Human Responses to a Simulated 35,000-Foot Instantaneous Decompression and the Subsequent Descent Profile Required by FAA Policy

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16. Abstract

Sudden decompression of an airliner passenger cabin due to structural failure or damage is unlikely, but it poses a potentially life-threatening event for occupants. We investigated a worst-case scenario, where the passenger fails to receive supplemental oxygen during a rapid decompression (RD), and the subsequent emergency descent to 25,000 ft required by Federal Aviation Administration (FAA) policy. Our research question was whether an individual's oxygen stores will be depleted prior to the aircraft descending to an altitude that will permit inward fluxes of oxygen that exceed the resting oxygen consumption requirement.
Methods: We exposed 24 subjects to normobaric instantaneous decompressions to a simulated altitude of 35,000 ft. The peak altitude was maintained for 10 s and then followed by a 5000 ft/min descent to 25,000 ft. Resting oxygen consumption was measured prior to the hypoxia exposure. During each trial, tidal volume, respiratory rate, breath-by breath inhalation, and end-tidal O_2, CO_2, and N_2 tensions were measured and net directional oxygen flux computed.
Results: All subjects had an initial reversal of the direction of oxygen flux following the RD that persisted until after the descent commenced with outward flux predominating at higher altitudes of the profile. Return to net inward flux almost always occurred near 29,000 ft, the altitude at which the mixed venous and alveolar PO_2 gradient approximates nil. The inward flux of oxygen approached but never surpassed each subject's resting oxygen consumption as the altitude approached the 25,000 ft endpoint. Based on our data, we used computational methods to predict the O_2 fluxes that would have occurred during normobaric exposures to 40,000 and 45,000 ft, along with Boyle's law effects expected during an actual rapid decompression.
Discussion: These data are unique to our knowledge, as they are the first to result from actual human exposure to the descent profile required by FAA policy. This research serves to quantitatively define this risk associated with a high altitude decompression, and may be useful in future policy decisions.

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HUMAN RESPONSES TO A SIMULATED 35,000-FOOT INSTANTANEOUS DECOMPRESSION AND THE SUBSEQUENT DESCENT PROFILE REQUIRED BY FAA POLICY

Sudden decompression of an airliner passenger cabin due to structural failure or damage is unlikely, but it poses a potentially life-threatening event for occupants. This has been addressed through Federal Aviation Administration (FAA) airworthiness regulations and by the Society of Automotive Engineers (SAE) Aerospace Standards. Cabin occupants of transport aircraft are provided continuous-flow style oxygen masks for emergencies; however, a delay or inability to don these masks will result in exposure to ambient oxygen levels and many would quickly become incapacitated.

In 1996, FAA Amendment 25-87 revised the "pressurized cabin" airworthiness standards for subsonic transport airplanes. It created three new requirements governing the cockpit/cabin environment:

- § 25.841(a)(2)(i) - Cabin pressure not to exceed 25,000 feet for more than two min.
- § 25.841(a)(2)(ii) - Cabin pressure not to exceed 40,000 feet for any time.
- § 25.841(a)(3) - Fuselage, structure, engine and system failures are to be considered in evaluating the decompression.

In 2006, the FAA issued an interim policy that changed the procedure for certifying new airliners again, increasing the maximum cabin pressure altitude ceiling from 40,000 ft to 45,000 ft. The new policy allows aircraft a total of 3 min to descend below 25,000 ft in the event of a rapid decompression (RD) with 1 min above 40,000 ft. Both standards require pilots to execute a flight profile that will result in a continuously changing cabin environment mirroring the actual aircraft altitude.

The aeromedical research community's challenge has been to quantify the potential for significant neurological damage and death under these specific flight conditions, which do not permit direct investigation. Previous work was typically conducted in altitude chambers, using static profiles at the maximum altitudes. The adaptation of earlier studies' data has been a frequent strategy, with reliance on calculated values derived from equations developed for the steady state. Recent computational models (Wolf & Garner, 2007, 2009) have impressively addressed the ventilatory responses to hypoxia-inducing altitudes, but the models did not consider the fluxes of oxygen between the organism and the environment that would ultimately determine survivability of the event.

Total body exchangeable oxygen reserves for a 70 kg human are estimated to be 1150 ml: 730 ml will be dissolved in plasma and bound to hemoglobin (Hgb), with the remaining 420 ml distributed in the tissues (Cross et al., 1968). Our research question was whether an individual's oxygen stores will be depleted prior to the aircraft descending to an altitude that will permit inward fluxes of oxygen that exceed the resting oxygen consumption ($\dot{V}_{O_2}$) requirement.

We exposed human subjects to normobaric instantaneous decompressions to a simulated altitude of 35,000 ft. The peak altitude was maintained for 10s, followed by a 5,000 ft/ min descent to 25,000 ft. The subjects breathed a gas mixture that duplicated the partial pressure of oxygen (PO_2) that would be present in ambient air during this flight profile. This simulated the worse-case situation in which passengers fail to don their oxygen masks. Inhaled and exhaled gas composition, arterial hemoglobin oxygen saturation, heart and respiratory rate, tidal volume, changes in cardiac output, and blood flow velocity in the middle cerebral arteries were measured. Algebraic summation of O_2 loss/gain was compared to the subjects' resting $\dot{V}_{O_2}$, to see if there was an organismal O_2 deficit resulting from the flight profile.

MATERIALS AND METHODS

Subjects

A convenience sample of volunteer research subjects that met the requirements for altitude chamber training was recruited from the pool of registrants for FAA physiological training classes. Each subject provided written informed consent before participating, completed a health questionnaire, and possessed a current Class III Airman Medical Certificate. Measures from 24 healthy subjects (21 males and 3 females; ages 18-29, mean = 23.7), not acclimated to high altitude comprise the dataset. The study protocol was approved in advance by the Civil Aerospace Medical Institute (CAMI) Institutional Review Board for the Protection of Human Subjects, which conforms to the Belmont Report, and Title 45, U.S. Code of Federal Regulations, Part 46, Protection of Human Subjects. (revised January 15, 2009).

