Perception of verticality and cardiovascular responses during short-radius centrifugation

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Abstract.
BACKGROUND: Artificial gravity using short-radius centrifugation has been proposed as an integrative countermeasure during spaceflight.
OBJECTIVE: To determine the rotation parameters of a short-radius centrifuge so that subjects rotating in the dark would feel as if they were standing upright.
METHODS: Twelve subjects were lying supine in a nacelle on a 2.8 m-radius centrifuge with their head closer to the axis of rotation and their feet pointing radially outwards. Subjects verbally reported body orientation for 26 combinations of centrifuge rotation rate and nacelle pitch tilt. ECG and respiratory responses were also recorded.
RESULTS: Five subjects felt like they were vertical when centrifugation elicited 1 g at their center of mass along their body longitudinal axis, whereas seven subjects felt they were vertical when they experienced about 1 g at ear level, regardless of the nacelle tilt angle. Heart rate variability varied with the subjects’ perception of verticality.
CONCLUSIONS: These results suggest that one group of subject was relying principally on the otolith organs for the perception of verticality, whereas the other group was also relying on extravestibular somatosensory receptors. The crewmember’s perception of verticality might be a factor to take into account for the prescription for artificial gravity during spaceflight.

Keywords: Subjective vertical, otoliths, vestibulo-autonomic reflex, artificial gravity

1. Introduction

Artificial gravity generated by centrifugation during spaceflight has been proposed as a multi-purpose countermeasure against bone, muscle, and cardiovascular deconditioning resulting from prolonged exposure to weightlessness. Continuous rotation of the entire spacecraft has considerable engineering, architectural, and financial implications. An alternative approach being explored is to provide astronauts with a small spinning bed [26]. They would lie on their back with their head near the center of rotation and their feet pointing radially outward (Fig. 1). Thus their lower body could be loaded for a specific period of time each day in approximately the same way as under normal Earth gravity. While not expected to be as efficient a solution from a physiological standpoint, given the acceleration gradient effects and intermittent exposure, short-radius centrifugation may prove effective. The engineering costs and design risks would certainly be lower as compared to designing a rotating spacecraft [2].

There are differences and similarities between being centrifuged on Earth and in orbit. On Earth, the gravitational force adds to the centrifugal force vectorially and produces a net specific gravito-inertial force that is tilted relative to the horizontal (Fig. 1). In weight-
lessness only the centrifugal force is present. However, both on Earth and in weightlessness, the centrifugal force increases with the distance from the axis of rotation, so there is a gravity gradient throughout the longitudinal body axis. The primary objective of this study was to evaluate the effects of this gravity gradient on the perception of verticality in subjects exposed to centrifugation on a short-radius centrifuge.

In absence of visual cues, the neurovestibular system, through the otolith organs and the somatosensory receptors, plays a major role in the subjective vertical. The otolith organs also play a role in the activation of the sympathetic nervous system in response to changes in posture [10,18,25]. Previous studies have demonstrated that approximately 64% of Space Shuttle astronauts experienced profound orthostatic intolerance when standing after landing, possibly due to inadequate sympathetic activation after adaptation to weightlessness [1,6,24]. This is a source of concern for intermittent centrifugation in orbit, which will mimic transient return in Earth gravity, and for adequate immediate post-flight functioning in a gravitational environment.

It is reasonable to believe that, to be the most efficient in mimicking Earth gravity, centrifugation should give the sensation to the subjects that they feel vertical like on Earth. Recent studies have shown that orthostatic intolerance could occur when subjects had the visual illusion of standing upright from a supine position, without actual changes in body tilt [22]. The secondary objective of this study was therefore to evaluate whether the mode of cardiac control during centrifugation was also influenced by the subject’s perception of verticality.

2. Material and methods

2.1. Subjects

Twelve healthy male subjects participated in this study. On average, they were 33 years old (range 26–42), 1.76 m tall (range 1.67–1.83), and weighed 73.5 kg (range 57.5–87). All participants received a comprehensive clinical assessment and gave their informed consent prior to the beginning this study. The experiment took place in the MEDES Flight Clinic at the CHU of Rangueil in Toulouse, France using the European Space Agency Short-Arm Human Centrifuge (SAHC). The experimental protocol had received the agreement from the local ethical committee.

