not vary greatly and is unlikely to have influenced our findings, although we note that long-duration astronauts are typically at least a decade older than this study's participants. Our findings do support using the device at the intended thenar site rather than the foot, where measurements were unreliable.

In the course of assessing this technology we obtained data on StO_2 during changing gravity conditions. This data is preliminary in nature and the usual limitations of parabolic flights apply, including a small sample size, short exposure times, and the potential for physiological effects of one phase (microgravity or hypergravity) to carry over into the subsequent alternate phase. Notwithstanding these limitations and the background variability, across multiple repeat measurements a small fall in StO_2 was observed in each individual on transition to microgravity. Such a small decrement has no physiological significance in itself, and an artifactual explanation cannot be excluded, but it is interesting to speculate whether this fall might represent the beginning of a larger effect of microgravity on tissue oxygenation that would have continued to develop had the weightless state been maintained beyond 17 seconds.

Although microgravity does not cause major impairment of gas exchange in the lungs (Prisk, 2014), limited evidence from a series of measurements on the Mir space station suggests that tissue oxygenation may nevertheless be somewhat decreased during spaceflight, perhaps due to slightly altered ventilation/perfusion matching in the lungs (Baranov, 2011; West, 2001). It is unfortunate that standard arterial blood gas analyses have not yet been performed in space, as these would be very helpful in interpreting isolated findings such as these, particularly in the light of the many 'hypoxia-mediated physiologic concerns' NASA has identified that could conceivably arise from or be worsened by a moderately hypoxic atmosphere in space (Norcross et al., 2013). These concerns include: visual impairment/intracranial pressure syndrome, sensorimotor performance deficits,

neurocognitive impairment, sleep disturbance, acute mountain sickness, diminished exercise capacity and cardiovascular performance, immunosuppression, oxidative stress and damage, nutritional deficiencies, and increased bone resorption with acceleration of bone loss and higher risk of renal stones (Norcross et al., 2013). The true potential for any of these adverse factors to impact on future space missions is currently unknown, but would presumably be greater if the effects of a hypoxic cabin environment were superimposed on any underlying impairment of tissue oxygenation inherently associated with microgravity.

Although the use of a hypobaric exploration-class atmosphere of this kind is many years away, the acute combination of microgravity and mild hypoxia is likely to be experienced much sooner with the anticipated commencement of commercial suborbital spaceflights. For suborbital operators utilizing an airline-style cabin pressure, several minutes of microgravity will be superimposed on mild background hypoxia, and for spaceflight participants these factors will together interact with any influence of age, smoking, or pre-existing disease, and contribute to in-flight hypoxemia (as has been observed on a parabolic flight (Mackenzie et al., 2007)). In addition to the period of weightlessness, suborbital spaceflights will also include significant high-*g* exposures which are in fact more likely to cause hypoxemia, and arterial oxygen desaturation has been demonstrated during normoxic centrifuge studies simulating anticipated suborbital acceleration profiles (Blue et al., 2014; Blue et al., 2012). Of course the true acceleration-weightlessness-acceleration profile of suborbital spaceflight cannot be simulated, and in-flight studies will be required to characterize the associated physiology when suborbital operations commence.

In summary, we have established that StO_2 monitoring is possible in microgravity and demonstrated the potential for exploring the use of this technology in space. In theory, astronauts could use this technology to detect a degree of tissue hypoxia that may not otherwise be apparent during future spaceflight operations, although the noise from background variability would need to be overcome, possibly with multiple repeat measurements. This evaluation has highlighted our incomplete understanding of the physiological interaction between microgravity and hypoxia, and further research into the effects of changing gravity conditions on oxygenation is warranted.

ACKNOWLEDGEMENTS

This work was supported by the NASA Flight Opportunities Program and the Medical Research Fund of the University of Oxford. We thank Hutchinson Technology Inc. for loaning additional portable StO_2 monitors for use in this study. The funding sources had no role in the design and conduct of the study, in the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

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