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Experimental paper

Hypoxia and hypercapnia effects on cerebral oxygen saturation in avalanche burial: A pilot human experimental study

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Abstract

Background: A sufficient supply of oxygen is crucial to avoid hypoxic cardiac arrest and brain damage within 30 min in completely-buried avalanche victims. Snow density influences levels of hypoxia and hypercapnia. The goal of this study was to investigate the effects of hypoxia and hypercapnia on cerebral oxygenation (ScO_2) in humans breathing into an artificial air pocket.

Methods: Each subject breathed into a closed system (air-tight face mask – plastic tube – snow air-pocket of 4 L) up to 30 min. Each subject performed three tests in different snow densities. ScO_2 was measured by a near-infrared spectroscopy (NIRS) device. Measurements included peripheral oxygen saturation (SpO_2), end-tidal carbon dioxide ($ETCO_2$), air pocket gases and blood gases. Snow density was assessed via standard methods and micro-computed tomography. Based on predetermined criteria, tests were classified based on whether they were terminated before 30 min and the reason for termination. The categories were: completed tests (30 min), tests terminated before 30 min when SpO_2 dropped to $\leq$75% and tests that were terminated before 30 min by requests of the subjects. General linear models were used to compare termination groups for changes in ScO_2, $ETCO_2$, SpO_2 and air pocket gases, and a multivariate analysis was used to detect factor independent effects on ScO_2.

Results: ScO_2 was decreased in the group in which the tests were terminated for $SpO_2 \leq 75\%$ caused by a decrease in oxygen supply in high snow densities. In the completed tests, an increase in ScO_2 occurred despite decreased oxygen supply and decreased carbon dioxide removal.

Conclusions: Our data show that ScO_2 determined by NIRS was not always impaired in humans breathing into an artificial air pocket despite decreased oxygen supply and decreased carbon dioxide removal. This may indicate that in medium to low snow densities brain oxygenation can be sufficient, which may reflect the initial stage of the triple H (hypothermia, hypoxia, and hypercapnia) syndrome. In high snow densities, ScO_2 showed a significant decrease caused by a critical decrease in oxygen supply. This could lead to a higher risk of hypoxic cardiac arrest and brain damage.

Keywords: Avalanche, Hypoxia, Hypercapnia, Cardiac arrest, Cerebral oxygenation, Near-infrared spectroscopy

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Introduction

Survival of completely buried avalanche victims (i.e. head and chest below the snow) decreases with increasing burial time[1,2] and depends on whether breathing is possible or not. Several studies have shown that breathing in avalanche debris is possible in the presence of a patent airway with or without an air pocket (i.e. any space in front of mouth and nose).[3–6] Yet, the absence of an air pocket may increase the likelihood of asphyxia due to rapidly emerging hypoxia and hypercapnia.[4] About two-thirds of completely buried avalanche victims die within 30 min from cardiac arrest associated with hypoxia and hypercapnia. Breathing into an air pocket allows longer survival, as the higher oxygen availability slows oxygen desaturation.[5] Increased porosity of the snow surrounding the air pocket seems to favour oxygen (O_2) diffusion into and carbon dioxide (CO_2) out of the air pocket, decelerating the development of hypoxia and hypercapnia.[3] When oxygen supply and carbon dioxide removal are sufficient and burial time exceeds approximately 30 min, completely-buried avalanche victims are likely to develop accidental hypothermia (core temperature $<35\,^{\circ}C$) in the so-called triple H (hypothermia, hypoxia, and hypercapnia) syndrome.[5,7]

A sufficient supply of oxygen is crucial to avoid hypoxic brain damage. Monitoring cerebral oxygenation (ScO_2) by noninvasive near-infrared spectroscopy (NIRS) allows the continuous assessment of oxygenated haemoglobin concentration in a defined volume of cortical and subcortical brain tissue.[8] ScO_2 measurements are sensitive to changes in both arterial oxygen and carbon dioxide blood content and in cerebral blood flow (CBF).[9,10] In an avalanche burial in which hypoxaemia and hypercapnia may occur prior to hypothermia, NIRS could provide valuable information on a decreased in ScO_2 caused by these factors. To date, no data related to ScO_2 in avalanche victims have been reported.

The goal of this study was to investigate the effects of hypoxia and hypercapnia on cerebral oxygen saturation in humans breathing into artificial air pocket for up to 30 min. The goal of the study could only be achieved using simulated burials. We measured the contributions of the reason for interrupting the test, snow density, end-tidal carbon dioxide ($ETCO_2$), peripheral oxygen saturation (SpO_2), and O_2 and CO_2 concentrations in the air pockets on changes in cerebral oxygenation.