2.2. Experiment protocol

Subjects were lying supine in a nacelle on a 2.8 m-radius centrifuge with their head closer to the axis of rotation and their feet pointing radially outwards. A canopy was placed over the upper part of the subject’s body to ensure that the subject had no visual cue or any moving reference. A headset was used by the subject to communicate with the operators outside the centrifuge room and to suppress any auditory orientation cues. A five-point harness restrained the subject’s upper body in the nacelle. A custom headrest was used to prevent head movements.

During each run, the centrifuge was accelerated at 3°/s² until constant velocity was achieved. The rotation rate of the centrifuge could be adjusted from 15 to 40 rpm and the nacelle could be tilted in pitch from 0° (horizontal) to 45° (head up) by increments of 5°. After 1 minute of constant velocity, the subjects were prompted by the operator to verbally report their orientation relative to horizontal. After about 3 min, the centrifuge was then decelerated at 3°/s² until full stop. A rest period of 1 min separated two centrifuge runs.

The subjects estimated the orientation of their body relative to horizontal in Earth-centric coordinates using a clock scale. For example, when the subjects judged their body as Earth-horizontal (0°), the response was “15 min past the hour”; when the subjects judged their body as Earth-vertical (90°), the response was “30 min past the hour”, etc. Generally the responses were made with an attempted precision of 0.5–1 min [21]. In agreement with previous studies [8], subjects reported a single tilt for the whole body. Occasional failures to respond prompted a dialog between the operator and the subject. In only one instance was one subject unable to respond (missing data < 1.5%).

The subjects experienced a practice run with the centrifuge during the clinical assessment. Approximately two weeks after this practice run, the experiment took place in the lab during two visits separated by a few days. During the first visit, the subjects were first placed in a horizontal position (nacelle tilt = 0°). The rotation rate ranged from 27.1 to 27.5 rpm (depending on subject’s height), so that Gz at their center of mass was 1 g. Verbal reports of body tilt, as well as ECG and respiratory responses were recorded. Then, a series of 12 centrifuge runs followed, where various combinations of rotation rate and nacelle tilt were used. During the second visit, 12 other combinations were used. During these 24 centrifuge runs, six nacelle tilt angles (0°, 5°, 10°, 15°, 30°, 45°) and four
Fig. 1. When rotating at constant velocity ($\omega$) on a short-radius centrifuge, subjects on Earth experience a gravito-inertial force (GIF), i.e., the resultant of the centrifugal force ($F_c$) and the gravitational force ($F_g$). The projection of GIF on the body longitudinal axis is $G_z$. The magnitude of $G_z$ depends on the rotation rate ($\omega$), the tilt of the nacelle relative to the horizontal ($\alpha$), and the distance to the axis of rotation. $G_z$ is the largest at the feet, and the smallest at the ear level where the otoliths are located. In this example, $\omega = 31.8$ rpm; $\alpha = 25^\circ$; $G_z$ at the subject’s center of mass (COM) = 1.8 g; $G_z$ (feet) = 2.7 g; $G_z$ (ear) = 1.15 g; $G_z$ gravity gradient = 57%.

rotation rates per angle were used. During all of these centrifuge runs, the subjects reported the orientation of their body relative to horizontal. In the last centrifuge run, the rotation rate and nacelle tilt were set so that all subjects reported the perception of being vertical, and ECG and respiratory movements were again recorded for 4 minutes.

During a pilot study, a digital weight scale was placed under the feet of one of the subjects to measure his body weight during centrifugation in the supine position that generated 1 g at his center of mass. We found that the body weight measured during centrifugation and the body weight measured when standing upright on the scale on the floor in the lab were different by less than 1%. This indicates that the shearing force between the back of the subject and the nacelle was small enough to be neglected in this study.

2.3. Data analysis

For each combination of centrifuge rotation rate and nacelle tilt, the centrifugal force directed along the subject’s body longitudinal axis ($G_z$) was calculated at the subject’s feet, center of mass (COM), and ear level (where the otolith organs are located). The $G_z$ gravity gradient was also calculated by taking the difference between $G_z$ at the feet and $G_z$ at the ear, divided by $G_z$ at the feet, multiplied by 100 (Fig. 1).