Medical Screening

Prior to the experiment, all subjects were given a complete pulmonary function test (PFT; VMax 229 Encore Respiratory Diagnostics System; Care Fusion, Inc.; Yorba Linda, CA), and a 12-lead electrocardiogram (ECG; Page Writer Xli; Hewlett Packard Company; Palo Alto, CA). Pulmonary function testing was performed with the subjects in sitting posture using a mouthpiece (dead space = 50 ml) and a nose clip. The system calculated total lung diffusing capacity for carbon monoxide (DLCO) using standard Jones-Meade criteria (Jones & Meade, 1961) and an anatomic dead space (ADS) algorithm (Hart, Orzalesi, & Cook, 1963). DLCO measurements were adjusted for the subject's own total hemoglobin value (Masimo Rainbow SET®, Masimo, Irvine, CA) and then converted to DLO_2 using the method of Comroe et al., 1962). The system was calibrated before each experiment by using a certified (± 3%) 3-liter syringe. Additionally, each subject was given a 6-min, sub-maximal Åstrand Bike Test (Åstrand & Ryhming, 1954)

to provide an estimate of $\dot{V}_{O_2}$max. The test was conducted on a Velotron Dynafit Pro computer-controlled, precision electronic bicycle ergometer/trainer (Racermate, Inc.; Seattle, WA). These tests, along with the health questionnaire, were used as a screening tool by the Medical Monitor (a physician) to rule out any evidence of disease that would constitute unacceptable risk, and thus exclusion from participation in the experiment.

The Normobaric Breathing Apparatus (Figure 1)

Normobaric exposures were accomplished using a reduced oxygen breathing device (ROBD; Environics, Inc; Tolland, CT). The ROBD uses thermal mass flow controllers to mix breathing air and nitrogen to produce the sea level equivalent atmospheric oxygen contents for altitudes up to 35,000 ft and is calibrated on a primary flow standard traceable to the National Institute of Standards and Technology (NIST). The ROBD outlet hose was connected to the inlet port on a two-way non-rebreathing valve (Hans Rudolph, Inc; Shawnee, KS) having three ports. The inhalation and exhalation ports each had a unidirectional diaphragm that directed flow to and from the mouth. This valve was connected in series with a heated (37°C), low dead space pneumotachometer that had a linear voltage output from 0 to 800 l/min (model 3813A series; Hans Rudolf, Shawnee, KS; dead

Figure 1. The normobaric apparatus.

space, 87.8 ml; flow resistance, 0.3 to 8.2 cmH$_2$O/80-800L/ min). The pneumotachometer was connected to a differential pressure research pneumotachograph system (Model RS100HR; Hans Rudolf; Shawnee, KS). A spirometry microbial/moisture filter mouthpiece (Care Fusion, Inc.; Yorba Linda, CA; dead space: 50 ml) was attached to the pneumotachometer. Total dead space in the apparatus was 223.1 ml. A sampling line connected to a mass spectrometer (model MGA-110; Perkin-Elmer; Waltham, MA) monitored the composition of inhaled and exhaled gasses.

As an orientation, all subjects breathed ground-level ambient air through the circuit for 2 min prior to the altitude exposure. That the apparatus had negligible physiological effects was evidenced by lack of changes in arterial Hgb oxygen saturation (SPO$_2$) or end-tidal CO$_2$ concentrations.

Procedure

The percentage of oxygen the device delivered was adjusted to account for the differential effects of water vapor pressure on inspired gas using the technique of Conkin (2011). To simulate the inspired partial pressure of O$_2$ (PIO$_2$) seen at 35,000 ft, we set the ROBD to deliver 4.05% O$_2$, which produced an inspired PIO$_2$ of 27.48 mm Hg.PO$_2$ The ROBD held this altitude for 10s and then ramped down to the PIO$_2$ computed for 25,000 ft (58.8 mm Hg; 7.23% O$_2$) over 120 s (the flight profile is shown in Figure 2). At 25,000 ft, the ROBD switched to 100% O$_2$ until baseline SPO$_2$ was reestablished. Barometric pressure in the laboratory was monitored with a NIST-traceable precision absolute manometer (model M2O$_2$; Meriam Process Technologies; Cleveland, OH) and was used each time to calculate the desired percentage of O$_2$ the ROBD delivered.
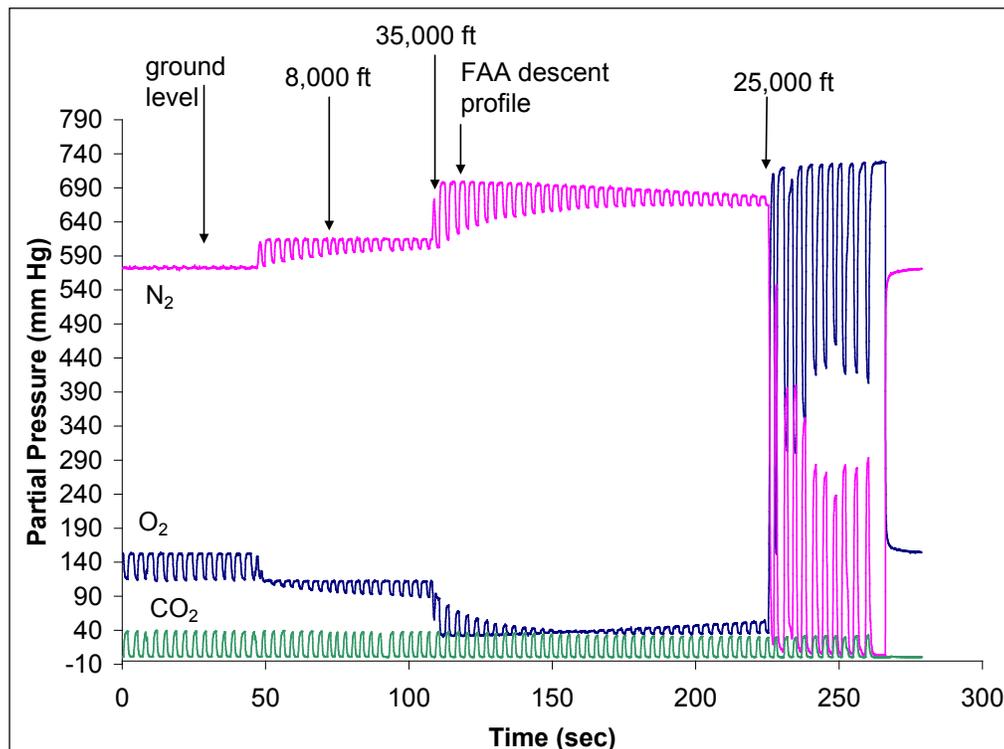
Figure 2. Breath-by-breath inhaled and exhaled respiratory gases during a normobaric instantaneous decompression to simulated 35,000 ft, 10-s plateau phase and subsequent 2-min descent to 25,000 ft. The subject was switched to 100% oxygen immediately upon reaching 25,000 ft.