Materials and methods

The Institutional Review Board of the General Hospital of Bolzano (No. 0147248) approved the experimental design. We conducted the study in agreement with the World Medical Association Declaration of Helsinki and relevant guidelines and regulations. All subjects gave written informed consent before enrollment in the study. All tests were performed in the Braies valley, Bolzano, Italy (elevation 1499 m).

Subjects

Twelve healthy Caucasians were consecutively recruited within winter recreationists and mountain rescue providers. Subjects of both sexes, with age $\geq$18 years old and classified according to the American Society of Anesthesiologists as ASA class I were considered eligible.

Experimental methods

The subjects performed three tests, each separated by one month, i.e. January (test session 1), February (test session 2) and March (test session 3). Each test consisted of breathing into an artificial air pocket through a tube as outlined in detail below. Before each test a snow pile with a vertical wall mimicking an avalanche deposit was prepared.[3] The snow was shoveled down a slope where it was piled against a wooden wall. After snow sintering and wooden-wall removal, cylindrical air pockets of 4 L in volume were cut out of the snow wall. The pockets were sealed with a well-fitted, custom-made metal lid to ensure a closed breathing circuit. After instrumentation and before the test, the subjects rested in a sitting position for approximately 30 min (outside of the snow, and protected from the cold with blankets, warm clothes and gloves). Subsequently, an oro-nasal face mask (V2 Series Reusable Mask, Hans Rudolph inc., Shawnee, KS) with a dead space of 99 mL was fitted without leaking. After an additional 5 min (baseline measurement) the mask was connected to the artificial air pocket by a 20 cm long flexible plastic tube with a diameter of 20 mm (dead space 60 mL).

The test duration was scheduled to be 30 min. Tests were terminated if one or more of the following criteria were met: $SpO_2 \leq 75\%$; fractional inspired $CO_2 > 8\%$ (hypercapnia); or the subject asked to terminate the test because of symptoms such as dyspnoea, dizziness or headache). After test termination, the tube was disconnected from the air pocket and data collection continued for an additional 2.5 min.

Measurements

Clinical parameters

Parameters that we measured non-invasively and continuously were mean arterial pressure (MAP), heart rate (HR) and SpO_2 (Monitor HeartStart MRx™, Philips Medical Systems, Andover, MA); respiratory rate (RR), minute ventilation (VE) and tidal volume (VT) (Oxycon™ mobile device, CareFusion Germany 234 GmbH, Hoechberg, Germany); main stream $ETCO_2$ (EMMA™Mainstream Capnometer, Masimo, Milano, Italy) and bilateral ScO_2 (Nonin SenSmart Model X-100 Universal Oximetry System™, Burke & Burke S.p.A. Assago, Italy). NIRS sensors were placed bilaterally and high on the forehead in order to avoid any influences from the frontal or sagittal sinuses on the NIRS signal. Blood gases were measured from mixed capillary blood (ABL90 Flex™, Radiometer, Copenhagen, Denmark) temperature corrected to 37 °C at the beginning of the test, after 5 and 15 min, and at completion or early termination of the test when the tube was still connected to the air pocket.

Air pocket parameters

The fractional O_2 and CO_2 concentrations in the air pocket (O_2 pocket and CO_2 pocket) were recorded continuously (X-AM 7000, Dräger, Vienna, Austria).

Snow parameters

Snow density was measured with three different methods. First, snow density was determined by weighing a pre-defined snow volume of the air pocket (i.e., bulk density). Second, snow density was determined by weighing snow samples randomly taken from the sidewall of the cavity (i.e., cutter density).[11] Third, snow density was determined by small samples scanned by micro-computed tomography (μCT).[3,12]

The bulk density, the mean cutter density and the mean μCT density were averaged.

Statistical analysis

The data are available from the corresponding author upon reasonable request. Based on predetermined criteria, tests were classified based on whether they were terminated before 30 min and the reason for termination. The categories were: completed tests (30 min), tests terminated before 30 min when SpO_2 dropped to ≤75% and tests that were terminated before 30 min by requests of the subjects. General linear models, with the subject as the random factor, were used to compare termination groups for changes of ScO_2, $ETCO_2$, SpO_2, air pocket O_2 and air pocket CO_2 at three different time points by means of ANOVA. For each termination group the following statistical analyses were carried out: (1) a correlation analysis by means of a correlation coefficient for repeated observations [13] to detect whether during the test phase changes over time of ScO_2 were correlated with changes in $ETCO_2$, SpO_2, air pocket O_2 and air pocket CO_2; (2) a multivariable analysis using a linear mixed model (LMM) to detect whether $ETCO_2$, SpO_2, air pocket O_2, air pocket CO_2, snow density and time had an independent effect on ScO_2 during the test phase; (3) a comparison between parameter values at start and at 2.5 min post-test by means of paired samples *t*-tests. The Holm-Bonferroni method was used to correct *p*-values for multiple comparisons. To evaluate agreement between the two sensors of the NIRS signal we calculated intraclass correlation coefficients (ICCs) based on a mean-rating, absolute agreement, 2-way absolute effects model. The mean of the two sensors was considered to be the value for ScO_2. Parameters were visually checked for normality by means of normal probability plots. SPSS version 25 statistical

Table 1 – Cerebral and peripheral oxygenation, respiratory-gas and ventilatory parameters, blood gases values, and mean arterial pressure at different timepoints per termination group.

