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Coriolis-induced cutaneous blood flow increase in the forearm and calf

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ABSTRACT: Using venous occlusion plethysmography, Sunahara et al. reported that Coriolis-induced nausea was accompanied by an increase in forearm blood flow, suggesting a decrease in sympathetic activity to this vascular bed. No significant blood pressure and heart rate changes were observed. Vasodilation of the limbs theoretically impairs orthostatic tolerance, particularly if blood flow is shown to increase simultaneously in the lower limbs. This study examined the latter possibility. Seventeen subjects were exposed to the Coriolis cross-coupling effects induced by 20 RPM yaw rotation, and a simultaneous 45° pitch forward head movement in the sagittal plane every 12 s. Forearm and calf skin blood flow were monitored in real-time using laser Doppler flowmetry (PeriFlux 4001). Our results indicated a significant ($p < 0.001$) simultaneous forearm and calf skin blood flow increase as a result of Coriolis cross-coupling across all 15 susceptible subjects. No significant changes in blood pressure and heart rate were observed. Coriolis-induced cardiovascular changes may confound previous reports on reduced G tolerance using ground-based centrifuges that invariably evoke cross-coupling effects. © 2001 Elsevier Science Inc.

KEY WORDS: Vestibular, Hyperemia, Hypotension, Nausea.

INTRODUCTION

The Coriolis illusion, named after Gustave Gaspard de Coriolis (1792–1843) is a common perceptual illusion that causes almost as much confusion in its discussion as in its experience. After a prolonged rotation about the yaw axis, the cupulae of the lateral semicircular canals return to the neutral position and the sensation of rotation ceases. If the subject pitches forward to 90°, the lateral semicircular canals are removed from, and the anterior and posterior canals have been inserted into the plane of rotation. The angular momentum of the endolymph in the lateral canals dissipates slowly. The torque resulting from the continued rotation of the endolymph causes the cupulae in the lateral semicircular canals to be deviated, and the sensation of angular motion occurs in the roll plane relative to the body. Simultaneously, the endolymph in the anterior and posterior canals acquires the angular momentum because they have been brought into the plane of rotation. The torque required for this change in momentum causes deflection of the cupulae and a sensation of rotation in the yaw plane relative to the body. The combined effect of the cupula deflection in all three semicircular canals is that of a suddenly imposed angular rotation in a plane in which no angular acceleration relative to the subject has occurred. The resulting Coriolis illusion experienced is one of rolling and yawing to the right.

Psychophysiological studies on the effects of Coriolis cross-coupling include the induced symptom complex of motion sickness, and autonomic responses as indicated by heart rate variability and forearm blood flow changes. The results of heart rate variability measurement are controversial. Most studies have found very small, variable, or inconsistent changes, despite substantial symptoms of nausea and disorientation experienced by the subjects [3,16].

However, provocation of nausea accompanied by an increase in forearm blood flow without significant changes in blood pressure and heart rate appears to show relatively consistent findings [19, 21,22]. Forearm blood flow increases were also observed during pseudo-Coriolis stimulation [12] without significant changes in heart rate and blood pressure. These studies employed venous occlusion plethysmography in which the rate of swelling of the forearm (represented by the measured slope of forearm circumference versus time) was taken as the index of blood flow. It was concluded that the forearm blood flow increase and the symptoms of motion sickness, however caused, are concomitant, and that the increase in forearm blood flow probably occurs in the skeletal muscle of the forearm. However, there were no direct measurements from the forearm muscle group. Depending on the uniformity of the data, in some cases, it is difficult to quantify with absolute confidence that changes in arm circumference correspond to changes in blood flow.

Despite its generally accepted accuracy and validity, venous occlusion plethysmography measures total regional blood flow with a low sampling rate. As a result, conclusions regarding control of the skin or muscle components of forearm blood flow must rely on evidence from separate studies in which independent measurements of skin blood flow or muscle blood flow were made. In some cases independent measurements have shown that there were little or no changes in forearm muscle blood flow in spite of regional changes. For example, no changes were observed in forearm muscle blood flow during whole-body heating [4], prolonged leg exercise [13], or moderate local warming of the limb

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[5]. Similarly, if increment in blood flow to the forearm during motion sickness is confined to the skin, as in the above examples, then changes in skin blood flow can be measured with reasonable accuracy from increment in total forearm blood flow.

Peripheral vasodilation in the limbs could theoretically impair orthostatic tolerance, particularly if these changes were documented in the lower limbs. In this study we investigated whether the increment in forearm blood flow during motion sickness could be detected by direct measurement of forearm skin blood flow using laser Doppler flowmetry. Secondly, we attempted to quantify skin blood flow changes simultaneously in the forearm and calf during Coriolis stimulation, and investigate how the time course of the blood flow changes correlate with the subjective reports of symptoms of motion sickness.

MATERIALS AND METHODS

Subjects

Seventeen healthy subjects (14 males, 3 females) between the ages of 22 and 46, participated in the study. Approval for this study was obtained from the DCIEM Human Ethics Committee and subjects gave informed consent before participation. They had no known history of ophthalmologic, oculomotor, or vestibular disorders, and they had no spontaneous nystagmus nor Romberg's sign with eyes opened or eyes closed. There was no known history of cardiovascular abnormalities. None of the subjects had frequent problems in any kinds of everyday motion environment. All subjects were instructed to strictly abstain from alcohol, tobacco, and over-the-counter and prescribed medication for at least 24 h prior to the experiment. All but two subjects had no previous experience with Coriolis stimulation.

