Combined effects of microgravity and reduced gas density on an exhaled biomarker for airway inflammation

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Background
During future planetary exploration, astronauts risk to inhale toxic Lunar and Martian dusts, which can cause airway inflammation (Linnarsson et al 2012). Measurement of exhaled nitric oxide (NO) is a simple and reliable way to diagnose airway inflammation and to monitor lung health (Alving et al 1993). We have previously shown that both gravity (Karlsson et al 2009) and gas density (Hemmingsson et al 2012) modify NO turnover in the lungs and therefore also exhaled NO. In these studies the effects of changes in gravity and gas density were studied separately and not in combination as would be the case in future planetary habitats. Our hypothesis based on preliminary data is that there is an interaction between the effects of gravity and gas density such that a reduction of gas density in microgravity will promote diffusive transport of NO in the lungs, whereas such an effect may not be obvious in normal gravity. Such an interaction would greatly impact the interpretation of data for exhaled NO obtained during manned planetary exploration. It would therefore be of great interest to determine how combined changes of gravity and gas density modify exhaled NO under conditions similar to those in future planetary habitats.

Methods
The study “Airway Nitric Oxide in Space here denoted AM) consisted of two different lung tests; exhaled nitric oxide partial pressure at multiple flows (PENO), and lung diffusing capacity for nitric oxide (DLNO). The tests were performed on astronauts before and during their stay on ISS. All measurements were performed both at normal ambient pressure (1013 hPa) and at reduced ambient pressure (700 hPa). During the sessions with lowered ambient pressure the oxygen level was increased to 27.5%. On Earth the reduced pressure sessions were performed in a hypobaric pressure chamber at the NASA Neutral Buoyancy Laboratory (Johnson Space Center, Houston, Texas USA), and aboard ISS in the US airlock (which normally is utilized for extravehicular activities, space walks).

Exhaled nitric oxide
The atmospheric pressure (and the associated changes in gas density and diffusivity for NO in the background gas) did not have any impact on exhaled NO at the standardized exhaled flow of 50 ml*s⁻¹ (PENO50), so data from the two pressures were pooled for each session. The mean values for all preflight sessions (on the average 138 days before launch) in 9 subjects was 2.46 (0.24) (mean(SEM)) mPa. Corresponding values inflight were day 67 inflight and 1.51 (0.15) mPa. Thus PENO 50 fell significantly by 39 % (P= 0.0004) in agreement with our earlier findings.

![Fig 1. Exhaled NO (PENO) at exhalation flow 50 ml/s as a function of time (day 0 = launch day) for nine subjects.](image_url)

Figure 1 shows PENO50 in all subjects as a function of time during the preflight and inflight periods. The diagram suggests a general trend that PENO50 fell with time, but this was not true for a few subjects resulting in no significant change for the group preflight and a trend inflight (P=0.072). This trend in a majority of the subjects deserves further study and may be related to factors related to the preflight training program, including EVA training and hyperoxia.
Lung diffusing capacity for nitric oxide (DLNO)

With our DLNO experiments on ISS we have performed the first ever direct measurements of the lung diffusing capacity for nitric oxide (the speed of gas diffusion from the lung gas to the blood) in microgravity and in addition in combined microgravity and reduced ambient pressure.

Fig 2. Preliminary data (means, n=9) of lung diffusing capacity for NO (DLNO) from the first nine subjects from which we obtained complete data sets under all four experimental conditions. In normal gravity DLNO did not differ between pressures, whereas in microgravity there was a significantly increased DLNO with the lower ambient pressure (P=0.003).

Lung diffusing capacity for NO in the 9 subjects for which there are data from all 4 conditions (1 G normal and reduced pressure, micro G normal and reduced pressure) is shown in figure 2. Our preliminary data support the hypothesis of interaction between microgravity and reduced pressure/ gas density; reduced density (increased diffusivity) in the gas phase enhances uptake of NO into the blood in micro G but not in normal G.

Conclusions and perspective

Our preliminary data support the notion of a combined influence of gravity and gas density on the pulmonary turnover of NO. Thus normal values of exhaled NO obtained on ground will not be useful as a reference for data obtained during space exploration, and individual normal values need to be established in flight before a possible exposure to toxic dust.

A limitation in the design of the present experiments was that the ambient pressure and the gas density during the hypobaric sessions was higher than the corresponding values foreseen in a future Lunar habitat. This was so since concerns for astronaut safety precluded exposure to hypoxia, since hypoxia might aggravate the Space Flight–Associated Neuro-ocular Syndrome (SANS), a condition that may include an elevation if the intracranial pressure. We are therefore planning a new set of ISS experiments using normoxic helium mixtures to obtain the desired gas density, about 50% of that with normobaric air. These experiments have recently been accepted by the European Space Agency for technical accommodation studies.

References


