# The effect of spaceflight on the otolith-mediated ocular counter-roll

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## Abstract

The otoliths of the vestibular system are seen as the primary gravitational sensors and are responsible for a compensatory eye torsion called the ocular counter-roll (OCR). The OCR ensures gaze stabilization and is sensitive to a lateral head roll with respect to gravity and the Gravito-Inertial Acceleration (GIA) vector during e.g., centrifugation. This otolith-mediated reflex will make sure you will still be able to maintain gaze stabilization and postural stability when making sharp turns during locomotion. To measure the effect of prolonged spaceflight on the otoliths, we measured the OCR induced by off-axis centrifugation in a group of 27 cosmonauts before and after their 6-month space mission to the International Space Station (ISS). We observed a significant decrease in OCR early post-flight, with first-time flyers being more strongly affected compared to frequent or experienced flyers. Our results strongly suggest that experienced space crew have acquired the ability to adapt faster after G-transitions and should therefore be sent for more challenging space missions, e.g., Moon or Mars, because they are noticeably less affected by microgravity regarding their vestibular system.

## Keywords

otolith deconditioning, ocular counter-roll, spaceflight, centrifugation, learning effect

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**Acronyms/Abbreviations**

| | |
|---|---|
| BDC | Baseline data collection |
| CCW | Counterclockwise |
| CW | Clockwise |
| GIA | Gravito-Inertial Acceleration |
| ISS | International Space Station |
| OCR | Ocular counter-roll |
| R+$x$ | $x$ days after return |
| SCC | Semicircular canals |
| VVIS | Visual and Vestibular Investigation System |

## 1. Introduction

### 1. Human vestibular organ: a multisensory system

Humans highly depend on the vestibular system, located bilaterally in the inner ear, for the coordination of movements and to ensure balance and gaze stabilization [1]. The vestibular organs consist of the semicircular canals (SCCs) that are stimulated by angular accelerations, and the otoliths that detect the vector sum of linear accelerations acting upon the head, known as the gravito-inertial acceleration (GIA) vector. The otoliths are the primary graviceptors of the vestibular organ by registering linear accelerations on the one hand, including gravity, and lateral tilts of the head on the other hand. Otoliths transmit their information to the brain to determine the spatial vertical, which is essential for controlling our posture and eye movements. An important otolith-mediated ocular reflex is the ocular counter-roll (OCR) that is generated when the head is laterally tilted, e.g., during centrifugation or while driving around a corner. The OCR tends to rotate the eyes in the opposite direction to the roll tilt and towards the GIA [2]. As a result, you will still be able to maintain postural stability and gaze stabilization when making sharp turns during locomotion.

### 2. Effect of prolonged spaceflight

Cosmonauts who are in the International Space Station (ISS), orbiting around Earth, are subjected to microgravity ($< 10^{-6}$g). The lack of gravitational input will cause a deconditioning of the otoliths by decreasing the gain (ratio of eye torsion over head tilt) of otolith-mediated reflexes [4]. Also, the assessment of the real vertical will be impaired when there is a loss of otolith input to the brain in microgravity [7]. Deconditioning of otolith-mediated reflexes following microgravity exposure has been proposed as one of the multiple causing factors of the postural, locomotor, and gaze control problems experienced by returning astronauts [5]. These symptoms are generally maintained until the otoliths are re-adapted to Earth's gravitational level [4].

The OCR has previously been used as a measure for microgravity's effect on the otoliths [7,8,9,10]. However, these studies overall provide conflicting results, which is most likely explained by variations in mission duration, methodological choices, and sample size. Our group has previously demonstrated a decrease in the OCR reflex after long-duration spaceflight based on 25 datasets, which returned to baseline on average 9 days after return to Earth.

The aim of this study was to examine the effect of prolonged spaceflight on the otolith-mediated OCR in a study sample of 44 datasets, extending the results from our prior work [4]. Considering the increasing number, longer duration, and more distant destinations of future planned space missions, it is necessary to know to what extent the otoliths are affected. There are only few studies examining long-term exposure to microgravity, so that the consequences of such exposure on otolith-mediated reflexes are still not well understood. This study may provide more insight, especially for the upcoming long-term space missions to the Moon and eventually to Mars.