Termination group	Parameter	Start	5 min	Stop	2.5 min post	*p*-Value for start*vs.* 2.5 min stop[b]
Completed tests (n = 18)	ScO_2 (%)	69 ± 5.3	71 ± 5.2	74 ± 4.0	73 ± 6.5	0.028
	SpO_2 (%)	98 ± 0.9	94 ± 2.0	92 ± 5.5	98 ± 3.1	1.000
	$ETCO_2$ (mmHg)	31 ± 3.6	36 ± 3.9	41 ± 11.6	30 ± 5.8	0.932
	PcO_2 (mmHg)	63 ± 6.4	58 ± 5.1	56 ± 4.9	–	–
	$PcCO_2$ (mmHg)	36 ± 2.5	40 ± 2.1	45 ± 4.4	–	–
	pH	7.43 ± 0.02	7.41 ± 0.02	7.37 ± 0.04	–	–
	Air pocket O_2 (%)	20 ± 0.4	13 ± 1.2	12 ± 1.7	21[a]	<0.001
	Air pocket CO_2 (%)	0 ± 0.3	4 ± 0.4	5 ± 0.5	0[a]	<0.001
	RR (rpm)	15 ± 4.5	17 ± 6.1	24 ± 7.5	16 ± 8.6	1.000
	VT (l)	1 ± 0.6	2 ± 0.8	3 ± 0.7	1 ± 0.6	0.387
	VE (l/min)	13 ± 3.9	26 ± 11.6	55 ± 19.9	19 ± 11.5	0.602
	MAP (mmHg)	107 ± 9.8	111 ± 10.6	121 ± 17.8	111 ± 11.3	0.293
Termination before 30 min by request (n = 5)	ScO_2 (%)	68 ± 5.3	73 ± 4.1	69 ± 1.9	74 ± 10.2	1.000
	SpO_2 (%)	98 ± 1.1	92 ± 1.1	79 ± 3.2	100 ± 0.4	0.129
	$ETCO_2$ (mmHg)	32 ± 2.6	38 ± 4.1	62 ± 6.9	29 ± 7.3	1.000
	PcO_2 (mmHg)	64 ± 8.7	58 ± 7.6	50 ± 4.3	–	–
	$PcCO_2$ (mmHg)	37 ± 0.9	42 ± 3.1	50 ± 4.7	–	–
	pH	7.43 ± 0.03	7.39 ± 0.01	7.33 ± 0.02	–	–
	Air pocket O_2 (%)	20 ± 0.0	13 ± 1.2	10 ± 1.6	21[a]	0.001
	Air pocket CO_2 (%)	0 ± 0.1	5 ± 0.5	6 ± 0.6	0[a]	0.001
	RR (rpm)	18 ± 4.3	18 ± 4.9	31 ± 3.7	18 ± 0.9	1.000
	VT (l)	1 ± 0.3	2 ± 0.6	3 ± 0.5	1 ± 0.5	1.000
	VE (l/min)	12 ± 3.4	38 ± 11.9	97 ± 13.4	18 ± 8.6	0.897
	MAP (mmHg)	111 ± 4.9	119 ± 6.8	130 ± 8.4	117 ± 10.7	1.000
Termination for $SpO_2 \leq 75\%$ (n = 13)	ScO_2 (%)	72 ± 4.1	70 ± 7.2	61 ± 4.6	79 ± 4.0	<0.001
	SpO_2 (%)	98 ± 1.7	86 ± 6.8	74 ± 1.1	99 ± 1.4	1.000
	$ETCO_2$ (mmHg)	32 ± 4.8	39 ± 3.2	47 ± 7.0	33 ± 5.4	1.000
	PcO_2 (mmHg)	65 ± 6.0	48 ± 5.9	38 ± 2.7	–	–
	$PcCO_2$ (mmHg)	35 ± 2.5	41 ± 2.4	46 ± 3.1	–	–
	pH	7.44 ± 0.04	7.39 ± 0.04	7.36 ± 0.04	–	–
	Air pocket O_2 (%)	20 ± 0.1	12 ± 1.1	10 ± 1.4	21[a]	<0.001
	Air pocket CO_2 (%)	0 ± 0.1	5 ± 0.4	6 ± 0.6	0[a]	<0.001
	RR (rpm)	14 ± 4.0	14 ± 5.3	18 ± 7.4	16 ± 4.2	0.866
	VT (l)	1 ± 0.8	2 ± 0.6	3 ± 0.6	1 ± 0.6	0.181
	VE (l/min)	14 ± 4.8	28 ± 14.2	47 ± 22.4	14 ± 5.6	1.000
	MAP (mmHg)	106 ± 12.0	115 ± 12.8	124 ± 24.5	101 ± 12.0	0.402

