Chapter 4

Effect of G-load and duration of centrifugation on the symptoms of SIC

The study described in this chapter investigated the characteristics of the gravito-inertial stimulus that is required for SIC to occur. Twelve non-astronaut subjects were exposed to centrifugation at 2 and 3G$_x$, for a duration of 45 and 90 minutes. A standardized head movement protocol was used to evoke SIC after centrifugation. The results show that in six out of 12 subjects (50%) no serious symptoms were elicited. In the other subjects, the effects of the 3G runs exceeded those of the 2G runs, and within each G-level symptom intensity was higher for the 90 min. exposure than for the 45 min. exposure. An exponential fit on this data showed that the time constant of adaptation to the gravito-inertial stimulus was about one hour.

This chapter describes a study that looked further into the nature of the gravitational stimulus that evokes vestibular adaptation and the accompanying symptoms of SIC. Generally speaking, adaptation takes time and it may be anticipated that a very short exposure to an altered gravito-inertial state will not result in SIC. The transitions following the rather short lasting hyperG exposure as experienced by a fighter pilot, for instance, do not trigger any symptoms of SIC, neither do the phases of

parabolic flight[6]. The experiences of the D1-astronauts indicated that 30 minutes of centrifugation at 3G is already sufficient to evoke SIC, but symptom-severity markedly increased after another 30 minutes of exposure. Apart from the duration of centrifugation, the magnitude of the gravito-inertial difference might be a second factor affecting the adaptation process. The fact that Albery and colleagues (1996) observed symptoms of SIC in subjects who were exposed to a load of $2G_z$ for a duration of 90 minutes furthermore suggests an interaction between the applied G-load and duration of centrifugation.

The aim of the study described in this chapter was therefore to systematically investigate the interaction between the G-level difference and duration of centrifugation in the occurrence of SIC. Apart from contributing to the fundamental knowledge about adaptation to altered gravito-inertial states, insight in this dose-effect relationship helps to determine the G-dose minimally required for SIC to occur in the first place, which is of help for future ground based research on SIC and SAS. It may also be of interest for selecting, training, and habituating future astronauts before their space flights. In addition, the (neuro-vestibular) consequences of gravity transitions relate to the application of intermittent artificial gravity (AG) during space flight and to the risks that are present during and after (re-) entry into Planet's gravity. These two topics are both identified as highly relevant for space research (see e.g. Clément & Bukley, 2007, and the Bioastronautics Roadmap[7]).

As the most simple model, it was hypothesized that at low to moderate G-levels the level of SIC is related to the product of the G-level *difference* and the time of exposure, $\Delta G \cdot t$. To validate this hypothesis subjects were repeatedly exposed to a hypergravity-load, using four different combinations of G-load and duration. A head movement

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[6] Although the repeated GIA changes occurring during parabolic flight may induce motion sickness symptoms too, these changes will not trigger adaptation processes similar to those involved in SIC.

[7] NASA/SP-2004-6113, available at http://bioastroroadmap.nasa.gov/.

protocol was used to trigger symptoms of SIC after centrifugation. Instead of letting the subjects perform self-paced head movements (as was the case in the astronaut studies), head movements were provoked using a stimulus-response paradigm (De Graaf & De Roo, 1996). Using this test, De Graaf & De Roo showed that head movement performance and symptom severity are mutually dependent: the severity of the symptoms is dependent of the velocity and amount of head movements, but, on the other hand, SIC susceptible subjects showed to move their heads slower than non-susceptible subjects. Thus, in order to compare the effect of the four centrifuge conditions, head movement performance was taken into account in the determination of SIC-severity.

The experiments to be described in Chapters 5 and 6 were carried out as a part of the same study, using the same subjects.

METHODS

Twelve male (non-astronaut) subjects participated in this study (aged 23.0±3.2 yrs.). All were free from any vestibular, cardiovascular, neurological and pulmonary disorders, as checked by a MD. The study was approved by the Medical Ethics Committee of the Utrecht University Hospital, The Netherlands. All subjects gave written informed consent prior to the study. In the selection procedure that preceded the experiment, the subjects were medically checked and then familiarized with the centrifuge during a run at $3G_x$ for 10 minutes only (see Chapter 2 for a description of the centrifuge facility). From all subjects their susceptibility to Earthly motion sickness was assessed by the Motion Sickness Susceptibility Questionnaire (Golding, 1998).

