Original articles

Effects of Valsalva manoeuvres and the 'CO_2-off' effect on cerebral blood flow

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Abstract

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Introduction: Previous research has shown that a rapid drop in inhaled carbon dioxide (CO_2) partial pressure reduces cerebral blood flow and may induce faintness – the 'CO_2-off' effect. The aims of this study were to investigate the effects of performing Valsalva manoeuvres while experiencing the 'CO_2-off' effect and whether symptoms occur that are sufficient to jeopardise submarine tower escape.

Methods: Twenty male volunteers, mean (SD) age 34.7 (8.5) years each completed three tests. The first test was to perform Valsalva manoeuvres breathing air. The second and third tests involved breathing a high CO_2 mix (5% CO_2/16% O_2/79% N_2) for 1 h prior to switching to breathe O_2 and performing Valsalva manoeuvres, or switching to breathe air for 1 min then O_2 and performing Valsalva manoeuvres. Blood pressure, cerebral blood flow velocity, electrocardiogram, and respiration were monitored throughout. A subjective questionnaire was administered at intervals to monitor symptom type and severity.

Results: Valsalva manoeuvres breathing air resulted in a 31% reduction in cerebral blood flow. Breathing high CO_2 caused a sustained increase in cerebral blood flow and symptoms of breathlessness and headache. Following the gas switch from high CO_2, some subjects reported faintness, headache and nausea. Cerebral blood flow dropped by 34% when switching from breathing high CO_2 to O_2, by 35% when switching to air then by a further 3% when switching from air to O_2. In both circumstances there was a further drop of 14% after performing the Valsalva manoeuvres. The drop in cerebral blood flow in subjects that reported faintness was greater than that in the subjects who did not, but this difference was not significant.

Conclusion: Transient faintness or headache may occur in the escape tower during pressurisation, but this should be short-lived and not incapacitating.

Key words

Hypercapnia, Valsalva, cerebral blood flow, Doppler, physiology, submarine

Introduction

Royal Navy submarines are fitted with tower escape systems allowing survivors to escape from a distressed submarine (DISSUB). There may be a long wait in the submarine prior to starting tower escape during which the partial pressure of carbon dioxide (PCO_2) may rise despite use of a CO_2 absorbent. Submariners may switch from breathing a hypercapnic and hypoxic atmosphere in the DISSUB to a normocapnic and normoxic atmosphere in the escape tower. The submariner is subject to rapid pressurisation in the escape tower to equalise with the surrounding sea pressure, and then decompression as he ascends to the surface. During the pressurisation the escaper will also be exposed to a hyperoxic atmosphere, with the inspired partial pressure of oxygen (P_iO_2) reaching as high as 398 kPa at the maximum permitted escape depth (180 m).

Fainting usually occurs when a person is in the upright position and can be provoked by anything that reduces cerebral perfusion.[1] CO_2 is a cerebral vasodilator whilst O_2 is a cerebral vasoconstrictor. Thus the switch from breathing a hypercapnic gas in the DISSUB to a hyperoxic gas whilst stood in the escape tower may lead to transient cerebral vasoconstriction resulting in cerebral hypoperfusion, which could in turn result in fainting. Fainting in the escape tower could endanger the escaper and hinder escape for the rest of the crew by blocking the tower with the escaper's body.

A previous study examined the physiological effects of the rapid replacement of a hypercapnic breathing gas with 100% O_2 – the 'CO_2-off' effect.[2] Subjects breathed a mixture of 5% CO_2/16% O_2/79% N_2 (high CO_2) for one hour and then switched to breathing O_2 for 15 min. Mild or moderate faintness was the most frequently reported symptom following the gas switch. Transcranial Doppler (TCD) was used to measure middle cerebral artery blood flow velocity (MCAv). There was a significantly greater percentage drop in mean MCAv in subjects who had symptoms of faintness that developed after the switch to O_2 when compared with those who did not.