$ETCO_2$, end-tidal carbon dioxide; MAP, mean arterial pressure; $PcCO_2$, partial pressure of carbon dioxide in capillary blood; PcO_2, partial pressure of oxygen in capillary blood; RR, respiratory rate; ScO_2, cerebral oxygenation; SpO_2, peripheral oxygen saturation; VE, minute ventilation; VT, tidal volume.

[a] Ambient air values.

[b] After Holm-Bonferroni correction. Values are given as mean ± standard deviation.

software (IBM Corp., Armonk, NY) was used. Tests were two-sided and $p < 0.05$ was considered statistically significant. We report the results as mean ± standard deviation, except for snow density, which we report as median (range). We report agreement between the two sensors as ICC (95% confidence interval (CI)) and the estimates of the LMM as mean (95% CI).

Results

Twelve males were enrolled in the study. The mean age was 34 ± 7 years, weight 78 ± 8 kg and height 179 ± 5 cm. Each subject underwent three test series. All tests were included in the final data analysis.

In total 36 study tests were performed: 18 of 36 tests lasted 30 min; 13 tests were terminated prematurely due to hypoxaemia ($SpO_2 \leq 75\%$), and 5 tests were terminated at the subject's request due to clinical symptoms [dyspnea (n = 3), dizziness (n = 1), and dyspnea and headache (n = 1)].

Median snow density was 310 kg/m^3 (range 155–481 kg/m^3) in test session 1, 434 kg/m^3 (range 354–475 kg/m^3) in test session 2 and 209 kg/m^3 (range 159–443 kg/m^3) in test session 3. ScO_2, SpO_2, $ETCO_2$, partial pressure of oxygen in capillary blood (PcO_2), partial pressure of carbon dioxide in capillary blood ($PcCO_2$), pH, air pocket O_2 and CO_2, RR, VT, VE and MAP at different time points are shown in Table 1. Agreement between the two sensors of the NIRS signal was 0.91 (95% CI 0.82–0.95) at baseline, 0.92 (95% CI 0.84–0.96) at 5 min, 0.95 (95% CI 0.90–0.97) at the end of the test and 0.93 (95% CI 0.85–0.96) at 2.5 min in the post-test phase.

Test phase

Single subject data for ScO_2, $ETCO_2$, SpO_2, air pocket O_2 and CO_2 of each group and snow density are shown in Fig. 1. Group changes in ScO_2, $ETCO_2$, SpO_2, air pocket O_2 and air pocket CO_2 from baseline to 5 min, to the last measure, and to 2.5 min post-test are shown in Fig. 2. At the end of the tests, changes in ScO_2 between groups were different, with the highest decreases found in the group in which the tests were terminated for $SpO_2 \leq 75\%$. These tests were all performed in snow densities higher than 350 kg/m^3. Additionally, at the end of the test air pocket O_2 was lower and air pocket CO_2 was higher in the two groups of tests terminated before 30 min compared to the group of completed tests (Fig. 2). In the group of completed tests, ScO_2 values progressively increased, despite a decrease in O_2 supply and increase in CO_2. In the group in which the tests were terminated before 30 min by request, ScO_2 (and SpO_2) showed intermediate

