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Short comunication

Space travel in a high altitude environment: Biology by-passing the pressure laws of physics and BioSpaceForming

Viaje espacial en un entorno de gran altura: condiciones biológicas que superan las leyes de presión de la física y adaptación biológica en el espacio

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ABSTRACT

After the accident on Apolo1, with 100% oxygen in the cabin, all spaceships now travel with a sea level pressure and 20.9% oxygen. Extravehicular activity requires lowering the pressures. It is complex and time consuming. Permanently reducing the cabin pressure would be a great advantage. A paper by NASA in 2013, proposed for the spaceflight environment: 8 psia / 32% O_2 (reducing the sea level pressure (14.7 psi / 20.9% O_2), but increasing the fraction of oxygen in order to replicate the sea level PaO_2). However, we question this proposal, as it is based on the fear of hypoxia. Our proposal back in 2007 suggested that space travel should take place in a hypobaric environment of 9.5 psi / 20.9% O_2 (like in the city of La Paz-Bolivia (3,600m) [11,811ft]). The logic behind it is that at all altitudes on planet Earth, life thrives in a 20.9% Oxygen, 79% Nitrogen. $PaCO_2$ also needs to be considered. In a physiological manner, over 200 million inhabitants of high altitude above 2,000m [6,561ft], have perfectly normal lives. The astronauts could benefit of a Extra-Vehicular Activity (EVA) suit pressure of only 149 mmHg [2.8psi] (lighter, much more comfortable and efficient spacesuits) and space travel anemia could be reduced. The preparation prior-to-space travel could be carried out by adapting and living in a high altitude environment. We consider chronic hypoxia a fundamental step in BioSpaceForming (Adaptation to life in space). As all living beings start to move out of Earth into space, they will have to change their biology and adapt to new conditions.

Keywords: space travel; chronic hypoxia; EVA; spacesuits; high altitude; adaptation.

RESUMEN

Después del accidente del Apolo 1, ocurrido con 100 % de oxígeno en la cabina, todas las naves espaciales viajan con una presión de nivel del mar y 20,9 % de oxígeno. La actividad extravehicular requiere que se reduzcan las presiones. Es un proceso complejo que consume mucho tiempo. Reducir la presión de la cabina de manera permanente sería una gran ventaja. En un artículo de la NASA de 2013 se proponen las siguientes condiciones para el entorno de los vuelos espaciales: 8 psia / 32 % O2 (reduciendo la presión de nivel del mar (14,7 psi / 20,9 % O2), pero incrementando la fracción de oxígeno para replicar la PaO2 de nivel del mar). Sin embargo, nosotros nos cuestionamos esa propuesta, ya que está basada en el miedo a la hipoxia. La propuesta que hicimos en 2007 sugería que los vuelos espaciales se realizaran en un entorno hipobárico de 9,5 psi / 20,9 % O2 (como en la ciudad de La Paz, Bolivia (3 600 m) [11 811 ft]). El fundamento lógico es que en el planeta Tierra la vida se desarrolla a todas las alturas con 20,9 % oxígeno, 79 % nitrógeno, aunque también hay que tener en cuenta la PaCO2. Desde el punto de vista fisiológico, más de 200 millones de habitantes de grandes alturas de más de 2 000 m [6 561 ft] tienen una vida perfectamente normal. Para la Actividad Extra-Vehicular (EVA) a los astronautas les convendría más que el traje tuviera una presión de sólo 149 mmHg [2,8 psi], es decir, un traje más ligero y mucho más cómodo y eficiente, a la vez que se reduciría la ocurrencia de anemia espacial. La preparación previa al vuelo espacial podría basarse en la adaptación a un entorno de gran altitud y la vida en el mismo. Consideramos que la hipoxia crónica es un paso fundamental en la adaptación biológica y la supervivencia en el espacio. Todo organismo vivo que se traslade de la Tierra al espacio debe cambiar su biología y adaptarse a las nuevas condiciones.

Palabras clave: viaje espacial; hipoxia crónica; EVA; trajes espaciales; gran altitud; adaptación.

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INTRODUCTION

In space, humans travel not only in micro-gravity, but also in an environment similar to earth where the barometric pressure resulting from the weight of the atmosphere has to be simulated. Gravity pulls the gas molecules of the atmosphere toward earth and this 'weight' becomes essential as it allows for enough pressure to transport oxygen, through diffusion, to the tissues as a fundamental catalyst of life. It is actually a respiratory cascade, pressure driven, where downstream are the cells in dire need of oxygen. Consequently, the space capsule has to be pressurized simulating the weight of the atmosphere on earth.

