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Highly Demanding Resistive Vibration Exercise Program is Tolerated During 56 Days of Strict Bed-Rest

Abstract

Several studies have tried to find countermeasures against musculoskeletal de-conditioning during bed-rest, but none of them yielded decisive results. We hypothesised that resistive vibration exercise (RVE) might be a suitable training modality. We have therefore carried out a bed-rest study to evaluate its feasibility and efficacy during 56 days of bed-rest. Twenty healthy male volunteers aged 24 to 43 years were recruited and, after medical check-ups, randomised to a non-exercising control (Ctrl) group or a group that performed RVE 11 times per week. Strict bed-rest was controlled by video surveillance. The diet was controlled. RVE was performed in supine position, with a static force component of about twice the body weight and a smaller dynamic force component. RVE comprised four different units (squats, heel raises, toe raises, kicks), each of which lasted 60–100 seconds. Pre and post exercise levels of lactate were measured once weekly. Body weight was measured daily on a bed scale. Pain questionnaires were obtained in regular intervals during and after the bed-rest. Vibration frequency was set to 19 Hz at the beginning and progressed to 25.9 Hz (SD 1.9) at the end of the study, suggesting that the dynamic force component increased

by 90%. The maximum sustainable exercise time for squat exercise increased from 86 s (SD 21) on day 11 of the BR to 176 s (SD 73) on day 53 ($p = 0.006$). On the same days, post-exercise lactate levels increased from 6.9 mmol/l (SD 2.3) to 9.2 mmol/l (SD 3.5, $p = 0.01$). On average, body weight was unchanged in both groups during bed-rest, but single individuals in both groups depicted significant weight changes ranging from -10% to $+10\%$ ($p < 0.001$). Lower limb pain was more frequent during bed-rest in the RVE subjects than in Ctrl ($p = 0.035$). During early recovery, subjects of both groups suffered from muscle pain to a comparable extent, but foot pain was more common in Ctrl than in RVE ($p = 0.013$ for plantar pain, $p = 0.074$ for dorsal foot pain). Our results indicate that RVE is feasible twice daily during bed-rest in young healthy males, provided that one afternoon and one entire day per week are free. Exercise progression, mainly by progression of vibration frequency, yielded increases in maximum sustainable exercise time and blood lactate. In conclusion, RVE as performed in this study, appears to be safe.

Key words

Berlin Bed-Rest Study · microgravity · de-conditioning · vibration · immobilisation · human physiology

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Introduction

In the recent years, exercise, as a countermeasure against de-conditioning, has become common practice in a number of clinical fields, such as during haemodialysis, in patients with osteoporosis, or in the rehabilitation of patients with leukaemia. However, little is known about the appropriate types of exercise to prevent de-conditioning during bed rest. Currently, the Space Agencies are organising bed-rest (BR) studies [9,21,25], which serve as ground based models of microgravity, in search for appropriate countermeasures that will allow long term space missions. (Bed rest studies are either performed with the subjects in horizontal position, or with -6° head down tilt [14] when the effects of microgravity on the cardiovascular system are to be mimicked more specifically). Most likely, the results of these studies will also provide insights into how clinical immobilisation may be treated. However, whilst training countermeasures need to be evaluated in terms of their preventive effects on the musculoskeletal system, any regimen needs to be feasible and well-tolerated by the subjects.

Among the different possible countermeasures for musculoskeletal disuse, one would intuitively choose resistive exercise to maintain the musculoskeletal system. This has been done in the Toulouse Long Term Bed-rest (LTBR) study, which tested the efficacy of squat and calf press exercises every three days with a gravity-independent resistive device [4]. Such regimen was found to be well tolerated and to completely preserve the thigh muscles. However, it prevented calf muscle atrophy and bone loss to only 50% [21,1,30]. Conversely, Shackelford et al. have tested the efficacy of a maximum resistive type of training which was performed 3 times per week for the upper and lower body, and 6 times for the plantar flexors [25]. That regimen provided better protection against musculoskeletal de-conditioning, but was also associated with a higher rate of exercise-related complaints (10% of all required exercise sets were missed). It therefore seems difficult to define the “intensity” and frequency of resistive exercise that is required and tolerated during bed-rest.