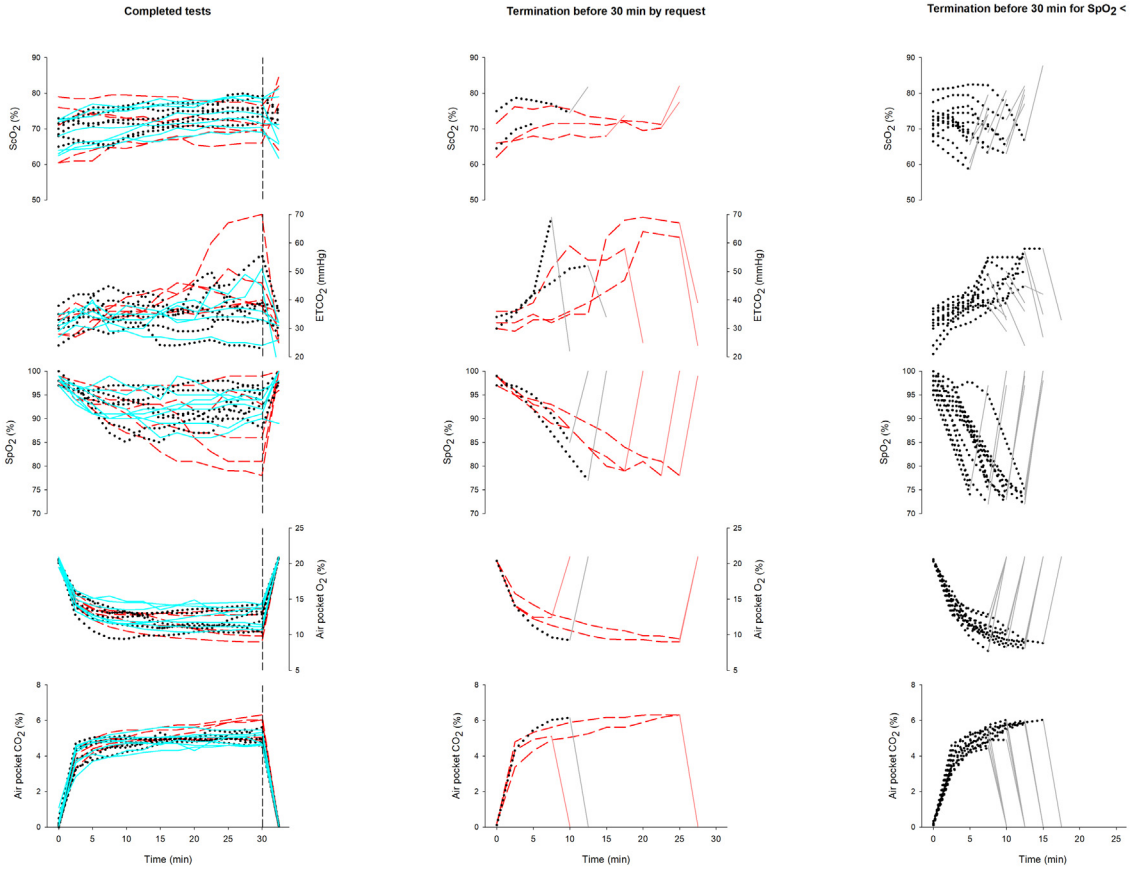

Fig. 1 – Curves of individual single subject data for ScO_2, $ETCO_2$, SpO_2, air pocket O_2 and air pocket CO_2 during the tests. Dashed red lines represent tests done breathing into an air pocket surrounded by snow density ≤250 kg/m^3, solid blue lines by snow density from 251–350 kg/m^3 and dotted black lines by snow density >350 kg/m^3. The black vertical dashed line in the group of completed tests represents the end of the 30 min test. For the termination before 30 min by request and termination for $SpO_2 \leq 75\%$ groups the post-test phase is depicted in solid light red for snow density ≤250 kg/m^3 and solid grey for snow density >350 kg/m^3.

