



The impact of long-term confinement and exercise on central and peripheral stress markers



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HIGHLIGHTS

- Brain activity and cortisol were assessed during 520 days of confinement.
- Global brain activity decreased during the confinement.
- Saliva cortisol increased during the confinement.
- Chronic stress results in a decrease of brain activity, exercise is able to counteract this.

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ABSTRACT

Long-term isolation has been reported to have impact on psycho-physiological performance in humans. As part of the 520 days isolation study (MARS500, $n = 6$) from June 3rd 2010 to November 4th 2011, this study aimed to show that stress caused by isolation and confinement is mirrored in cortical activity and cortisol levels and that exercise is a valid countermeasure.

Cortical activity was measured by electroencephalography (EEG) pre- and post-moderate exercise every two weeks, salivary cortisol was taken every 60 days.

Data show a decrease of global cortical activity, in both alpha- and beta-activity ($p < .05$ – $p < .001$), and an increase of salivary cortisol ($p < .05$ – $p < .001$), during the isolation, indicating that isolation acts as a chronic stressor with impact on cortical activity and cortisol levels. Moderate exercise leads to an increase ($p < .01$) in cortical activity. Therefore, during long-term space missions the factor isolation must be kept in mind as the reduction of cortical activity and the heightened stress level could impair performance. However moderate exercise might be able to counteract this impairment.

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1. Introduction

During long-term space flights humans are confronted with special environmental conditions and constraints that are different from living on Earth. Besides altered physical parameters (e.g. microgravity and radiation), psychological factors such as isolation, limited room, heavy workload, communication delays and lack of a diversified environment [1,2] exert influence on the human body. Isolation and confinement are known to act as stressors on the human body and can provoke physical as well as mental and emotional strains, affecting mission success and mission safety [3]. Previous studies already investigated the effects of long-term isolation as it occurs during space flights on human

behavioural health. These studies were especially concerned about the early detection and identification, as well as the reduction and the coping of the impacts of these stressors to optimize performance and interaction between individuals, in order to increase mission efficiency and safety [4–8]. The existence of psychological effects also suggests a neuronal adjustment towards these stressors [9,10]. Nevertheless, the influences of long-term confinement on the human brain are barely investigated. A non-invasive practical method indicating physiological alterations might be the measurement of neocortical dynamic functions by electroencephalography (EEG) [11].

From June 2010 to November 2011 the Institute of Biomedical Problems (IBMP) and the European Space Agency (ESA) together with the German Aerospace Center (DLR) conducted the MARS500 isolation study in Moscow, investigating the psychological and physiological issues of a simulated Mars mission. Six participants of different nations lived in a mock-up spacecraft for 520 days under complete isolation

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[12]. This study did not only provide an isolated and confined environment over a long period but offered also highly controlled and reliable conditions.

From a previous isolation study (MARS105) it is known that confinement has an impact on brain physiology as well as on affective state [3]. Over the three months of isolation a general decrease of brain activity, measured by EEG, as well as a decrease in perceived physical state and motivation was noticeable. In the same study moderate exercise could be verified as a countermeasure. However, since this study lasted only for three months, the results are certainly not sufficient to predict effects of a longer isolation period (18 months) and thus to prepare for a long-term spaceflight, e.g. to Mars.

The aim of the current study was to investigate the effects of a prolonged isolation on stress reaction and the advisability of exercise as a non-psychological treatment. It was hypothesized that 18 month of isolation will result in an increasing level of stress, classified by saliva cortisol and EEG alpha and beta activity. Furthermore exercise was hypothesized to counteract this deconditioning.

2. Material and methods

2.1. Participants & facility

Six male participants of different nationalities between 27 and 38 years old at the beginning of the study (age 31.3 ± 4.1) were selected by the IBMP and ESA on selection criteria applied for astronauts, and lived together in confinement for 520 days. After approval by the local Research Ethics committee all participants signed an informed consent. The isolation facility consisted of four connected habitat modules (medical module, habitable module, storage module and mars landing module) and one external module, simulating the Martian surface (www.esa.int/MARS500) [12]. During the study, the participants had a routine schedule for daily activity, such as performing facility inspection, doing operative work, preparing and implementing scientific experiments, physical training and so on.

2.2. Protocol

The experiment was integrated in the routine operation and consisted of an exercise session with electroencephalographic measurements before and after exercise and was performed every two weeks. The EEG method was chosen in order to allow – unlike PET- or MRT-scanning – measurements on site and within reasonable time. Saliva was collected before, after and every 60 days within the isolation period. Participants were trained before the start of the mission to undertake all measurements on themselves without the need for an investigator to enter the facility.

