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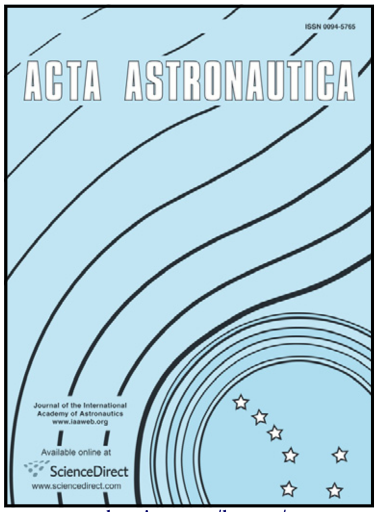

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Gender specific changes in cortical activation patterns during exposure to artificial gravity

Stefan Schneider[1,2], Ryan Robinson[1], Craig Smith[1], Melanie von der Wiesche[3], Nandu Goswami[4]

[1] Institute of Movement and Neurosciences, German Sport University Cologne.

[2] Faculty of Science, Health, Education and Engineering, University of the Sunshine Coast, Maroochydore, Queensland, Australia.

[3] Institute of Aerospace Medicine, German Aerospace Center (DLR), Cologne, Germany.

[4] Institute of Physiology, Medical University Graz, Austria.

Corresponding author: Priv.-Doz. Dr. Dr. Stefan Schneider

Institute for Movement and Neurosciences

German Sport University Cologne

Am Sportpark Müngersdorf 6

50933 Köln

Germany

Tel.: +49.(0)173.7078760

Fax: +49.(0)221.4973454

Mail: schneider@dshs-koeln.de

A B S T R A C T

Keeping astronauts healthy during long duration spaceflight remains a challenge. Artificial gravity (AG) generated by a short arm human centrifuges (SAHC) is proposed as the next generation of integrated countermeasure devices that will allow human beings to safely spend extended durations in space, although comparatively little is known about any psychological side effects of AG on brain function.

16 participants (8 male and 8 female, GENDER) were exposed to 10 minutes at a baseline gravitational load (G-Load) of +0.03Gz, then 10 minutes at +0.6Gz for females and +0.8Gz for males, before being exposed to increasing levels of AG in a stepped manner by increasing the acceleration by +0.1Gz every 3 minutes until showing signs of pre-syncope. EEG recordings were taken of brain activity during 2 minute time periods at each AG level. Analysing the results of the mixed total population of participants by two way ANOVA, a significant effect of centrifugation on alpha and beta activity was found ($p < .01$). Furthermore results revealed a significant interaction between G-LOAD and GENDER alpha-activity ($p < .01$), but not for beta-activity.

Although the increase in alpha and beta activity with G-LOAD does not reflect a general model of cortical arousal and therefore can not support previous findings reporting that AG may be a cognitively arousing environment, the gender specific responses identified in this study may have wider implications for EEG and AG research.

Keywords: EEG; artificial gravity; exercise; brain cortical activity; alpha activity; gender

INTRODUCTION

Artificial gravity (AG) has been suggested as a key integrated countermeasure for astronauts to combat the physiological deconditioning that occurs during long duration spaceflight [1]. Centrifugal forces would impart +Gz acceleration to the body and these 'head to toe' forces would provide sufficient gravitational loading to stimulate various physiological systems of the body in a way to preserve their normal physiological functions as for example bone and muscle strength [2]. However, the optimal 'dose' of AG for astronauts has not yet been determined [3].

Beside a study by Biernacki et al. [4] reporting no changes in subjective enjoyment during centrifugation, but instead positive changes in arousal such as increased energy and reduced tension currently no further information exist concerning psychophysiological effects of artificial gravity and accordingly further work seems necessary to determine exactly how AG is affecting cognition and the brain. Although AG may indeed bring benefits in terms of preventing the physiological deconditioning normally associated with long duration spaceflight, if it is lowering mood, raising the stress levels [5, 6] or impairing the cognitive abilities [7] of astronauts already working in a pressured and technical environment, then its suitability as a countermeasure during spaceflight may have to be reconsidered.