Centrifuge conditions and design

The four centrifuge conditions that were used in this study are depicted in Table 4.1. By using the levels of 2 and 3G for centrifugation, the G-level *difference* relative to Earth's gravity (*ΔG)* equaled 1 and 2G respectively.

In combination with the chosen durations, the product $\Delta G \cdot t$ was equal in two of the four conditions (45, 90, 90 and 180 G-minutes respectively). The conditions will be referred to as 2G45, 2G90, 3G45 and 3G90, respectively.

Subjects came in one day a week for four subsequent weeks and received each load-duration combination once. The order in which the conditions were presented was determined by a digram balanced Latin square design. Subjects were uninformed about the stimulus characteristics, except for the maximum duration (90 min.) and the maximum G-load (3G). Although body and head movements were possible during centrifugation to a small extent, the subjects were instructed to refrain from making head movements. They were allowed to close their eyes, but sleeping was prevented.

TABLE 4.1
Characteristics of the four centrifuge runs.

Condition	Total gravito-inertial load during centrifugation (G-units)	Duration (min)	Magnitude of the G-transition after centrifugation (ΔG, in G-units)	Dose ($\Delta G \cdot t$, in G-minutes)
2G45	2	45	1	45
2G90	2	90	1	90
3G45	3	45	2	90
3G90	3	90	2	180

After centrifugation the subjects were transported to the test-facility by wheelchair (approximately 200 m from the centrifuge) to minimize variability in the amount of body motion before the SIC assessment. Using a head movement protocol to evoke symptoms of SIC (see below), one entire test day consisted of a pretest, a centrifuge run and four posttest measurements approximately at 15, 60, 120, and 210 min. after centrifugation. The eye movement tests described in Chapters 5 and 6

were also part of the protocol, as depicted in Figure 4.1. During the breaks in between test sessions no restrictions were imposed on the subject's behaviour. After every test day, an evaluation form was deployed assessing the time they were free of symptoms.
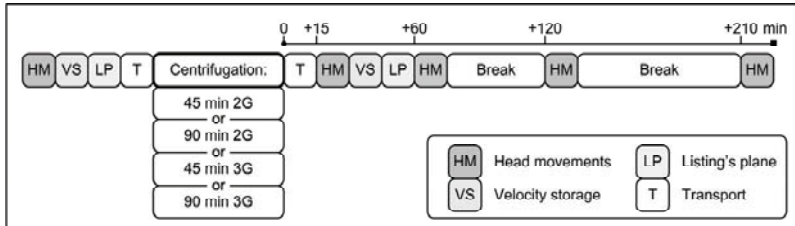

Figure 4.1: Time line of the experiment. The head movement test (HM) to assess SIC-severity was carried out before and repeatedly after the centrifuge run. The measurements on Listing's plane (LP) are further described in Chapter 5, the measurements on velocity storage (VS) in Chapter 6.

Head movement protocol

A standardized head movement protocol was used to test subjects for SIC, adapted from De Graaf & De Roo (1996). In this protocol the subject stood erect with the head in the center of a rectangular box (dimensions 1.4×0.7×0.7 m, front and bottom open, see Figure 4.2). In front of the subject, a cue display was mounted at eye level with four LED's to indicate the desired direction of head movement: up, down, left, or right. Four target displays showing random numbers were attached to the upper, left, and right side of the box and a fourth display below, on a small stand right in front of the subject. In order to see the target displays, the head had to be rotated over an angle of at least 50°.

Subjects were instructed to look at the cue display and turn their head in the indicated direction, read the random number that appeared on the target display, and turn the head back to its original position. They were to move 'reflexively', as if they were tapped on the shoulder or someone called their name. They had 5 s to complete each movement, followed by

a 2 s break. Each test session consisted of a maximum of 40 head movements, 10 in each direction, presented in random order. During the test, head orientation and velocity were measured using a small magneto-inertial motion and tilt sensor that was attached to the subject's head (Xsens MT9, Xsens Technologies BV, The Netherlands). Signals were digitized at 50 samples/s.

Figure 4.2: Experimental set-up for the head movement test. The cue display, positioned in front of the subject, is shown in the upper left inset. This display indicated the direction of the required head movement. Three target displays are visible; the fourth was positioned below and in front of the subject. The subject wore a movement registration device to measure head position and velocity.

Symptom scores

To describe the symptoms that were evoked by the head movements, subjects completed the Simulator Sickness Questionnaire (SSQ, see Kennedy et al., 1993) after each head movement test. To the 16 motion sickness related symptoms that are rated in this questionnaire two SIC-specific symptoms were added: emesis and oscillopsia.

