Comparative Study on the Effects of +Gz Exposure and Oxygen Concentration on Small Airway Collapse.

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Primary Objective: To determine how exposure to +5Gz forces affects small airway function when breathing ambient air (21% oxygen) and oxygen enriched air (60% oxygen) , without the breathing component of the AGSMSecondary Objective: To explore the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON57426

Source
ToetsingOnline

Brief title
+Gz and Oxygen Concentration Effects on Airway Collapse.

Condition

- Other condition

Synonym
Acceleration Atelectasis, G-induced airway collapse

Health condition

Acceleratie Atelectase

Research involving
Human

Sponsors and support

Primary sponsor: Centrum voor Mens en Luchtvaart, Koninklijke Luchtmacht
Source(s) of monetary or material Support: Ministerie van Defensie

Intervention

Keyword: Acceleration Atelectasis, Centrifuge, impulse oscillometry, Oxygen concentration

Outcome measures

Primary outcome

The primary outcome measure of this study will be the change in airway compliance (xrs) before compared to after +5Gz exposure when breathing ambient air (21% oxygen) and oxygen enriched air (60% oxygen). Measuring airway compliance before +Gz exposure will serve as baseline measurement. The specific outcome measure provided by the tremoFlo IOS, that fits this primary parameter best is: Reactance Area (AX), a derived parameter representing the total energy loss due to airway distensibility or compliance, as reflected by the echo or rebound of oscillatory air waves.

Secondary outcome

Secondary outcome measures will provide a comprehensive assessment of changes in respiratory function in response to +Gz exposure, facilitating a detailed analysis of both central and peripheral airway mechanics under varying conditions of oxygen concentration. These include:

• Total airway resistance measured at a low-frequency oscillation of 5 Hz (R5), which reflects resistance across both central and peripheral airways.

• Central airway resistance, determined at higher frequencies of 19 Hz and 20 Hz (R19, R20), which isolates the resistance primarily in the larger, more central airways.

• Peripheral airway resistance, calculated by subtracting central airway resistance from total airway resistance (R5-R19, R5-R20), representing the resistance in smaller, more distal airways.

• Reactance at 5 Hz (X5), which captures the elastic properties of the airways and lungs, indicating how easily airways return to their resting state following inhalation.

• Tidal volume (VT), the volume of air inhaled and exhaled with each breath during normal breathing, providing an indicator of lung ventilation efficiency.

Other study parameters (if applicable)

Through asking by a researcher the additionally data is collected on the following factors:

• Subjective ratings of perceived breathing difficulty during and after +Gz exposure expressed in the following categories: no difficulty, mild, moderate and severe.

• Incidence of acceleration atelectasis symptoms (e.g., couching and chest pain).

• Visual symptoms (either tunnel vision or grey-out) during +Gz exposure.

Study description

Background summary

In recent years, the increase in reports of unexplained physiological events in military aviation emphasize the need for a better understanding of the effects of in-flight stressors (i.e. hypoxia, temperature, vibration) on physiological processes. Among these stressors, exposure to positive G-forces in the cranio-caudal direction (+Gz) during high speed flight maneuvers, poses unique challenges that can significantly impact pilot health and performance. One notable consequence of +Gz exposure is the development of acceleration atelectasis, a condition characterized by the collapse of terminal airways in the basal alveoli. This phenomenon occurs when +Gz causes inadequate ventilation despite maintained perfusion, resulting in atelectasis.

Acceleration atelectasis, or G-induced atelectasis, has been studied since the 1960s. Langdon and Reynolds were the first to describe how increased levels of sustained +Gz combined with a 100% oxygen concentration led to alterations in basal lung segments and produced post-flight signs and symptoms such as, inability to take a deep breath, substernal tightness and paroxysmal coughing. Additionally, Levy et al. reported ten cases of post-flight basilar sub-segmental acceleration atelectasis, which were typically asymptomatic, though some individuals experienced chest pain and cough. Importantly, they noted that this condition is usually self-limiting, with symptoms resolving and clear chest x-ray findings within 48 hours post-flight. Hyde et al. demonstrated that exposure to +3.5 Gz, coupled with the inhalation of 100% oxy-gen while wearing an anti-G suit, resulted in a 40% decrease in vital capacity. Later research has corroborated these findings, documenting similar mechanisms and symptoms.