PHYSIOLOGICAL MEASURES

Resting Oxygen Consumption

Resting oxygen consumption ($\dot{V}_{vo_2}$) was measured immediately prior to the normobaric hypoxia exposure. Breath-by-breath respiratory gas exchange was measured with the VMax 229 Encore Respiratory Diagnostics System (Care Fusion, Inc.; Yorba Linda, CA) using a flow-through mask. The system analyzed expired gas for oxygen concentration using a paramagnetic oxygen analyzer and for carbon dioxide concentration by using a nondispersive infrared analyzer. Gas analyzers were calibrated before each measurement using three known standard gas concentrations (16% O_2, 4% CO_2; 26% O_2, 0% CO_2; room air 20.94% O_2, 0.05% CO_2). The duration of the measurement was variable depending on how long it took the subject to reach stable values (5 consutive $\dot{V}_{o_2}$ values differing by 2% or less). Management and storage of data from the VMax 229 was done in CardioSoft/VMax Vision software for Windows (version 6.51, Care Fusion, Inc.; Yorba Linda, CA). In practice, the subjects were tested in the same sitting position as the subsequent hypoxia exposure.

Measurement of inhaled atmospheric and end-tidal air composition

A Perkin-Elmer Medical Gas Analyzer, MGA-1100 (Perkin-Elmer Life and Analytical Sciences, Inc.; Waltham, MA), was utilized for real-time measurement of the percentages of atmospheric gases (N_2, O_2, CO_2 and H_2O) delivered by the ROBD, and in the subjects' exhaled end-tidal gasses. Voltage output linearity was 0.5% of full scale for all gasses. Two-point calibrations were performed before each experiment using room air and a certified calibration gas (3% CO_2, 0% O_2, 97% N_2; ± 1%).

Ventilation

Ventilatory flow (Ambient Temperature, Pressure and Water Saturation; ATPS) and respiratory rate were measured with a heated, low dead space pneumotachograph (previously described) and acquired at a sampling rate of 1KHz on a personal computer for subsequent analysis. Tidal volume (V_t) was calculated on a breath-to-breath basis after digital integration of the flow signal at actual barometric pressure using LabChart Pro software V.7 (AD Instruments; Colorado Springs, CO). The system was calibrated before each experiment.

Oxygen Flux Rates

Breath-by-breath oxygen consumption and loss ($\pm \dot{V}_{o_2}$) was measured during the entire profile. Inhaled and end-tidal O_2, CO_2, and N_2 percentages, inhalation volume (V_{in}) converted to standard temperature pressure dry (STPD) volumes, and respiratory rate were recorded. V_{in} was adjusted for both anatomic and spirometry apparatus dead space. Anatomic dead space was estimated in each subject as a function of height using the relation $V_d = [7.585*(height^{2.363})]*10^{-4}$ established by Hart et al. (1963; r=.917)). $\dot{V}_{o_2}$ was then computed using the Haldane transformation (Haldane, 1912 & 1922) of the Fick principle through the following equation:

$$\dot{V}O_2 = \left(\dot{V}_{in} * \%O_{2_{in}}\right) - \left[\left(\frac{\%N_{2_{in}}}{\%N_{2_{exp}}} * \dot{V}_{in}\right) * \%O_{2_{exp}}\right] * bpm$$

Data Acquisition and Recording Scheme

Analog signals from all monitoring equipment (except ventilatory and ECG sensors) were digitized at 20 samples/s and recorded with a custom-built LabView data acquisition instrument (National Instruments Corp.; Austin, TX). Ventilatory signals (flow, volume, and rate) and ECG were digitized at 1 KHz and recorded using a modular Bio Amp (Powerlab Model ML880, AD Instruments; Bella Vista, Australia). Data files were synchronized *post hoc* by introducing a generated square wave with a function generator (Hewlett Packard model 3310B; Palo Alto, CA) into both data acquisition systems during the experiment.

Analysis

Statistical analysis was performed using programs available in the SPSS statistical package (SPSS, version 15.0, Chicago, IL). Significance was set *a priori* at alpha ≤ 0.05. Measurements are presented as means ± SD. All variables were tested for normal data distribution. Bivariate analysis between variables was carried out using Pearson product-moment correlation coefficients.

Based on the subjects' mean functional residual capacity (FRC), ADS, and breath-by-breath O_2 flux measurements made during the normobaric simulated 35,000-ft profile, we predicted the expected fluxes and O_2 deficits that would occur during 40,000 and 45,000-ft RD/descent profiles (Table III). Additionally, using the Boyle's law relation for RD-induced gas expansion, we calculated the additional O_2 loss expected during an actual rapid decompression. We treated ADS and FRC as discreet compartments with different gas compositions.