Because the SSQ does not provide insight into the temporal build up of symptoms *during* the test, the level of sickness was also scored on the Misery Scale (MISC). The version used in this study differed slightly

from the scale used in the astronaut studies, in that it clarifies the meaning of the scores, especially in the lower range (see Table 4.2).

TABLE 4.2
Misery Scale (MISC)

Symptoms		Score
No problem		0
Uneasiness (no typical symptoms)		1
Dizziness, warmth, headache, stomach awareness, sweating, ...	vague	2
	slight	3
	fairly	4
	severe	5
Nausea	slight	6
	fairly	7
	severe	8
	retching	9
Vomiting		10

Subjects were instructed about all symptoms possibly anticipating nausea (Graybiel et al., 1968; Reason & Brandt, 1975, pp38-54) leading to scores 2-5, which are also listed in the SSQ (Kennedy et al., 1993). The new MISC also takes into account that the order of symptoms other than nausea generally varies over subjects, while nausea, if present, always directly precedes retching and vomiting. It is equal to the MISC used and validated by Wertheim et al. (1998), with the exception that once nausea is experienced, a minimum MISC of 6 is rated (instead of 5), and the symptoms below a rating of 6 are pooled instead of ordered. As with the previously applied MISCs, this new MISC is easy to use during the test and has the advantage that it reflects the momentary subjective score (De Graaf & De Roo, 1996; Bles et al., 1997; Bos et al., 2005). It was the main sickness measure used in the current study. MISC scores were

collected prior to the test and after every 10 head movements. The test was aborted when the MISC exceeded 7.

Data analysis

Head movement performance was described by the maximum head angular velocity (ω_{max}), defined as the maximum magnitude of the 3D angular velocity vector. For every subject, ω_{max} was averaged over all yaw and pitch trials within one session. Head position data (i.e., head orientation) was used to check whether the task was performed properly.

As stated in the introduction of this chapter, MISC scores are affected by head movement velocity and vice versa. Because a particular head movement velocity was not strictly prescribed during the test, there is a chance that head movements were performed deliberately at a low rate in order to prevent sickness. This would lead to an underestimation of MISC scores, which could hamper the comparison of centrifuge conditions. Such behaviour (i.e., low MISC scores and low angular velocity) would deviate from the inverse relationship between MISC scores and movement velocity that normally is observed. It would also result in a low linear correlation between MISC scores and maximum angular velocity. When such deviating behaviour is indeed found, and the correlation between MISC scores and maximum angular velocity is low, both measures have to be taken into account to enable a consistent comparison of centrifuge conditions. Thus, depending on the results of a linear regression analysis between MISC scores and ω_{max}, the data will be combined in a single measure. This measure then, will be used to determine the subject's susceptibility to SIC and to investigate the effects of ΔG and duration of centrifugation on the occurrence of SIC.

RESULTS

The head movement data of one subject had to be disregarded for further analysis. This subject was so disturbed by his first centrifuge run (2G90)

that he also refrained automatically from making any rapid head movements following the other runs, regardless of the gravito-inertial stimulus. Such behaviour was not observed in the other subjects. A second subject was so disturbed by the first posttest following the 3G90 run (terminated after 9 head movements) that he was unable to perform the second test session 45 minutes later (MISC>7). Missing head movement performance data for this session was replaced using linear interpolation.

The symptom scores obtained after each centrifuge run showed large differences between centrifuge conditions and between subjects. Where none of the subjects experienced nausea (MISC≥6) following the head movement test after the 2G45 centrifuge condition, 5 of the 12 subjects did so after the 3G90 run. However, before we could identify subjects as SIC-susceptible and subsequently compare the effect of the four centrifuge conditions, it was checked whether head movement performance was deteriorated after centrifugation. As mentioned in the Methods section, a deterioration of head movement performance could lead to an underestimation of the MISC scores. Therefore we will start this section with an analysis of head movement performance. It will be shown that ω_{max} was indeed decreased after centrifugation, but that the correlation between ω_{max} and MISC scores was low. This necessitated a correction of the MISC scores, as described below.