Apparatus

Subjects were seated upright on the vertically oriented rotation axis of a motorised platform rotating at 20 rotations per minute (RPM) or 2.1 radians per second. A headrest served to guide the forward and downward movements of the subject's head through an angle of 45° within 2 s in the sagittal plane relative to the seated subject. As a result, all head movements made were guided active head movements beginning with a head down movement from the natural head erect position.

Physiological Measurements

Laser Doppler flowmetry is a convenient, safe, and noninvasive method to measure cutaneous microvascular flow from multiple sites with relative ease. It depends on the Doppler shift of coherent (laser) light reflected from the tissue. This frequency shift is due to the velocity of moving particles (red blood cells) within the tissue and, therefore, is directly related to tissue blood flow. The varying distribution of capillaries in the skin below the probe at different locations, and local variations in flow through these capillaries, make this technique site specific. However, it has the limitation of providing only the relative value of blood flow changes among trial conditions. A comparison study by Johnson et al. [14] suggested that laser Doppler flowmetry correlates well with venous occlusion plethysmography techniques with a correlation coefficient of 0.94–0.98.

Continuous forearm and calf blood flow (BF) changes were monitored using the Perimed Periflux 5001 laser Doppler system in combination with two Perimed #413 integrating probes (Perimed Inc., Stockholm, Sweden) intended for use on areas with large spatial variation in blood perfusion, such as forearm and calf. An integrating probe was positioned on the lateral surface of the left forearm in the region of largest circumference. The second integrating probe was positioned on the dorsal surface of the left calf, left of the midline in the region of largest circumference. Blood pressure (BP) and heart rate (HR) were monitored using the Portapres Model 2.0 (TNO, Amsterdam, The Netherlands) and respiration (RSP) was monitored using model 3993/10 Biolog, (UFI, Morro Bay, CA, USA). Ambient temperature of the labora-

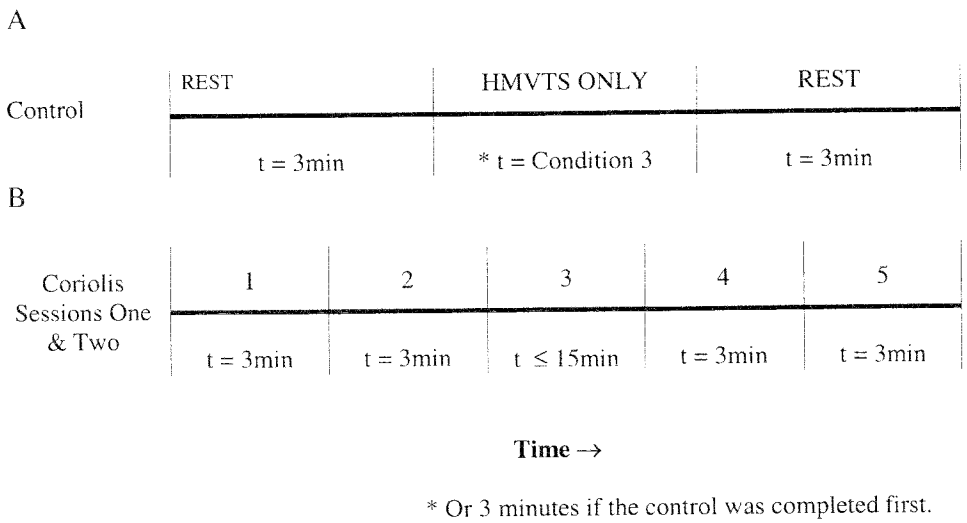

FIG. 1. Experimental procedures for (A) the control and (B) Coriolis sessions. For the control: REST = sitting upright, at rest; HMVT ONLY = sitting upright with pitching head movements every 12 s, and reporting symptoms of nausea according to the Golding's scale after each head movement. For the Coriolis sessions: (1) sitting upright, at rest; (2) yaw rotating at 20 rpm; (3) yaw rotation at 20 rpm with pitching head movement every 12 s, and reporting symptoms of nausea according to the Golding's scale at the end of each head movement. The end point for the trial is reaching a rating of 7 on the Golding's scale or 15 min, whichever came first. Condition (4) is identical to (2), and condition (5) is identical to (1).