Vibration exercise is a comparatively new type of exercise, that may be specifically suitable to prevent and increase bone mass [24,29,28]. We have speculated that vibration, in combination with resistive exercise, might be a suitable training modality. Therefore, we designed a resistive vibration exercise (RVE) program with two training sessions on most days. Vibration is well known to elicit detrimental responses in humans, but in the recent past a number of studies have shown that, with appropriate modalities, vibration can indeed be beneficial [8,6,31,22]. In consequence, safety of such a highly demanding RVE program during bed-rest is an important topic. The present study, therefore, aimed to assess the feasibility of that program, and how well it can be tolerated during 8 weeks of bed-rest.

Material and Methods

The Berlin Bed-Rest (BBR) study was approved by the Ethical Committee of the Campus Benjamin Franklin in Berlin and by the Bundesamt für Strahlenschutz. It was organised between

February 2003 and June 2004 in the Hospital of the Campus Benjamin Franklin.

Subject recruitment

Healthy, highly motivated men between 20 and 45 years were searched for. Smoking, current medication, any relevant medical disorder, current competitive sports, and a body mass index (BMI) below 20 or above 28 were exclusion criteria.

After announcements in the media, subject recruitment involved four steps.

- *Step 1:* Telephone questionnaire, assuring general suitability (694 applicants).
- *Step 2:* Psychological screening, with two personality questionnaires (Freiburger Persönlichkeits-Inventar and TSS) and a biographic information sheet (376 applicants). (The TSS is a questionnaire which is intellectual property of the DLR (Deutsches Zentrum für Luft- und Raumfahrt) team that contributed to this study).
- *Step 3:* An interview with an experienced team of psychologists from the Institute for Aerospace Medicine (DLR Hamburg) and the principle investigators (119 applicants).
- *Step 4:* Medical screening (57 applicants, of which 20 subjects were included in the study, plus 4 individuals as back-ups).

Subjects were randomised either to the RVE group (exercise), or to the non-exercising control group (Ctrl). In order to balance seasonal effects, the study was organised in 5 campaigns, each comprising 4 subjects. The first campaign started in February 2003, and the last campaign ended in May 2004. In all campaigns, 2 subjects from the RVE group were living in one room and 2 subjects from the Ctrl group in a different room.

Study protocol

During the BR, subjects were by no means allowed to stand up, to lift their trunk in bed to more than to 30° , to move their legs briskly, or to elicit large muscle forces with their leg muscles other than during testing sessions or training units (RVE group only). As far as possible, adherence to this protocol was controlled by continuous video recordings and by force transducers in the frames of the bed.

Ingestion of alcohol or nicotine, excessive doses of caffeine, as well as the regular intake of any drug or medication was prohibited.

The diet was balanced with regards to caloric intake, using the Harris-Benedict equation [12] with an adjustment by an activity factor of 1.2 for BR. Calcium input was set at 1000 mg per day. Daily diet plans were prepared, using the nutrition-software EBISpro (Dr. Erhardt, University of Hohenheim, Germany). All meal components were weighed, and their nutritional contents were taken from prepared meal charts. Occasionally, higher caloric intakes were allowed to keep up motivation. Resting energy expenditure was regularly assessed to correct the caloric intake if necessary.

Because of the known effects of heparin on bone metabolism, no anticoagulation was prescribed [19]. Instead, subjects were screened for a predisposition to develop a deep vein thrombosis

(factor 5 mutation, prothrombin mutation, plasma levels of protein S and Protein C) and colour coded Doppler ultrasound scans of the leg veins were taken regularly. Moreover, gentle massage of the legs was administered twice weekly in order to improve venous flow. During the massage, the leg joints were passively mobilised without stretching the muscles and, if desired, back muscles were massaged.