To further investigate how the brain responds to hypergravity, it is necessary to record brain activity during centrifugation itself. Given the practical limitations of working within such an environment [8], electroencephalographic (EEG) recordings are an ideal method to employ for such a task. The location of particular interest is the frontal cortex, as it is associated with higher cognition, mood and motivation [9]. Traditionally alpha activity in the frontal cortex has been the main focus of investigations. The traditional model of arousal assumes that the slower alpha activity (8-12Hz) is predominant in a more relaxed state, whilst a decrease of alpha activity and an increase in beta activity (12-35Hz) is associated with stress and arousal [10].

As gender differences in cognition and responses to stressful situations have been observed previously [11], and coupled with the fact that males and females show differences in +Gz acceleration tolerance [12], it seems likely that centrifugation may have some gender specific effects on the brain in terms of mood and cognition.

This study was carried out under the hypothesis that centrifugation would induce a stress related state within individuals and would result in observable changes in frontal cortex activity, with beta activity expected to increase whilst alpha activity decreases. This hypothesis was tested by using a short arm human centrifuge to expose participants to increasing levels of AG and measuring cortical activity using EEG in the alpha and beta frequency bands. Additionally, by testing a mixed population, gender specific differences in responses to centrifugation were hypothesised.

METHODS

Participants and Procedures

After providing informed consent, 16 healthy volunteers (8 male and 8 female; mean age 26.7 ± 4.43 years) with no prior history of vasovagal syncope were selected for this study. None of the participants had any experience with artificial gravity or microgravity. Participants completed a medical examination to confirm suitability, no further exclusion or inclusion criteria existed. Ethical approval was obtained for this study (Ethik-Kommisssion der Ärztekammer Nordrhein, Düsseldorf, Germany) in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Participants could withdraw from the study or terminate participation at any time.

The European Space Agency (ESA) Short Arm Human Centrifuge (SAHC) (Verhaert Space, Belgium) at the DLR Institute for Aerospace Medicine (Cologne, Germany) was used to expose participants to increasing levels of artificial gravity in a stepped manner. One participant at a time lay supine on a nacelle of the SAHC, positioned with their heads towards to the centre and feet pointing outwards. All participants were instructed to remain relaxed and refrain from head movements during the experiment. Two separate protocols for males and females were used based on previous findings of gender differences in +Gz tolerance [12]. The protocol began with 60 minutes in a 6° head down tilt position to simulate the cardiovascular shifts that occurs during spaceflight before returning to a supine position to begin the centrifugation run. Next, participants were exposed to 10 minutes of a BASELINE centrifugation speed of 5 RPM, producing +0.03Gz (Note that all +Gz levels quoted in this study are as measured at heart level), followed by 10 minutes of +0.8Gz for males or +0.6Gz for females. The differences between male and female were chosen in order to guarantee a sufficient number of stages to be completed before signs of presyncope occur. Previous experience with the SAHC showed that female participants show signs of presyncope earlier than male participants (unpublished observation by the SAHC team at DLR). Female participants were tested in the middle of their menstrual cycle. From this point the artificial gravity level was increased by +0.1Gz every 3 minutes. Centrifugation increased in this manner until the point at which any symptoms of pre-syncope occurred, as identified by a trained medical monitor.

EEG recordings

Two minute EEG recordings were taken at each level of centrifugation, during which time the participants were asked to close their eyes so that artefacts from muscle activity such as blinking would be minimised and were asked not to move or speak. During set up, participants were fitted with an EEG cap with 32 active Ag/AgCl electrode sensor sites (ActiCap - Brain Products, Germany) in the positions FP1, FP2, F7, F3, Fz, F4, F8, FC5, FC1, FC2, FC6, T7, C3, Cz, C4, T8, TP9, CP5, CP1, CP2, CP6, TP10, P7, P3, Pz, P4, P8, PO9, O1, Oz, O2, and PO10 as per the international 10-20 system [13]. Two additional references electrodes (GROUND and REF) were also used. To aid signal transduction, prior to fitting the EEG cap each electrode was pre-filled with electrolyte gel (SuperVisc™, EasyCap GmbH, Herrsching, Germany). Additional electrolyte gel was applied using a syringe and blunt cannula to ensure sufficient conductivity between the scalp and the electrode. Sufficient conductivity was confirmed by checking to ensure the impedance of all electrodes did not exceed ten kilo Ohm (kΩ). Analogue EEG signals were converted to digital and stored using a Brain Vision Amplifier and RecView software (Brain Products GmbH, Munich, Germany) with a sample rate of 500 Hz.