Submariners are trained to minimise ear discomfort by equalising pressure across the tympanic membrane using Valsalva manoeuvres (Valsalvas). Valsalvas are known to cause a drop in MCAv when in the upright position.[3] This is a mechanical effect of the raised intra-thoracic and intra-abdominal pressure causing reduced venous return and cardiac output. Therefore, we hypothesized that performing Valsalvas following a switch from breathing high CO_2

might exacerbate the drop in MCAv caused by the switch in breathing gas previously observed and possibly worsen any symptoms such as faintness or nausea.

Methods

The study was approved by the QinetiQ Ethics Committee (ethical protocol SP792 v 2.0), and carried out at the QinetiQ Hyperbaric Medical Unit, St. Richard's Hospital, Chichester, UK. Volunteers gave their written informed consent and the study was conducted in accordance with the principles of the Declaration of Helsinki (revised 2008).

STUDY DESIGN

It was hypothesised that Valsalvas would further increase the observed drop in mean MCAv caused by a gas switch from high CO_2. A power test (power = 0.8 and alpha = 0.05) using R statistical software (version 2.10.1) determined that 16 subjects would be required to detect a significant increase in the mean percentage drop in mean MCAv of a further 10% over that caused by the switch to 100% O_2 alone. To allow for possible subject withdrawal, or increase in the observed standard deviation in mean MCAv, 20 subjects were recruited.

SUBJECTS

Twenty male volunteers participated in the study, with mean (SD) age of 34.7 (8.5) years; height 179.8 (4.9) cm; body mass 84.4 (14.5) kg. Subjects were requested to refrain from alcohol the day before each test. They were requested to have a light breakfast and their normal caffeinated drink on the morning of each test. The subjects performed each of three test conditions on separate visits with a period of at least 24 hours between each.

PROCEDURES

All tests were carried out at normobaric ambient pressure. British Oxygen Company supplied cylinders of medical quality 5% CO_2/16% O_2 balance N_2, hereafter termed 'high CO_2' (note that in the previous study this was termed $5CO_2/16O_2$[2]). Medical O_2 and air were obtained from the hospital supply. Breathing gases were contained in Douglas bags and breathed via plastic tubing and a silicon mouthpiece. A four-way gas switching block (Hans Rudolph Inc.) was used to control the gas delivered.

The three tests were conducted as shown in Table 1. Test 1 was conducted first for all subjects, allowing familiarisation with equipment and procedures. The order of Tests 2 and 3 was randomised.

VALSALVA MANOEUVRES

A calibrated pressure transducer (General Electric, Druck, 800–1200 mbar range) was connected to the mouthpiece

Table 1
Procedures for Tests 1, 2 and 3 (see text for more details)

Time (min)	**Test 1**	**Test 2**	**Test 3**
0	Start air (standing)	Start high CO_2 (seated)	Start high CO_2 (seated)
5	6 x Valsalva		
10	End		
50		Stand up	Stand up
60		Switch to O_2	Switch to air
61		6 Valsalva	Switch to O_2
62		Switch to air	6 Valsalva
63		Sit	Switch to air and sit
68		End	End

assembly to ensure Valsalvas were performed consistently. Subjects wore a nose-clip throughout. Valsalvas were performed by the subject occluding the mouthpiece exhale valve with the right hand while attempting to breathe out to achieve a mouthpiece pressure of 40 mmHg (5.3 kPa) above ambient for 2 s. A traffic light system displayed when sufficient effort had been achieved. Six Valsalvas were performed in 30 s by each subject.

INSTRUMENTATION

A flow meter (KL Engineering Spirometric module S430A) placed in the inhale tubing allowed measurement of respiratory rate and minute volume. Subjects were instrumented for the duration of the test allowing measurement of:

- brachial blood pressure (BP mmHg) (General Electric, DINAMAP ® Pro 1000) from the right arm;
- O_2 saturation (General Electric, DINAMAP ® Pro 1000) from a finger on the left hand;
- blood velocity in the middle cerebral artery (measured continuously) using Transcranial Doppler transducer (Comtec TCD II) held in position at either left or right temporal region with a Rimed probe holder LMY2;
- electrocardiogram (ECG) using two independent ECG monitors (LifePulse10 HME Ltd and General Electric DINAMAP ® Pro 1000) showing leads I and II;
- inspired and expired O_2 and CO_2 concentrations via a capillary tube from the centre of the mouthpiece to a Servomex 1440 fast-response gas analyser.