Vibration exercise device

Exercise was done with a dedicated device (Galileo Space, Novotec, Pforzheim, Germany). The construction was derived from a commercially available device for vibration exercise in standing position (Galileo 2000, Novotec, Germany) with specific modifications for the use in BR (see Fig. 1).

In brief, the device consists of a vibration platform suspended on a trolley. The platform's central axis of rotation thus enabled side-alternating, sinusoidal vibration with frequencies between 5 and 30 Hz. Elastic springs were attached to the trolley for the subjects to attach themselves through belts with their shoulders, hips, and hands. This generated a static force equivalent to approximately 2 times the body weight.

The vibration of the foot plate was elicited by a counter-phase, eccentric rotation of a mass under the right and left part platform (for an explanation see [23]). By virtue of that construction (pre-set vibration frequency), the acceleration of the platform mass changes with vibration frequency. The vibration amplitude A (in mm) is given by the distance from the centre of rotation s (in mm, typically 180 mm) as $A=0.0214 \cdot s$. If the vibrations were completely inelastic, then the peak force F (in N) would be given by the vibration frequency frq (in Hz) as

$$F = 507 \cdot frq^2/s \quad \text{Equation (1)}$$

where the value of 507 is a result of pi and the rotating masses' inertias. However, passive leg movements were clearly observable during vibration exercise. Therefore, we expect the oscillatory force component to be considerably smaller than given by equation 1.

Exercise scheme

Exercising with the Galileo Space (in supine position) device turned out to be much more demanding than with the Galileo 2000 device (standing position). Four different exercise units were performed:

1. Squatting exercise: Knees were extended from 90° to almost full extension in cycles of 6 seconds for each squat (knee extensors).
2. Heel raises: With knees almost extended, heels were raised to fatigue. Only then, brief rests (< 5 seconds) were allowed with the entire foot on the vibration platform in order to recover, and subjects started to raise their heels again (foot plantar-flexors).
3. Toe raises: Similar to 2, but toes were raised instead of heels (foot dorsi-flexors).
4. "Kicks": With the same loading as in 1–3, knees were extended as quickly and forcefully as possible. The platform was struck with the balls of the feet, and legs rested on the Galileo Space framework inbetween the kicks. This was done



Fig. 1a “Galileo Space” training device for usage in bed-rest. The subjects attach themselves to a vibrating platform by belts with their waist, their shoulders, and their hands. Vibration is generated by means of eccentrically rotating masses on the other (= left) side of the platform.

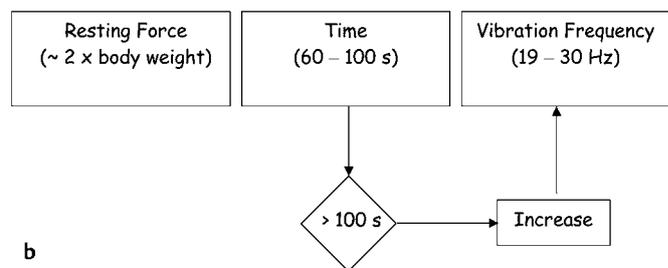


Fig. 1b Illustration of the standardisation of training intensity during the morning sessions. For each unit (1–3, see text), the vibration frequency was increased in the subsequent session in the time that the subject was able to exercise longer than 100 s.

ten times with 10 seconds of rest inserted. The rationale for this unit was the idea to generate high strain rates with a 10-second insertion, which has been found to have osteogenic effects in animals [26].