ECG and respiratory responses were continuously recorded (1 kHz and 200 Hz, respectively) by the LifeShirt monitoring system from VivoMetrics Inc. (California, USA). The QRS waves were automatically detected in Matlab (v. 7.8, The MathWorks) using the Signal Processing Toolbox and the BioSig Toolbox. The results were visually inspected to avoid improper detection. A time series of occurrences of R peaks was constructed, and the RR-intervals (RRI) were computed as the time differences between two consecutive R peaks.

The respiratory sinus arrhythmia (RSA), i.e. the high-frequency (0.15–0.4 Hz) component of heart rate variability, is a cardiorespiratory interaction mediated by the vagus nerve. RSA is considered a marker of the parasympathetic modulation of heart rate [9]. RSA was computed over every three breathing cycles, according to the method described by Migeotte and Verbandt [13]. A mean RRI and a mean RSA were then calculated for each subject over the 4-min centrifugation run (one run when the subjects were horizontal during the first visit, and one run when all subjects felt being vertical during the second visit).

Linear regression, multivariate analyses of variance (ANOVA) and $t$-tests were performed using SPSS v. 2.0. A $p$ value of less than 0.05 was considered statistically significant. Data are presented as mean ± SD.

3. Results

3.1. Perception of verticality

Figure 2 shows the perception of tilt relative to horizontal reported by all 12 subjects during the 26 centrifuge runs they were exposed to. There was a spectrum with inter-individual differences in the perception of tilt for the various g levels. Five subjects (COM group) had the sensation to be vertical, i.e. reported a 90° tilt, when they were supine and exposed to nearly 1 g at their center of mass. The seven other subjects (OTO group) reported being tilted head-up by only 45°
in average when they were exposed at 1 g at their center of mass. All the OTO subjects reported being vertical for 2 g at their center of mass. Simple linear regressions fit to the individual data indicated that the regression coefficients were significantly different from zero in both groups. Student t-tests on the coefficients indicated that the slope of the linear regression was significantly different between the two groups of subjects \[ p = 0.029 \].

The subjects in the COM group had the sensation of being vertical, just like standing upright on Earth, for the following rotation rates and nacelle tilts: 27.7 ± 1 rpm at 0°, 27.2 ± 1.3 rpm at 5°, 25.7 rpm ± 0.8 at 10°, 24.6 ± 2.4 rpm at 15°, 21.3 ± 2.3 rpm at 30°, and 18.1 ± 2.1 rpm at 45°. These values corresponded to a Gz acceleration of approximately 1.10 g ± 0.03 at their COM, regardless of the nacelle tilt angle (Fig. 3A, COM).

The subjects in the OTO group had the sensation of being vertical for the following rotation rates and nacelle tilts: 39.3 ± 4.3 rpm at 0°, 38.0 ± 1.5 rpm at 5°, 37.1 ± 3.1 rpm at 10°, 33.4 ± 3.1 rpm at 15°, 30.5 ± 3.3 rpm at 30°, and 20.9 ± 2.4 rpm at 45°. These values corresponded to a Gz acceleration of approxi-
Fig. 4. Time series of changes in R-R Intervals (RRI) and Respiratory Sinus Arrhythmia (RSA) during centrifugation generating 1.3 g (Gz) at the COM ($\omega = 27.8$ rpm, $\alpha = 15^\circ$) in one typical subject.

Immediately 2.14 ± 0.44 g at the COM when the nacelle was horizontal and 1.20 ± 0.22 g at the COM when the nacelle was tilted at 45° (Fig. 3A, OTO). The difference in Gz at the COM between the two groups of subjects when they had the perception of being vertical was significant [$p = 0.004$].

Interestingly, the subjects in the OTO group had the sensation of being vertical when the centrifuge rotation rate generated approximately 1.05 ± 0.08 g at the ear level, regardless of the nacelle tilt angle (Fig. 3B). The difference in Gz at the ear level between the two groups of subjects when they had the perception of being vertical was also significant [$p = 0.004$].

The Gz gravity gradient ranged from 75–25% across all the conditions tested, and was not significantly different between both subject groups (Fig. 3C).