## 2. Material and Methods

### 2.1. Experiment timeline and subjects

The Visual and Vestibular Investigation System (VVIS), located in the Gagarin Cosmonaut Training Centre in Star City near Moscow (Russia), was used to induce the OCR. We investigated 27 cosmonauts, of whom several were tested twice or even more times during consecutive spaceflight missions to the ISS. As a result, 44 experiments were performed in total, 31 were conducted for experienced flyers (N=16 second-time, N=8 third-time, N=4 fourth-time, and N=3 fifth-time flyers), while the other 13 experiments were conducted for the remaining first-time flyers (N=13 first-time).

The cosmonauts were tested before and after their 6-month space mission in the ISS between ISS increment mission 16 in October 2007 to increment 61 in April 2020. The pre-flight experiments consisted of 2 baseline recordings defined as *baseline data collection* (BDC), and the post-flight experiments consisted of 2 to 3 OCR recordings. The first post-flight measurement was taken 1 to 3 days after their return to Earth, defined as R+1/3. The second post-flight measurement was taken 4 to 7 days after their return, R+4/7. The

third post-flight measurement was taken 8 to 12 days after their return, R+8/12. It was impossible to test all cosmonauts on the same day after their return, due to medical and logistical limitations.

The experiment protocol was designed in accordance with the ethical standards defined in the 1964 Declaration of Helsinki and was accepted by the Human Research Multilateral Review Board (HRMRB) and European Space Agency (ESA). Cosmonauts gave their voluntary informed consent prior to their participation in this study.

### 2.2. Visual and Vestibular Investigation System

The cosmonauts were securely fastened, by a five-point safety harness with a restriction of head movements, and seated upright on the rotation chair, 0.5 m away from the vertical rotation axis.

The experimentation room was darkened to avoid fixation or visual motion feedback during centrifugation. A visual display, mounted in front of the cosmonaut's face, was used to project visual targets during parts of the experiment. Binocular 3D video-oculography with infrared video goggles was used to enable continuous recordings of dynamic changes in ocular torsion.

At standstill, the calibration of the video goggles and a baseline recording were performed. After an acceleration phase of $30°/s^2$, the cosmonaut was subjected to constant angular velocity of $254°/s$ resulting in an outward centripetal acceleration Ac of 1g first for 5 minutes in a Counterclockwise (CCW) direction. The chair was decelerated with a rate of $3°/s^2$ to stand still. The chair was then manually 180° rotated, and subsequently the protocol was repeated for 5 minutes in a Clockwise (CW) direction. In between both centrifugation directions, the cosmonaut remains seated while the operator changes the centrifuge configuration to the subsequent (CW) direction. The cosmonaut faced the direction of motion, with the right ear outwards during CCW rotation and the left ear outwards for the CW rotation. The vector sum of the gravitational acceleration Ag and the centripetal acceleration Ac is called the Gravito-Inertial Acceleration (GIA). This GIA was perceived by the subject as the 'spatial vertical' and exerted a shear force on the otolith system which caused an illusory 45° perceived roll-tilt during rotation. As a result, an OCR was induced that tended to orient the eyes towards the GIA and thus away from the direction of the perceived tilt.

### 2.3. OCR measurements

The OCR measurements were taken before, during, and after centrifugation according to a fixed protocol. The first and fourth OCR measurements were respectively taken before and after centrifugation during standstill, where no centripetal force was acting upon the body and thus an OCR of 0° was observed as expected. The second OCR measurement was taken 40 seconds after the steady-state phase of constant rotational velocity was reached, because we only wanted to assess the contribution of the otolith system to the OCR. During the 40 seconds, the cupula of the horizontal semicircular canals (SCCs) returns to its original position and no longer contributes to the OCR. The third OCR measurement was taken 40 seconds before the start of the deceleration phase. The time interval between the second and third OCR measurements was 3 minutes and 40 seconds. During centrifugation, the second and third OCR measurement, an OCR of on average 5°-7° [18] was expected to be measured because of GIA stimulating the otoliths. Each OCR measurement was recorded for 20 seconds, while the cosmonaut observed a fixation dot on the visual display. The fixation dot was used to cancel out other eye movements, e.g., saccades, during centrifugation. The OCR was calculated as the difference of the average eye torsion over these 20 second recordings, consisting of 600-1000 frames, between rotation and standstill.

