Influence of long-term spaceflight on neuromechanical properties of muscles in humans

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1Département de Génie Biologique, CNRS UMR-6600, Université de Technologie, F-60205 Compiègne cedex, France and 2Y. A. Gagarin Cosmonauts Training Centre, Star City, 141160 Moscow Region, Russia

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Lambertz, Daniel, Francis Goubel, Rustem Kaspranski, and Chantal Pérot. Influence of long-term spaceflight on neuromechanical properties of muscles in humans. J Appl Physiol 94: 490–498, 2003. First published September 20, 2002; 10.1152/japplphysiol.00666.2002.—Reflex and elastic properties of the triceps surae (TS) were measured on 12 male cosmonauts 28–40 days before a 3- to 6-mo spaceflight, and a few days later (R+5/+6). H reflexes to electrical stimulations and T reflexes to tendon taps gave the reflex excitability at rest. Under voluntary contractions, reflex excitability was assessed by the stretch reflex, elicited by sinusoidal length perturbations. Stiffness measurements concerned the musculoarticular system in passive conditions and the musculotendinous complex in active conditions. Results indicated 1) no changes (P > 0.05) in H reflexes, whatever the day of test, and 2) increase in T reflexes (P < 0.05) by 57%, despite a decrease (P < 0.05) in musculoarticular stiffness (11%) on R+2/+3. T reflexes decreased (P < 0.05) between R+2/+3 and R+5/+6 (−21%); 3) increase in stretch reflexes (P < 0.05) on R+2/+3 by 31%, whereas it decreased (P < 0.05) between R+2/+3 and R+5/+6 (−29%). Musculotendinous stiffness was increased (P < 0.05) whatever the day of test (25%). Between changes in reflex and stiffness were also studied by considering individual data. At R+2/+3, correlated changes between T reflexes and musculoarticular stiffness suggested that, besides central adaptive phenomena, musculoarticular structures took part in the reflex adaptation. This mechanical contribution was confirmed when data collected at R+2/+3 and R+5/+6 were used because correlations between changes in stretch reflexes and musculotendinous stiffness were improved. In conclusion, the present study shows that peripheral influences take part in reflex changes in gravitational unloaded muscles, but can only be revealed when central influences are reduced.

musculotendinous stiffness; musculoarticular stiffness; H reflex; T reflex; stretch reflex

Since the beginning of manned spaceflight, a weightlessness environment has apparently abolished the vital stimulus for the maintenance of musculoskeletal function. The most striking feature of exposure to weightlessness has been reported as the loss in muscle mass in animals and humans due to atrophy (for a review, see Refs. 12 and 14). Nevertheless, orbital microgravity also represents a unique environment, which allows the study of adaptation in muscle elastic properties and reflex excitability assumed to be involved in postural and movement control mechanisms.

Some insight into mechanical adaptations, by use of a simulated nonweightbearing environment, has been gained from animal and human experiments, in which a decrease in muscle and tendon stiffness was observed (1, 7, 23). A balance between an increased musculotendinous stiffness and a decreased passive musculoarticular stiffness has recently been reported after long-term spaceflight (26). This increase in musculotendinous stiffness was mainly attributed to changes in neural drive already hypothesized by others (4, 22). Thus it can be suggested that muscle control can also be affected by microgravity, in reflex as well as in voluntary conditions.

Changes in reflex excitability after a period of microgravity (real or simulated) have already been reported in the literature, but such studies remain scarce. In humans, results of Russian teams, cited in the review of Edgerton and Roy (12), were the first to report higher H reflexes when tested in a lying position after bed rest or dry water immersion. In a bed-rest case study, Duchateau (11) confirmed these results and ascribed the reflex potentiation to a higher synaptic efficacy. The same type of interpretation was proposed to explain the higher H reflexes in awake rats after a period of unloading by hypokinesia-hypodynamia (3). Reschke et al. (38) also found a potentiation of H reflexes after spaceflight, tested during vertical linear acceleration; this increase was considered to reflect changes in the influence of the vestibular apparatus on the reflex pathway. Only the study of Yamanaka et al. (42) reported a decrease in H reflexes after bed rest in standing subjects and attributed it to a higher presynaptic inhibition in such a position (5).

As reviewed by Edgerton and Roy (12), Russian studies also concerned changes in T reflexes due to simulated or real microgravity. However, no consistency of the direction of changes was found, even if decreases in
the Achilles tendon reflex were more often reported than increases. After simulated microgravity, Anderson et al. (3) reported a decline in T reflexes in awake rats. The reverse changes between H and T reflexes illustrate that mechanically elicited reflexes are also influenced by peripheral mechanisms such as tendon stiffness and muscle spindle sensitivity (36). Thus the lower T reflexes in rats can be related to a decrease in muscle and tendon stiffness (1, 7).