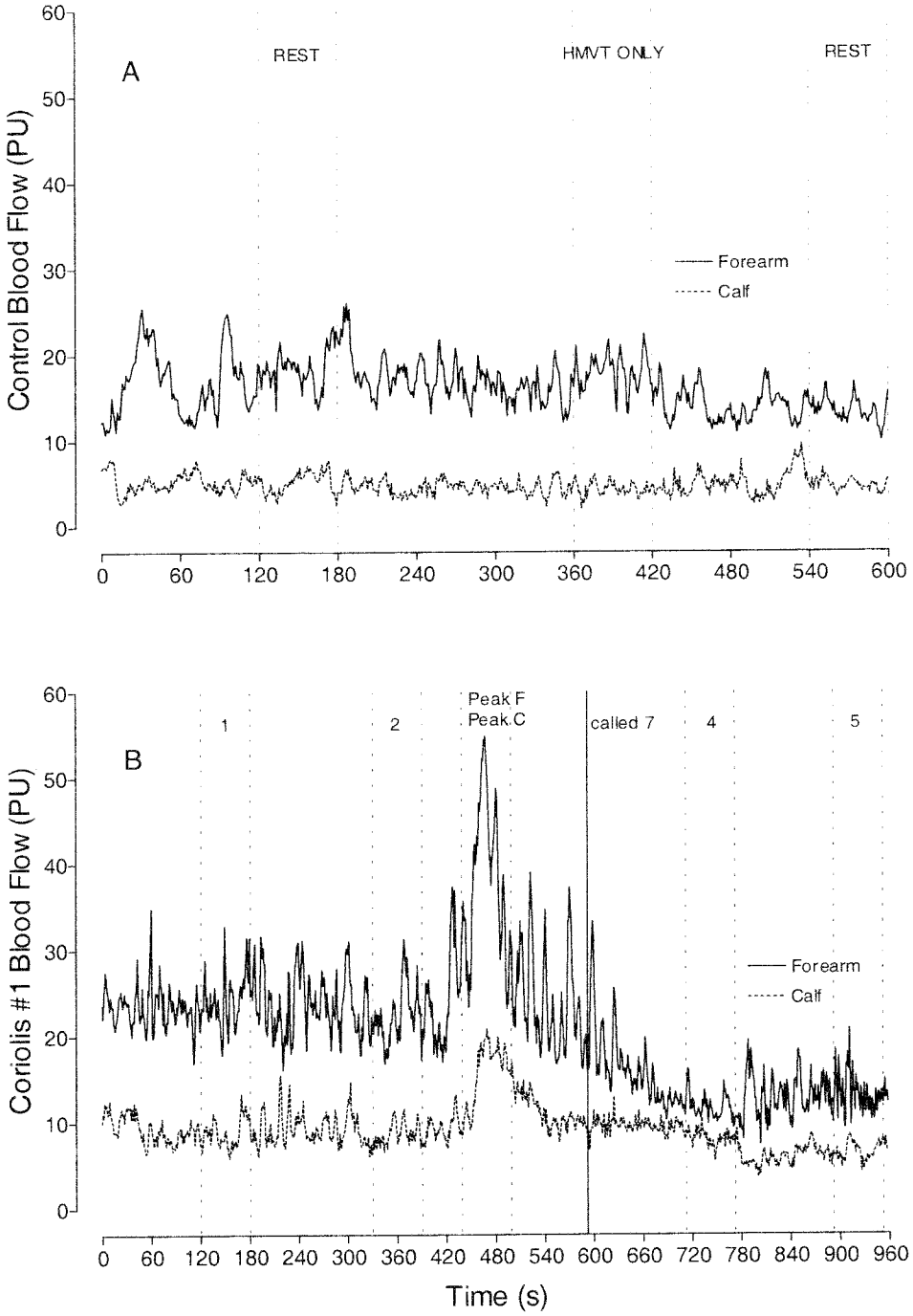

FIG. 2. Raw traces of forearm and calf skin blood flow (PU) recorded from the same subject during (A) the control session, and (B) a Coriolis session, in which a rating of 7 was called after peak forearm and calf blood flow were reached. The basic unit of measurement used in the PeriFlux is the Perfusion Unit (PU), which is an arbitrary value equal to the analogue output of 10 mV. This relationship is only valid when the instrument has been calibrated using the PF1000 calibration device. Since the PU is arbitrary it cannot be given any physiological definition such as the actual number of cells flowing through a given volume of tissue during a given time period. In this study measurements of blood flow in response to different motion stimuli were expressed as percentage changes from the calibrated zero.

tory was maintained between 22 and 24°C and subjects were instructed to wear lightweight, loose clothing. Because skin blood flow could be affected by emotion and temperature, comparisons were only made during each single placement of the probe. Subjects were instructed to relax without active movement during the measurement period.

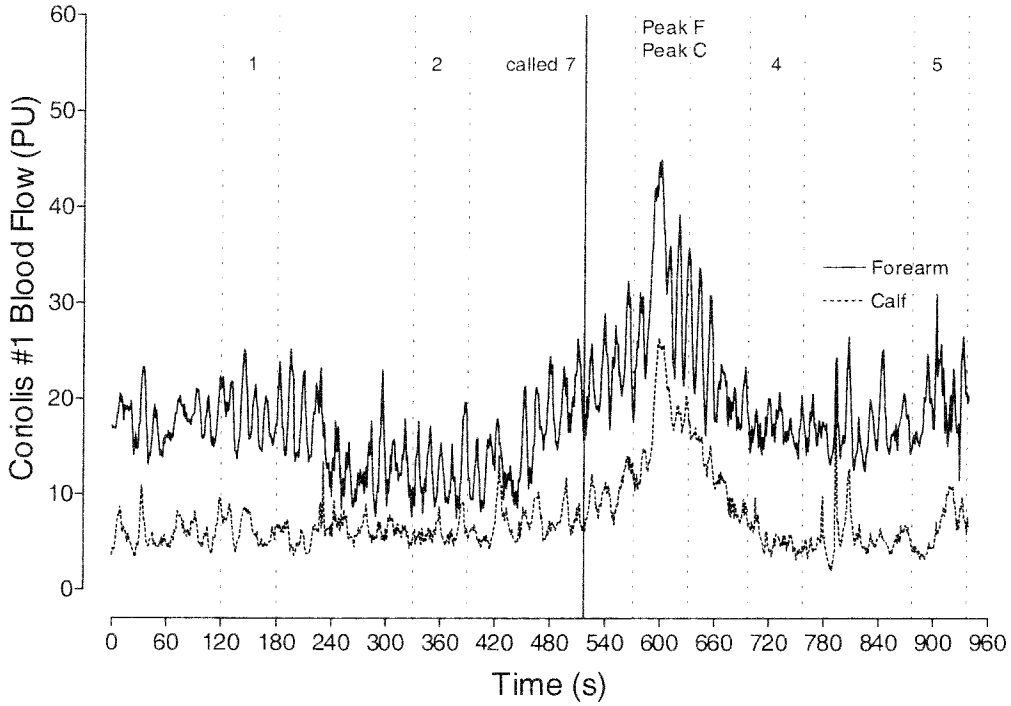

FIG. 3. Raw traces of forearm and calf skin blood flow (PU) recorded during the Coriolis trial of another susceptible subject, in which a rating of 7 was called before peak forearm and calf blood flow were reached.

