Chapter 3

Exploratory research on the effects of sustained centrifugation: an overview

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This chapter provides an overview of the research that was performed in the past to characterize the effects of sustained centrifugation on postural stability, motion and attitude perception and vestibularly driven ocular responses. This is complemented with data on subjective vertical measurements that were performed within the framework of the present thesis. Together, these data did not reveal significant effects of sustained centrifugation on perceptual measures, but ocular responses were found to be affected.

Apart from testing subjects for SIC-susceptibility, several vestibular tests have been performed over the years to quantify the effect of sustained centrifugation on behavioural tasks, and elucidate the mechanism underlying SIC. They all focused on the otolith system and related responses (see Table 3.1 for an overview). Below, the most important results are summarized. For a detailed description of the results the reader is referred to the original manuscripts listed in Table 3.1. This research is then complemented with some new data, described in the second part of this chapter.

TABLE 3.1
Overview of available literature on the effects of sustained centrifugation in humans

Reference	Stimulation	n	Test	Description
Bles et al., 1989	90 min $3G_x$	3	Stabilometry	Postural stability during quiet stance, with and without vision
			Tilting Room	Postural stability in a dynamically tilting visual environment
			Subjective Vertical	Setting oneself upright while seated in a tilted chair
			Visual Motion Perception	Visual motion perception during fore-aft linear oscillation
			Optokinetic Nystagmus	Modulation of horizontal slow phase velocity that is elicited during linear oscillation by optokinetic stimulation
			Double Task Performance	Simultaneous performance of a tracking task and a continuous memory task
			Caloric Nystagmus	Recording of caloric nystagmus in different head orientations in pitch
Bles & De Graaf, 1993	60 min $3G_x$	3	Vision during centrifugation	Effect of vision during centrifugation on SIC-severity
			Head movements supine	Ranking provocativeness of yaw, pitch, and roll head movements in an erect and a supine posture
	60 min 3G	7	Direction of G-load	Difference in SIC severity following G_x, G_y, and G_z centrifugation
			Tiling Room	Postural stability in a dynamically tilting visual environment
	90 min $3G_x$	8	Attitude perception	Attitude perception after deceleration of the centrifuge (while lying in centrifuge gondola)
		8	Stabilometry	Postural stability during quiet stance, with and without vision
Albery & Martin, 1996	90 min $2G_z$	9	Postural stability	Postural stability assessment under different vestibular and visual conditions
De Graaf & De Roo, 1996	60 min $3G_x$	15	Psychomotor Performance	Yaw and pitch head movements while standing in combination with a psychomotor task (placing a peg in a hole)
Groen et al., 1996b	60 min $3G_x$	11	Static Ocular counter rolling	Ocular counter rolling during static lateral body tilt
			Torsional VOR	Ocular counter rolling during dynamic body roll about an Earth vertical and Earth-horizontal axis
Groen, 1997	60 min $3G_x$	9	Subjective Vertical	Indication of the subjective visual vertical during lateral body tilt
		9	Horizontal VOR	Recording of horizontal nystagmus during vertical axis rotation

Review of previous studies

Postural stability

Of all tests performed on the D1-astronauts (Bles et al., 1989), postural stability appeared to be the parameter that was most affected by centrifugation. When deprived of visual information, postural sway was greatly increased during quiet stance. One astronaut showed a major increase in visual dominance after centrifugation, as assessed in a tilting room. The astronaut was standing on an Earth-fixed stabilometer platform, while the visual surround (a 2.5×2.5×2 m cabin) was dynamically tilted about the roll axis located at ankle height. After centrifugation this astronaut was much more de-stabilized by the visual tilt than before centrifugation. Interestingly, similar results were also found in the same astronauts after spaceflight (Bles & Van Raay, 1988).

The effect of sustained centrifugation on postural measurements was further investigated by Bles & De Graaf (1993). They observed an increased postural sway following centrifugation during standing upright with the eyes closed, that markedly increased when head movements were made. In some subjects the head movements resulted in a complete loss of postural control. In addition, subjects reported that standing in the sharpened Romberg position (feet positioned in front of each other, heel to toe) remained very difficult until hours after centrifugation. In these experiments the SIC-susceptible subjects did not behave statistically different from the non-susceptible subjects.

Albery & Martin exposed subjects to $2G_z$ stimulation and observed no real changes in postural stability after a 40 minute exposure, but found a significant reduction after an exposure of 90 minutes.