Clinical Monitoring

To ensure subject safety, real-time clinical non-invasive monitoring of cardiovascular, pulmonary, and neurological indexes was carried out by the Medical Monitor. These included:

Hemoglobin oxygen saturation and heart rate

Percent hemoglobin saturation, expressed as the ratio of oxyhemoglobin to reduced hemoglobin in arterial blood, was measured with a pulse oximeter clamped to the index finger of subjects' non-dominant hand and with a forehead sensor placed above the right supraorbital ridge. Absorption ratios and heart rate (HR) were computed by a pulse oximeter (Nellcor Model N600-X; Covidien Corp.; St. Louis, MO) and displayed as percent saturation and beats per minute (bpm), respectively.

Finger plethysmographic hemodynamic variables

Beat-to-beat monitoring of arterial blood pressure and its first derivative was employed using finger photoplesthysmography (NexFin; BMEYE B.V.; Amsterdam, The Netherlands). Stroke volume was determined by a three-element model of arterial input impedance (Nichols & O'Rourke, 1990). Cardiac output was calculated as the product of stroke volume and heart rate.

Intracranial blood flow

Continuous mean, systolic, and diastolic blood flow velocity in the right and left middle cerebral arteries (MCAs) were measured in all subjects. Backscattered Doppler signals, available as analog voltages, were continuously and simultaneously monitored by means of a ST3 pulsed digital transcranial Doppler (TCD) system (model # PMD 150; Spencer Technologies; Seattle, WA). Ipsilateral MCA velocity measurements were made using 2-MHZ probes via the posterior temporal windows immediately above the zygomatic arch. Middle cerebral arteries were identified bilaterally within depths of isonation between 35 to 56 mm.

Serum S100b measurements

To confirm that the hypoxia exposures were not resulting in clinically significant brain anoxia, we measured the serum levels of the protein S100b. Whole blood samples were collected from an indwelling catheter placed in the left antecubital vein in Serum Separator Tubes (BD Vacutainer® SST™ 367986; BD, Franklin Lakes, NJ) at four times, designated *Baseline, T2, T3,* and *T4.* The first sample was collected immediately before altitude exposure. Remaining samples were collected immediately after the hypoxia exposure, 15 min after exposure, and 2 h after exposure. After at least 30 min, SSTs were centrifuged at 1300xg for 10 min in a swinging bucket centrifuge pre-chilled to 4°C. Serum was aliqoted into ~500uL aliquots and stored at -80°C until assayed. S100b concentrations were determined from 50uL/well in triplicate on a custom Milliplex® Map magnetic bead sandwich ELISA kit (Cat. # HNDG4MAG-36K, Millipore Corp; Billerica, MA) measured on a BioPlex 100 (BioRad Laboraties; Hercules, CA) according to the manufacturer's recommended protocol and instrument settings. Statistical analysis was performed with pairwise.t.test in R v2.15 (Gentleman) with multiple testing correction by the Bonferroni method. For assays below the level of quantitation (LOQ=11 pg/mL), 5 pg/mL was assigned.

RESULTS

Data from 24 of the original 35 subjects comprise the dataset. Six subjects were disqualified after medical screening and five subjects failed to complete the profile due to incapacitation (manifested by their inability to maintain a mouthpiece seal). None of the subjects had increases from baseline in serum S100b (a biomarker for cerebral anoxia) following their hypoxia exposure to levels previously shown to be clinically significant.

All subjects had an initial reversal of the direction of oxygen diffusion following the RD that persisted until after the descent commenced, with outward flux predominating at higher altitudes of the profile. Return to net inward flux almost always occurred near 29,000 ft, the altitude at which the mixed venous and alveolar PO_2 gradient approximates nil. The net inward flux of oxygen approached but never surpassed each subject's resting O_2 as the altitude approached the 25,000 ft endpoint (Figure 3).

Subjects exhibited variable ventilatory responses to the profile. Typically, Vt increased during the 1st minute of the profile, with respiratory rate either decreasing or remaining unchanged (Figure 4). For cross-subjects comparison, we also computed an average minute volume (MV) during the 130-s profile. SPO_2 and heart rate sensors reported large changes after the RD commenced (Figure 5), with the finger probe showing declines in arterial oxygen saturation that always exceeded the forehead sensor by an average of 19.75%. Changes in finger SPO_2 exhibited a response latency that followed the HR and forehead sensor, by an average of 15s. Return of HR and SPO_2 to baseline levels began after completion of the 2-min profile once 100 % O_2 was breathed.

Although all subjects had an O_2 deficit resulting from the profile, variation in individual physiological measures existed within the subject pool. Mean cardiovascular and respiratory parameters, along with ranges and standard deviations (SD) are presented in Table I.

Bivariate one-tailed Pearson correlation tests were applied between these variables and revealed several significant relations (Table II). The strongest relationship was seen between the final V_t before the RD and the flux of O_2 during the first breath following the RD. Furthermore, the average alveolar PO_2 during the profile was strongly related to FRC, cardiac output, and the total O_2 deficit.