Psychophysical Measurements

The procedure used to quantify the subjective severity of sickness before and after each trial was that modified from Graybiel et al. [8], including consideration of pallor, nausea, and vomiting. During the exposure of Coriolis cross-coupling stimulation, the subjective rating scale by Golding and Kerguelen [7] was used. Subjects rated their degree of motion sickness after every head movement on the following scale: 1 = No symptoms; 2 = Any symptoms, however slight; 3 = Mild symptoms, e.g., stomach awareness but no nausea; 4 = Mild nausea; 5 = Mild to moderate nausea; 6 = Moderate nausea but can continue; 7 = Moderate nausea, want to stop. The motor driven headrest was stopped when the subject reported a rating of 7, or after 15 min for those subjects who did not achieve a sickness rating of 7. They were informed that although the scale was ordinal, they did not have to follow the scale in the written sequence, but rather to pair symptoms they experienced at a particular instant with a specific level on the scale.

Since the individual's level of anxiety during nauseogenic and stressful stimulation may affect the physiological response [2,6], an attempt to monitor anxiety was made. State-Trait Anxiety Inventory (STAI), form Y, (Mind Garden, Inc., Redwood City, CA, USA) was used to measure the subject's level of anxiety before and after exposure to Coriolis stimulation in all trials. The state-anxiety scale is a sensitive indicator of changes in transitory anxiety experienced by subjects [6].

Procedure and Design

Each subject participated in three trials: one control and two Coriolis trials. The order of the trials was counter-balanced across subjects. Each trial was separated by at least 7 days to prevent habituation to the stimulus. The control trial consisted of sitting at rest for 3 min, head movements for 3 min, and followed by sitting at rest for another 3 min. The Coriolis trial consisted of sitting at rest for 3 min, yaw rotation for 3 min, yaw rotation and head movements for 15 min or when subject reached the end point; followed by yaw rotation and sitting at rest for 3 min, respectively. The experimental protocol for the control and the Coriolis trials is summarised in Fig. 1.

A repeated measure factorial design was employed with three factors: trial type, probe location, and motion stimulus. Trial types consisted of control, Coriolis 1, and Coriolis 2, while probe locations consisted of forearm and calf. Motion stimuli consisted of "at rest," "head movements only," and "at rest" in the control trial. Motion stimuli in the Coriolis trials consisted of "at rest," "20 RPM yaw rotation," "20 RPM yaw rotation and head movements-Coriolis stimulation," "20 RPM yaw rotation," and "at rest." Each head movement consisted of pitching the head forward to approximately 45° from upright and maintained at this position for 12 s followed by return head movement to upright position and maintained for another 12 s before the next pitching forward movement. At the end of each head movement the subject was instructed to rate their symptoms according to Golding's scale and report the rating verbally. The end point for the trial is either reaching a rating of 7 on the scale or 15 min of stimulation, whichever comes first. During the Coriolis trials, rotation at 20 RPM was continued for another 3 min after head movements were stopped, unless subjects chose to abort the trial.

Statistical Analysis

Prior to the analyses, artefacts from raw BF, BP, HR, and RSP data from each trial were reviewed and excluded from further analyses. Artefacts constituted less than 1% of the recorded data. With the exception of condition 3 in the Coriolis trials, the last 60 s

