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Research report

The impact of chronic stress burden of 520-d isolation and confinement on the physiological response to subsequent acute stress challenge

Buqing Yi[a,*], Sandra Matzel[a], Matthias Feuerecker[a], Marion Hörl[a], Camilla Ladinig[a], Vera Abeln[b], Alexander Choukèr[a,*], Stefan Schneider[b,c,**]

[a] Department of Anaesthesiology (Research Group Stress and Immunology), Hospital of the University of Munich (LMU), Munich, Germany
[b] Institute of Movement and Neurosciences, German Sport University Cologne, Cologne, Germany
[c] Faculty of Science, Health, Education and Engineering, University of the Sunshine Coast, Maroochydore, Queensland, Australia

HIGHLIGHTS

- We exposed the Mar520 participants and a control group to an acute stress challenge.
- We observed enhanced cortical activities and elevated cortisol and adrenaline levels.
- A group effect was revealed showing higher cortisol peak levels in the Mars520 group.

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ABSTRACT

Collective evidence indicates that previous exposure to stressful condition might be able to induce changes in brain structure, HPA axis activity and related neurotransmission, and accordingly affect physiological responses to subsequent challenges. During long-term spaceflight, space travelers have to live under the condition of isolation and confinement in the spacecraft for a long period. It is still largely unknown if this kind of chronic stress burden can induce any long-lasting changes. To address this question, following 520-d isolation and confinement simulating a flight to Mars, the participants and a matched control group were exposed to an acute stress challenge called parabolic flight. Brain cortical activity, HPA axis activity, and sympathetic adrenal-medullary system response were monitored by EEG signal, cortisol secretion, and catecholamine production, respectively. We observed enhanced EEG signals, elevated cortisol levels and increased adrenaline productions. A group effect on cortisol output was revealed showing higher cortisol peak levels in the Mars520 group as compared to the control group, suggesting that HPA axis was to a certain extent more activated in the subjects who had chronic stress experience.

1. Introduction

Human interplanetary travel has been anticipated for several decades. One major challenge for the success of interplanetary exploration is that space traveler has to be confined and isolated in the spacecraft for a long period. For example, a flight to Mars will likely take more than 500 days. It is still largely unknown how the chronic stress burden of long-term "isolation and confinement" can affect human beings physiologically, such as whether this kind of chronic stress experience has any long-lasting effect on subsequent activities.

Both animal studies and a few human studies have suggested that exposure to chronic stress can induce changes in brain structure (such as hippocampal volume), HPA axis activities, and related neurotransmission, which accordingly affect cognitive and emotional functions and alter behavioral responses [1–3]. There is a growing concern about the persistence of changes induced by chronic stress burden [2]. A few studies revealed that chronic

* Corresponding author at: Department of Anaesthesiology (Research Group Stress and Immunology), Hospital of the University of Munich (LMU), Marchioninistrasse 15, 81377 Munich, Germany. Tel.: +49 89 4400 76422; fax: +49 89 4400 78886.
** Corresponding author at: Institute for Movement and Neurosciences German Sport University Cologne Am Sportpark, Müngersdorf 6, 50933 Köln, Germany.
E-mail addresses: buqing.yi@med.uni-muenchen.de (B. Yi), alexander.chouker@med.uni-muenchen.de (A. Choukèr), Schneider@dshs-koeln.de (S. Schneider).

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stress experience was able to cause long-lasting changes in subsequent stress responses, mainly characterized by sensitizing the neuroendocrine output to secondary stressors [4–8]. Previous isolation studies performed in social animals using acute stressors such as cold stress or acoustic startle also indicated that chronic isolation experience may enhance HPA responsiveness to new stressors [9,10].

However, there are only few human studies addressing this topic mainly due to the difficulty of finding a proper study model that all the subjects could experience similar chronic stress with comparable duration and severity. In a 520-d isolation-and-confinement study simulating a flight to Mars, six healthy males lived in an isolation-and-confinement condition for 520 days and they showed persistent high-level cortisol during the prolonged isolation period, indicating changes of HPA axis activity [11]. It provided an extraordinary chance for investigating the potential effect of chronic stress experience. In addition, we would like to know whether this kind of chronic stress experience is able to affect physiological response to the highly tough landing process, which is known to cause high physiological stress to the human body. Currently, only one model called parabolic flight can somehow simulate the landing process by producing 30 rounds free-fall conditions (called 30 parabolas, see Fig. 1), which could induce strong physiological stress responses and has been established as an acute stress model [12].