We attempted to predict the magnitude of O_2 flux/deficit for 40,000 ft and 45,000 ft profiles, with and without the effects of gas expansion resulting from Boyle's law, based on the 35,000 ft measurements reported here (Table III).
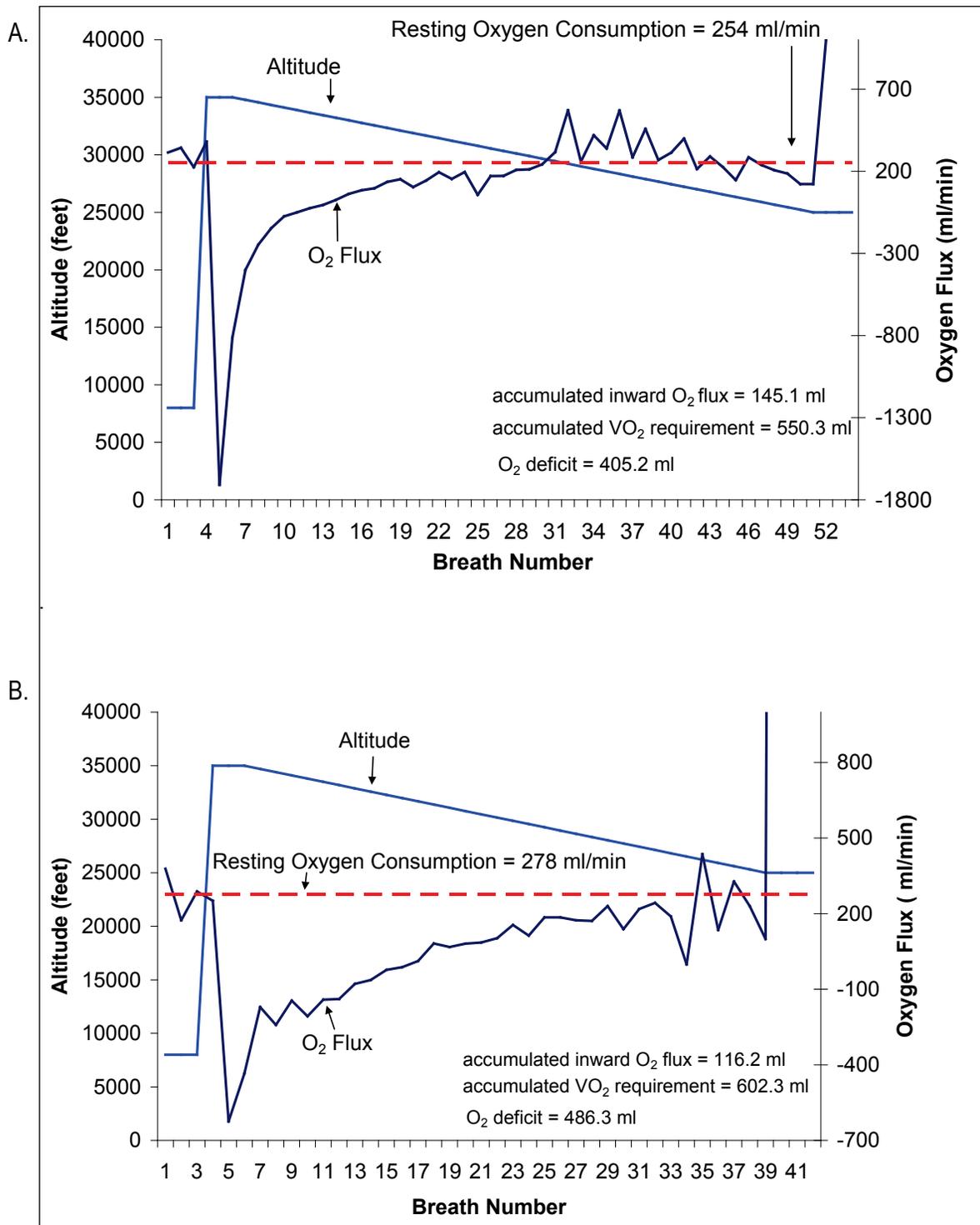
Figure 3. Breath-by breath oxygen fluxes in 2 subjects (A. and B.) resulting from the 35,000 ft RD profile. Shown are the altitude profile, resting O_2 measured just prior to the experiment, and O_2 flux. Negative values reflect outward flux. The abrupt increase in O_2 flux, seen as the profile descended through 25,000 ft, results from switching the subjects to 100% oxygen. The saw-tooth pattern in O_2 fluxes late in the profiles reflect changes in FRC (Wessel et al, 1979; di Prampero & Lafortuna, 1989) resulting from the progressive hypoxic ventilatory response.