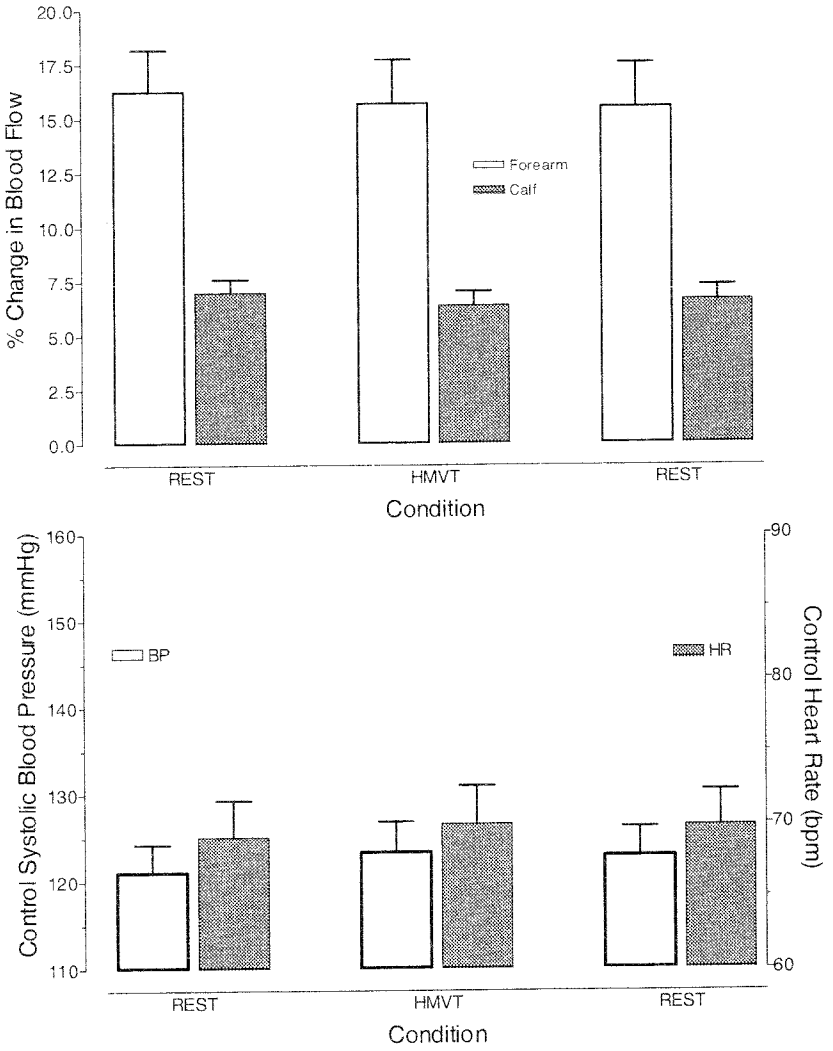

FIG. 4. Mean % change from calibrated zero in forearm and calf blood flow perfusion units(A) and mean systolic blood pressure and heart rate (B) for each control condition (error bars are standard error of the means, SEMs).

of BF, BP, HR, and RSP data during identical motion stimuli, in all trials, were used in the final analyses. In condition 3, the time for peak forearm and peak calf blood flow for each Coriolis trial was identified, and 30 s before and after each peak was also used in the analyses of BF. The corresponding 60-s window in the BP, HR, and RSP data were also analysed. Data were analysed by repeated measures ANOVA using Statistica by Statsoft, with the significance level α set to ≤ 0.01. All post hoc testing was completed using planned comparisons; p-values for factors with more than two levels were adjusted using Greenhouse-Geisser's epsilon correction factor.

RESULTS

In the control trial, based on subjective reports, 15 of 17 subjects were shown to be susceptible to the Coriolis stimulation; they exhibited the cardinal symptoms of motion sickness such as pallor, epigastric discomfort, and nausea. These subjects also demonstrated an increase in rhythmic blood flow fluctuation in the forearm and calf simultaneously. Raw blood flow data in Figs. 2 and 3 illustrate the difference in BF changes during the control (Fig. 2A) and the Coriolis trial (Fig. 2B) of one of the "susceptible subjects." As in all susceptible subjects, there was a distinct shift of the rhythmic blood flow as indicated by the increase in perfusion units. The two subjects who demonstrated resistance to the Coriolis stimulus lacked identifiable forearm and calf blood flow increase. Of the 15 susceptible subjects, two did not complete the second Coriolis trial due to the severity of sickness experienced.

Blood Flow

From the control trial, a 2 (probe location) $\times$ 3 (motion stimulus) repeated measures ANOVA revealed that the magnitude of forearm blood flow in general was significantly greater than calf blood flow in each of the three motion conditions, [$F(1,16) = 33.93$, $p \leq 0.01$]. However, there was no significant difference between the motion stimulus conditions, which suggested that head movement and verbal report of symptoms did not cause any

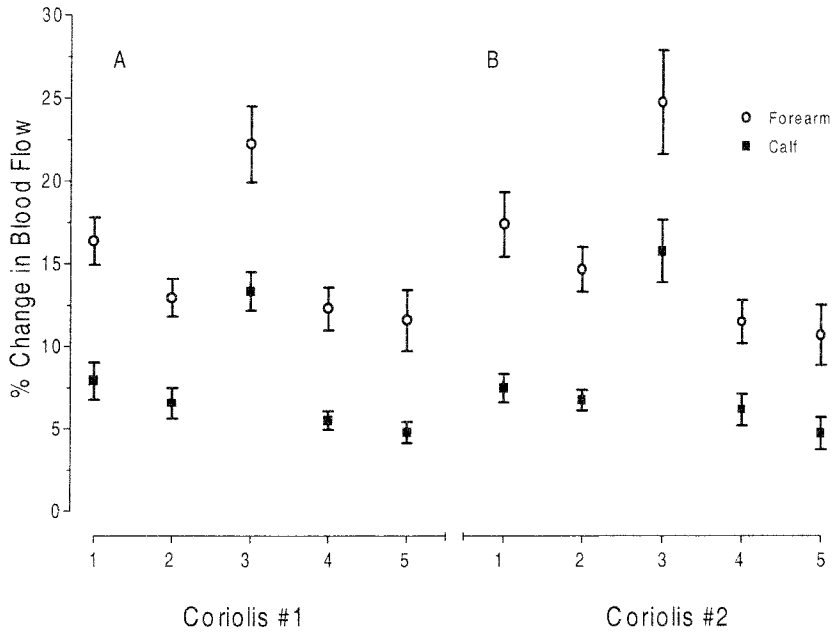

FIG. 5. Mean % change in forearm and calf skin blood flow for each motion stimulus condition during the Coriolis sessions (error bars are SEMs).

changes in BF. Figure 4A illustrates the lack of mean blood flow changes during the control trial.

A 2 (trial type) × 2 (probe location) × 5 (motion stimulus) repeated measures ANOVA performed on the combined BF data from Coriolis 1 and Coriolis 2 revealed a significant main effect for probe location [$F(1,10) = 61.78$, $p \leq 0.01$], and a significant interaction between motion stimulus and probe location [$F(4,40) = 48.44$, $p \leq 0.01$, $\in = 0.43944$]. Similar to the control trials, magnitude of forearm BF was significantly greater than calf BF (i.e., main effect for probe location). Within both forearm and calf probe locations, BF increase was significantly higher during condition 3 (yaw rotation plus head movements) than any other conditions (Fig. 2). Most importantly, it is significantly higher than conditions 2 and 4 (yaw rotation only), $p < 0.001$ for all comparisons, which indicated that the forearm and calf BF were induced by Coriolis stimulation. There was an immediate two- to threefold increase. Similar pattern of blood flow increases within all conditions in the two Coriolis trials was evident suggesting a test and re-test reliability, and this is illustrated in Fig. 5.