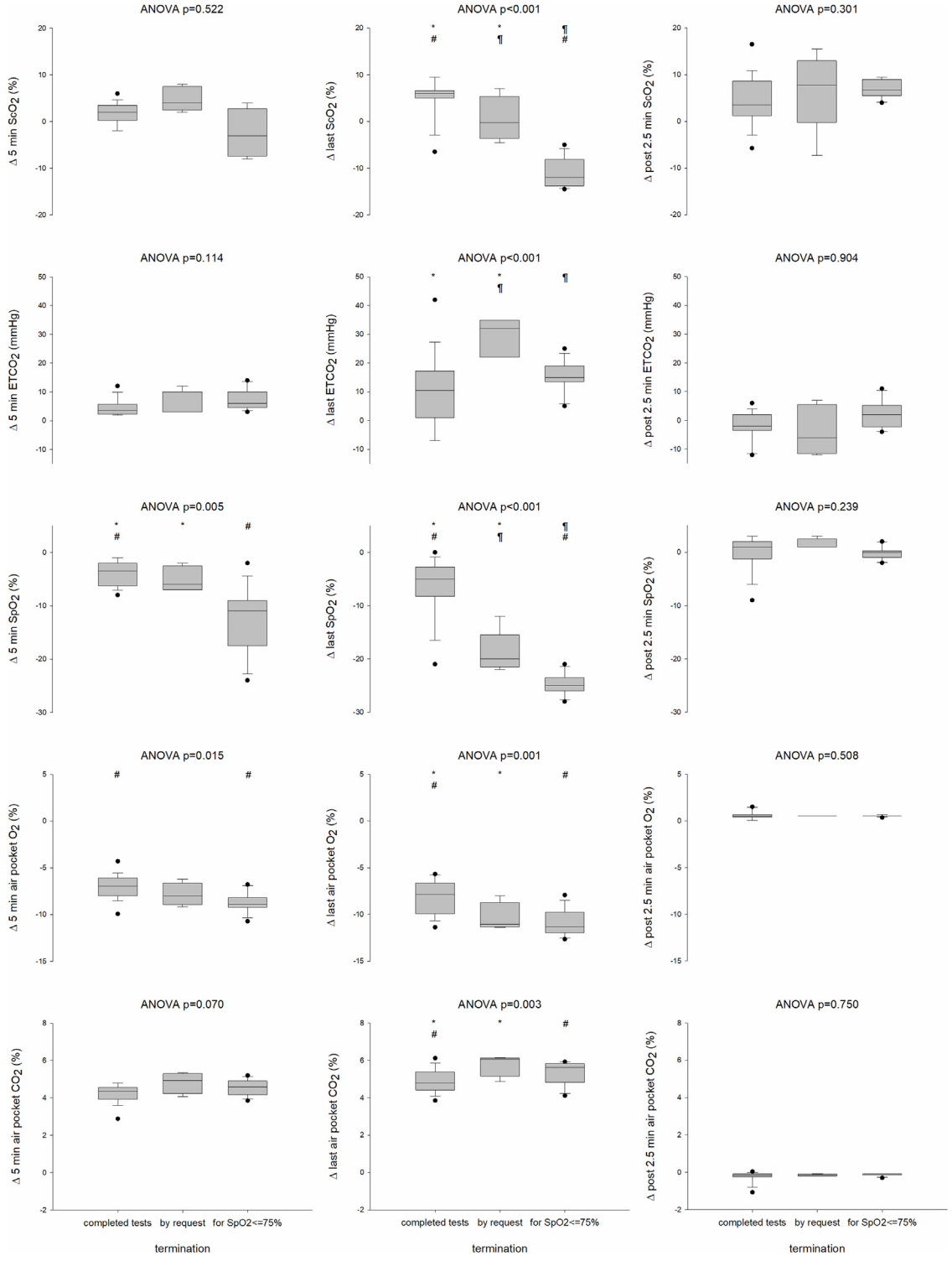

Fig. 2 – Boxplots of difference from baseline to 5 min (left), from baseline to last measure (middle) and from baseline to 2.5 min post-test (right) of data for ScO_2, $ETCO_2$, SpO_2, air pocket O_2 and air pocket CO_2 per termination group. * indicates a significant difference ($p < 0.05$) between completed tests and termination before 30 min by request groups, # indicates a significant difference ($p < 0.05$) between completed tests and termination for $SpO_2 \leq 75\%$ groups and ¶ indicates a significant difference ($p < 0.05$) between termination before 30 min by request and termination for $SpO_2 \leq 75\%$ groups.

values within the other two groups, while $ETCO_2$ was the highest (Fig. 2). At the end of the tests, changes in $ETCO_2$ were similar in the other two groups.

In the group in which the tests were terminated for $SpO_2 \leq 75\%$, changes in ScO_2 were positively correlated with changes in SpO_2 ($r = 0.749$, $p < 0.001$) and air pocket O_2 ($r = 0.527$, $p = 0.010$), and negatively with changes in $ETCO_2$ ($r = -0.475$, $p = 0.022$) and air pocket CO_2 ($r = -0.529$, $p = 0.009$) (Table 2). The LMM analysis detected only an effect of SpO_2 on ScO_2 (Table 3) indicating a positive correlation between them as the LMM estimated that a decrease of 1% of SpO_2 predicted a decrease of 0.7% (95% CI 0.4–0.9%) in ScO_2. In the group of completed tests, changes in ScO_2 were positively correlated with changes in $ETCO_2$ ($r = 0.282$, $p = 0.004$) and air pocket CO_2 ($r = 0.412$, $p < 0.001$) and negatively with changes in air pocket O_2 ($r = -0.423$, $p < 0.001$) but not with changes in SpO_2 (Table 2). The LMM analysis showed effects of time, snow density, $ETCO_2$ and air pocket O_2 on ScO_2 (Table 3). The estimated mean of ScO_2 increased during the first 10 min of test [64% (95% CI 58–70%) at baseline, 74% (95% CI 70–78%) at 10 min, 75% (95% CI 71–79%) at 20 min and 74% (95% CI 70–78%) at 30 min] and was higher in subjects breathing in snow densities in the range of 251–350 kg/m^3 [76% (95% CI 71–80%) vs. 70% (95% CI 66–74%) for $\leq$250 kg/m^3 and 72% (95% CI 68–76%) for >350 kg/m^3]. The LMM estimated that an increase of 1 mmHg of $ETCO_2$ predicted an increase of 0.1% (95% CI 0.0–0.2%) in ScO_2 and that a decrease of 1% in air pocket O_2 predicted a decrease of 0.9% (95% CI 0.2–1.6%) in ScO_2.