During each session, units 1–4 were done in ascending order. Training “intensity” was controlled by (i) the resting force (F_{Rest}), (ii) vibration frequency, and (iii) by the time for each unit. For the morning sessions, the standardisation is illustrated in Fig. 1b. F_{Rest} was controlled by the belts' lengths, and was typically adjusted to twice the body weight. On Wednesday mornings, subjects were asked to exert themselves and do each exercise unit as long as possible, as if for competition (F_{Rest} and frq as the day before). Blood lactate was then measured from capillary samples obtained before and 0, 1, 3, and 5 minutes after the squatting exercise by an enzymatic photometric method (Boehringer, Mannheim, Germany). (Blood lactate was measured only in the last 4 campaigns [i. e., 8 out of 10 subjects]).

During afternoon sessions, subjects exercised with a resting force of only about 1.4 times their body weight, but ran through units 1–3 for 60 seconds each as many times as possible. All training sessions were supervised by specially trained staff, and subjects were frequently encouraged.

Table 1 Subject characteristics

	Age (years)	Height (cm)	Weight (kg)	BMI (kg·m ²)	FM (%)	LM (%)	FQ (mets/week)
Ctrl	33.4 (6.6)	185 (7)	79.4 (9.7)	23.3 (1.7)	17.4 (5.2)	78.9 (4.8)	85.3 (89.5)
RVE	32.6 (4.8)	183 (9)	81.7 (14.4)	24.2 (2.6)	21.4 (6.8)	75.1 (6.5)	33.1 (28.0)

Subject characteristics at baseline. Given are the mean values for each group and the standard deviation in brackets. Weight was assessed on day BR01. BMI = body mass index. FM = Fat mass, assessed by DXA; LM = lean body mass, assessed by DXA; FQ = Freiburg questionnaire score, in metabolic units per week. None of these measures was different among groups ($p > 0.1$)

During the first campaign, subjects expressed that the exercise scheme was too hard. We interpreted this as over-training and therefore, starting from week 4, left the Wednesday afternoon and all Sundays free of exercise after the second week. There was also no training whenever it interfered with other measurements (e.g., muscle biopsy). Thus, during the 56 days of BR, 89 exercise sessions were scheduled for each subject.

Measurements

Baseline data collection (BDC) started 3 days prior to the BR. Upon arrival, subjects filled in the “Freiburg” questionnaire to assess their pre-study habits of aerobic exercise in terms of Metabolic Units (Mets) expended in exercise per week [10]. Body weight was measured with a “seca 985” bed scale (Seca, Hamburg, Germany) daily at 7 o’clock a.m., after voiding the bladder. From that, the change in weight from the first day of BR (BR01) was computed for days BR02 to BR56. Body composition was measured by dual x-ray absorptiometry (DXA, Hologic Delphi).

Clinical investigation, with special attention to any kind of pain, signs of venous thrombosis, and mood was performed by physicians on a daily basis. Subjects filled in a pain questionnaire during BDC and on days BR01, BR04, BR13, BR27, BR41, BR53, R + 1, R + 2, R + 3, R + 4, R + 7 and R + 14 (R = recovery). These questionnaires covered any current pain or discomfort. If necessary, the pain location was marked on a body chart and the pain intensity was rated with a visual analogue scale (VAS) [7].

Statistical analyses

Statistical analyses were carried out with the SPSS software version 11.5.0 (as of Sep. 6, 2002, www.spss.com). Data is given as means with their standard deviation (SD). Significance was assumed if $p < 0.05$.

Progression of the training was assessed by the preset exercise parameters (F_{Rest} , frq, and duration of the exercise = T), which were compared between days BR10, when all subjects were familiar with the exercise, and BR51 by a paired-samples *t*-test. Changes in the capacity to perform RVE were assessed on the “competition” days BR11 and BR53, for which peak blood lactate levels after squatting exercise and the maximally sustainable duration of the exercise were compared by the paired-samples *t*-test.

The relative change in weight on days BR56 and R + 4, and also the weight gain from day BR56 to R + 4, was tested for significant differences from 0 (one-sample *t*-test, separately for each group). Moreover, the total (absolute, i.e., root mean square) % changes

in weight from day BR01 were tested with a repeated measures ANOVA for group and time effects and for time·group interaction.