Blood Pressure and Heart Rate

There were no significant changes in BP and HR during the control trials (Fig. 4B). A 2 (trial type) × 6 (motion stimulus) repeated measures ANOVA performed on the combined BP and HR data from the two Coriolis trials revealed no significant changes in BP and HR between yaw rotation alone (condition 2) and Coriolis stimulation (conditions 3F and 3C). Due to the fact that in some subjects, the forearm and calf blood flow increase during Coriolis stimulation did not arise at exactly the same moment, the corresponding systolic blood pressure and heart rate for the forearm and calf were plotted separately as 3F and 3C, respectively. However, blood pressure was significantly lower when the subjects were at rest (conditions 1 and 5). Figure 6A illustrates the changes in systolic blood pressure across all conditions during the Coriolis trials. Figure 6B demonstrates the lack of statistical significance in heart rate measurement between conditions 2 and 3 (3F and 3C) during the Coriolis trials.

Respiration

A 2 (trial type) × 6 (motion stimulus) repeated measures ANOVA was performed on the combined RSP data from Coriolis 1 and 2 and no significant findings were observed across difference stimulus conditions (Fig. 7). Similarly, there were no significant changes during the control trials.

Subjective Reports of Sickness and State-Anxiety Rating

Both the state-anxiety level (Fig. 8A) and the subjective reports of motion sickness (Fig. 8B) of susceptible individuals increased significantly from the pre-Coriolis to post-Coriolis exposure, $p < 0.001$. There were no significant changes in the control trials, indicating that head movements alone did not affect the anxiety level or provoke sickness symptoms.

DISCUSSION

It has been suggested that microcirculatory blood flow and vessel diameter of the caliber of arterioles are temporally and spatially variable and that this variability manifests itself in the rhythmic luminal changes that cause corresponding flow variation [10]. The cyclical variations of blood flow observed in our recordings (Figs. 2 and 3) might represent the arteriolar vasomotion. Our primary interest was to investigate whether Coriolis-induced nausea could affect skin blood flow changes, i.e., blood flow changes between conditions 2 and 3; 3 and 4. Results indicated that all of the subjects who were susceptible to the Coriolis stimulation showed a significant increase in both forearm and calf skin blood flow, from condition 2 (yaw rotation only) to condition 3 (yaw rotation and pitching head movements). Once the Coriolis stimulation was removed, blood flow decreased back to the state of

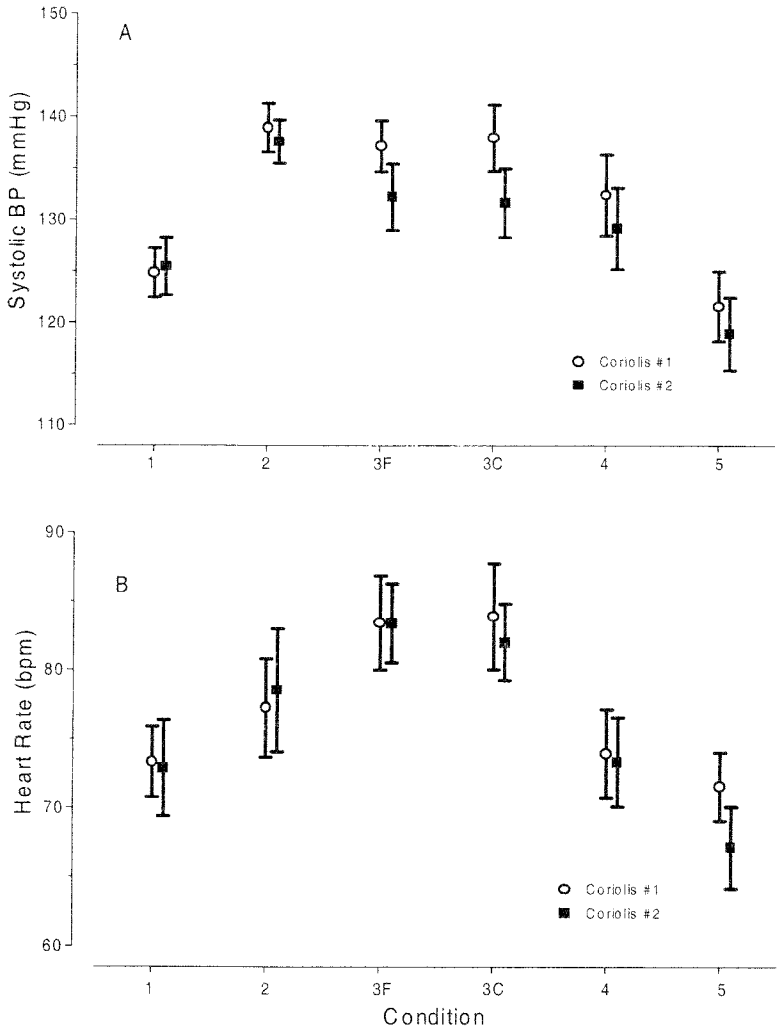

FIG. 6. Mean systolic blood pressure and heart rate for each motion stimulus condition during the Coriolis sessions (error bars are SEMs). Due to the observation that in some subjects, there is a phase difference between the forearm and calf blood flow, their corresponding systolic pressure and heart rate were plotted separately as indicated by 3F and 3C, respectively.