When tests were terminated before 30 min by request, changes in ScO_2 were positively correlated with changes in the air pocket CO_2 ($r = 0.772$, $p = 0.005$) and negatively with changes in the air pocket O_2 ($r = -0.733$, $p = 0.010$) (Table 2). No correlation with changes in SpO_2 or $ETCO_2$ was found. In the LMM analysis none of the parameters showed an effect on ScO_2 (Table 3).

Post-test phase

Changes in ScO_2, $ETCO_2$, SpO_2, air pocket O_2 and CO_2 from baseline to 2.5 min in the post-test phase were not different in the three termination groups (Fig. 2). Within 2.5 min from test termination, all parameters returned to baseline level, with the exception of ScO_2 that was higher than baseline in the group of completed tests ($p = 0.028$) and the group in which the tests were terminated for $SpO_2 \leq 75\%$ ($p < 0.001$) (Table 1).

Discussion

As far as we know, this is the first study investigating the effects of hypoxia and hypercapnia on cerebral oxygen saturation in humans breathing into artificial air pockets in snow. The study helps to describe the contribution of snow density and physiological components to asphyxia development in avalanche victims within the first 30 min of burial. ScO_2 determined by NIRS was not consistently impaired despite a decreased level of O_2 and an increased level of CO_2 in the air pocket. ScO_2 showed a significant decrease in the group in which the test was terminated for $SpO_2 \leq 75\%$. This decrease was driven by a decrease in oxygen supply associated with high snow densities. In the group of completed tests, there were mild increases in ScO_2 despite decreased oxygen supply and limited CO_2 removal. Such an increase

Table 2 – Correlation coefficients (r) of changes in cerebral oxygenation with changes in $ETCO_2$, SpO_2, air pocket O_2 and air pocket CO_2 depending on termination group.

Parameter	Completed tests (n = 18)		Termination before 30 min by request (n = 5)		Termination for $SpO_2 \leq 75\%$ (n = 13)	
	r	*p*-Value	r	*p*-Value	r	*p*-Value
$ETCO_2$	0.282	0.004	0.127	0.653	−0.475	0.022
SpO_2	−0.078	0.403	−0.292	0.291	0.749	<0.001
Air pocket O_2	−0.423	<0.001	−0.733	0.010	0.527	0.010
Air pocket CO_2	0.412	<0.001	0.772	0.005	−0.529	0.009

$ETCO_2$, end-tidal carbon dioxide; SpO_2, peripheral oxygen saturation.

Table 3 – *p*-Values for fixed effects of linear mixed models with cerebral oxygenation as dependent variable depending on termination group.

Fixed effect	Completed tests	Termination before 30 min by request	Termination for $SpO_2 \leq 75\%$
Intercept	<0.001	0.746	0.170
$ETCO_2$	0.005	0.379	0.680
SpO_2	0.115	0.217	<0.001
Air pocket O_2	0.015	0.934	0.462
Air pocket CO_2	0.856	0.970	0.432
Snow density[a]	<0.001	0.951	[b]
Time	0.002	0.672	0.553

$ETCO_2$, end-tidal carbon dioxide; SpO_2, peripheral oxygen saturation.
[a] $\leq$ 250, 251–350 and >350 kg/m^3 groups (the same subdivision as in Strapazzon et al., 2017).
[b] Not evaluable: when terminated for $SpO_2 \leq 75\%$, all cases with snow density >350 kg/m^3.

could have been driven by an increase in cerebral blood flow. Despite the omission of hypothermia from our experimental model, we think that this experimental design adequately simulates the early stages of a real avalanche burial. Within 30 min of avalanche burial, cooling data reported in the literature suggest that accidental hypothermia is not probable and therefore does not significantly affect brain metabolism or physiology at this early stage.[7,14]