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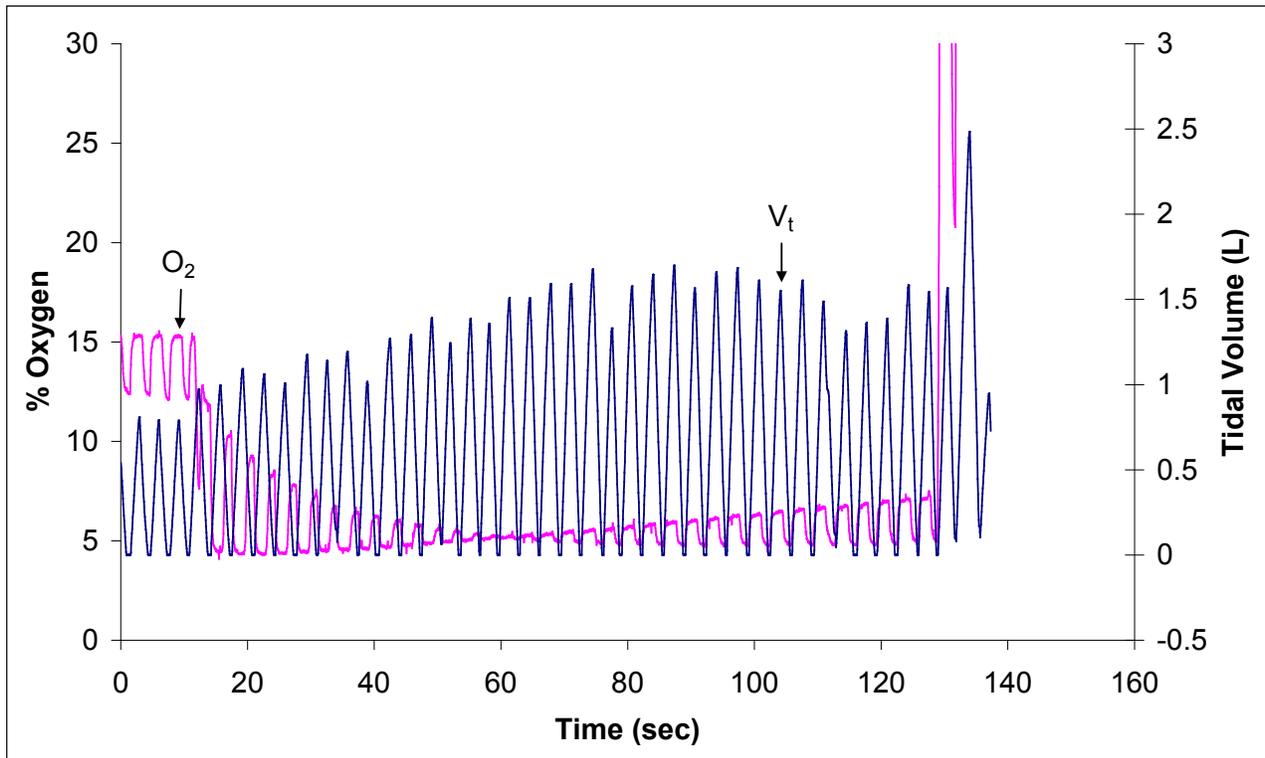
Figure 4. Inspired and expiratory O_2 percentage and ventilation (ATPS) during the profile in one subject. The peak of the O_2 trace (inspiration) and nadir (expiration) reverse initially after the RD, and then reverse again as the altitude decreases over time. A vigorous ventilatory response to the hypoxic gas mixture can be seen.
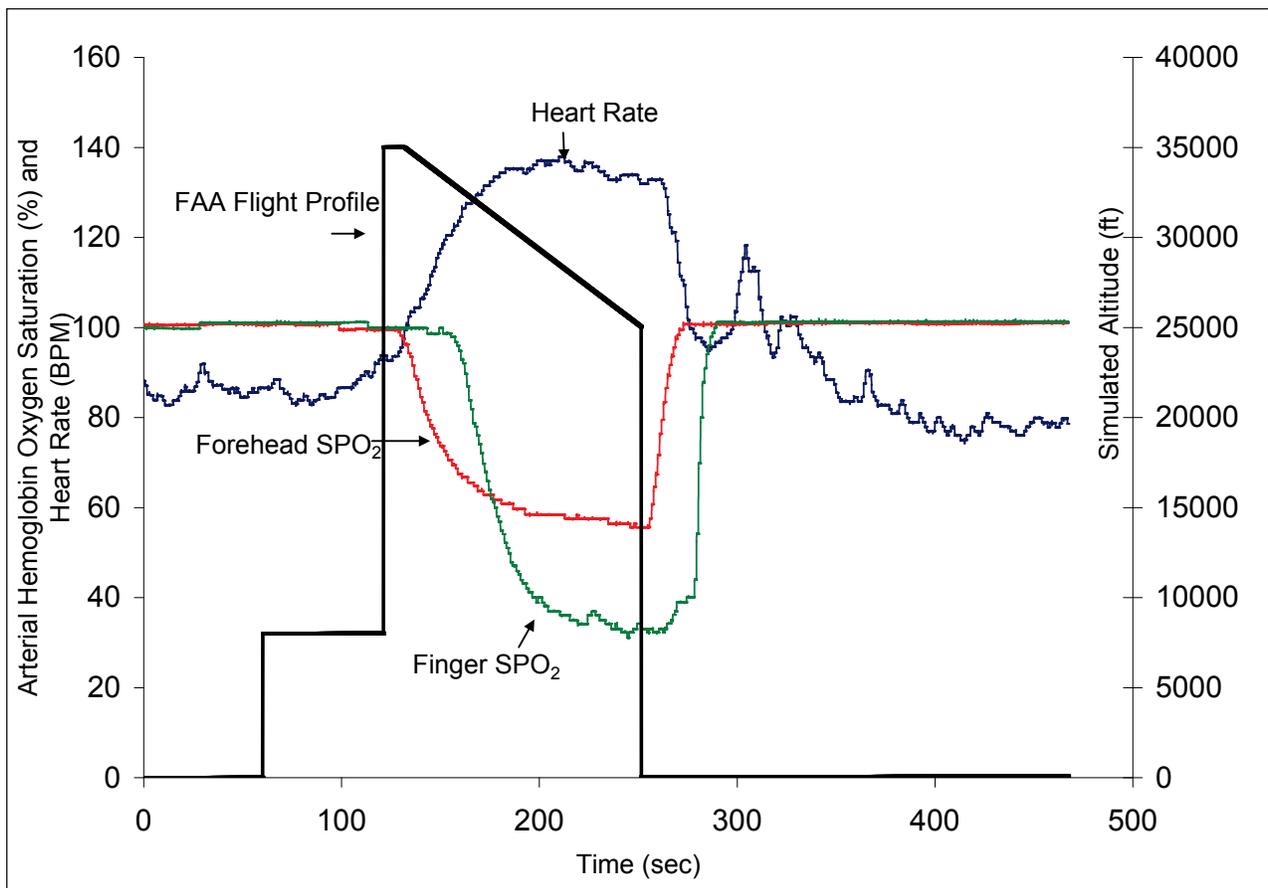
Figure 5. Profile altitude superimposed on arterial hemoglobin oxygen saturation and heart rate in one subject. 100% oxygen was breathed upon reaching 25,000 ft at the end of the profile, with heart rate and SPO_2 returning to baseline values.

Table I. Descriptive statistics for physiological parameters collected prior to (DLO$_2$, FRC, $\dot{V}_{O_{2\,max}}$, and ADS) and during the flight profile. Average PAO$_2$ values reflect both inhalation and exhalation during the 130-s profile. Tidal volume before RD values were for the single breath just prior to the RD. Negative flux values reflect outward movement of oxygen from the respiratory tract. Cardiac output was averaged over the 130-s profile.