pre-Coriolis stimulation. There were no significant differences between conditions 2 (pre-Coriolis yaw rotation only) and 4 (post-Coriolis yaw rotation only). The two subjects who were resistant completed 15 min of Coriolis stimulation and did not show any forearm or calf skin blood flow changes between conditions 2 and 3. Therefore, our data suggested that the previously observed forearm blood flow increase using venous occlusion plethysmography [21] during Coriolis stimulation is attributed at least in part to an increase in forearm skin blood flow. The difference in blood flow changes between motion sickness-susceptible and the two resistant subjects appears to be consistent with previous findings by Isupov et al. [11]. They suggested that resistance to motion sickness is related to the nature of compensatory and adaptive reactions of the cardiovascular system and that it could manifest under conditions other than vestibular stimulation. Specifically, they observed that the circulating blood volume in the upper body decreased in motion sickness-susceptible subjects and remained unaltered in motion sickness-resistant subjects upon occlusion of their femoral vein.

Although it was mentioned by Sunahara et al. [21] that blood flow increases were also observed in the calf, no data was presented and no information was available regarding the temporal sequence of blood flow increases in these two regions. With few exceptions, the susceptible subjects showed a simultaneous blood flow increase in the forearm and calf. There were two subjects who showed increase in the forearm before the calf, the phase difference was within 60 s. Surprisingly, three other subjects showed BF increase in the calf before forearm; the phase difference range was from 24, 43, and 44 seconds. The temporal sequence of blood flow increase is relatively consistent within subject but varies across the subjects. The temporal pattern of blood flow changes across subjects can roughly be separated into two groups. The first group showed a peak increase in forearm and calf blood flow before announcing the end point of 7 on the rating scale. The second group announced the end point before their blood flow increase reached a maximum. This temporal difference could have been caused by the possibility that some subjects might have either exaggerated or minimized their symptoms. However when we

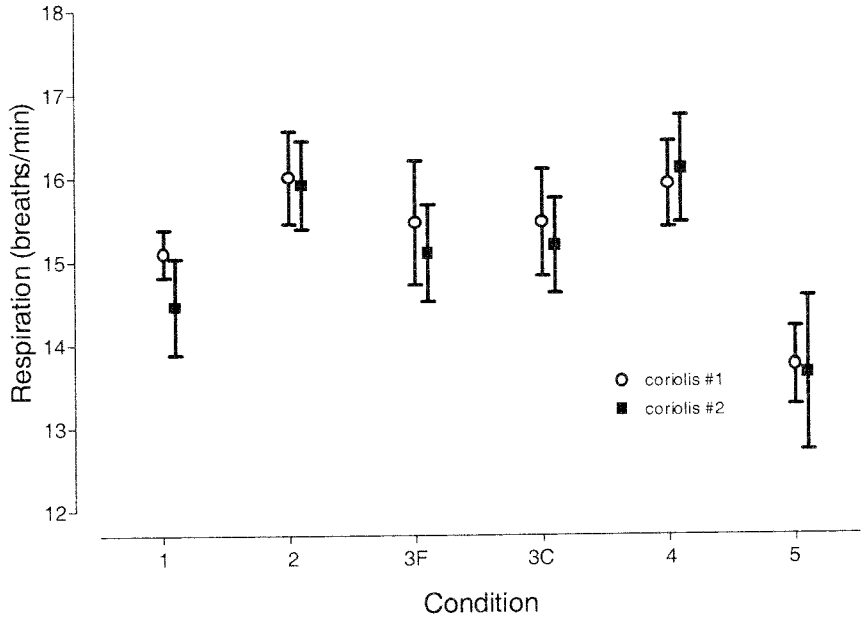

FIG. 7. Mean respiration for each motion stimulus condition during the Coriolis session (error bars are SEMs).

compared the two Coriolis trials within subjects who participated in both trials, the temporal sequence of peak blood flow and their subjective end point was relatively consistent. By observing the blood flow recordings, it was possible to predict when the subject would signal the end point. However, rate of blood flow increases was not uniform across subjects: three of the susceptible subjects showed a gradual increase that was correlated with their subjective symptoms rating. The remaining subjects showed a more abrupt increase and reached a maximum.

Similar to previous findings, during BF increases, there were no significant changes in blood pressure and heart rate among all conditions, both in the control and the Coriolis trials. In a few subjects where increased heart rate was evident, the increase was transient, did not reach statistical significance, and returned to normal, while blood flow increase remained elevated. When the seated subjects were exposed to rotation about their spinal axis, their limbs were positioned away from the centre of axis of rotation. The significant increase in blood pressure and heart rate observed between the "at rest" and "yaw rotation" (conditions 1 and 2; conditions 4 and 5) could be the result of the radial acceleration gradient.

Based on the observation that in response to Coriolis stimulation there was an almost immediate increase in respiration as well as forearm blood flow [19], Sinha suggested that hyperventilation is the cause of hypercaemia, the well known peripheral vasodilator effect of a low $PaCO_2$ level. However, we did not observe hyperventilation and there was no significant difference in rate of respiration between the different motion stimulus conditions. Respiratory changes are inconsistent and not an invariable concomitant of motion sickness [18].

Anxiety plays an important role in stressful experiments [20] and it shares many of the same signs and symptoms as occur during motion sickness; symptoms such as sweating, dizziness, upset stomach, flushing, pallor, and in some cases, hyperventilation. Our data indicated that the anxiety level prior to Coriolis stimulation was similar in the control and Coriolis trials. Hence, anxiety has a marked increase post-Coriolis stimulation. Although the state-anxiety questionnaire was administered at the end of the trial, it appears that the anxiety level remains elevated long after blood flow has returned to normal levels. It is likely that skin blood flow increases during Coriolis stimulation are part of the anxiety-induced response but had a much shorter duration.