Head movement performance

The head movement velocity data is shown in Figure 4.3. A 2(ΔG) × 2(duration) × 5(session) × 2(movement plane) within subjects ANOVA revealed that ω_{max} was lower for pitch than for yaw movements ($F(1,10)=407$, $p<.001$). Inspection of head position data learned that the amplitude of yaw movements was higher than the pitch amplitude (65±7° vs. 53±8°). Apparently, subjects voluntarily rotated further than necessary in yaw. The interaction of G × session was significant ($F(4,40)=7.78$, $p<0.001$) and a posthoc Tukey test indicated that ω_{max} was significantly

lower after 3G stimulation, but not following the 2G runs. Large interindividual differences are reflected by the many outliers in Figure 4.3. These outliers indeed correspond to the behaviour of SIC-susceptible subjects, as will be shown later. The absence of a significant interaction of G-load × movement plane × session indicated that the velocity decrease was present in both yaw and pitch movements.
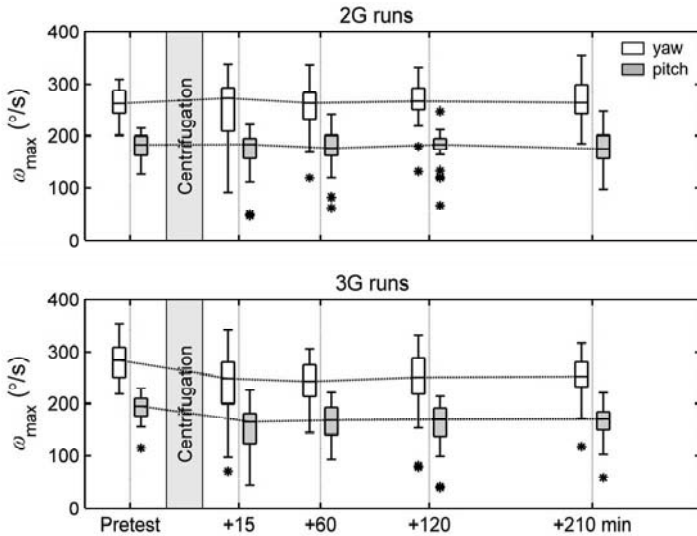

Figure 4.3: Boxplot of the averaged ω_{max} for the two G-levels. Pitch head velocity was lower than yaw velocity, and both were affected by the 3G-condition. Stars indicate extremes.

As to symptom severity, subjects who experienced nausea after centrifugation indicated that only the pitch movements were provocative and that their experienced level of nausea decreased again after a few yaw movements. This implies that the build up of symptoms was directly related to movements involving changes in head orientation with respect to gravity. It also explains the absence of a gradual MISC increase within one session. Therefore, the maximum MISC score within each session

(*MISC$_{max}$*) was taken as a measure for SIC-severity, rather than the score at the end of the test. The *MISC$_{max}$* scores of the first posttest are shown in Figure 4.4, plotted against head movement performance (ω_{max}, averaged for pitch and yaw). The focus will lie on the results of the first post test, since in this session the effects are largest.

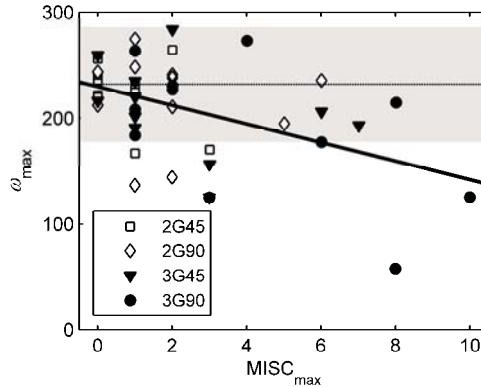*Figure 4.4: Mean ω_{max} vs. the maximum MISC score of the first post test following each centrifuge run (n=11). The regression line (solid) and the mean velocity of the pretest (dashed) are indicated. The gray area represents the mean pretest velocity ±2SD.*

A linear regression analysis revealed the anticipated inverse relationship between maximum head velocity and MISC scores (ω_{max} = 229.7 − 8.8·*MISC$_{max}$*, $r=$ −0.47, $p<.01$): subjects suffering from nausea (i.e., high MISC scores) generally prevented rapid head movements (i.e., low ω_{max}). For clarity, the average pretest performance (± 2SD) is also depicted in Figure 4.4 by the dashed line and shaded area. The fact that the accounted variance of the regression equation is low ($r^2 = 0.22$) indicates that different behaviour (e.g., high MISC scores with high ω_{max}) is observed as well, depending on the received stimulation and the subject's susceptibility. Most obvious in this respect are the data points in the lower left corner of Figure 4.4: ω_{max} is well below the pretest average *despite* a low *MISC$_{max}$* score. These points represent subjects who most

likely refrained from rapid head movements to prevent serious nausea. It is likely that $MISC_{max}$ scores in this latter group would have been higher when head movements were performed at a higher rate.