Measure	N	Minimum	Maximum	Mean	SD
DLO$_2$ (ml/mm Hg/min)	24	25.10	62.60	40.4204	9.54306
FRC (L)	24	1.44	6.56	3.1763	1.06690
$\dot{V}_{O_{2\,max}}$ (ml/kg/min)	24	16.90	72.64	40.1171	11.78329
Resting $\dot{V}_{O_2}$ (ml/min)	24	219.0	333.0	270.41	36.23
Anatomic Dead Space (ml)	24	124.89	200.00	155.5679	16.94774
Total Inward Flux (ml)	24	32.90	373.60	149.3604	85.56427
Avg minute volume (ml)	24	9.02	28.41	14.5621	4.40735
Increase in HR (BPM)	24	23.20	55.00	41.4717	10.11964
Avg RR (cycles/min)	24	7.27	42.20	18.1603	7.06571
Lowest finger SPO$_2$ (% Hgb SAT)	24	31.40	76.18	55.5295	8.74035
Average PAO$_2$ (mm Hg)	24	36.78	41.82	38.3758	1.25361
Profile O$_2$ deficit (ml)	24	292.40	662.40	436.5	94.42754
Tidal Volume before RD (L)	24	.17	1.58	.5376	.37321
1st Breath Flux (ml)	24	-1708.00	-51.04	-376.874	334.93621
Average Cardiac Output (L/min)	22	7.43	13.7	11.81	1.51

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Table II. Significant Pearson correlations along with their p values between physiological measures. All other possible relationships from Table I were not significant.

	Anatomic Dead Space	O_2 Deficit	Average PAO_2	Resting VO_2	1st Breath O_2 Flux	HR Increase (BPM)
DLO_2	0.531 $p=.004$	0.388 $p=.030$				
O_2 Deficit			0.507 p=.006			
FRC	0.555 $p=.002$		0.671 $p=.000$	0.504 $p=.006$		
Pre-RD Tidal Volume					-0.77 $p=.000$	-0.473 $p=.010$
Average MV					-0.656 $p=.000$	
Lowest SPO_2			0.369 $p=.038$			
Total Inward O_2 Flux			-0.639 $p=.000$			
HR					0.543 $p=.003$	
Average PAO_2	0.493 $p=.007$	0.507 $p=.006$				
Cardiac Output		0.483 $p=.011$	0.513 $p=.007$			

Table III. Measured and Predicted (italics) Oxygen Fluxes and Deficits

Measure	35,000 ft profile	40,000 ft descent profile (2 min) prediction	45,000 ft descent profile (3 min) prediction
Resting VO_2 (ml/min)	270.4	**270.4**	270.4
O_2 Flux RD to 30K (ml)	-97.53	*-125.4*	*-208.9*
Additional O_2 loss resulting increased time above 30,000 ft (ml)	-	*27.9*	*111.4*
Total O_2 Flux for Profile (ml)	+ 149.3	*+121.4*	*+37.9*
Total O_2 Requirement for Profile (ml)	585.8	*585.8*	856.3
Total O_2 Deficit for exposure (ml)	-436.5	*-464.1*	*-818.4*
Added O_2 Loss Resulting From Boyle's Law Gas Expansion (ml)	*-296.5*	*-325.9*	*-349.5*
O_2 Deficit With Boyle's Law Effects (ml)	*-733.0*	*-790.0*	*-1167.9*

40,000 and 45,000ft flux estimation technique. The mean total outward O_2 flux during the 1st 69.9 s (elapsed time from the 35,000 ft RD until descending through 30,000 ft) was 97.53 ml. This was then divided by the elapsed time to get a baseline O_2 flux/s. The baseline flux was multiplied by the time required by the 40,000 ft (89.95 s) and 45,000 ft (149.9 s) profiles to reach the same 30,000 ft. This provided an estimate of the additional outward flux attributable to the increased time required to reach 30,000 ft in the 40,000 and 45,000- ft profiles. These estimated fluxes were then added to the mean O_2 flux measured for the entire 35,000- ft profile to yield predicted 40,000 ft and 45,000 ft predictions.

Compensation for Boyle's Law Effects. To account for the effects of Boyle's law, which would be seen during an actual RD (but not a ground-level exposure) on the volume of gas residing in the subjects' FRC and anatomic dead space (ADS), we made the following calculations. The mean FRC and ADS for the 24 subjects were 3.18 L and 155.6 ml, respectively, yielding an end-expiratory volume subject to expansion of 3.329 L (ATPS).

We treated the ADS and FRC as discreet compartments with different compositions. During the RD, ADS gas (FIO_2 = .209; 4.89% of total volume) would exit first, followed by FRC gas (FIO_2 = .125; 95.1% of total volume). The original volume of O_2 residing in ADS +FRC O_2 at 8,000 ft was 430 ml (ATPS).

Using the Boyle's law relation ($P_i V_i = P_f V_f$), we solved for the final volume where Pi = 564.5 mm Hg (8,000 ft); Pf = 178.9 mm Hg (35,000 ft), 140 mm Hg (40,000 ft) 108.5 mm Hg (45,000 ft) and Vi = 3.329 L. This gave post-RD volumes of 10.5 L, 13.4L, and 17.3L respectively . Of these, 3.329 L would remain in the FRC + ADS space, leaving 7.17 L, 10.1L, and 13.9 L that would actually exit the respiratory tract. Mean peak expiratory flow for the subjects measured during their pulmonary function studies was 9.2 L/s, indicating that all of the expanded volume could easily be lost within the 1st 2 s following the RD. The amount of O_2 in the exiting ADS and FRC was calculated for each altitude, converted back to its 8,000 ft equivalent, and then subtracted from the measured and predicted normobaric O_2 deficits.

DISCUSSION

The probability of engine rotor failure-induced decompression at altitudes of 40,000 to 45,000 ft is exceedingly small and a number of current airliners, including the Boeing 747 and 737 aircraft, have been exempted to fly at maximum altitudes above 40,000 ft. Relative to current operations, no incidents of decompression above 40,000 ft have been recorded in the United States. However, the calculated relative risk of an RD although small, has led to concern in the civil aeromedical community because of the event's potential lethality.

A previous FAA report (2004) concluded that altitude exposure limits of 40,000 with a 2-min descent time to 25,000 ft involved significant risk for pathologic injury to cabin occupants, and that the new policy involved a greater degree of risk of permanent neurological injury and death to unprotected aircraft occupants. These conclusions were based primarily on animal studies conducted by British researchers who evaluated the physiological aspects of altitude exposure as applied to the development of the Concord supersonic aircraft. This body of work emphasized the potential lethality of such exposures.