Currently, space programs use sea level pressures (760 mmHg) [14.7psi] and normoxia (21% oxygen fraction) in space capsules. When astronauts need to go for a space walk, the pressure in the spacesuit, has to be reduced to 1/3 that of sea level (240 mmHg) [4.6psi], similar to the pressure on Mount Everest. The Fraction of Inspired Oxygen (FIO_2) is increased to around 60% during some hours, in order to continue breathing as if at sea level.This implies that in order to avoid decompression sickness (DCS) and acute mountain sickness (AMS), complex and time consuming procedures need to be carried out. This makes the space suits very voluminous and rigid in order to sustain the pressure in space. Furthermore, the spacesuits have to protect the astronauts from radiation and a cooling vest is used in order to keep their body temperature within normal values. Here we question a paper by NASA that proposed a reduction of cabin pressure but with an increase of the oxygen fraction. Our proposal is to use a high altitude simulated environment without changing the inspired oxygen tension.

HYPOTHESIS

In 2013, NASA published a paper with a proposal for reducing the pressure of space vehicles in order to surpass the difficulties of pressure changes. It is entitled "Effects of the 8 psia / 32% O_2 Atmosphere on the Human in the Spaceflight Environment".(1) The reduction of the pressure in the cabins is good, however the permanent increase of the FIO_2 from 20.9% (normal earth oxygen concentration) to 32%, and hence Nitrogen at 68%, is questionable (Fig. 1).

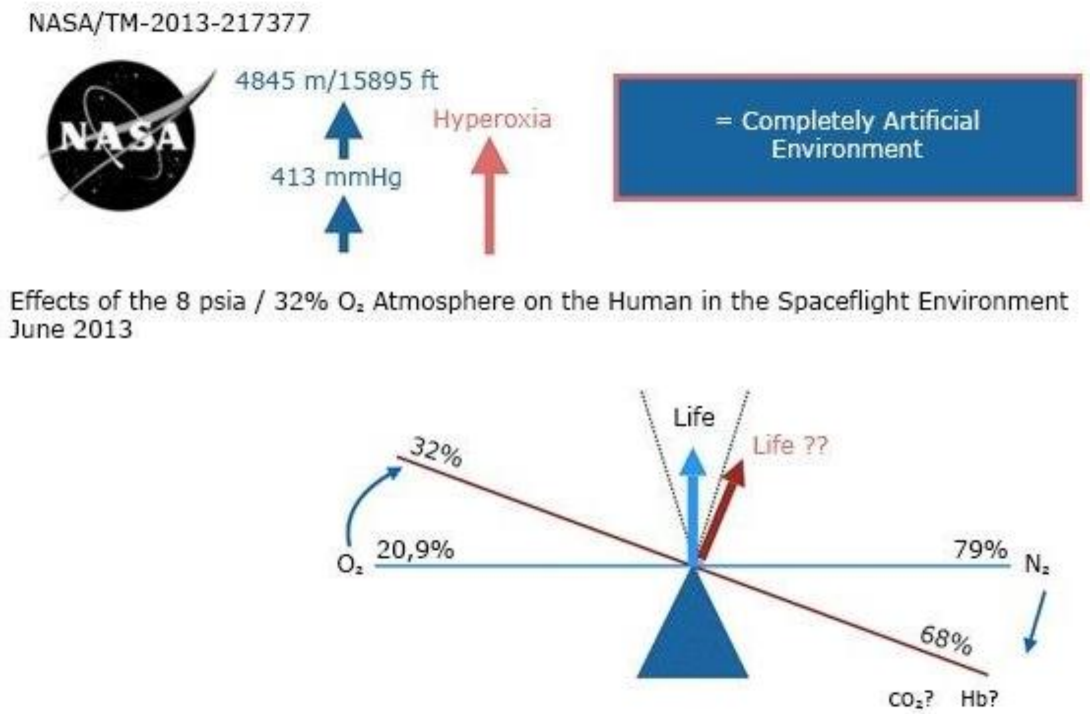

Fig. 1. The NASA article questioned for it's un-physiological proposal. Shown in a horizontal line, is the normal physiological and biological balance of 20.9% oxygen and 79% nitrogen. The tilted line shows the disruption when oxygen is increased to 32% forcing a reduction of the nitrogen to 68%, with a questionable displacement of the balance, in the pointing arrow of life.