An avalanche burial is a life-threatening situation. Avalanche accident statistics indicate that avalanche victims do not survive for more than 30 min with obstructed airways.[1,15] Survival times of avalanche victims may be extended with a patent airway and may even be further prolonged with an air pocket.[1] 13 of the 36 tests (36%) were terminated prematurely due to hypoxaemia, 5 (14%) were terminated at the request of the subjects, and 18 (50%) were completed. Epidemiological data show that approximately 70% of completely buried avalanche victims die of asphyxia within ~30 min.[7] Asphyxia can result from obstruction of the upper airway caused by inhaled avalanche debris or vomitus, or because of airway obstruction due to anatomical reasons, compression of the chest by avalanche debris and ice mask formation. A combination of hypoxia and hypercapnia due to inadequate gas diffusion may also lead to asphyxia (as shown in our study). Asphyxia from any cause finally results in hypoxic cardiac arrest.[5,6,16] Brain oedema, loss of gray and white matter differentiation, or hypodensity of basal ganglia have been reported even after short burial and return to spontaneous circulation on site.[17] In all tests that were prematurely terminated by severe hypoxemia when snow density was >350 kg/m^3, there was an impairment of ScO_2. When snow density exceeds 350 kg/ m^3, subjects might not be able to compensate for hypoxemia and, despite an expected increase in CBF, ScO_2 decreases. It can be expected that in such scenario avalanche victims will die from asphyxia in spite of the presence of an air pocket. In tests in which the subjects completed the full 30 min, ScO_2 values showed an increase, despite a decrease in O_2 supply and CO_2 removal. In this scenario O_2 and CO_2 concentrations in the air pocket have only changed to a limited extent, possibly because of adequate diffusion of the gases into and out of the pocket favored by medium to low snow densities, which allowed subjects to compensate for the altered respiratory gases in the air pocket. Since ScO_2 changes depend, amongst other factors, on CBF, this could reflect an increased CBF due to a combined vasodilatory effect of hypoxia and hypercapnia.[18] There is a curvilinear relationship between $PaCO_2$ and CBF.[19,20] Under normothermic, normoxic conditions for every 1 mmHg change in $PaCO_2$ CBF changes ~3% in the same direction.[21] Consistent with this response, in the present study ScO_2 correlated not only with decrease O_2 concentration in the air pocket but also with different degrees of increase in CO_2 concentration in the air pocket over time. Despite a lack of studies investigating CBF in an experimental model of avalanche burial, we expect that the development of hypoxia and hypercapnia will lead to an increase in CBF in normothermic subjects breathing into an artificial air pocket.[3,5,6] How long this will take will likely be closely related to individual vasomotor reactivity and the extent of hypoxia and hypercapnia.

The course of tests in which the subject completed the test without premature termination might represent the initial stage of the triple H syndrome, before the subject becomes hypothermic.[1,22] Our results show that when air pocket O_2 reduction and CO_2 accumulation are limited, brain oxygenation can be maintained up to 30 min and possibly until accidental hypothermia occurs. Adequate brain oxygenation seems to be crucial for good neurological outcome. Breathing into medium to low snow densities (i.e. snow densities from 251−350 kg/m^3) probably allows sufficient diffusion of O_2 into the pocket and of CO_2 out of the pocket. [3] On the contrary, snow densities higher than 350 kg/ m^3 might limit diffusion leading to test interruptions (and to asphyxia in a real-life scenario).

Limitations

This was a pilot human experimental study. Both sexes were eligible for recruitment, but the first twelve subjects were all male. Despite that most ski tourers (70%),[23] and mountain rescue service providers are male in our area, only the inclusion of both sexes allows to apply results to all population. We have already foreseen a future larger study including both females and males to further investigate the physiological mechanisms and clinical implications of the current findings. In this study, the additional effect of cooling during snow burial on brain oxygenation could not be investigated for ethical reasons. All subjects remained insulated and normothermic throughout. In some of the tests, subjects may have resembled patients at risk of developing asphyxia. In other tests, subjects might have resembled patients that develop triple H syndrome and survive avalanche burial for longer than 30 min. To avoid the effects of skin vasoconstriction on NIRS measurements[24] each subject's forehead and NIRS probes remained covered throughout the tests. Insulation of the skin and probes avoided interaction between measurements of skin and cerebral tissue. No measurement of cerebral oxygen metabolism was performed. The subjects did not perform any cognitive task (e.g., verbal fluency task) related to frontal cortex activation.

Conclusions

Our data show that ScO_2 determined by NIRS was not always impaired in humans breathing into an artificial air pocket despite decreased oxygen supply and decreased carbon dioxide removal. A mild increase in ScO_2 can occur despite decreased oxygen supply and carbon dioxide removal. This may indicate that in medium to low snow densities brain oxygenation can be sufficient. This may reflect the initial stage of the triple H syndrome. In high snow densities, ScO_2 showed a significant decrease caused by a critical decrease in oxygen supply. This could lead to a higher risk of hypoxic cardiac arrest and brain damage. The study helps to describe the contribution of snow density and physiological components to asphyxia development in avalanche victims within the first 30 min of burial. Our experimental model might enable further study of factors that affect CBF and ScO_2. Studies in real avalanche rescue operations are needed to evaluate the effect on outcome when non-invasive measures of cerebral oxygen saturation are used to guide triage and treatment.

Author contribution

GS, HG, MFa, PP, MFk, JS and HB contributed to study design. GS, SM and HB enrolled study subjects. GS, HG, MFa, TDC, SM, RT, KS, PP, MFk, JS and HB participated in clinical/snow-property data collection and analysis. TDC and MFk performed the statistical analysis. GS, MFa, and HB oversaw the interpretation of results. GS, MFa and TDC did the literature review and wrote the manuscript. All

authors critically reviewed the final draft of the manuscript and have given approval for the version submitted.

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Conflict of interests

No conflict of interests exists for any author.

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