Subjective Vertical

In addition to a deterioration of postural balance changes were observed by Bles and colleagues (1989) in the perception of the vertical. The astronauts were seated in a chair that was put in a tilted position and the astronauts were to set the chair upright again. After centrifugation they showed a consistent backward bias, indicating that in the *actual* upright position, a forward tilt was perceived. Such a directional bias in the perceived direction of gravity was also suggested by the postural measurements of Bles & De Graaf (1993) mentioned above, where subjects generally showed a tendency to fall backwards.

Groen investigated the effect of sustained centrifugation on the perception vertical in the roll plane. Non-astronaut subjects were to align a visual line with gravity under various angles of lateral body tilt. It was observed that subjects tended to underestimate the tilt at larger tilt angles (A-effect, that is, the visual line was tilted towards the body axis), but no effect of centrifugation was found.

Eye movements

Torsional eye movements were of particular interest, because they are assumed to be predominantly driven by otolith signals (see e.g. Miller, 1962). Groen and colleagues (1996b) recorded ocular counter rolling during static lateral body tilt and found a decrease in the gain of this response after sustained centrifugation. The dynamic torsional response was assessed during angular oscillation of 0.25 Hz about an Earth-vertical axis (no otolith stimulation) and about an Earth-horizontal axis. The gain of the response was found to be increased after centrifugation during rotation about an Earth-horizontal axis (i.e., with otolith stimulation). This might seem to be contradictive with the results of the static measurements, but they are explained by the finding that in these subjects stimulation of semicircular canals alone led to a higher response gain than stimulation of both semicircular canals and otoliths. Thus, apparently the otolith contribution counteracted the canal contribution. Therefore a reduced otolith gain after centrifugation would decrease the counteracting effect of the otoliths, thereby increasing the total gain of the response. This opposite effect of semicircular canals and otoliths on the torsional response was however not replicated in a later study using the same subjects (Groen et al., 1999).

Apart from the torsional vestibulo-ocular reflex (VOR), Groen (1997) also investigated the horizontal angular VOR during constant velocity Earth-vertical axis rotation. The gain of this response was unaffected by sustained centrifugation, but the dominant time constant of the decay-rate of slow phase velocity was found to be significantly decreased.

Head movements

The findings of Bles & De Graaf (1993) showed that in an erect posture only pitch and roll head movements were provocative, while in a supine posture pitch and yaw movements were provocative. This indicated that only those head movements were provocative that changed the orientation of the head relative to gravity, in line with earlier reports of the D1-astronauts.

De Graaf and De Roo (1996) developed a head movement test that included a psychomotor task. Subjects were to turn their head in a visually indicated direction (up, down, left, or right) where another visual trigger was shown. Depending on the latter trigger they either were to press a button or to put a peg in a small hole. It was observed that subjects who were suffering from SIC moved their heads significantly slower than subjects who were not suffering from SIC. Although this velocity decrease was present in both pitch and yaw movements, only the pitch movements were rated provocative. Task performance was not affected by centrifugation.

Mode of centrifugation

Bles & De Graaf (1993) also tested whether the direction of the applied gravitational load affected the aftereffects of centrifugation. To that end they positioned the subjects in a supine body position in the centrifuge while changing the position of the head relative to the GIA. Pitching the head forwards over 90º yielded G_z-stimulation, rotating the head 90º about the longitudinal body axis yielded G_y stimulation and keeping the head in line with the body yielded G_x stimulation. These three conditions, however, had comparable effects on postural stability. The only difference between conditions was that after G_x stimulation pitch head movements were rated as more provocative than roll head movements (while erect) and after G_y stimulation roll was rated more provocative than pitch. Yaw movements, that did not change the orientation of the head relative to the vertical, were not provocative in both cases. G_z stimulation did not change the rank order of the provocativeness of head movements and the effects of was similar to G_x stimulation.

In three subjects the effect of vision on SIC was investigated and it was observed that SIC-severity was increased when subjects kept their eyes open during centrifugation. (Bles & De Graaf, 1993).

ADDITIONAL EXPLORATORY RESEARCH

Within the framework of this thesis, additional vestibular testing was performed both in the four astronauts who participated in a centrifuge experiment between 2003 and 2007, and in a group of non-astronaut subjects. The two main experiments focused on the effect of sustained centrifugation on ocular responses and are described in Chapters 5 and 6. Here the results of the other additional tests are described.