BACKGROUND

Life on earth has thrived in an atmosphere where oxygen is present in 20.9 % balanced with around 79% nitrogen (and some other minor gas concentrations). *We believe that this balance is a fundamental physiological environmental condition that allows for the growth and development of life of humans, and of all living beings including plants, animals, bacteria, and others.* It is evident that living beings can be exposed to extreme environments in relation to temperature, pressure, however the balance of 20.9% O_2 and 79% nitrogen is present at all altitudes and all sea depths. The main changing variable is the pressure, which can affect the temperature and humidity of the atmosphere.

One may assume that only the sea level Arterial Oxygen Partial Pressure (PaO_2) value is what counts, but actually, the balancing gas Nitrogen in its 79% fraction is also transcendental for good health. Nitrogen is fundamental also for plant life,(2) and space travel has to look into survival with the use of plants. Nitrogen is the inert gas, that does not participate in gas exchange during breathing, however it plays a fundamental role in respiration, as it maintains the alveoli distended so that they do not collapse. Furthermore, high oxygen environments are deleterious to human health as observed in the presence of retinal dysplasia in newborns, or the existence of Reactive Oxygen Species (ROS) which are aggressive on metabolism. It has been found that lung cancer is present in greater quantities in oxygen rich environments at sea level, as compared to high altitude locations. Toxic effects of hyperoxia on the lung have also been reported. The skin plays a fundamental role in life as it is the "spacesuit" of humans on earth. So exposing it to a higher oxygen concentration is yet to be studied. Increasing the PIO_2 is also questionable as the tissues in the nasopharinx, trachea, bronchi and even alveoli are exposed to these higher levels of oxygen and superoxide dismutase may act as a defense mechanism. This condition is well tolerated in hospitals temporarily, but to make it permanent could have other consequences. Furthermore, the risk of fires in a spaceship with higher oxygen concentrations is evident. One has to recall the tragic accident and immediate death of 3 astronauts on Apollo 1, before takeoff when 100% oxygen was used. 32% is obviously not as risky as 100%, however it is more risky than 20.9% in an environment packed with cables, electricity.

Astronauts suffer, among many other complex micro-gravity alterations, anemia (the reduction of the hemoglobin and hematocrit) that upon return to sea level has to be normalized to pre-flight levels due to it's disadvantage on earth. The reason that anemia presents, is fundamentally due to a lower requirement of oxygen by orthostatic muscles in the legs and thorax, in microgravity.(3) Currently, the O_2 pressure in the cabin is too high, in relationship to the oxygen consumption so the body reduces the hemoglobin quantity and produces neocytolisis.(4) Exercise in space, reduces bone and muscle wasting, and ongoing studies are being carried out in order to solve lumbar spine problems upon re-entry.

Over 200 million high altitude residents live above 2,000m (6,560ft) of altitude, and they have adapted perfectly to life in the mountains. They live their lives as if they were at sea level. They reproduce and practice sports, all this with a higher hematocrit. They even have proved extended longevity.(5)

PROPOSAL

High altitude residents have adapted to life under chronic hypoxia during thousands of years. The city of La Paz, Bolivia's capital, between 3,100m [10,170ft] and 4,100m [13,451ft] with over 2 million inhabitants, is a flourishing city visited by many tourists, just as any other city at sea level. In fact, it is one of the 7 Wonderful cities in the world, according to the New 7 Wonders Organization, selected in 2014 from over 1200 cities. Life is perfectly normal and even carried out with several advantages like having low incidence of asthma, more angiogenesis, and even extended longevity,(5) among others. Consequently, the first author of this article previously proposed in 2007, in a dissertation for a Doctor of Medical Sciences Degree, at the University of Copenhagen, as a visiting professor, the original idea of space travel in a high altitude environment but it was misunderstood and seriously questioned. This resulted in the rejection of the degree by the opponents who even acknowledged their poor experience on high altitude issues.(3) Interestingly, the main opponent is one of the authors of the NASA paper published in 2013, source of our analysis.(1) Furthermore, the thesis of the dissertation caught the german's attention and was published as a book in Germany in 2010.