DATA RECORDING

Heart rate, BP, respiration rate, respiratory minute volume, and mean MCAv were recorded each minute for 5 min then every 5 min until 60 min then at 1 or 2 min intervals to the end.

A subjective symptoms questionnaire was administered each minute for the first 5 min of high-CO_2 breathing, then after a further 5 min and then at 10 min intervals until the switch, when it was administered more frequently. The subject

Table 2
Mean ± 95% CI absolute and % change in physiological parameters during Test 2

Test 2	Air baseline	1 min CO_2	5 min CO_2	30 min CO_2	Final min CO2	1 min O_2	Valsalva	1 min air	Final min air
Resp rate (breath·min^{-1})	11 ± 1.8	12 ± 1.8	13 ± 2.2	16 ± 1.9	17 ± 1.8	15 ± 1.8	10 ± 1.9	14 ± 2.2	13 ± 1.9
% change		9	18	45	55	36	-9	27	18
Resp minute vol (L·min^{-1})	6 ± 1.0	11 ± 1.9	17 ± 2.5	25 ± 2.4	28 ± 3.3	20 ± 2.9	NA	10 ± 1.9	6 ± 1.0
% change		83	183	317	367	233	NA	67	0
Mean BP (mmHg)	91 ± 1.9	96 ± 3.1	95 ± 3.1	96 ± 3.3	105 ± 3.7	103 ± 3.3	NA	101 ± 3.7	96 ± 3.3
% change		5	4	5	15	13	NA	11	5
Heart rate (beat·min^{-1})	61 ± 3.7	64 ± 3.1	62 ± 3.5	63 ± 3.5	73 ± 4.3	72 ± 4.9	79 ± 6.5	74 ± 5.3	57 ± 4.7
% change		5	2	3	20	18	30	21	-7
MCAv (cm·s^{-1})	65 ± 4.9	75 ± 6.9	79 ± 7.6	75 ± 7.3	76 ± 8.4	50 ± 6.5	40 ± 4.7	46 ± 5.9	63 ± 6.1
% change		15	22	16	17	-23	-39	-29	-3
$ETCO_2$ (kPa)	5.3 ± 0.2	6.0 ± 0.2	6.4 ± 0.2	6.3 ± 0.2	6.3 ± 0.2	4.3 ± 0.8	NA	4.4 ± 0.4	5.0 ± 0.2
% change		13	21	19	19	-18	NA	-17	-6

Table 3
Mean ± 95% CI absolute and % change in physiological parameters during Test 3

Test 3	Air baseline	1 min CO_2	5 min CO_2	30 min CO_2	Final min CO_2	1 min air	1 min O_2	Valsalva	Final min air
Resp rate (breath·min^{-1})	11 ± 1.4	12 ± 1.4	13 ± 1.6	16 ± 1.4	16 ± 1.4	16 ± 1.4	15 ± 1.4	12 ± 2.4	13 ± 1.8
% change		9	18	45	45	45	36	9	18
Resp minute vol (L·min^{-1})	6.5 ± 1.2	11 ± 2.0	18 ± 2.0	24 ± 2.0	28 ± 2.9	22 ± 3.1	13 ± 2.0	NA	6.5 ± 1.2
% change		69	177	269	331	238	100	NA	0
Mean BP (mmHg)	92 ± 2.5	95 ± 2.9	96 ± 3.3	96 ± 3.1	106 ± 3.3	104 ± 2.9	101 ± 3.3	NA	97 ± 2.2
% change		3	4	4	15	13	10	NA	5
Heart rate (beat·min^{-1})	64 ± 5.3	70 ± 4.7	65 ± 4.5	66 ± 4.7	74 ± 4.7	76 ± 5.1	80 ± 5.3	81 ± 6.3	58 ± 3.7
% change		9	2	3	16	19	25	27	-9
MCAv (cm·s^{-1})	65 ± 8.0	76 ± 7.6	81 ± 9.6	74 ± 9.4	79 ± 10.2	51 ± 6.9	49 ± 6.3	37 ± 5.3	58 ± 6.8
% change		16	23	14	20	-22	-26	-43	-11
$ETCO_2$ (kPa)	5.2 ± 0.2	6.0 ± 0.2	6.5 ± 0.2	6.4 ± 0.2	6.4 ± 0.2	4.3 ± 0.6	4.4 ± 0.4	NA	5.0 ± 0.2
% change		16	25	23	23	-16	-15	NA	-4