Provocativeness of head movements

Earlier results, as mentioned above, showed that after centrifugation only those head movements were provocative that changed the orientation of the head relative to gravity. Thus, pitch and roll when erect and pitch and yaw when supine. These results were replicated in a group of 4 astronaut subjects and 11 non-astronaut subjects. They all were exposed to $3G_x$ for 60 min. and rated the provocativeness of yaw, pitch and roll head movements (maximal 10 per axis, performed at a frequency of about 0.25 Hz), both when standing and when lying supine. The effect of the head movements was scored on a 11-point numeric MISC scale (see Table 2.1) A nonparametric ANOVA (Friedman ANOVA by ranks) on these MISC scores showed that pitch movements were ranked as most provocative, while yaw and roll-movements were ranked equally provocative (χ^2=8.44, p=.015). In a supine position there was a trend for roll to be ranked *least* provocative, while pitch and yaw were ranked about equally provocative, (χ^2=4.7, p=.097). When subjects were asked afterwards what they found the most provocative movement, it was generally pitch, both in an erect and supine posture.

Postural stability and visual-vestibular interaction

Postural stability during quiet stance and during dynamic tilt of the visual surround (in the tilting room) was also performed on two of the four astronauts who were tested within the framework of this thesis (exposed to 60 min at $3G_x$). One of them was susceptible to SIC and the other one was not. During all recordings, the astronauts stood on a layer of foam rubber that was placed on the stabilometer platform to reduce the relative weighting of proprioceptive cues. The sway of the centre of pressure was recorded in the fore-aft and the lateral direction, at a sample frequency of 20 Hz. Recordings were obtained during quiet stance with eyes open, with eyes closed and with the neck extended (eyes closed). These conditions were always performed in this order. Figure 3.1 displays the results of the static postural stability recordings of the two astronauts (i.e., stationary visual surround). Shown are values for sway in the fore-aft direction, lateral sway was generally smaller but followed a similar pattern. The astronaut who was not affected by the centrifuge run in terms of SIC exhibited very little postural sway. Only a little increase during the first posttest in the 'Neck extension' condition was observed. In contrast, the other astronaut, who was reasonably affected by the centrifuge run, clearly showed a different pattern over sessions, especially in the 'Neck extension' condition. Instead of a steady decrease of the postural sway over sessions (which is normally observed in repeated recordings) the sway increased in the second and especially in the third session. The third session was also the session were the highest MISC scores were observed. In this astronaut behaviour was not back to baseline within 4 hours after the centrifuge run.

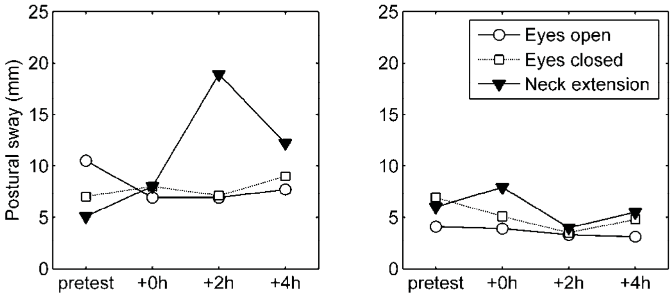

Figure 3.1: Postural stability recordings for the three experimental conditions in two astronauts (Each panel shows the data of one astronaut). Postural sway is expressed as the root-mean-square value of the sway of the centre of pressure.

The dynamic measurements (oscillation of the visual surround at 0.025 Hz and 0.2 Hz) in pitch or roll showed no large increases in postural sway, indicating that the astronauts were not affected by movement of the room. This was also not deteriorated by sustained centrifugation.

Subjective vertical measurements in the pitch plane

In two separate experiments it was investigated whether sustained centrifugation affected the perception of body orientation in space in the pitch plane, as was suggested by earlier findings (Bles et al., 1989; Bles & De Graaf, 1993). They were performed on a total of 10 subjects (2 astronauts and 8 non-astronaut subjects) who were exposed to 60 min at $3G_x$. Both experiments were performed shortly before and after centrifugation.

The first experiment focused on the perception of the vertical and of body orientation under different conditions of pitch body tilt, using a tactile indicator. Experiments were perfomed in the TNO tilt-chair, that enabled rotation about the pitch axis through the center of the head. Blindfolded subjects were seated and secured with a five-point belt. They were oriented in different positions and in each position they were to align the manual indicator first with their perceived longitudinal body axis (Subjective Body axis, SB, defined as 'parallel to your spine") and subsequently with the gravitational vertical (Subjective Vertical, SV). Figure 3.2 shows the error in these two measurements as a function of tilt.