The video files obtained during the VVIS experiment contain recordings of the eye movements and were analyzed in a visual programming language (custom made by H.M. in LabVIEW - National Instruments -11500 N Mopac Expwy. Austin, TX, USA) to measure the OCR in degrees.

### 2.4. Statistical analysis

The OCR measurements were statistically analyzed in JMP® (version Pro 16. SAS Institute Inc, Cary, NC, 1989-2001), with $p<0.05$ as significance threshold, using linear mixed models. We first tested our main variables as fixed effects and then systematically tested all interaction terms. The variables included were *Timepoint* (BDC1, BDC2, R+1/3, R+4/7, and R+8/12), *Days After Return* (1 to 12 days), *Flight* (first-time vs experienced flyers). The significance threshold used for selecting the fixed effect was set at $p=0.001$. Non-significant terms were removed until all combinations were tested and only the significant ones remained. In all models, *Cosmonaut* was entered as random intercept to account for the non-independence between observations from the same cosmonaut. As random slope terms *Cosmonaut\*Flight* and *Cosmonaut\*Flight\*Timepoint* were included according to their Likelihood ratio tests

(p<0.0001). The residuals of all models were checked for normality and homoskedasticity.

## 3. Results

We evaluated the OCR measured across different time points (BDC1, BDC2, R+1/3, R+4/7, and R+8/12) and different experience levels of the cosmonauts (first-time to experienced flyers). We showed an effect of time and previous spaceflight experience on the OCR (p<0.001) (**Figure 1**). There was also a significant interaction effect of time and previous flight (p<0.001). A post-hoc Dunnett's correction was performed to compare the OCR between BDC1 and all subsequent measurements. BDC2 did not differ from BDC1, proving a good test-retest reliability of the data. The OCR significantly decreased early postflight at R+1/3 and R+4/7 compared to BDC1. At R+8/12, OCR was back to preflight level. Overall, these results show that the OCR is decreased early after spaceflight and that it returns to baseline within two weeks after spaceflight. Moreover, the change in OCR over time differs between first-time and experienced flyers, with experienced flyers being less affected (**Figure 2**).
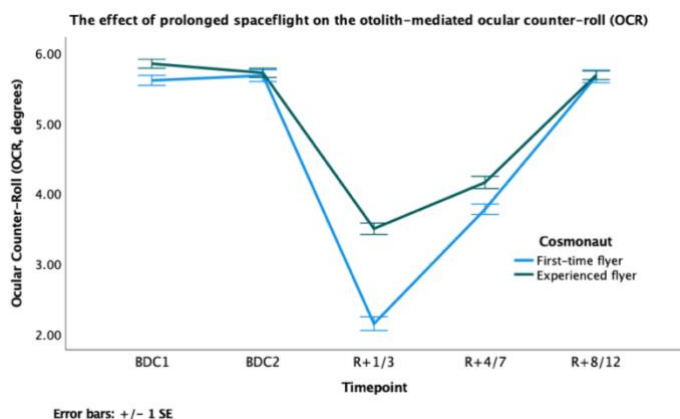


**Figure 1 Difference between first-time and experienced flyers regarding the effect of long duration spaceflight on the OCR. Error bars represent standard errors of the mean with multiplier 1.**

Using an independent sample T-test, as an approximation, we found a significant difference between the first-time and experienced flyer at R+1/3 (p<0.0001). The first-time flyers showed a decrease until $2.15 \pm 0.10$, where only the experienced flyers showed a decrease until $3.50 \pm 0.08$.
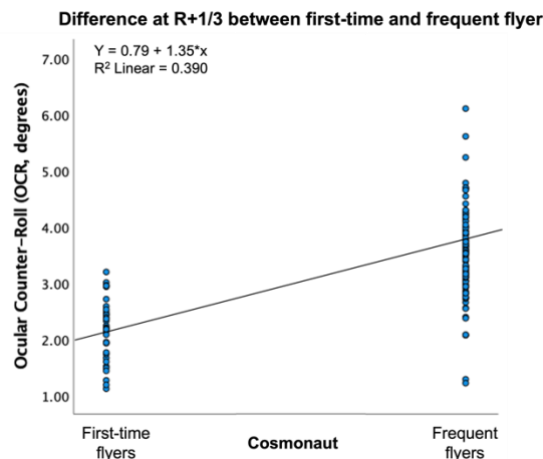


**Figure 2 The difference between first-time and frequent flyers early post-flight (R+1/3).**

## 4. Discussion

The aim of this study was to examine the effect of prolonged spaceflight on the otolith-mediated OCR in a relatively large study sample of 27 cosmonauts. The main findings of this study were that (i) the OCR showed to be consistent for test-retest as assessed by repeated preflight measurements, (ii) the OCR is decreased early post-flight compared to pre-flight, (iii) the OCR returns to baseline levels as measured on average 9 days after the space mission, and (iv) the OCR change over time is dependent on previous experience in space.