EEG data analysis

EEG data was analysed offline using Brain Vision Analyzer (Brain Products GmbH, Munich, Germany). High and low pass filters were applied so that the majority of signals below and above between 0.5 to 70 Hz were eliminated (time constant 0.318 s; 24 dB/octave). A notch filter was also applied at 50Hz to remove interference signals from power sources. 10 second sections at the beginning and end of each 2 minute 'eyes closed' period were discarded, leaving a 100 second recording to analyse. This was segmented further into 4 second sections, with a 10% overlap between each section. A combination of automatic artefact rejection (maximal amplitude = 200μV; minimal amplitude = -200μV; gradient < 50 μV/ms) and manual artefact rejection (visual inspection of the data for excessive noise, movement artefacts or electrodes producing no signal) allowed for the identification and removal of abnormal electrodes signals or segments. Any electrodes signals that were removed in such a manner were recalculated using topographic interpolation (spline interpolation; order = 4; degree = 10; lambda = $1e^{-05}$). Abnormal segments were not recalculated. Application of a fast Fourier transformation (half spectrum; maximum resolution; Hanning Window = 10%) allowed for analysis of frequency spectra within EEG signals. The remaining segments were then combined, producing an averaged frequency activity for each electrode at a specific +Gz level. Finally, the activity from electrodes covering 5 main areas of the cortex were pooled together (frontal = Fp1, Fp2, F3, F4, F7, F8, FC1, FC2, FC5, FC6, Fz; temporal = T7, T8, TP9, TP10; parietal = P3, P4, P7, P8, PO9, PO10, Pz; central = C3, C4, CP1, CP2, CP5, CP6, Cz; occipital = O1, O2, Oz), with raw sums of activity exported for alpha activity (7.5Hz-12.5Hz) and beta activity (12.5Hz-35) in each pooled region.

Statistics

For statistical analysis data was normalised by using log-transformation [V'=ln(V)]. To analyse differences in gender as well as to indicate whether possible changes in frontal activity are region specific, a two way ANOVA was used with factors GENDER (Male, Female), REGION (frontal, parietal, central, temporal, occipital) and G-LOAD (repeated measures: BASELINE, BASELINE + 1, MAXIMUM - 1, MAXIMUM). If ANOVA results were significant, post-hoc analysis was carried out using Fisher's LSD test.

R E S U L T S

Alpha activity

Whereas the statistical analysis revealed no significant interactions between GENDER, REGION and G-LOAD ($F_{(12, 210)} = .19$, $p = .99$), an effect of G-LOAD and GENDER was noticeable ($F_{(3, 210)} = 4.19$, $p < .01$ – Figure 2). Post hoc analysis revealed a significant increase of alpha activity for male participants comparing the three measurements during G-load with baseline data ($p < .01$). No effect for G-LOAD and REGION was noticeable ($F_{(12, 210)} = 1.37$, $p = .18$).

Beta activity

No significant interactions between GENDER, REGION and G-LOAD could be obtained for beta activity ($F_{(12, 210)} = .25$, $p = .99$). In contrast to alpha activity, no G-LOAD*GENDER effect was noticeable ($F_{(3, 210)} = 1.01$, $p = .39$) but a main effect for G-LOAD was noticeable ($F_{(3, 210)} = 4.96$, $p < .01$ — Figure 2). A following post-hoc analysis revealed an increase comparing BASELINE with BASELINE+1 ($p < .001$) and MAXIMUM ($p < .01$) whereas MAXIMUM-1 missed significance marginally ($p = .08$). Again no differences between REGIONS over G-LOAD were detectable ($F_{(12, 210)} = .88$, $p = .57$).

DISCUSSION

This study was designed to study the effects of artificial gravity on the activity of the frontal regions of the brain commonly associated with mood and cognition. EEG recording was chosen as the most suitable form of brain imaging technique to be used during artificial gravity. Beside a global increase of cortical beta frequency ranges with increasing G-loads, a male specific increase in global alpha activity could be noted within this study.