The pain data was categorised according to body region (plantar area of foot, dorsal area of foot, ankle joint, m. triceps surae, knee joint, m. quadriceps, m. hamstrings, m. glutealis, lumbar spine, thoracic spine, cervical spine, and other). Data from the bed-rest period (BR01 through BR53) and recovery period (R + 1 through R14) were examined separately and the data was pooled across body region and side of body. To enable meaningful statistical analysis, raw VAS scores were not used. Instead, the occurrence (VAS > 0) or absence of pain (VAS = 0) was used to reclassify the pain information. Data was also further pooled to express the number of subjects with any pain, the number of subjects with lower limb pain, the number of subjects with lower limb muscle pain, and the number of subjects with knee and ankle joint pain. A binary logistic regression was used with an intention-to-treat approach, treating missing data as absence of pain.

Results

Baseline data

The characteristics of the study subjects are given in Table 1. There were no group differences in age, height, weight, body mass index or in the Freiburg Questionnaire score.

Exercise

Vibration frequency (frq), which was set to 19 Hz in the first training session, was augmented, according to the subjects’ capability, from 20.7 Hz (SD 1.0) on day BR10 to 25.9 Hz (SD 1.9) on day BR51 ($p < 0.001$). On the same days, the leg component of the resting force increased from 981 N (SD 119) to 1049 N (SD 96, $p = 0.016$), respectively, and the preset period of squatting exercise (T_{Squat}) increased from 80 s (SD 10) to 101 s (SD 20, $p = 0.003$). An even larger increase was observed in the maximally sustainable period of squatting exercise ($T_{max,Squat}$) assessed on the “competition days” (Wednesdays), which increased from 86 s (SD 21) on day BR11 to 176 s (SD 73) on day BR53 ($p = 0.006$).

On these days, blood lactate levels after squatting exercise increased from 6.9 mmol/l (SD 2.3, see Fig. 2) on day BR11 to 9.2 mmol/l (SD 3.5) on day BR53 ($p = 0.01$), while resting levels were unchanged (1.2 mmol/l, SD 0.4 on BR11 and 1.5 mmol/l, SD 0.8, $p = 0.29$).

Lactate after Squat Exercise

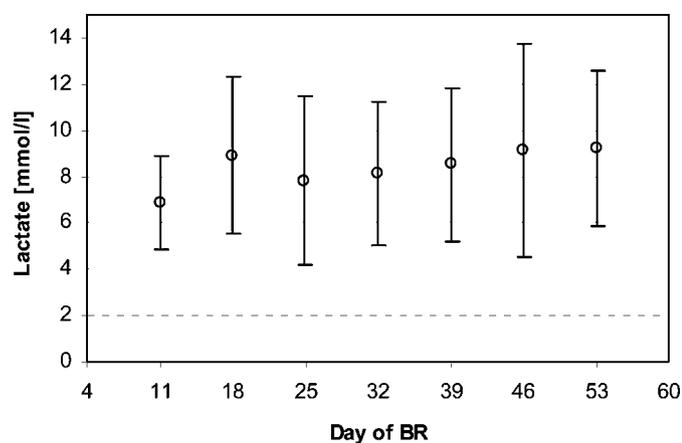


Fig. 2 Blood lactate after squat exercise. Peak blood lactate concentration after squat exercise and standard deviation, as assessed on the “competition” days in week 2 to 8 of the bed rest. Levels on day BR53 were significantly larger than values on day BR11 ($p = 0.01$).