Sea level physicians and scientists are fearful of hypoxia, due to their poor exposure to low levels of oxygen, thus they proposed that astronauts travel in a sea level environment. Actually, space has practically not only a 0 mmHg barometric pressure, but also 0% oxygen. The question is: Would it not be better that astronauts use the knowledge of adaptation to life at high altitude so that they are prepared for life in hypoxic environments in space? *As humans, we are traveling from an oxygen rich environment on earth to where there is hardly any oxygen in the Universe.*

Sedentary high altitude residents have an additional stimulus (hypoxia) that forces their organisms to outperform the sedentary residents of sea level. Life under chronic hypoxia is an "exercise" that renders the possibility of survival much greater under harsh conditions. Several athletes train at high altitude. Sea level residents have a limiting disability: poor tolerance to hypoxia.(6)

The advantages gained by traveling in a high altitude environment similar to that of the city of La Paz, i.e. 9.5 psi / 20.9% O_2 are very significant (Fig. 2). Recall that at sea level it is 14.7 psi / 20.9% O_2. Above all, this condition has already been proved to be effective over thousands of years. There are many mechanisms of adaptation to hypoxia. Upon arrival to high altitude, the sea level hemoglobin, hematocrit and red blood cells are insufficient for an effective oxygen transport to the tissues. Consequently the organism has to find physiologic mechanisms of survival.[7] Initially, this is achieved by increasing ventilation, the amount of air entering the lungs in 1 minute on one hand and increasing cardiac frequency on the other. If the ascent is too fast some subjects could possibly collapse on minimal exercise, but generally travelers to the city of La Paz - Bolivia take several hours to reach this altitude by road or through long plane flights where the cabin pressure on commercial planes is around 2500m [8,200ft]. This exposure contributes to the adaptation process for arrival to high altitude, as a stimulus to cope with hypoxia. Nowadays thousands of travelers arrive to the airport in the city of El Alto at 4100m [13,451ft]. At first, some people feel headache, and most feel some shortness of breath on mild exercise, like climbing some stairs. If the person is healthy, these symptoms most probably are not too bad and disappear gradually in the acute phase, in one or two days. The shortness of breath likewise goes away when full adaptation is achieved. Hematological adaptation has been studied to take around 40 days.[7] Other mechanisms of adaptation include angiogenesis, more efficiency of the mitochondria, etc. However when the symptoms persist or complications arise, a medical precise diagnosis, makes pre-existing conditions evident. So hypoxia, is also a test of good health. A great test for astronauts, who should also be selected for their excellent health.