Corrected MISC score

Given the weak correlation between $MISC_{max}$ and ω_{max}, and the fact that these variables are mutually dependent, they both had to be taken into account in the comparison of centrifuge conditions. To that end, MISC scores were corrected for the level of performance: the scores were increased when the head movement velocity was lower than the pretest average. Thus, it was assumed that the performance decrease was due to (anticipated) nausea. As such, the corrected measure should estimate the symptom level that would have been reached when the head movements had been performed at the pretest level. The magnitude of the correction was based on the regression analysis presented above. On average, a 1-point increase in $MISC_{max}$ was accompanied by a decrease of 8.8 °/s in ω_{max} (slope of the regression line). This would be a perfect correction factor when the variance in $MISC_{max}$ was totally accounted for by the variance in ω_{max}, i.e. $r^2=1$. However, r^2 was in fact only 0.22, implying that the decrease in head movement velocity was also affected by other factors and thereby making the correction of 1 MISC-point per 8.8 °/s too strenuous. Instead, the variance accounted for was taken into account by dividing the slope of the regression line by r^2. This resulted in a correction of 1 *MISC*-point per 40°/s decrease in ω_{max}. The group average of the pretest ($\overline{\omega}_{max\ pretest}$, equal to 232°/s) was taken as a reference velocity relative to which the velocity change of each subject and each centrifuge condition was determined. The corrected score, denoted by *CMISC*, then became:

$$CMISC = MISC_{max} + \frac{\overline{\omega}_{max\ pretest} - \omega_{max\ posttest}}{40} \qquad (4.1)$$

For example, a MISC score obtained after head movements performed with an average velocity of only 152º/s instead of the pretest average of 232º/s would be increased with 2 MISC points. Since one cannot get sicker than sick, scores were ceiled at a *CMISC* of 10. This corresponded to the assumption that if a subject would have made a more vigorous head movement, he would have vomited.

This new variable has subsequently been used to categorize the subjects. Subjects were considered susceptible to SIC if their *CMISC* of the first posttest following the 3G90 centrifuge run was 6 or higher, i.e. if they were suffering from nausea (or would be if they had made more vigorous head movements).

Comparison of centrifuge conditions

Based on their *CMISC* scores, six out of 12 subjects were considered susceptible to SIC. Figure 4.5 summarizes their CMISC scores. These scores were submitted to a 2(ΔG) × 2(duration) × 5(session) within subjects factorial ANOVA, with SIC-susceptibility as a between-subjects factor. The results show that the effects of the 3G runs exceeded those of the 2G runs ($F(1,9)=43.7$, $p<0001$) and the effects of the 90 minute exposure exceeded those of the 45 minute exposure ($F(1,9)=17.9$, $p<.01$). Also a main effect for test session was found ($F(4,36)=40.2$, $p<.0001$). Given the large differences between the SIC and non-SIC group ($F(1,9)=22.8$, $p<.01$) it is not surprising that the interaction between SIC and respectively ΔG ($F(1,9)=21.1$, $p<.01$), duration ($F(1.9)=9.4$, $p<.05$), and session ($F(4,36)=18.6$, $p<.0001$) were also significant. Furthermore, an interaction-effect was found for ΔG × session ($F(4,36)=19.4$, $p<.0001$), duration × session ($F(4,36)=8.5$, $p<.0001$) and ΔG × session × SIC ($F(4,36)=11.1$, $p<.0001$). Post hoc testing revealed that for the non-SIC group, no significant differences were found; centrifugation did not significantly increase the *CMISC* scores. For the SIC-group, on the other hand, *CMISC* scores were significantly increased after the 2G90 run and both 3G runs. Comparing the magnitude of the effect measured in the