Changes in brain activity related to G-load

Although alpha- and beta-activity in the frontal cortex increased with G-load, these changes where mirrored in global activity and therefore could not necessarily be identified to reflect specific emotional or mental changes. Whilst previous studies [5, 6] reported increased arousal during artificial gravity being related to changes in frontal cortex activity, this is not reflected in an increase of beta or decrease of alpha activity ion this study.

It must be noted that one difficulty in assessing the context of the findings of this study within the wider EEG literature is partly down to the variability results previously reported. In a review paper summarising the changes in EEG activity that accompany meditation, Cahn and Polich [14] showed that that from several dozen studies there is no clear consensus on whether specific frequency bands increase or decrease during meditation. Compounding this issues is the fact that different classifications for EEG frequency bands have been used previously, with some studies labelling the frequency range of 6-9Hz as theta activity, whilst labelled this range as ‘sub alpha’ activity [15]. Additionally, the majority of EEG studies with altered gravity levels have come from studies with data only from males [4, 16]. In terms of previous studies investigating EEG responses to stimuli, Corsi-Caberera et al. [17] reported that during a task solving experiment relative alpha power decreased equally for both sexes whilst theta power increased, although this study specifically looked at the parietal lobes. This discrepancy between the EEG changes during task based responses and this current study (where alpha power increased only in males and did not change in females) may hint at some of the unique cognitive processes that occur during stress.

But also the reliability of a general model of arousal, i.e. that alpha activity decreases in response to stress, whilst beta activity increases, is questionable. Recent studies reporting changes in brain cortical activity after exercise, provoking similar cardiovascular effects as reported during artificial gravity, revealed that changes in the lower (delta, theta) as well as the higher (beta, gamma) frequency bands were of similar magnitude to those observed in the alpha range [18, 19]. Therefore no more than an overall cortical activation after exercise could be posited. Whilst the described model of arousal seems to be a decent way to analyze changes in psychological arousal, such cortical activation patterns might be superposed by physiological arousal and therefore a different way of analysis like for example cortical current density as proposed by Smith et al. [6] seems more applicable. Further research seems necessary to distinguish different ways of analysis in one cohort of participants.

Gender differences

Alpha activity showed a significant interaction between gender and the effects of centrifugation. Additional analysis confirmed an increase in alpha-activity in the male but not female population.. Gender differences in beta-activity and gender interactions with G-LOAD could not be identified. Whilst links between increased alpha activity and increased cortical activity have been noted previously [20], questions remain as to the underlying reasons for the observed gender differences.

In a study by Matud [11] comparing stress coping mechanisms, females were reported to suffer more stress than men, and have more emotional based coping mechanisms. Women also showed significant changes in the oxy-haemoglobin responses in the prefrontal cortex, whilst men did not, as measured by near infrared spectroscopy [21]. In a study using a noxious heat stimulus applied to the hand, Paulson et al. [22] found that females had a significantly greater activation of the contralateral prefrontal cortex in comparison to males when as measured by changes in regional cerebral blood flow as detected by positron emission tomography (PET) and also subjectively rated a 50°C stimulus as significantly more intense than males. As alpha activity is negatively correlated with brain activity, the findings in this study support these ideas. Biernacki et al. [4] also reported increases in positive arousal effects from centrifugation, and importantly their study was composed of only male cadets as participants, who likely experienced centrifugation as more of a ‘positive thrill’.

Gender differences in +Gz tolerances could possibly also explain some of these changes, as however maximal G-loads experiences by both males and females were found to be comparable.

Although gender differences were previous identified to exist with regards to baseline EEG activity and during cognition tasks, this study is noteworthy in that it highlights gender specific responses to the stimulus of centrifugation. It will be important to confirm whether this effect seen in this study is unique to centrifugation alone or whether this can be seen in response to other such stimuli, perhaps then revealing if the physiological demands of centrifugation are key to these findings.

Limitations and implications for AG as an effective countermeasure.

AG devices are proposed to be a ‘next generation integrated countermeasure’ that will enable astronauts to stay healthy during extended periods of microgravity. However, given the array of psychological challenges that are likely to be faced during such missions [23], then further studies are necessary determining whether higher intensities of AG are perhaps negatively affecting mood and cognition [6].