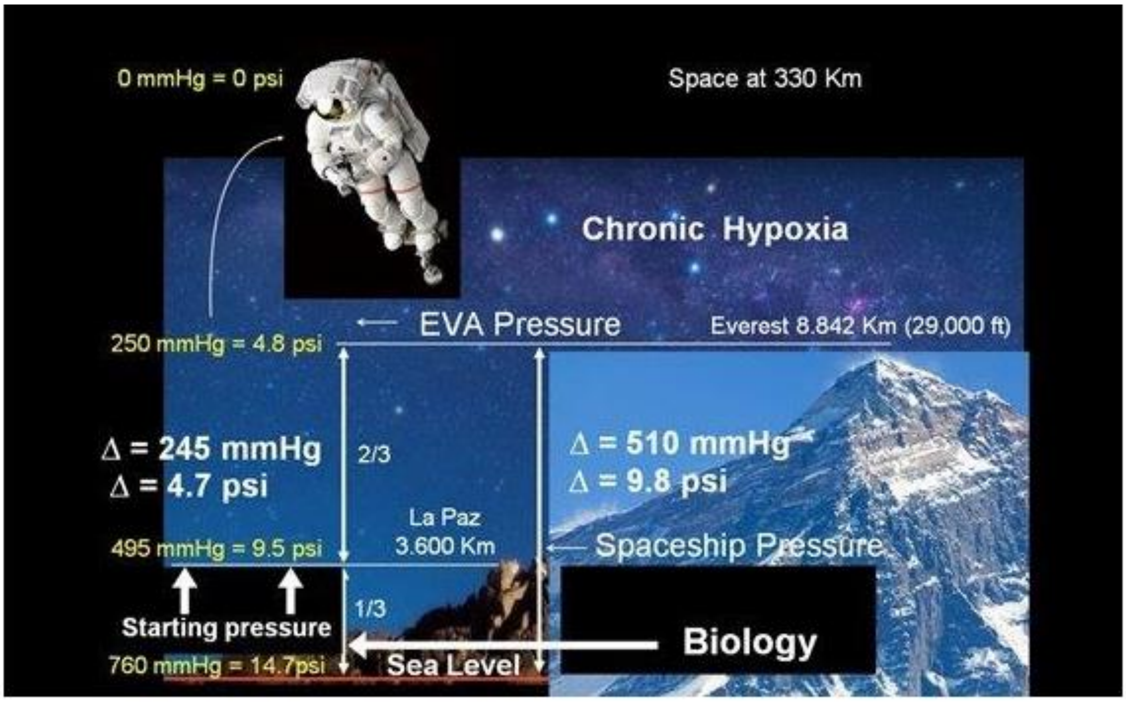

Fig 2. The diagram shows the benefits of a reduction of the spaceship cabin pressures to a similar pressure of that of the city of La Paz (3600m), maintaining the 20.9% oxygen 79% nitrogen balance. Shown, on the left, are the different altitudes starting at sea level and going to 3600m which is 1/3 of the altitude up to mount Everest 8542m (similar to a pressure used in the EVA). However in terms of pressure differences, due to the exponential shape of barometric pressure of the atmosphere, it becomes ½, reducing from 9.8psi (510mmHg) to 4.7 psi (245 mmHg). The starting point for the spaceship pressure becomes 9.5 psi (in the middle) and exit to an EVA suit pressure on top is significantly reduced. Also shown is the advantage gained by allowing biology (with adaptation to high altitude) to by-pass the pressure laws of physics.

Several variables need to be taken into account for adaptation within Earth. In the dissertation at Copenhagen University, 3 "lags" of travel from Copenhagen at sea level to the city of La Paz at 3,600m [11,811ft], were described. First, the jet lag, which is actually a time lag, due to the 5 to 6 hours time difference (daylight saving time) in a rapid (flight) change of longitude on the planet. This implies a change in the circadian rhythm that alters the sleeping hours. The second lag was the "season lag", actually a temperature lag, going from Copenhagen in the North latitude to La Paz in the South latitude (summer to winter and vice versa). The third lag was the "oxygen lag", actually an "altitude lag" going from sea level to 3,600 m. Although the oxygen fraction is still 20.9% (maintaining the physiological balance with nitrogen), the barometric pressure is reduced (1/3 less than at sea level) to 495mmHg [9.5psi]. Correspondingly, the Partial Inspired Oxygen Pressure (PIO_2) is reduced from 150 mmHg [2.9psi] to 94 mmHg [1.81psi] (1/3 less of the pressure decrease). This, likewise reduces the PaO_2 from 98 to 60 mmHg. Nevertheless the respiratory cascade, with lower pressure differences, still achieves an optimal delivery of oxygen at the cellular level. Oxygen transport, at high altitude, from blood to muscle mitochondria, apparently is not affected by chronic hypoxia.[8] *This makes life possible at high altitude, and is proof of genetic pre-conditioning for such environmental circumstances.*

So in order to adapt to high altitude, the organism has to find the most energy efficient mechanism for the transport of oxygen to the tissues. This is achieved, following the High Altitude Adaptation Formula = time/altitude Δ.[7] The red blood cells with hemoglobin have the role of capturing oxygen and transporting it to the tissues, abundantly, in a low volume, greatly surpassing the dissolved oxygen content in plasma in a very efficient manner. The hemoglobin is linked to the PaO_2 by the formula of oxygen content. At high altitude, the reduction of the environmental pressure reduces the saturation of the hemoglobin, so the organism chooses to increase the quantity of hemoglobin as a fundamental trait of adaptation, thereby reducing the energy expenditure of the extra work of the lungs and the heart. With the adaptation formula in a period of 40 days for the altitude of La Paz, the red blood cells along with the hematocrit and hemoglobin achieve an optimal level (a plateau with no further increase).(7) During the initial arrival to high altitude the subject is short of breath upon minimal exercise, however when adaptation is achieved, the organism is able to perform almost as well as at sea level. The sub maximal exercise capacity is improved. For example the current American Consul in La Paz, is a high level competitor in running (not so much uphill) and swimming even in the Titicaca Lake at 3800m [12,467ft]. He could be an excellent astronaut.