first posttest between centrifuge conditions, the 2G90 run did not differ significantly from the 3G45 run, whereas the 3G90 run effects exceeded all other runs.
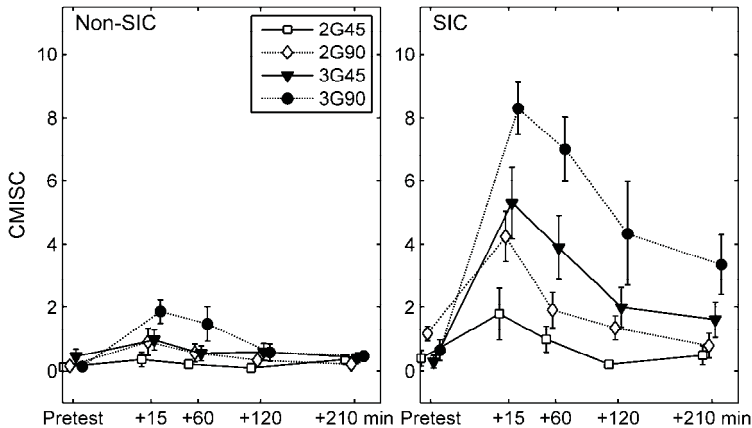

Figure 4.5: Mean CMISC scores for each test session and centrifuge condition. Error bars indicate standard error of mean.

The recovery rate differed per condition. For the 2G90 run the scores were already back to the pretest level in the second posttest, whereas for the 3G45 run this has occurred in the third posttest. In the 3G90 condition recovery has begun (scores in the third posttest are significantly lower than the first posttest) but was not yet complete in the last posttest. The scores then were still higher than the pretest level. To estimate the time constant of the recovery process, the post-centrifugation data of the SIC-group was fitted with an exponential decay curve ($CMISC(t) = A \cdot e^{t/\tau}$). Time constants equalled 74 and 85 s (2G) vs. 135 and 194 s (3G) for respectively the 45 and 90 min. exposure. The amplitude A increased in a same manner, 2, 5, 6, and 9 *CMISC*-points, respectively.

Other symptoms

Although motion sickness is the most prominent component of SIC, a range of other symptoms were observed. Subjects often could not walk in a straight line and had difficulties with taking corners and maintaining balance. Some subjects reported motion illusions during vertical movements. Figure 4.6 shows the incidence of the symptoms that were scored after the head movement test following each centrifuge run. Many subjects were not completely free of symptoms after the end of the last post test, especially after the heaviest condition. Subjects were still suffering from nausea, dizziness and fatigue for the rest of the day. In one subject, head movements remained provocative up to 6 hrs after the run. Another subject experienced motion illusions when lying in bed at night. In all cases symptoms had vanished completely the following morning. It is interesting to note that sleep in between the test-sessions also had a positive effect on recovery.
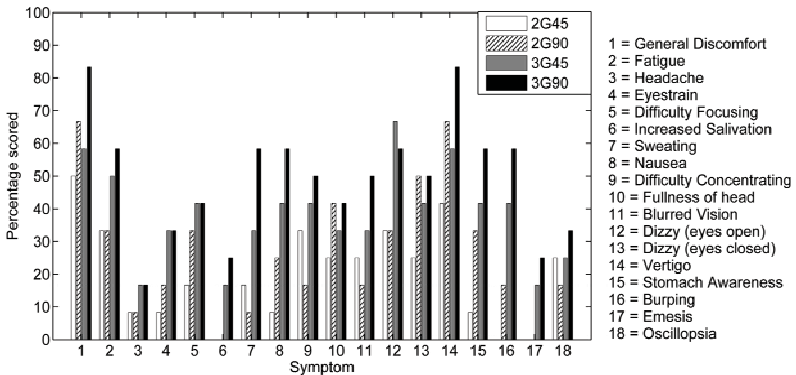

Figure 4.6: Histogram of symptom scores for each centrifuge condition in the first posttest (n=12). Symptoms are listed on the right.

Susceptibility to Earthly motion sickness

Six out of the 12 subjects were considered susceptible to SIC. Following the MSSQ (Golding, 1998), all subjects rated themselves as not (*n*=10) or

slightly susceptible (n=2) to *Earthly* motion sickness. MSSQ scores ranged from 0 to 60.5, (mean=18.5, SD=21.5) with the mean score being equal to the 20th percentile score (Golding, 1998). Although the MSSQ scores were fairly low, the SIC-susceptible group had significantly higher MSSQ scores than the non-susceptible group (t=3.1, p<.01). Furthermore, the MSSQ scores were significantly correlated with the *CMISC* scores of the first posttest after the 3G90 run (r=0.83, p<.01).