3.2. Cardiovascular responses

Transient changes in RRI and RSA during centrifugation are shown in Fig. 4. As expected the RRI decreases during centrifugation, i.e. the heart rate increases as a result of the increased hydrostatic pressure gradients. RSA also decreases under increased g-load. These changes in RRI and RSA are similar to those observed in previous studies [12,14] and indicate a reciprocally coupled sympathetic activation and parasympathetic inhibition mode of cardiac control. Decreases in RRI and RSA were transient, returning to pre-centrifugation levels within 1 min (Fig. 4).

Multiple ANOVAs were performed with subjects’ perception of body tilt (horizontal or vertical) and subject group (COM or OTO) as independent variables, and physiological parameters (RRI and RSA) as dependent variables. There was a main effect of the perception of body tilt on RRI and RSA [$F(1, 10) = 33.772; p < 0.001; \eta^2 = 77.2\%$ and $F(1, 10) = 19.823; p < 0.001; \eta^2 = 66.5\%$, respectively]. When testing the interaction between the subject group and the perception of body tilt, the $p$ value was superior to 0.05 [$F(1,10) = 0.411; p = 0.062$]. However, because the magnitude of this effect was relatively high ($\eta^2 = 30.6\%$) this interaction cannot be neglected. A larger number of subjects should presumably give rise to a significant interaction effect.

RRI and RSA were significantly smaller [$t(6) = 2.46$, $p = 0.004$; and $t(6) = 2.45$, $p = 0.007$; respectively] for the subjects of the OTO group between the centrifuge runs where they perceived being vertical (90°) compared to those runs where they perceived being tilted in average by 32.1° (SD 16.3°) relative to the horizontal (Fig. 5). However, RRI and RSA were
not significantly different for the subjects of the COM group between the centrifuge runs where they felt vertical with no nacelle tilt, and those runs where they felt vertical with the nacelle tilted. These results indicate that RRI and RSA depend on g level. In other words, cardiovascular response is stronger in the OTO group because stimulation of body graviceptors is also stronger.

We were unable to demonstrate a statistically significant correlation between the degree of change in cardiovascular responses and the individual measures of tilt perception or the Gz value at their COM for the entire group of 12 subjects. Indeed, although RRI and RSA decreased when the magnitude of Gz at their COM increased in the subjects in the OTO group, this was not the case for the COM group. Also, RRI and RSA were not different in both groups when the subjects perceived being vertical, although the Gz at their COM was significantly different (1.15 g ± 0.14 g in the COM group, vs. 1.58 g ± 0.31 g in the OTO group; t(4) = 2.78, p = 0.03).

4. Discussion

Our results demonstrate that short-radius centrifugation of subjects in the lying down position can elicit the perception of standing upright and transient autonomic responses. These changes are caused by changes in otolith or other body graviceptors, or baroreceptors that may contribute to cardio-respiratory control. These results are consistent with other data in humans and animals suggesting that graviceptive inputs contribute to the cardiovascular response to a change in posture [25].

Although the main source of gravitational and inertial information is certainly expected to be the labyrinth, somatic graviceptors are thought to exist within the trunk as well [15]. Ground-based studies using tilt tables and centrifuges with healthy individuals, as well as labyrinthectomized, paraplegic, or nephrectomized subjects have investigated these extravestibular mechanoreceptors [16]. Their results demonstrated that the influence of the proprioceptive receptors that measure forces acting on the limbs and/or the skin on the vertical subjective during tilt or centrifugation is minimal. On the other hand, they suggested the existence of two potential somatic graviceptive systems located at the height of the last ribs, i.e., near the body’s center of mass. One is a “vascular” graviceptive system, which would be activated by fluid shift during postural changes via afferent fibers from peripheral sensors (e.g. baroreceptors) and vagal withdrawal or sympathetic activation. The other is a “truncal” graviceptive system, which would take advantage of the dense liquid-filled kidneys structures and their pressure receptors. The results obtained with the labyrinthectomized subjects indicate that the effects of these somatic gravity receptors on the z-axis component of the postural control system are, on average, equal to or even larger than that of the otoliths [16]. Recent models of human spatial orientation also postulate the existence of an internal estimate of gravity that determines the perception of self-orientation with respect to gravitational and inertial forces [3,11].
In our study, the perception of verticality and the related cardiovascular responses of 7 out of 12 subjects (58.3%) during centrifugation were based on the Gz force measured at ear level. A nearly 1 g vector at the ear level elicited the sensation of being vertical, regardless of the higher force levels on the other body parts and the gravity gradient. These subjects were therefore strongly otolith-dependent. The other five subjects (41.7%) were more sensitive to extravestibular mechanoreceptors situated near their center of mass, i.e. they were more dependent on the somatic graviceptors or the internal estimate of gravity. These subjects felt that they were vertical when centrifugation elicited 1.10 g at the center of mass, which corresponds to nearly 1 g at the heart level.