2.3. Exercise

The training was moderate and was conducted for 30 min on different devices. The number of possible exercise devices needed to be adapted to the special circumstances of the MARS500 facility and was limited to six training-devices: two different treadmills, a bicycle ergometer, the MDS (*Multifunctional Dynamometer in Space*), expanders and a vibration platform were used for this study. The assignment of the subjects to the six exercises was randomized across the 18 month of isolation to prevent a familiarization- and/or time effect [13]. Regardless of the training, the participants performed a five-minute warm-up before every training session, mainly consisting of stretching and toning.

2.4. Cortisol

Saliva was collected in the morning immediately after awaking (between 7 to 8 am) using the Salivettes® sampling device (Sarstedt,

Nümbrecht, Germany). Samples were frozen till the end of the study on site. Salivary cortisol concentrations were quantified with an automated immunoassay system based on the principle of electrochemiluminescence (Elecsys 2010, Roche, Mannheim, Germany). Cross-reactivity and interfering substance testing was applied to the saliva measurement, therefore according to the manufacturer's instructions, no repeated testing was needed. The minimum detectable concentration was 0.018 µg/dL. The intra-assay variation coefficient ranged from 1.5% to 6.1% and the corresponding inter-assay variation coefficients ranged from 4.1% to 37.1%.

2.5. EEG recording and analysis

EEG data collection took place before and directly after each exercise in a sitting position for three minutes. As exercise sessions were more or less randomly assigned and living was organised in shifts, EEG recordings were not fixed to a time of day. But due to the fact that EEG recordings were averaged over two months and six participants (see statistics), any constant circadian influence can be neglected. For EEG recordings participants were seated in a relaxed position, with eyes closed. Data were recorded using Brain Vision Amplifier and RecView software (Brain Products GmbH, Munich, Germany) at 500 Hz. A 16-channel active EEG system (Brain Products GmbH, Munich, Germany) with electrodes on sites Fp1, Fp2, F7, F3, F4, F8, T7, T8, C3, C4, P7, P3, P4, P8, O1 and O2) was placed according to the international 10–20 system. To facilitate signal transduction, electrode gel (SuperVisc, EasyCap GmbH, Herrsching, Germany) was applied on each electrode position via a syringe with a blunt-top needle.

EEG recordings (pre- and post-exercise) were edited with Brain Vision Analyzer 2.0 software (Brain Products, Munich, Germany). The EEG-data were filtered with phase shift free Butterworth filters (low cut-off at 2 Hz, high cut-off at 40 Hz, time constant at 0.0265 s, 48 dB slope) including a Notch-filter at 50 Hz. EEG-channels with impedance above 10KOhm were excluded from further analysis. The remaining recordings were divided in 4-second segments each allowing a 10% overlap. An automatic artefact correction algorithm was applied, which allowed a maximum voltage step of 50 µV per data sample and an amplitude range of –200 to 200 µV. Identified artefacts were marked and removed from further analysis. Fast Fourier Transformation (FFT) was used defining the raw sum of global field power (GFP, µV²) for the frequency bands of alpha (7.5–12 Hz) and beta (12.5–35 Hz). Finally all remaining segments were averaged and GFP of the pooled channels was exported via area information export for the specific wave bands. Due to the limited number of channels it was decided to not further differentiate between different brain regions.

2.6. Statistical analysis

For statistical analysis EEG-data was normalised using $x' = \ln(x)$ [3] and in order to improve the statistical validity measurement results of two consecutive months were summarised and averaged. This revealed nine time periods during isolation (P1–P9) plus the additional measurements before and after the confinement (pre-isolation: –21 days, P1: 1st and 2nd month, P2: 3rd and 4th month, P3: 5th and 6th month, P4: 7th and 8th month, P5: 9th and 10th month, P6: 11th and 12th month, P7 13th and 14th month, P8: 15th and 16th month, P9: 17th and 18th month, post-isolation: +8 days). For comparing reasons, the arithmetic mean of all measurements of one subject was determined and the percentage for each time point calculated. The pre-isolation measurement was set at 100%. Changes across time (TIME) as well as changes from pre-exercise to post-exercise (PREPOST) were determined using repeated measures analysis of variance (ANOVA). Fisher LSD test was used for a post hoc test if appropriate. All statistical tests were performed using Statistica 7.1 (StatSoft, Tulsa, USA).

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