The decrease in OCR measured at R+1/3 reflects a deconditioning of the reflex as a result of a prolonged reduction in gravitational input during the space mission. It has long been established that the vestibular system is affected during space travel and that this causes various symptoms and functional changes during the first weeks in space, as well as the first weeks back on Earth. Specifically, postural control, locomotion, and gaze stabilization are affected during this time frame, which can be attributed to the vestibular system still being adapted to the condition of microgravity [6, 9, 10, 14, 16]. The decrease in OCR therefore strongly points to such an adaptation. Further establishing the association between OCR changes and functional changes will be essential for future missions to the Moon and Mars, where multiple gravitational level transitions will be made, forcing the vestibular system to adapt multiple times [13, 18].

Although a decrease in OCR after spaceflight has been demonstrated before [6, 16, 12, 17], some studies show conflicting results with ours. For example, one study showed no change in OCR

after spaceflight [3]. This is potentially explained by the different methodological approach to trigger the OCR. In that study, the OCR was induced by static tilting of the head as opposed to the off-axis centrifugation used in our study. Moreover, the mission duration was less than two weeks as opposed to six months for our study. Possibly, the mission duration alone could explain why others have not observed OCR changes. Specifically, the vestibular system might only be slightly adapted compared to cosmonauts spending six months in space, meaning that the readaptation upon return to Earth takes place more quickly. In this case, the OCR is not found to be altered after spaceflight, possibly due to the otoliths being fully re-adapted at the time of measurement. This would highlight the importance of taking into account the mission duration concerning measurements of the vestibular system in space travelers.

Concerning the re-adaptation of the OCR when back on Earth, we found that the measurements taken on average 9 days post-flight did not significantly differ from pre-flight values. While this time frame has a reasonable correspondence with the time window in which cosmonauts present with gait, posture, and locomotion issues, we were not able to prospectively investigate such an association. On the other hand, our data corroborate with those of Kornilova and colleagues, who independently reported a similar time frame of OCR re-adaptation than we do. Interestingly, it has been shown that the vestibular system at the cortical level still presents with connectivity and activity changes 9 days post-flight compared to pre-flight [15,16,17]. This suggests that vestibulo-oculo reflexes are more quickly readjusted to Earth's gravity, while the brain needs more time, up to three months [17], for readjusting.

Lastly, we found that cosmonauts who flew in space before showed a lesser post-flight decrease in OCR compared to first-time flyers. This is a novel finding, as often sample sizes are not large enough in both groups. These data indicate that the otoliths of first-time flyers are more affected than in experienced flyers. We hypothesize that previous time spent in microgravity triggers learning behavior at the level of the neural reflex circuits, providing a resistance against OCR deconditioning. Previous spaceflight experience is known to have a beneficial effect for in-flight adaptation and post-flight re-adaptation at the level of sensorimotor function. For example, experienced flyers recover more quickly regarding locomotor function and are often not as susceptible to space motion sickness than first-time flyers [19]. Based on our OCR data, we

demonstrate clearly that the OCR is less deconditioned in experienced flyers, advocating for sending humans to the Moon and Mars who have prior experience in microgravity. Due to the multiple gravity level transitions that will be characteristic for such missions, it would be beneficial to send experienced flyers due to their vestibular system seemingly adapting better to microgravity than first-time flyers. These findings might therefore open a new line of research into the exact requirements regarding experience for Moon and Mars missions.

## 5. Conclusion

Our study showed that the otolith-mediated OCR reflex decreases early post-flight, corroborating several other studies in long-duration mission cosmonauts. We further demonstrate a re-adaptation of the OCR to Earth's gravity levels around 9 days post-flight. Lastly, we show that prior experience in microgravity results in less deconditioned OCR reflexes, which may have beneficial consequences for functional adaptations during future space missions, such as to the Moon or Mars.

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