DISCUSSION

The re-introduction to Earth's gravity following a sustained exposure to hypergravity can elicit symptoms that resemble those of SAS (e.g. nausea, dizziness, visual illusions). The present study looked further into the nature of the gravito-inertial stimulus that is a prerequisite for the symptoms to occur, by investigating the interaction between G-level and exposure duration on the experienced symptom level (SIC). Subjects were exposed to centrifuge runs at $2G_x$ and $3G_x$ for 45 and 90 minutes and carried out a head movement protocol to elicit SIC.

The results showed that 50% of the subjects were suffering from SIC after one or more centrifuge conditions. This corresponds to the amount found in previous studies (Bles et al., 1997; De Graaf & De Roo, 1996) and is in the same order as the incidence of SAS (e.g. Davis et al., 1988; Homick, 1979; Matsnev et al., 1983). In line with the findings of De Graaf & De Roo (1996), the present results show that both yaw and pitch movements were performed at a significantly lower rate after centrifugation, whereas only the latter provoked nausea. Apparently, susceptible subjects adopted a strategy to limit *all* head motion, regardless of its direction. Although the main trend in our data was that head velocity decreased with an increasing symptom severity, other behaviour was also observed (see Figure 4.4): subjects moving slowly, while experiencing only mild symptoms. This resulted in a weak correlation between $MISC_{max}$ and ω_{max}. As such, the data necessitated the correction of the symptom scores for performance, by means of the

CMISC. Although there are obviously more ways to combine the two measures, the method used here is simple, and based on the statistical analysis. This correction yielded a more pronounced distinction between the SIC- susceptible subjects and the non-susceptible ones as well as a more consistent comparison between centrifuge conditions.

The main finding of this study is that, within the measured range, both G-level and duration affected the symptom level as defined by the *CMISC* scores. The scores following the 3G exposures exceeded those of the 2G exposures and the effects of the 90 minutes exposure exceeded those of the 45 minute exposure. However, it was after the 3G90 exposure only that the average *CMISC* of the SIC-susceptible group was substantially higher than 6 ("mild nausea"). The remainder of this discussion will elaborate on the parameter driving the adaptation process, and possible implications for space flight are discussed.

Time course of adaptation

The results of the current study suggest that the G-level difference is the signal that drives the adaptation during centrifugation and re-adaptation to 1G. The *CMISC* scores of the SIC-susceptible group are higher after 45 minutes centrifugation at 3G than at 2G. The adaptation to 3G is however not yet complete after 45 minutes, given the increase in *CMISC* scores with prolongation of the exposure. It is, however, likely that the effects saturate at a certain time interval, that is, when adaptation is complete. This is in line with the preliminary qualitative results from Bles and colleagues, who showed that the difference between an exposure of 60 and 90 minutes to $3G_x$ was small as compared to the difference between a 30 and 60 minute exposure. This suggests a nonlinear interaction between *ΔG* and duration. To make a first order estimation of the time constant of the adaptation process, an exponential function of the form $CMISC = A \cdot (1 - e^{-t/\tau})$ was fitted through the data of the first posttest (SIC-group only). These first posttest data were assumed to reflect the status of adaptation just at the end of the centrifuge

run. It was furthermore assumed that the time constant of adaptation (τ) was independent of ΔG, but that ΔG did affect the amplitude A, the saturation value of *CMISC*. For instance, it is plausible that a prolongation of centrifugation at 2G does not significantly increase the *CMISC*, so that this value saturates well below 10. At a level of 3G, a level of 10 may be reached. As a first step, A was taken linearly dependent on ΔG so that the function to fit became $CMISC = c \cdot \Delta G \cdot (1 - e^{-t/\tau})$. When the parameter c was fixed at 5, implying a maximal value of 10 for *CMISC*, the time constant τ came to 58 minutes (see Figure 4.7). As can be seen in Figure 4.7, both the 2G and 3G curves intersect the SEM error bars, indicating that the adaptation process can be described by this simple model based on the difference between gravity levels and exposure duration only. Although this is just a first step in modelling the role of ΔG and exposure duration in adaptation, it already may give a fair indication of the order of magnitude of the adaptation time constant.
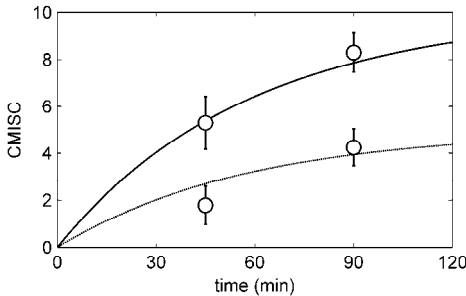

Figure 4.7: Fits on the CMISC data (SIC-susceptible group) as a model for adaptation to 2G (dashed line) and 3G (solid line). Bars indicate standard error of mean.