It may be important to use EEG imaging to determine whether any lingering signs of negative mood or stress remain after AG exposure, or whether the changes identified in this study are confined only to the period of AG itself. It would be also advisable to investigate whether the magnitude or duration of centrifugation could be reduced to the point where not only the physiological benefits of AG remained but also that astronauts do not find the experience unpleasant or stressful. Whereas higher G-loads seemed to be preferable for the adaptation of the skeletal system and longer duration (going along with lower G-loads) are preferred for cardiovascular adaptations, further investigation seems necessary to identify the individual load and duration of AG in order to maximize its effect on all physiological and psychological systems.

Future studies could also investigate whether changes in EEG activity are preserved, reduced or amplified during the exposure of daily centrifugation over several days in subjects with no prior experience of AG. If subsequently it is found that any negative changes in cognitive states diminished over time, then this would then lend weight to the idea that astronauts should receive prior training and familiarisation with AG environments.

That gender in itself is a factor that must be accounted raises questions as to which other factors must be must also be considered, investigated and controlled for to identify their significance to cognition and mood. Prior experience to AG environments may be another factor worth investigating.

Future studies should try to combine records of subjective experiences as well as other markers of stress and arousal to determine the emotional nature of centrifugation. Designing future experiments to carefully tease apart the direct contribution of centrifugation may be a challenging task, but not insurmountable.

A C K N O W L E D G E M E N T S

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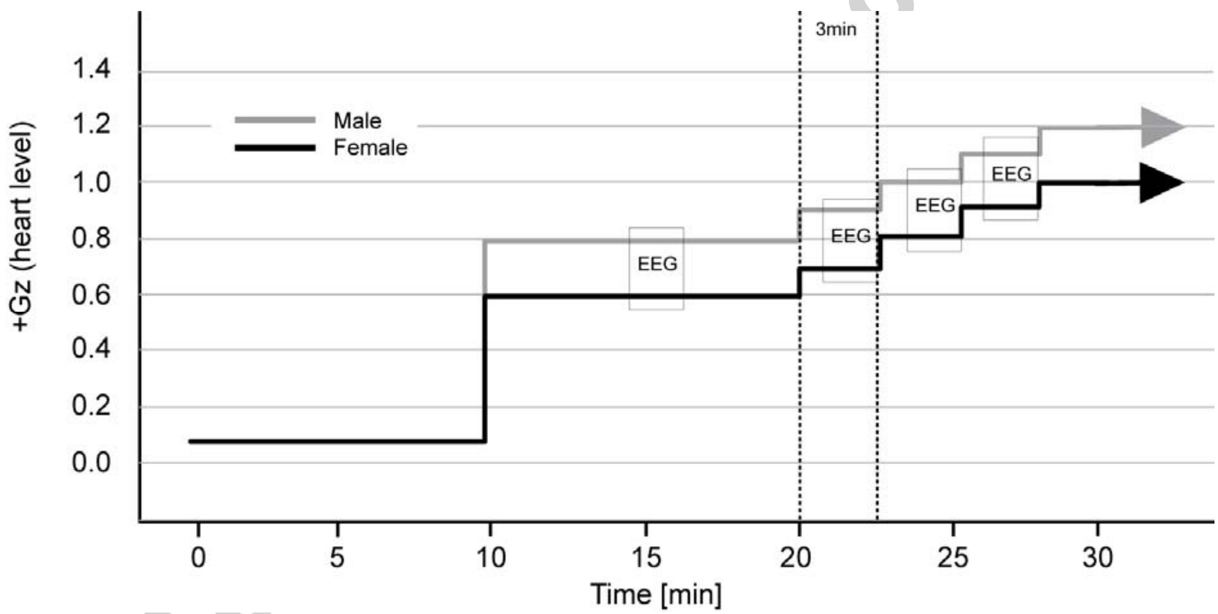

Fig 1: Diagram of centrifugation profile. Different protocols were used for males and females. Boxes labelled 'EEG' denote the time periods during which EEG recordings were analysed. The protocol continued increasing the +Gz acceleration in the stepped manner observed until the symptoms of presyncope occurred.