To investigate whether the chronic stress burden of long-term isolation and confinement can influence physiological response to subsequent challenges, Mars520 participants performed parabolic flight six months later after the completion of the Mars520 study when the participants were back to their regular lives. A matched control group with subjects who had no experience of long-term isolation and confinement also performed parabolic flight. The major focus of this study was to compare physiological responses to the acute stress challenge between the Mars520 group and the control group. A variety of systems in the body are involved in the responses to acute challenge. In the brain, stress hormones adrenalin and cortisol are secreted when facing acutely threating event, and increased circulating cortisol and adrenalin can subsequently regulate the behaviors of many organ systems [13–18]. In this study, brain activity (EEG), cortisol response, and catecholamine production were monitored during the procedure of parabolic flight. Our hypothesis is that exposure to the chronic stress imposed by 520-d isolation and confinement can sensitize the neuroendocrine output to subsequent acute stress challenge and it might also influence other related physiological aspects.

2. Material and methods

2.1. Participants and procedures

Six healthy male subjects participated in a 520-d isolation-and-confinement study simulating a spaceflight to Mars. Details about this study and the selection/exclusion criteria of the Mars520 participants are described in the supplementary material. One Mars520 subject reported that he had previous parabolic flight experience. To avoid a potential impact on the results interpretation, we excluded this subject from the final data analysis. A matched control group with five subjects was selected following a detailed medical history and physical exam, and the main exclusion criteria were same as that of the Mars520 study. Demographic data of the Mars520 group (mean ± SD; age (y): 34 ± 5; size (m): 1.76 ± 0.04; weight (kg): 76 ± 5; BMI: 25 ± 1) and the control group (mean ± SD; age (y): 33 ± 10; size (m): 1.80 ± 0.04; weight (kg): 77 ± 6; BMI: 24 ± 1) showed no difference ($p > 0.20$ for difference in age, size, weight, and BMI). With approval from the Caen University's ethics committee (which is by French law responsible for experiments on the A300 Zero-G airplane) the Mars520 subjects and the control subjects performed parabolic flight. All participants have given written informed consent. None of them reported taking any medication during the study.

Parabolic flight (PF) was conducted by NOVESPACE with an Airbus 300 (A300 Zero-G). Within a time period of 90 min, 30 experimental parabolas (parabolas 1–30) were performed, each characterized by 20 s of microgravity (free fall). The flight procedure and experimental procedure during parabolic flight are shown in Fig. 1, and the details of the flight procedure have been described elsewhere [19]. During the flight, each participant was secured with a safety belt for the first 25 parabolas. Participants were free to leave their seat and move about the cabin during the last five parabolas.

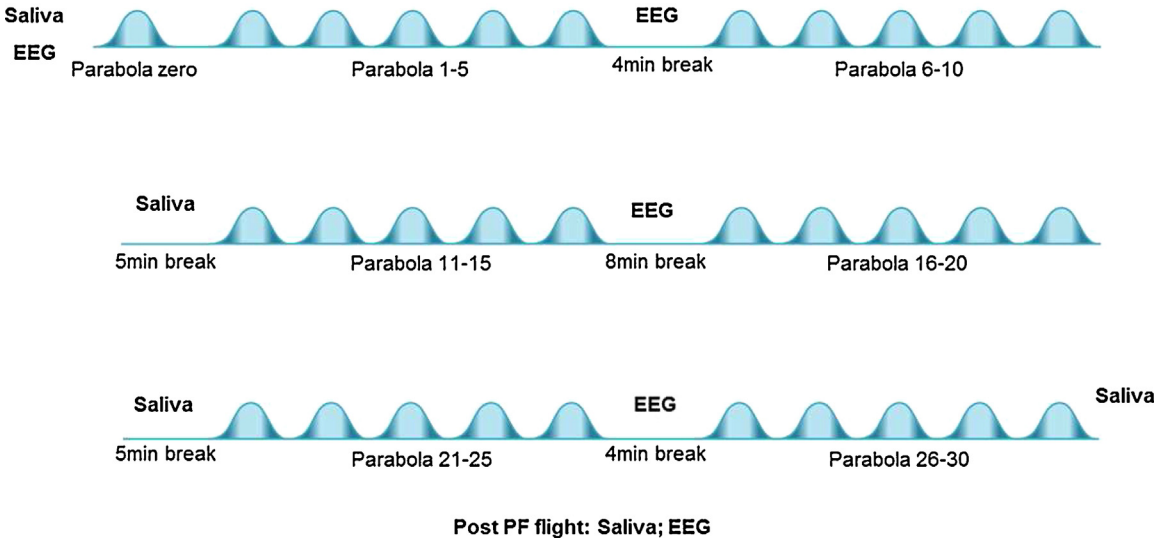

Fig. 1. The flight procedure and experimental procedure during parabolic flight. In total, thirty experimental parabolas (parabola 1–30) were performed. After each series of five parabolas there was a short 4–8 min break. Time points for saliva sample collection and EEG recording are indicated. Prior to parabola 0, saliva collection and EEG recording took place. EEG recording was repeated after parabola 5, 15, and 25. Saliva collection was repeated after parabola 10, 20, and 30. After 30 parabolas were finished, saliva samples were collected again shortly before landing. EEG recording was performed again 30 min after landing.