The tolerance to hypoxia is also fundamental as it carries a paradox of survival in high altitude environments.(6) At sea level, the PaO_2 is around 98 mmHg. If a person suddenly presents a PaO_2 of 60 mmHg, he/she is immediately entered into an Intensive Care Unit, as his/her life is at risk. However when a traveler flies to the city of La Paz, on arrival, the pressure is dropped gradually and when the door of the plane is opened, his PaO_2 drops to 60 mmHg. Very few present nausea and vomiting and hardly anyone fainting. Most arrive uneventfully, as thousands do every day. How is this possible? The tolerance to hypoxia equation is proposed as an explanation. Tolerance to hypoxia = Hemoglobin/$PaCO_2$ * 3.01, where $PaCO_2$ is the Partial Pressure of Carbon Dioxide. It turns out that the denominator is related to the immediate response at high altitude where there is hyperventilation upon arrival, so $PaCO_2$ descends. Whereas the numerator is the longer term response of the adaptation process that gives rise to an increase of hemoglobin to a suitable high altitude level.(7) Thereby, the organism finds that it can increase the numerator variable in order to save energy expenditure in a metabolic cellular proliferative way. Blood becomes slightly thicker accompanied by angiogenesis, vasodilation, and many other genetic expressions, in order to transport oxygen more efficiently, without any serious compromise to health. Accordingly, at the tissue level, cells receive enough oxygen in order to carry out the multiple metabolic processes of biology. Hence, *life thrives under chronic hypoxia successfully not only with a lower* PaO_2*, but likewise with a lower* $PaCO_2$ *than at sea level.*(6)

The hypoxic gene expression that includes HIF, and many other molecules are proof that in our genes, survival in a hypoxic environment is preprogrammed. Prof. Dr. Gustavo Zubieta-Castillo (Sr) 1926-2015, postulated that man can adapt to life even in the hypoxic environment of the highest mountain in the planet, Mt. Everest at 8,542m [28,024ft].(9) This, based on some facts that showed clinically that man can tolerate extreme hypoxia during disease at high altitude, and that the fetus in the womb is already in a very low oxygen level. Every human being on earth came to life at the hypoxic level of Mt. Everest. They originally have fetal hemoglobin, as a mechanism to tolerate extreme hypoxia. The numerator of the Tolerance to Hypoxia, under these circumstances, plays a fundamental role. Additionally, the NASA twins study,(10) is living proof of extensive gene expression during 1 year in space, proving that human genes, have resources for adaptation and BioSpaceForming, even beyond earth.

If a high altitude pressure and hence lower oxygen tension is used in space capsules, as proposed by us, the hypoxic stimulus, will sustain an adequate level of hematocrit for reentry to earth. The time frames for the decrease of the hematocrit on descent from high altitude to sea level, is a linear decrease lasting 20 days, coming from 3,600m [11,811ft] of altitude. Vice-versa, upon ascent to high altitude it is a logarithmic increase of the hematocrit taking 40 days to complete.(7) In space using a hypobaric pressure similar to the city of La Paz, will probably stimulate an increase of the red blood cells, as a physiologic solution, and counterbalance the space anemic phenomenon. Studies need to be performed to show the results of such a proposal. One can speculate that it is highly probable that the hematocrit can be regulated, to the most energy efficient mechanism to transport oxygen to the tissues in micro-gravity. Probably, hemoglobin would not increase to the normal average values of the city of La Paz males Ht = 50% and females Ht = 46%, but rather maintain itself close to the sea level values. This could be explained by the fact that the atmosphere barometric pressure on Earth creates the 4 vertical pressure zones in the lung. Whereas in space, it is highly probable that there is a completely even ventilation/perfusion in all levels of the lung making the gas exchange more efficient thereby contributing to further anemia as less hemoglobin is needed.

The fear about not sleeping well at high altitude, and not being able to adapt properly, can be well resolved with previous trials of stay in the city of La Paz, for at least 40 days. Once selected, the astronauts could prepare for space flights in the city of La Paz, or maybe in other high altitude locations with a similar altitude. Sleeping with hypoxicators could also be an alternative, while residing at sea level, but not as efficient, due to the daytime sea level normoxia.