was required to rate his level of discomfort as: none, mild, moderate, severe or intolerable in each of the categories: nausea, breathlessness, faintness and headache.

TEST TERMINATION CRITERIA

The test would be terminated:

- at the subject's request; on a subjective questionnaire response of 'intolerable' to any aspect;
- on failure of any equipment used to monitor withdrawal variables;
- on recording end-tidal CO_2 ($ETCO_2$) > 8.5 kPa for more than five consecutive breaths;
- if the subject began to vomit;
- if the subject fainted or requested assistance feeling faint;
- on subjective signs of impending panic;
- if BP was greater than either a systolic of 180 or a diastolic of 110 mmHg, sustained for over 1 min.

STATISTICAL ANALYSIS

The relative percentage change from baseline values in six physiological parameters (respiratory rate, heart rate, BP, MCAv, $ETCO_2$ and respiratory minute volume) was calculated at different time points. The relative percentage change in mean MCAv was calculated from the value immediately preceding and those following the switch from high CO_2 for Test 2 and Test 3. Data were compared using either paired or unpaired, unequal variance Student's *t*-tests. Differences were considered significant if $P < 0.05$.

Results

SYMPTOMS

All subjects completed each of the three tests successfully; there were no withdrawals and no subject fainted or vomited or was otherwise incapacitated at any stage. Four subjects did not report any symptoms throughout the tests. Fifteen of the 20 subjects reported symptoms during high-CO_2 breathing, compared with seven reporting mild or moderate symptoms of faintness, with headache or nausea after the gas switch and performing Valsalvas.

PHYSIOLOGICAL PARAMETERS

Tables 2 and 3 show absolute and percentage change in the mean physiological parameter values at defined points through Tests 2 and 3 respectively. No data for BP, respiratory minute volume and $ETCO_2$ are reported for the time at which the Valsalvas were performed, as the subjects were occluding the exhale valve, making these measurements inaccurate.

MCAv

Figures 1, 2 and 3 show the change in mean MCAv during Tests 1, 2 and 3 given as a percentage change from the baseline measurement. During Test 1 mean MCAv dropped by 31% after performing the Valsalvas, and then recovered towards baseline values. The changes in mean MCAv were very similar for both Test 2 and Test 3: MCAv increased to reach a peak of about 23% above baseline at 5 min of