Of particular note was the work of Nicholson and Ernsting (1967), who conducted a decompression study exposing baboons to 30,000, 42,500, and 53,000 ft. In the 30,000-ft decompression, the animals lost consciousness at the 22,000- ft level during ascent, regained consciousness at 15,000 ft on descent and made an apparently normal recovery from the hypoxic insult. During the 53,000-ft decompression, one animal was observed to be unconscious at 40,000 ft and respiration ceased at 43,000 ft. The animal did not survive the decompression. Another animal appeared unconscious at 30,000 ft on ascent and stopped breathing at 40,000 ft on descent. The animal died 5 days after the exposure. A third animal appeared unconscious at 35,000 ft and stopped breathing at 37,000 ft. The animal survived but sustained severe brain damage. A fourth animal demonstrated "gross respiratory embarrassment" from 35,000 ft and respiration ceased at 43,000 ft. The animal died 5 days after the exposure. In the 5 days before they died, the animals exhibited gross behavioral and neurological disturbances.

Additional work by Nicholson et al. (1970) reported on a study of behavior and neuropathology in 21 Rhesus monkeys as a sequelae of profound hypoxia resulting from decompressions to 42,500 ft. Altitudes were held until the occurrence of respiratory arrest followed by a rapid descent profile. Three animals died, and seven showed evidence of neuropathology.

In the current study, we have measured human physiologic responses to a simulated instantaneous rapid decompression to 35,000 ft and the subsequent emergency descent profile required by FAA policy. Further, we have used these data as the basis for predicting responses to both a 40,000-ft exposure, and the recent FAA policy change allowing a 3-min descent profile following an RD to 45,000 ft. These data are unique to our knowledge, as they are the first to result from actual human exposure to the descent profile required by FAA policy.

Our experimental design sought to examine the worst-case scenario of a passenger failing to don an oxygen mask, and their subsequent exposure to pure ambient conditions during the 2-min profile. We constructed the profiles to include a 10-s plateau phase at 35,000 ft prior to the descent. The plateau added a degree of realism to the exposure by simulating the time required for the pilots to recognize the problem, disengage the altitude hold function on the autopilot, and then execute a descent maneuver.

To confirm the absence of clinically significant cerebral anoxia resulting from exposure to hypoxic gas mixtures in our study, we tested all subjects for elevations in serum levels of the calcium binding protein S100b. S100b is secreted by astrocytes and is hypothesized to spill from injured cells and enter the bloodstream via a permeablization of the blood–brain barrier. S100b levels are a hallmark of brain injury resulting from prolonged hypoxia after cardiac arrest (Rosen et al., 1998, Siman et al., 2009). Elevations have also been seen in breath-hold divers, within 10 min of the end of the apneic phase (Andersson et al., 2009). S100b increases in these reports were all an order of magnitude higher than the modest and non-sustained elevations seen in our subjects.

We have shown that in a cohort of 24 healthy young adults, exposure to a normobaric RD to simulated 35,000 ft, followed by the 2-min FAA flight profile, the total inward O_2 flux was less than resting $\dot{V}_{O_2}$, requirements but did not exceed theoretical exchangeable reserves. This was true even when added O_2 loss resulting from Boyle's law gas expansion was considered. Based on our data, we used computational methods to predict the O_2 fluxes that would have occurred during normobaric exposures to 40,000 and 45,000 ft, along with Boyle's law effects expected during an actual rapid decompression. Although the 40,000 ft RD and subsequent 2-min descent profile yielded a predicted O_2 deficit well under the 1,170 ml of reserves, this was not the case for the 45,000- ft – 3 min profile. Here, the predicted O_2 deficit slightly exceeded the exchangeable O_2 reserves, emphasizing quantitatively, the increased risk involved in this RD scenario.

This work has several limitations. Our predictive technique may have underestimated the 40,000 ft and 45,000 ft O_2 losses, as we assumed the fluxes would be similar to the mixed venous-alveolar P_{O_2} gradients existing at 35,000 ft. Although the diffusion gradients would increase from 35,000 ft to 40,000 ft and 45,000 ft (12.5 mm Hg, 20.5 mm Hg, and 27.1 mm Hg, respectively, assuming mixed venous P_{O_2} = 40 mm Hg), we argue that this would result in minimal differences in the initial flux rates because of an increasing disequilibrium between pulmonary capillary blood and alveolar air as the final RD altitude increased. Oxygen transfer between the lungs and blood would become increasingly diffusion-limited because the process is operating on a progressively steeper part of the oxygen dissociation curve as P_{O_2} values decline (West et al., 2007). Hence, blood would be leaving the pulmonary capillaries before reaching equilibrium with alveolar oxygen, resulting in the initial reverse flux rate being smaller than the diffusion gradients would predict. Furthermore, our subjects were all healthy young adults who

passed rigorous medical screening. This is not true of the general flying public where age and disease processes would negatively impact hypoxia tolerance.

Although we terminated the hypoxic exposures at 25,000 ft by switching subjects to 100% oxygen, we caution that under real-world conditions, the flight profile would continue a descent to 10,000 ft, and the extent of oxygen deficit would likely be more severe than observed in this study. We chose a 25,000-ft termination point because the FAA interim policy only addressed flight profiles above this value, and we wished to limit the severity of the hypoxia exposure.

Permitting airplanes to fly above 40,000 ft does offer real and tangible benefits to the aerospace industry, the traveling public, and the U.S. economy by reducing air traffic congestion, pollution, and improving fuel economy. An analysis reported in the FAA Interim Policy on High Altitude Cabin Decompression (2004) showed that there is an average probability of an uncontained engine failure at cruise altitude of approximately 1×10^{-7} per engine hour. Because these events are rare, the FAA considers that the benefits of operating at higher altitudes compensate for the added risk. Our work serves to quantitatively define this risk and may be useful in future policy decisions.

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