Traveling from sea level to space and back with the current conditions, implies a big biological change. Traveling from high altitude to sea level on the planet does not imply a big biological change. Therefore, if space would adopt the high altitude conditions, astronauts, would be able to move faster between space, high altitude and sea level in certain aspects, uneventfully. Ideally, it would be best to have the launching site at high altitude so that the astronauts have a minor environmental change and that the space ships travel a shorter distance from earth to space. To travel from high altitude (4,000m)[13,123ft] to space, would also be energy efficient. It has already been proposed by us to move Cape Canaveral to El Altiplano (the high plateau) in August, 2006.

The knowledge acquired during 49 years of medical practice at high altitude, is applied to a proposal for a most efficient capsule environment for the human exploration of space.[(11)] A cabin pressure similar to the city of La Paz, Bolivia (495 mmHg) [9.5psi] i.e. 2/3 that of sea level (760 mmHg) [14.7psi], would not only maintain the hematocrit for re-entry, but furthermore, could significantly accelerate the preparation for Extra Vehicular Activity (EVA) that currently takes up several hours. Currently, the EVA space suits use 250 mmHg. We likewise propose that a lower pressure (149 mmHg) [2.8psi] or even lower, be used in space suits, making them more flexible and thereby reducing the risks of DCS and AMS(11). In this case, it implies only 346 mmHg [6.7psi] in pressure difference, from space capsule to space suit, as compared to 510 mmHg [9.8psi] in the current methodology. The laws of physics in relation to pressure changes cannot be broken. However, human biology with adaptation to lower pressures and lower levels of oxygen and carbon dioxide, which is the case of high altitude residents, can reduce the pressure gap significantly (Fig.2). Thereby, biology breaks the limitations of the pressure laws of physics.

Space travel will always have hypoxia as a fundamental threat, hence a hypobaric, normoxic space capsule environment results beneficial, practical and one more step in “BioSpaceForming” of human beings.[(11)] BioSpaceForming is the word created in order to explain the adaptation process that all living beings will have to carry out in order to survive in space. BioSpaceForming = Adaptation to life in Space. Adaptation is the fundamental biological resource of survival. It is noteworthy to mention that the astronaut Scott Kelly during 1 year of space flight had “decreased body mass, telomere elongation, genome instability, carotid artery distension and increased intima-media thickness, altered ocular structure, transcriptional and metabolic changes, DNA methylation changes in immune and oxidative stress-related pathways, gastrointestinal microbiota alterations, and some cognitive decline postflight".[10] This is a remarkable example of BioSpaceForming.

Another important aspect, is to pay attention to the arterial carbon dioxide tension ($PaCO_2$). $PaCO_2$ is transcendental according to our studies in the tolerance to hypoxia.[6] High levels of $PaCO_2$ reduce the tolerance to hypoxia. In fact, it is one of the crucial factors that allows for survival in extreme high altitude environments. The removal of CO_2 in spaceships needs to be improved, as this may be a factor in gene expressions in space,[10] and $PaCO_2$ is also fundamental for the acid-base equilibrium that sustains life.

CONCLUSION

It is fine to decrease the pressure of the space cabin but it is un-physiologic to increase the PIO_2 from 20.9% to 32%, as proposed in the aforementioned publication. Life is precious and it cannot be a source of experiment with hyperoxia, and much less in space. A decrease of the cabin pressure maintaining the 20.9% is totally physiologic. It could solve other current issues in space such as space anemia, likewise saving energy, time, and reducing expenses. It has also been proved by thousands of years of humans living at high altitude. For a sea level resident, the high altitude of the city of La Paz (3600m) [11,811ft], seems complex and sometimes, based on general comments, as something intolerable. This is definitely not true. Hundreds of thousands of visitors arrive to El Alto airport at 4100m [13,451ft] every year. Many even decide to move to high altitude leaving their sea level home. The equilibrium between PaO_2, $PaCO_2$ and nitrogen are all fundamental to life. Space travel would greatly benefit from these pragmatically effective concepts. Biology through adaptation helps, hereby, to surpass the pressure change limitations in space, and it is an important BioSpaceForming mechanism.

The full presentation during the Panam2019 Space Physiology Symposium can be accessed at: https://www.youtube.com/watch?v=h7IBqx_MwmM

The Dissertation and follow up is available at: http://altitudeclinic.com/Copenhagen/

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Conflict of interests

There is no conflict of interest in relation to the research presented.