The development of faster and more agile fighter aircraft in the 1980s and 1990s spurred further investigation into the effects of different gas mixtures on acceleration atelectasis, particularly with the introduction of on-board oxygen generating systems (OBOGS). These studies found that gas mixtures containing more than 70% oxygen were associated with an increased risk of acceleration atelectasis. They also found protective effects from argon and nitrogen dilutions, unassisted positive pressure breathing (PPB), and Anti-G Straining Maneuvers (AGSM). Consequently, the OBOGS was designed to limit the maximum oxygen concentration to 60% up to 15,000 feet cabin altitude and in unpressurized aircraft. Recent studies have reaffirmed that breathing 60% oxygen typically results in only mild acceleration atelectasis.

A major challenge in the study of acceleration atelectasis has been the measurement of outcomes. Conventional spirometry has long been the gold standard for evaluating lung function and airway collapse, but it necessitates forced inhalation or exhalation techniques, which can influence airway collapse measurements. Recently, the adoption of Forced Oscillation Techniques (FOT) and Impulse or Airwave Oscillometry (IOS and AOS) has gained traction as methods for assessing lung function and airway collapse. These oscillometric techniques measure airway resistance and compliance by generating airwaves at multiple frequencies, ranging from 5 Hz to 37 Hz. Lower frequencies penetrate deeper into the airways, providing insights into total airway resistance and compliance, while higher frequencies are indicative of central airway conditions.

Pollock et al. assessed lung function after repeated +5 Gz exposure using spirometry and FOT in two studies. In the first, subjects underwent five centrifuge runs at varying durations, breathing 94% oxygen in four runs and 21% in one, with FOT revealing no significant changes in air-way resistance or compliance. In a second study, five exposures at oxygen levels of 21, 35, 45, 60, and 75% also showed no significant effects. However, the single-frequency FOT measurements limited the ability to distinguish small from central airway function, which may be relevant for assessing acceleration atelectasis. In a collaborative study involving the Royal Netherlands Air Force and the Royal Canadian Armed Forces, researchers used Airwave Oscillometry to evaluate resistance and compliance after +9 Gz exposures while subjects donned anti-G trousers and performed AGSM. This study found significant reductions in resistance and increases in compliance post-exposure, highlighting the protective effect of positive intrathoracic pressure and raising questions about the duration of airway impedance changes.

Understanding changes in airway resistance and compliance at moderate +Gz levels, where full AGSM may not be necessary, is crucial. Experienced fighter pilots often personalize their AGSM techniques and adapt their efforts effectively. In current OBOGS systems the delivered oxygen concentration only exceeds 60% in unpressurized aircraft to mitigate acceleration atelectasis risks. Therefore, accurately assessing airway impedance measures at moderate +Gz levels while breathing 21% and 60% oxygen*before exposure, immediately post-exposure, and after a recovery period*is essential for determining any effects and the duration of any observed effects. While previous studies have predominantly used conventional spirometry or partly used oscillometry, it may provide more precise measurements by eliminating the need for forced maneuvers and differentiating between upper and lower airways.

This study aims to assess potential airway collapse during G-exposure at 21% and 60% oxy-gen, utilizing the full range of airwave oscillometry outcomes to differentiate resistance, reactance, and compliance among central, total, and small airways. The research questions focus on observable effects on airway resistance and reactance during G-exposure with both oxygen levels, with subjects wearing anti-G trousers and without performing AGSM breathing. The hypothesis posits that small airway resistance will increase and compliance will decrease due to small airway collapse. This investigation builds upon the foundational work of Pollock et al. and Cornelissen et al.