Figure 1
% change in mean MCAv (95% CI shown) from baseline during Test 1

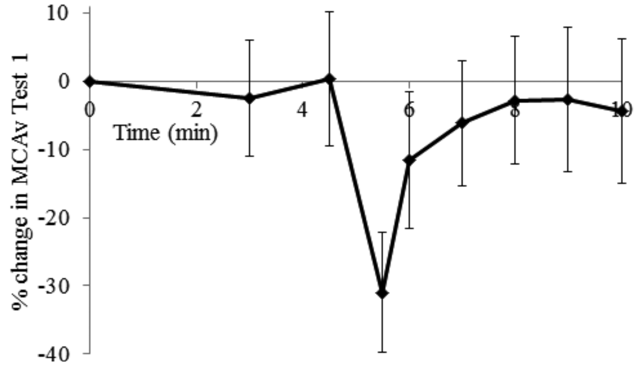


Figure 2
% change in mean MCAv (95% CI shown) from baseline during Test 2

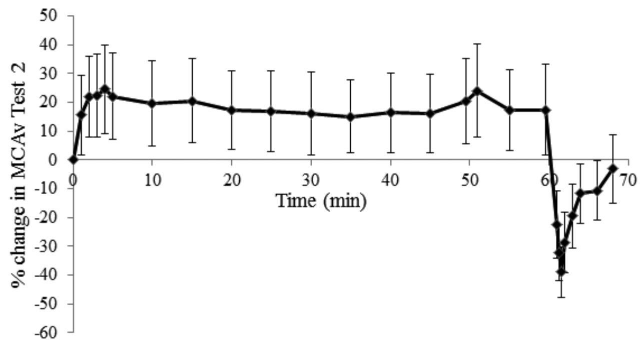


Figure 3
% change in mean MCAv (95% CI shown) from baseline during Test 3

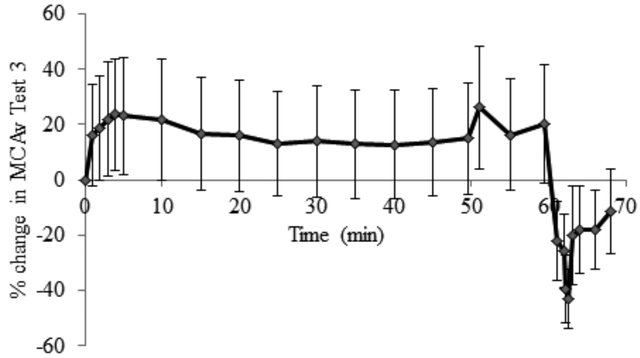


Figure 4
% change in mean MCAv (95% CI shown) post switch to O_2; Test 2 comparing faint and non-faint subjects (not significant)

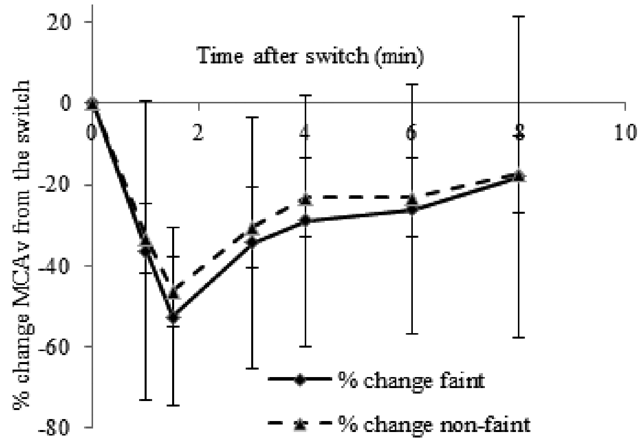
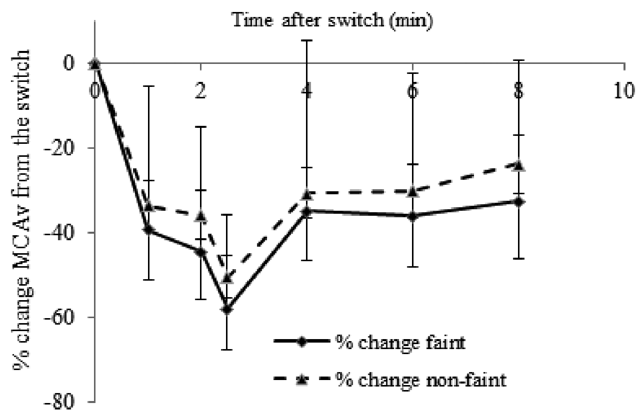


Figure 5
% change in mean MCAv (95% CI shown) post switch to air Test 3 comparing faint and non-faint subjects (not significant)



breathing high CO_2. There was then a decline; the mean MCAv was around 16% above baseline from 15 min until the subjects stood up when it increased to around 25%. The switch from high CO_2 in both tests caused a drop to around 23% less than the baseline and there were further decreases in mean MCAv with Valsalvas before a recovery towards baseline.