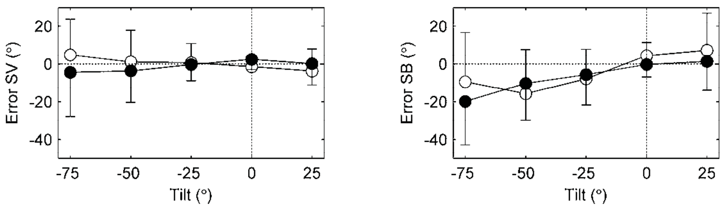

Figure 3.2: Errors in subjective vertical (SV) and subjective body axis (SB). Pretest values (mean and standard deviation) are indicated by the open symbols, values of the first posttest are indicated by the filled symbols.

For backward body tilt a positive error in SV yields an underestimation of tilt, thus the SV is tilted towards the body-axis (A-effect). This is visible for larger tilt angles in the pretest, and appears to be changed into an overestimation of tilt in the posttest. However, these effects of test session or tilt angle were not significant (Factorial ANOVA with Tilt and Test session as within subject factors). Interestingly, for the SB a significant effect of Tilt was found ($F(4, 32)=5.46$, $p<.01$): the body axis was perceived to be more tilted backwards (negative error) and this error increased with tilt angle. No significant effect of centrifugation could be demonstrated. Similar trends for SV and SB were observed in six control subjects who did not undergo centrifugation (see Nooij et al., 2006).

In a second experiment subjects were to reorient themselves to upright after a perturbation in pitch (<30° forward or backward). As in the previous experiment, subjects were blindfolded and seated in the tilt-chair. Each session consisted of six repetitions. The data showed that the magnitude of the error was weakly correlated with the magnitude of the perturbation (r=0.25, p=.01), but because this effect was small in comparison with the error magnitude, the values were not corrected for this trend. Analysis of variance revealed that the sign of the error in the perceived upright was dependent on the direction of the perturbation: when the perturbation was backwards, the perceived upright position was also tilted backwards and vice versa ($F(1, 72)=50.5$, $p<.001$). No effect of test-session (pre-/posttest) could be demonstrated for the error in the perceived upright, and also no differences between the behaviour of SIC-susceptible subjects and non-susceptible subjects. Over all, the error in the perceived upright ranged between −10.8° and +9.7° (mean +0.6°, SD 4.0°), whereas the average absolute error equaled 3.2° (SD 2.42°). In the second session the variability of the responses (standard deviation over the six repetitions) decreased significantly ($F(1,7)=6.4$, $p<.05$), suggesting that subjects got more acquainted with the task.

DISCUSSION

By recording the kinematic characteristics of the head movement, De Graaf and De Roo (1996) nicely showed that head movements were required to provoke SIC following centrifugation: SIC susceptible subjects performed the head movements slower than non susceptible subjects, in an attempt to minimize or prevent increasing symptoms of motion sickness. The results of previous studies regarding the provocativeness of head movements were replicated by new data: pitch head movements were most provocative both when erect and supine. Yaw movements were not provocative when erect, and roll movements were not provocative when supine. The observation that this provocativeness was not altered following G_z stimulation (Bles & De Graaf, 1993) suggests that the magnitude of the G-load is more important than the direction of stimulation, indicating the involvement of a central adaptation process. However, that G_y stimulation altered the order of provocativeness when compared to G_x stimulation suggest that a direction specific element should be involved as well, adding to the effect of the G-magnitude.

Next to symptoms of motion sickness, the second most obvious effect of sustained centrifugation is the deterioration of postural balance. As long as veridical visual information is available, balance could be maintained, but in more challenging situations (with eyes closed or head extended) postural sway increased. Although there were large differences between individuals (i.e., between the two subjects in Figure 3.1), no relationship between SIC-susceptibility and postural sway parameters could be demonstrated (Bles & De Graaf, 1993). This is comparable with the findings in astronauts following space flight. After space flight a similar deterioration of postural balance is found, both in astronauts who suffered from SAS and in astronauts who were free form SAS (e.g., Black et al., 1995; Reschke et al., 1998; Young et al., 1993)

Following centrifugation, head movements often resulted in postural overcorrections and loss of balance (Bles & De Graaf, 1993) showing that dynamic situations were more challenging than static situations. This furthermore hints at a disturbed interaction between semicircular canals and otoliths: both are involved in the estimation of the vertical in this situation. As mentioned in Chapter 1, this is in accordance with the hypothesis that a disturbed perception of the vertical during dynamic head tilt is related to the occurrence of motion sickness after centrifugation.