Provocation of nausea by Coriolis (vestibular) accompanied by an increase in forearm and calf blood flow suggests a decrease in sympathetic activity in this vascular bed. Both vasoconstrictor nerves and vasodilator nerves (nerves which directly or indirectly cause vasodilation) regulate the circulation through the skin of the forearm. Because there is no apparent change in blood pressure or heart rate concomitant with increased blood flows, in order to maintain this blood pressure it is likely that an increased vasoconstriction in other regions of the body must have occurred. Facial pallor in the frontal temporal and circumoral area is a consistent sign of motion sickness that is almost invariably observed before vomiting [9,17]. Pallor is the result of vasoconstriction in the skin, probably in response to an increase in the sympathetic nervous activity to the blood vessels of the skin. A recent study in cats by Kerman et al. [15] demonstrated that electrical vestibular stimulation leads to patterned changes of regional vascular tone, a decrease in hind limb resistance whereas the forelimb resistance increases. It is difficult to compare this reciprocal patterning of vascular changes with current results. Other than species difference, the blood flow to the muscle and skin cannot be distinguished in the former study. Furthermore, the calculated vascular resistance and conductance was based on measurements of blood pressure and blood flow velocity, with the assumption that venous pressure does not change independent of arterial blood flow.

Independent blood flow measurement is required to elucidate whether the observed forearm blood flow increase also originates from the respective skeletal muscle. Increase in forearm skin blood flow without significant changes in blood pressure and heart rate suggests a decrease in sympathetic activity to this vascular bed. The other possibility is an immediate increase in cardiac output by

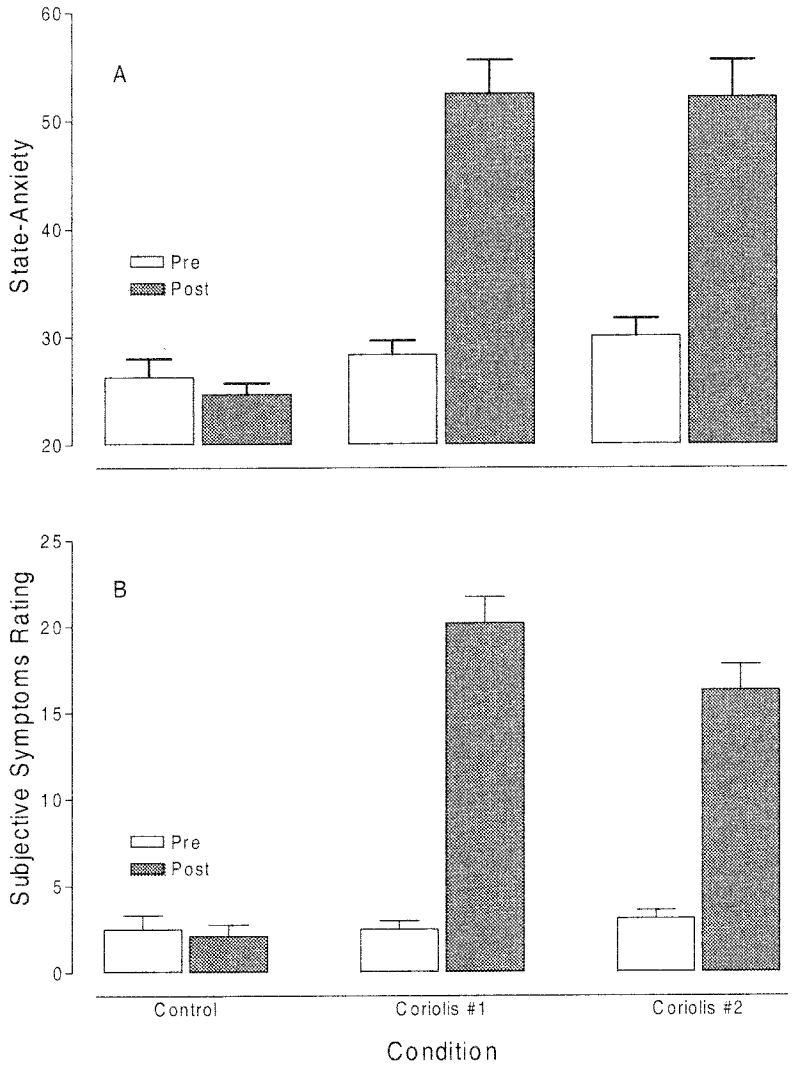

FIG. 8. Mean scores of (A) state-anxiety and (B) subjective symptoms ratings before and after exposure to the Coriolis stimulus (error bars are SEMs).

increase in the stroke volume (since heart rate does not change significantly). Vasodilation in the limbs could theoretically impair orthostatic tolerance, particularly when these changes were found in the lower limbs, as indicated by the results of this study. Our results have significant implications for the maintenance of G tolerance in flight when increased acceleration of the aircraft follows turns or other manoeuvres that could provoke the cross-coupling effects [1]. This could result in loss of G tolerance due to a fall in peripheral resistance below an already critical level followed by a decrease in arterial blood pressure. The Coriolis-induced cardiovascular changes observed might also confound previous studies on reduced G tolerance using ground-based centrifuge that will invariably evoke the cross-coupling effects. However, the exact mechanism and potential effect of Coriolis-induced cardiovascular changes during centrifuge and in-flight studies require further investigations.

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