Body weight

During the BR, body weight changed in many subjects, ranging from losses by 10% in some individuals to gains by 10% in others. On average, however, body weight was unchanged on day BR56 in both groups (+0.0%, SD3.1, $p = 0.97$ for Ctrl, and +2.4%, SD = 5.5, $p = 0.21$ for RVE). On day R + 4, there were trends to indicate a minor increase in weight from baseline (+2.0%, SD 3.5, $p = 0.076$ for Ctrl, and +3.7%, SD 5.8, $p = 0.011$ for RVE). Between day BR56 and day R + 4, significant weight gains (+2.0%, SD 1.1, $p < 0.001$ for Ctrl, and +1.3%, SD 1.2, $p = 0.007$ for RVE) occurred without any difference between groups ($p = 0.24$).

Repeated measure ANOVA of total (= root mean square) percent changes during BR (BR02 to BR56) revealed a time effect ($p < 0.001$), but no time * group interaction ($p = 0.21$). Analysis of the within-subjects contrasts revealed significant increases, with a linear ($p = 0.001$) and a quadratic ($p = 0.047$) term.

Clinical data and pain

Except for pain related entities (see below) and two cases of diarrhoea, a cervical syndrome (unrelated to the study), an effusion of the knee joint (RVE group, relieved after reducing training), and a bone-burst at the knee (Ctrl group, after bed-rest), no adverse effect occurred. No subject dropped out, and all subjects left the hospital in a good state of health.

During BR, RVE subjects complained more often of lower limb pain than the Ctrl subjects ($p = 0.035$, Table 2). This was mostly joint pain (4 out of 6 subjects) but also due to muscle pain.

During early recovery (R + 1 to R + 14), virtually all subjects suffered from muscle pain, which was most pronounced in the calves (Table 2). Plantar foot pain was more common in the Ctrl than RVE subjects ($p = 0.013$), where 8 out of 10 subjects complained of it. Likewise, foot dorsal pain was more common in the Ctrl group ($p = 0.074$). Although RVE subjects reported

Table 2 Regional distribution of pain

Region	Side	BR01 through BR56		R + 01 through R + 14	
		RVE	CTRL	RVE	CTRL
Foot plantar area	left	0	1	2	8 [#]
	right	0	1	2	8 [#]
Foot dorsal area	left	0	0	0	4
	right	1	0	1	4
	combined	1	0	1	5 ^b
Ankle joint	left	1	0	3	4
	right	1	0	2	4
Knee joint	left	2	0	3	4
	right	2	1	2	5
Triceps surae muscle	left	0	0	7	8
	right	1	0	8	9
Quadriceps muscle	left	0	0	1	1
	right	2	0	2	1
Hamstrings muscle	left	0	0	3	1
	right	0	0	3	1
Glutealis muscle	left	0	0	3	1
	right	0	0	3	1
Lumbar spine		2	2	3	4
Thoracic spine		0	2	0	4
Cervical spine		0	0	1	3
All regions pooled		6	3 ^a	8	9
All lower limb pain pooled		5	1 [*]	8	9
All lower limb muscle pain		2	0	8	9
Knee and ankle joints pooled		4	1	3	5

Totals indicate number of subjects with pain during the bed-rest or recovery period, respectively. Differences between groups: * $p = 0.035$, # $p = 0.013$, ^a $p = 0.082$, ^b $p = 0.074$, others $p > 0.10$

muscle pain more frequently than Ctrl subjects during recovery, this was not found to be significant.

Descriptively, of the 6 Ctrl subjects who experienced foot-plantar pain at R + 1 (median VAS 44), 4 still had pain at R + 14 (median VAS 24), whereas in the RVE group pain, if at all, tended to occur later (one subject at each R + 3 and R + 14, VAS of 29 and 26 respectively).

Discussion

Overall, the RVE was well tolerated by the subjects in this bed-rest study. This is, for example, reflected by the exercise progression. Vibration frequency increased from 19 Hz at the beginning to about 26 Hz at the end. Unfortunately, we were unable to measure the platform reaction forces. However, in an undamped, in-elastic oscillation this would lead to an increase from 1000 N to 1900 N (see equation 1). This is a rise by 90%. It should be noted that this figure is only an illustration, and that absolute comparisons cannot be made. However, it seems very likely that

the dynamic force component was increased substantially in the course of the study. By comparison, the increase in the leg component of the resting force (by 10%), although significant, was much smaller than the progression in dynamic force.