The percentage change in mean MCAv taken from the value immediately preceding the switch was calculated for Tests 2 and 3. During Test 2 the mean MCAv dropped by 34% when switching from high CO_2 to O_2, by a further 14% after performing the Valsalvas and then recovered towards baseline over the final 5 min. During Test 3 the mean MCAv dropped by 35% when switching from high CO_2 to air, by a further 3% when switching to O_2 and then by 14.5% when performing the Valsalvas. Recovery towards baseline values then continued over the final 5 min.

MEAN MCAv WITH OR WITHOUT FAINTNESS

Figures 4 and 5 show the percentage change in MCAv taken from the value immediately preceding the switch from high CO_2 for Test 2 and Test 3. Subjects are grouped as those who did or did not report feeling faint after the switch and/or Valsalvas. The drop in MCAv for the subjects reporting faintness or increased faintness following the switch was generally greater than the drop in MCAv for those who did not. However, this difference was not statistically significant.

Discussion

CHANGES WHILE BREATHING HIGH CO_2

The most frequently reported symptom while breathing high CO_2 was breathlessness, followed by headache and faintness, which is in agreement with our previous study.[2] The symptoms of breathlessness and headache were evenly reported between Tests 2 and 3 regardless of which was performed first, whereas symptoms of faintness were more likely to be reported on the first test with high CO_2 rather than on the second; possibly a learning effect, as subjects knew what to expect and therefore did not report as faint. Cerebral blood flow has been shown to increase when breathing 5% CO_2.[2,4] In the present study, mean MCAv increased by 23% after 5 min of breathing 5% CO_2.

CHANGES AFTER SWITCHING FROM HIGH CO_2

Transient mild or moderate symptoms of faintness, headache or nausea occurring after the switch to either air or O_2 were reported by seven subjects. Faintness or increased faintness was the most commonly reported symptom, being reported by 7/20 subjects (35%, 95% CI 15–59%). This is a higher incidence than in our previous study where 7/34 (20%, 95% CI 8–38%) subjects reported mild to moderate faintness after the switch to O_2. Therefore, proportionately more subjects felt faint after the switch and Valsalva than just from the switch alone, but this was not statistically significant.

Three subjects reported mild headache starting after the switch to O_2 on Test 2; however, this was also around the same time as they were performing Valsalvas. Activity-related headaches are well documented and are reported by sufferers during or shortly after a physical activity which typically incorporates a Valsalva, such as coughing, sneezing or straining while lifting heavy loads.[5,6] These 'cough headaches' are generally short-lived, lasting between 1 s and 30 min, without other associated symptoms.[5] It would be unlikely that this would in any way prevent safe escape from a submarine. Any headaches reported by subjects in our trial were resolved by the end of the tests.

Pre-fainting symptoms include headache and nausea and these additional symptoms were reported by subjects who also reported feeling faint. Fainting or feeling faint is associated with a decrease in MCAv and this is most commonly provoked in the standing position.[1] Hyperoxia and hypocapnia both reduce MCAv and the decrease seen in our study could have been caused by cerebral vasoconstriction due to hyperoxia from switching to 100% O_2 (Test 2) and/or the return to normocapnia from ceasing to breathe high CO_2 (Tests 2 and 3) – the 'CO_2-off' effect.

Differentiating between the symptoms reported after the switch from high CO_2 and those symptoms reported after the Valsalvas was difficult, because of the exact timings of administering the questionnaire at 1 min intervals at this part of the trial. However, in the debrief at the end of the tests, some subjects reported definite symptoms after Valsalvas and two subjects noted light-headedness after performing Valsalvas alone (Test 1).