Interestingly, a time constant of about one hour would imply that the effects after 90 minutes of stimulation would differ significantly from the effects of 60 minutes stimulation. Although this latter stimulus was often used in other centrifuge experiments (De Graaf & De Roo, 1996; Bles et al., 1997), the MISC data obtained there cannot be compared easily with

the *CMISC* scores reported here, because the scores are heavily dependent on the amount, the amplitude and the velocity of head movements made. To the experimenter's observation, the amount of movement required to elicit a particular MISC scores was less after an exposure duration of 90 minutes. A systematic comparison is however needed to be conclusive about this issue.

It can be assumed that different dynamics have to be incorporated in the model when higher G-levels are used. Obviously, there are limits to adaptation speed and to the saturation level of adaptation. Furthermore, the model does not incorporate the dynamics between the level of mal-adaptation and the eventual build up of sickness symptoms (see e.g Oman, 1982; 1990; Bos & Bles, 1998). Admission to more direct adaptation measures would be useful in this respect, especially when they can be monitored during centrifugation. Such a measure would probably also reveal more about the adaptation process in non-susceptible subjects. It is possible that they re-adapt more quickly, too fast to measure any effects, or that this group uses a different strategy to cope with G-transitions disregarding vestibular input altogether. Nevertheless, it can be concluded that the order of conditions showing increasing levels of sickness as revealed by the *CMISC*, i.e., 2G45, 2G90, 3G45 and 3G90, can well be explained by a first order approximation of the adaptation process based on the difference between gravity levels and exposure duration only.

Consequences for Artificial Gravity

The fact that G-transitions can cause disorientation and motion sickness has implications for space flight. Intermittent Artificial Gravity (AG) is currently a promising countermeasure against physiological deconditioning during space flight. However, the exact characteristics of the stimulus, like the optimal body position, frequency, duration, and load, still need to be determined (Clément & Pavy-Le Traon, 2004; Clément & Bukey 2007; see also the Bioastronautics Roadmap[7]). The

results of this study show once more that, from a vestibular point of view, locating the vestibular system on or close to the rotation centre is preferred in order to prevent repetitive G-transitions. The fact that both G_x and (the more often used) G_z stimulation may elicit symptoms of SIC (Albery & Martin, 1996; Beier, 1999; Beier et al., 2002; Takeda et al., 1996) suggests that the direction of stimulation is of minor importance as compared to the magnitude. Although the G-transitions experienced after AG exposure or entry into a planet's gravity field are generally smaller than the provocative 2G transition (i.e. from 3 to 1G) used in this study, one should keep in mind that adaptation to the *absence* of gravity forms a singular case within the gravitational continuum. During the stay in microgravity, the astronauts become more visually dependent and some of them eventually adopt a body centred reference frame instead of a gravity based reference frame (e.g. Glasauer & Mittelstaedt, 1998; Oman et al., 1986). Due to this adaptation, orientational responses are no longer required. Re-entry into any gravity field requires regaining of those responses, which can be accompanied by SIC. It is to be verified in space what G-difference is required for this process to occur.

Relation with Earthly motion sickness

A last issue that will be touched upon is the relation between SIC and Earthly motion sickness. Although susceptibility to SAS is correlated with that to SIC (see Chapter 2), no such correlation was found between SAS and Earthly motion sickness (Homick et al., 1987; Oman et al., 1986). The finding that the SIC-susceptible subjects had significantly higher scores on the MSSQ seems to contradict this. In may be too premature to draw conclusions based on our limited sample of subjects, whose MSSQ ratings were all low. Although in previous centrifugation experiments the MSSQ was not administered explicitly, it is known that there are subjects who are very susceptible to Earthly motion sickness, but not to SIC, and vice versa (Bles et al., 1995; Bles, personal communication).

Conclusion

The current study showed that the magnitude of the G-transition and the exposure duration both contribute to the experienced level of SIC after centrifugation. By means of a simple but adequate curve fit, the time constant of adaptation was estimated at about one hour. Although previous studies indicated that a stimulus of 60 minutes at 3G is sufficient to make the symptoms of SIC visible, these results imply that adaptation to 3G is not yet complete after this exposure duration.