There is also evidence that the exercise, and its progression, elicited training effects. This is reflected by the maximum sustainable exercise period, which was doubled during the bed-rest, but also by a moderate increase in post-exercise blood lactate levels (~15%). Generally, post exercise blood lactate levels were quite high, often exceeding 10 mmol/l (Fig. 2), which was unexpectedly high. In particular, these values are about twice as large as after exhaustive RVE on the Galileo device that is used in standing position [20]. This difference is probably due to the more difficult control of posture on the Galileo Space device, and to the subjects of this study being highly motivated. Taken together, thus, there is evidence that the RVE subjects engaged themselves seriously in the training program.

This was not related to an average change in body weight during BR. Also, no change in body weight was observed in the Ctrl group. However, it is noteworthy that substantial changes (from -10% to +10%) occurred in single individuals, an observation that is also seen in isolation [11] and confinement studies [16].

Importantly, these individual changes occurred independently of exercise. It seems, thus, that maintenance of the individual body weight during bed-rest constitutes a problem that needs to be dealt with by an intensified dietary control in future bed-rest studies.

During bed-rest, RVE subjects suffered from more lower-limb pain than Ctrl subjects, mainly due to joint pain. People undertaking long-term bed-rest commonly report low back pain in the initial days and weeks [13], although there is no specific consensus as to its origin [3,13,15,27]. Two subjects in the control group and one in the training group reported this. One training subject reported onset of back pain during training. This may have been due to mechanical overload in exceeding tissue strength [18]. Three subjects reported some knee pain (one with bilateral knee discomfort) at some stage during the training protocol. This may have been similarly due to excessive tissue loading. Pain resolved in all cases with appropriate modification of the training program. One training subject reported some bilateral ankle discomfort, occurring only during training. The subject only reported discomfort during the ankle plantarflexion-dorsiflexion exercise. This discomfort may be associated with movements to “end-of-range” in an ankle stiffening due to prolonged non-weight-bearing. One training subject reported some dorsal foot pain in the initial days of bed-rest. This resolved itself within days and the cause is unclear. Finally, three training subjects reported muscular pain at the biopsy site (two at the right quadriceps, one at the right calf). This may be due to relative strain being placed on an “injured” area.

Modifying the training resulted in resolution of pain in all cases. The above problems resolved in the course of few days to one

week, and only about 0.1% (12 out of >900) exercise sessions were cancelled because of pain. The majority of the cancelled sessions (7 sessions) occurred in the first 2 groups, indicating that with accumulating experience, adverse effects by RVE could be minimised.

Finally, our data suggests that RVE quite effectively prevented foot pain after re-ambulation. Personal experience suggests that such pain usually emerges from the plantar connective tissues, with tearing and inflammation upon re-ambulation. The pain presentation was similar to plantar fasciitis (pp465–466 in [5]). On the other hand, RVE did not prevent muscle pain after re-ambulation. It is uncertain in how far this was due to “regular” muscle soreness, or even to delayed onset muscle soreness (DOMS), which is known to occur in unconditioned individuals undertaking unaccustomed exercise [2,32], and which has also been reported in astronauts after return to Earth [17].

The present study has some limitations, as its outcome depends on the motivation of the subjects, introducing subjective factors. However, we have attempted to reduce these subjective factors by recruiting only highly motivated subjects for this study.

Conclusion

In conclusion, the present study indicates that resistive vibration exercise during BR was well tolerated twice daily, provided that at least 1.5 days during the week are reserved for recovery. Under these conditions, with the exercise progression relying predominantly upon increasing vibration frequency, and thus most likely involving increasing dynamic forces, symptoms of over-training were seldom and always manageable. However, our pain data suggest that the training can probably not be further intensified very much.

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