MCAv AND SYMPTOMS FOLLOWING VALSALVA MANOEUVRES

Other studies have reported that decreases in MCAv of about 50% are associated with faintness. Passive head-up tilt of healthy subjects reduces MCAv and induces feelings of faintness.[7] In our study, the drop in percentage MCAv for the group that noted faintness or increased faintness following the switch was, in general, greater than the drop for those that did not. However, in contrast to our previous study, this difference was not significant. Our previous study demonstrated a significant difference in percentage drop in mean MCAv between the subjects who had symptoms of faintness after the switch to O_2 and those who did not report faintness (decrease in MCAv of 51% versus 44% respectively).[2]

Valsalvas performed in the standing position reduce the mean MCAv to 50% of the value obtained during supine rest, whereas during supine Valsalvas the reduction in MCAv is of the order of 35%.[3] The authors concluded that in the upright position, expiratory straining may critically compromise cerebral perfusion.

In our previous study, where the subjects switched to breathing 100% O_2 but did not perform Valsalvas, there was a large drop in percentage MCAv in the first minute following the switch to O_2 (similar to the effect observed with this study) – any further drop in percentage MCAv after the first minute following the switch was not significant when compared with the drop in the first minute. Therefore, it is assumed that in our present study, the significant drop in percentage MCAv observed following Valsalvas was, in fact, due to the Valsalvas and not to a continued/prolonged effect of the switch to O_2. Although Valsalvas exacerbated the decrease in cerebral blood flow following the switch from high CO_2, the accompanying symptoms of faintness, headache and nausea were transient and not incapacitating.

RELEVANCE TO SUBMARINE TOWER ESCAPE

The procedure for performing the Valsalvas was a compromise between the operational scenario and achieving a reproducible effect. In submarine escape exercises conducted by RN instructors, the observed method of ear-clearing varies markedly between individuals but is likely to be more frequent.

During the debriefing of the subjects following each test there was a range of comments from the subjects regarding how they felt, from "*nothing of note*" and "*didn't notice any difference*" to comments that the transient faintness after the switch and Valsalva was "*pretty grim, I couldn't have done any physical work at that point*" and "*I couldn't have made a decision*". Despite these reports, all subjects successfully completed the six Valsalvas. This required them to coordinate repeatedly closing off the mouthpiece outlet with their hand while simultaneously ensuring that they were reaching the required exhalation pressure, and following instruction on when to inhale and exhale. Submariners are trained in using escape towers and the procedures should be familiar. Following pressurisation, the submariner will be ascending through the water column to the surface, with no physical work or decision making to perform. Submariners simply need to breathe normally during the ascent and by the time they reach surface any transient faintness or headache due to changes in the breathing gas/Valsalva manoeuvres should have resolved.

In the escape scenario, it is likely that the submariners will be at least partially immersed and thus subject to hydrostatic pressure which should help to support systemic BP and cerebral perfusion. The time from the start of flooding of the tower to the start of compression can take up to 190 s, depending on depth and type of escape tower, and this period may give a protective effect on cerebral circulation, reducing the risk of fainting in the escape tower.

Our study examined the effect of acute high CO_2 exposure. The effect of switching to air from a chronic high CO_2 exposure, as may be experienced in a DISSUB environment, is unknown.

Conclusions

The hypothesis that Valsalva manoeuvres would reduce MCAv over and above that caused by a switch from breathing high CO_2 was upheld; there was a further 14% decrease in MCAv. The percentage drop in MCAv occurring following the switch from high CO_2 to 100% O_2 (34%) was similar to that occurring following the switch to air (35%). Therefore, a 'CO_2-off' effect seems the best explanation of the observed results.

Seven subjects reported faintness after the gas switch and performing Valsalvas, some with additional symptoms of headache or nausea. Those subjects who reported feeling faint had a slightly lower mean MCAv than those who did not, but this was not statistically significant. Transient faintness or headache may occur in the submarine escape tower during pressurisation, but this should be short-lived and not be incapacitating.

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