A previous study by Vaitl et al. [19] indicated that changes in shifts of blood volume into or out of the thoracic cavity induced by lower body positive pressure (LBPP) or lower body negative pressure (LBNP) exerted on the lower body also led subjects to feel tilted head-up or head-down, respectively. When LBPP and LBNP were combined with centrifugation, the perception of verticality was influenced by both the otoliths and the fluid distribution in such a way that both interact in a compensatory manner [20]. It is reasonable to assume that the impact of the fluid distribution should be greater during the runs in which the Gz gravity gradient is high. Our results showing the largest difference in perception of verticality between the COM and the OTO subject groups when the gravity gradient is 75% seems to support this assumption.

It is interesting to note that the cardiovascular responses were not significantly different in both groups of subjects when the first group (OTO) was exposed to 1 g at the otolith and the second group (COM) to 1 g at the heart. Also, the measured cardiovascular responses to short-radius centrifugation causing 1–1.5 g at the heart are similar to standing, at least for a comparison based on centrifuge runs lasting 4 minutes. The gravity gradient for these low g levels seems not to interfere with tilt perception or cardiovascular responses. These results are in agreement with previous studies and they confirm the efficacy of short-radius centrifugation as a possible countermeasure to the cardiovascular deconditioning that occurs during spaceflight [7,14].

One might expect to find that the degree of change in cardiovascular reflexes during centrifugation would correlate with individual measures of tilt perception. This was the case for the subjects within a group but not between groups. For example, RRI and RSA were not significantly different in the COM subjects who felt being vertical and in the OTO subjects who felt tilted by only 32.1° relative to the horizontal. The cardiovascular responses in the OTO group, however, seem to depend on the g level, with stronger RRI and RSA responses corresponding to a stronger stimulation of the graviceptors. The small number of subjects coupled with the intrinsic variability in subjective and objective responses could be the reason for the lack of correlation between the magnitude of tilt perception and transitory cardiovascular responses across groups. It may also be possible that different pathways are used in the processing of acceleration information contributing to tilt perception and control of cardiovascular orthostasis, just as vestibular perceptual responses are dissociated from oculomotor function [3,4,17].

Our results are in agreement with those of Wood et al. [22] who elicited changes in the perception of verticality in supine subjects using static visual cues and demonstrated a visually mediated cardio-respiratory response. Transient decreases in mean blood pressure were measured in response to the illusory tilts. These responses were very similar to those that these same subjects manifested when exposed to an actual passive head-up tilt. As in our study, a significant correlation between the magnitude of physiological and subjective reports could not be demonstrated. The authors suggest that visual information contributing to tilt perception may also be processed on different pathways than those subserving visual control of cardiovascular orthostasis [22].

When one moves from the supine position to an upright stance, there are a number of mechanisms that serve to resist hypotension. As well, hypotension can be elicited by natural or electrical vestibular stimulation. Compensation for orthostatic hypotension is also impaired by vestibular lesions. Yates and Bronstein [23] have proposed that the background excitability of many types of sympathetic preganglionic neurons may be regulated by central vestibular or peripheral signals. Under conditions of vestibular pathology or altered gravitational states, the role that is played by graviceptors and perception of verticality in orthostasis may become more critical. Centrifugation provides the potential for future enhanced cardiovascular countermeasures to combat orthostatic intolerance in crewmembers returning from spaceflight [2,5,6]. Our data suggest that controlling for the subject’s perception of verticality during centrifugation testing is a wise course of action. The subjects’ position on the centrifuge could be individually adjusted to allow for the reproduction of the naturally perceived stand-
up position in all the subjects and an optimum stimulation of the otolith-autonomic reflex for cardiovascular orthostasis.

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