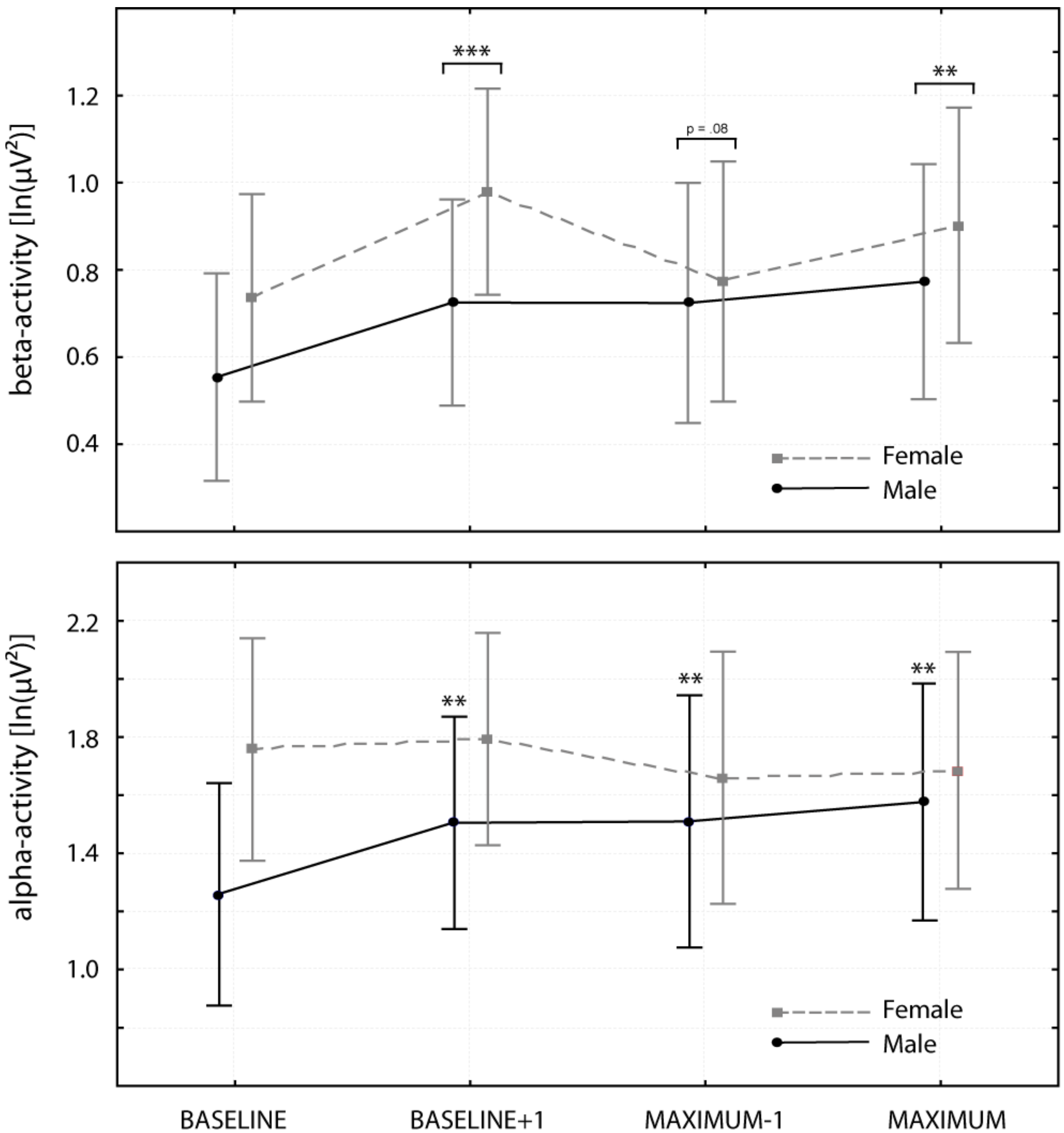

Fig 2: Changes in alpha-activity (bottom) and beta-activity (top) across G-LOAD (Baseline, Baseline+1, Maximum-1, Maximum) differentiated between GENDER (female n=8, dashed line, male n=8, solid line). An increase within the male population in alpha-activity as well as an increase in beta-activity for both populations could be obtained under G-load. Graphs show means +/- .95 confident intervals. *** indicates p < .001, ** indicates p < .01.

Highlights:

The brains reaction to artificial gravity was assessed using EEG.

Male participants showed an increase in alpha activity in the frontal cortex.

Increasing G-loads were accompanied by an increase in beta activity in both genders.

Gender specific responses may have implications for research in artificial gravity.