Study objective

Primary Objective: To determine how exposure to +5Gz forces affects small airway function when breathing ambient air (21% oxygen) and oxygen enriched air (60% oxygen) , without the breathing component of the AGSM

Secondary Objective: To explore the interaction between oxygen concentration and +Gz exposure on respiratory mechanics, focusing on both central and peripheral airway dynamics.

Study design

Study Type: A randomized crossover design where participants serve as their own controls, exposed to +Gz with breathing both 21% and 60% oxygen concentrations on separate days.

Blinding: Participants will be blinded to the specific oxygen concentration they are breathing during each run. The researchers involved in the data collection will not be blinded due to logistical constraints but will not interact with participants regarding study conditions.

Study Setting: Center of expertise for aerospace medicine and physiology.

Duration: 4 months (2 months for recruitment, 2 months for intervention (no follow-up)).

Exposure order of the participants to the oxygen concentrations will be randomly assigned. Exposure order will be counterbalanced.

Intervention

Day 1 - Control: Participants will undergo 2 centrifuge runs:
o Baseline measurement whilst seated and strapped in the centrifuge gondola.
o Relaxed G-profile to determine G-tolerance and visual symptoms (either tunnel vision or grey-out). With this run the participant knows which symptom indicates the need for more muscle strain to maintain consciousness. This profile takes usually somewhere between 45 and 60 seconds before visual symptoms appear and the participant terminates the run.
o +5 Gz profile with anti-G trousers, while breathing normal air (21% oxy-gen) through a breathing mask. In this profile the participants have to per-form a correct anti-G straining maneuver if needed, which is the isometric continuous straining of muscles in the lower extremities and abdomen.
o Second measurement of airway impedance using the Thorasys tremoFlo, whilst still seated and strapped in the centrifuge gondola.
o After this the subject is unstrapped, exits the gondola and takes place in a second mock-up ejection seat to maintain the same seated position or the next minutes until 30 minutes post-run.
o After 30 minutes post-run a third measurement is taken to determine if any observed effects are transient within 30 minutes or if they sustain.

Day 2 - Intervention: Participants will undergo 2 centrifuge runs:
o Baseline measurement whilst seated and strapped in the centrifuge gondola.
o Relaxed G-profile to determine G-tolerance and visual symptoms (either tunnel vision or grey-out). With this run the participant knows which symptom indicates the need for more muscle strain to maintain consciousness. This profile takes usually somewhere between 45 and 60 seconds before visual symptoms appear and the participant terminates the run.
o +5 Gz profile with anti-G trousers, while breathing 60% oxygen through a breathing mask. In this profile the participants have to perform a correct anti-G straining maneuver if needed, which is the isometric continuous strain-ing of muscles in the lower extremities and abdomen.
o Second measurement of airway impedance using the Thorasys tremoFlo, whilst still seated and strapped in the centrifuge gondola.
Withdrawal of individual subjects
o After this the subject is unstrapped, exits the gondola and takes place in a second mock-up ejection seat to maintain the same seated position for the next minutes until 30 minutes post-run.
o After 30 minutes post-run a third measurement is taken to determine if any observed effects are transient within 30 minutes or if they sustain.

Study burden and risks

Due to the nature of this study, which only involves benign levels of Gz in a controlled centrifuge environment, participants are not at risk of any serious or long lasting injuries. Participants are medically screened before participation so any participant with contra-indications for exposure to increased levels of Gz is excluded from participation.

Contacts

Public
Centrum voor Mens en Luchtvaart, Koninklijke Luchtmacht

Kampweg 53
Soesterberg 3769 DE
NL
Scientific
Centrum voor Mens en Luchtvaart, Koninklijke Luchtmacht

Kampweg 53
Soesterberg 3769 DE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Participants must be part of military personnel (either active military or reservist).
- Aged between 18 and 55 years old.

Exclusion criteria

- Presence of any chronical respiratory illness.
- Current or recent (past 2 weeks) respiratory illness, e.g. a cold.
- Unfit assessment following flight medical examination.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending

Start date (anticipated):	30-03-2025
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	04-04-2025
Application type:	First submission
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	**ID**
CCMO	NL88765.041.25