The perception of the vertical during *static* body tilt was not found to be affected by sustained centrifugation, neither in the roll nor in the pitch plane. The same was true for the perceived body orientation. Many studies demonstrated that the perception of the gravitational vertical can be quite veridical, but that this does not guarantee a veridical perception of body orientation relative to that vertical. The latter requires both ego- and allocentric information and thus, the perceived body orientation in space cannot be inferred from the subjective vertical setting alone (e.g., Mars et al., 2005; Mast & Jarchow, 1996; Van Beuzekom et al., 2001). This was also shown by the perceptual responses to pitch body tilt, as mentioned above. Subjects were able to indicate the vertical with only minor errors, but they made large errors in indicating their subjective body axis. Where subjective vertical settings are predominantly based on otolith input, somatosensory information is known to affect the perception of body posture in space (see e.g., Bisdorff et al., 1995; Bringoux et al., 2000; Ito & Gresty, 1997; Mittelstaedt, 1999). Somatosensory information most likely dominated the perception of the postural vertical in the task where subjects were to set themselves upright.

Although sustained centrifugation did not affect the perception of the vertical during lateral or pitch body tilt, it did affect the ocular response: the gain of ocular counterrolling was decreased. Because this response is mainly dependent on the magnitude of the utricular shear force (e.g., MacDougall et al., 1999; Merfeld et al., 1996a; Miller & Graybiel, 1971; Moore et al., 2001), this would suggest a decrease in otolith sensitivity to head tilt. The absence of an effect on the visual vertical, which is also largely dependent on otolith information, is however not in accordance with this hypothesis. Another possibility is that the otolith sensitivity remains unaltered but that the gain of the orientation response is decreased. Such a decrease would leave the subjective vertical setting unaffected. A general decrease in orientation responses could be a common way of the system to deal with unfamilar response patterns differing from expected patterns, as might be the case following sustained centrifugation. This would also be in accordance with the decrease in ocular counter rolling generally found after spaceflight (Dai et al., 1994; Hoffstetter-Degen et al., 1993; Vogel & Kass, 1986; Young & Sinha, 1998; but see also Moore et al., 2001). To study the effects of gravity on eye position and related orientation responses in more detail, a start was made to measure the orientation of the so-called Listing's plane within the framework of this thesis. As mentioned in the previous chapter, Listing's plane describes three-dimensional eye position during visual fixations and saccades, and its orientation is dependent on head tilt. Therefore the orientation of Listing's plane was expected to be informative about changes in otolith function and related orientational responses too.

Preliminary data in astronaut subjects indeed showed changes in the orientation of Listing's plane following sustained centrifugation. Therefore a separate study was dedicated to the effect of gravity on three dimensional eye position, which will be described in Chapter 5.

A last interesting finding that is discussed here is the decrease in the dominant time constant of the horizontal angular VOR. This dominant time constant specifies the rate of decay of the slow phase eye velocity during constant velocity rotation. For yaw rotation about an Earth-vertical axis it is about 20s, which is longer than expected based on the dynamics of the semicircular canals. The human cupular time constant is about 3.5-7 s (Dai et al., 1999). This prolongation of the VOR is attributed to a central process called *velocity storage* (Raphan et al., 1979), which is known to be dependent on otolith input too. For example, the time constant decreases with tilt angle: during Earth horizontal axis rotation the time constant is smaller than during Earth vertical axis rotation (see e.g., Haslwanter et al, 2000; Tweed et al., 1994, but see also Bos et al, 2002). Thus the decrease of the dominant time constant suggests that sustained centrifugation affects the interaction between otoliths and semicircular canals. Investigation of the velocity storage mechanism is also interesting given the observed relationship between the velocity storage time constant and motion sickness (e.g., Bos et al, 2002; Dai et al., 2003). This thus incited a separate study, that will be described in Chapter 6.

Conclusion

It can be concluded that gravity plays a major role in SIC: only those head movements are provocative that change the orientation of the head relative to the vertical. Furthermore, that the speed of those movements affects both SIC and postural balance hints at a disturbed interaction between canals and otoliths. Ocular responses that are mediated by gravity may shed more light on the exact mechanism underlying the observed effects.