To our knowledge, no study has been undertaken to investigate changes in stretch reflex activities after a period of unloading. Stretch reflexes of voluntary contracted muscles in response to imposed joint perturbations, studied to assess the effects of a specific training method (24, 41), mobilize the reflex pathway in a more natural way than electrical stimulations or tendon taps.

The present study dealt with the question of whether reflex excitability is altered by long-term spaceflight and whether possible changes in reflex excitability are due to central and/or peripheral mechanisms. For that, reflexes were tested at rest (H and T reflex) and during isometric contractions (stretch reflexes elicited by sinusoidal perturbations). Changes in H reflexes should reflect central mechanisms, with the knowledge that this reflex is obviously not influenced by changes in elastic properties of peripheral structures. On the other hand, changes in mechanically elicited reflexes could be influenced by such changes in elastic properties. Therefore, changes in passive musculoarticular stiffness were related to changes in the T reflex. In the same way, changes in musculotendinous stiffness were related to changes in the stretch reflex.

MATERIALS AND METHODS

Subjects and Apparatus

The experiments were performed on three male cosmonauts who participated in EuroMir'95 and '98-E space missions. Thanks to a special agreement between the French and the Russian space agencies, further experiments were done on 11 male cosmonauts (Mir missions EO 19–24). From these 14 cosmonauts, two cosmonauts were not able to perform the entire protocol. The remaining 12 cosmonauts (C1 to C12) performed a set of experiments 28–42 days before flight [baseline data collection (BDC); BDC1, BDC2], soon after spaceflight [return (R); R+2/+3], and on R+5/+6.

The cosmonauts spent ~180 days aboard Mir station, except for two (C1 and C2) who spent 90 days in flight. The cosmonauts were familiarized with the experiment during a preliminary session some days before starting the preflight tests. Cosmonauts gave their informed, written consent, and experiments were carried out according to the guidelines of the Declaration of Helsinki. The experimental protocol was approved by the committee of hygiene, safety, and ethics at the University of Compiègne and by the medical boards of the missions.

The experiment to test the neuromechanical properties of the triceps surae was performed by using a specific motor-driven ankle ergometer (29). Achilles tendon taps were carried out by using a custom-made electromagnetic reflex hammer. The reflex hammer was mounted on the foot support of the ankle ergometer. Electrical stimulations were applied using a commercially available isolated stimulator (Digitimer, DS7) with adjustable stimulation intensity. A round-headed cutaneous electrode was used as cathode, and a silver plate was chosen as anode. Electromyograms (EMGs) induced by these stimulations were sampled at a frequency of 10 kHz.

The technical support of the ankle ergometer to characterize the elastic properties of the plantarflexor muscles has been described in detail by Tognella et al. (40). Briefly, the ankle ergometer consisted of a power unit that contained the actuator, its power supply unit, a digital optical position transducer, a strain-gauge torque transducer, and a tachometer to capture angular velocity. The instrumentation included a 486 PC-type computer equipped with an analog-digital interface and a timer board. A specific menu-driven software controlled all procedures and recorded mechanical variables and EMG (1-kHz sampling frequency) for later analysis. A dual-beam oscilloscope gave the cosmonaut a visual feedback on the procedure in progress.

All EMG signals were recorded differentially, amplified, and band-pass filtered (1 Hz and 1 kHz).

Experimental Procedure

The cosmonaut lay comfortably in a prone position on an adjustable table with his left foot rigidly attached to the actuator of the ankle ergometer and maintained by restraint systems to keep his thigh and shoulders immobilized during the test. The horizontal bimallear axis coincided with the axis of rotation of the actuator. The hip angle was at −170°, the knee was extended to 120°, and the ankle was placed at 90° (i.e., reference position), the approved position for H-reflex studies (19). These angular positions were the same in pre- and postflight tests; meanwhile, hip, knee, and ankle positions currently adopted in microgravity were modified. This could influence the reflex excitability. Position of the hip was recently proposed as a controlling factor of spinal reflex excitability (21). However, such influences were of minor import in the present protocol, in which maximal H reflexes, less susceptible to be affected by such mechanisms than submaximal H reflexes, were elicited (9). Furthermore, it was necessary to test the reflexes in the same joint positions in pre- and postflight experiment; otherwise it was difficult to compare the reflex changes.

Surface EMGs were detected on each part of the triceps surae muscle group (TS), i.e., the soleus (Sol), the gastrocnemius lateralis (GL), and gastrocnemius medialis (GM), by using standard Ag/AgCl surface electrodes. In addition, EMG signals of the tibialis anterior (TA) were recorded to evaluate possible antagonist EMG activity. To reduce the electrode impedance to below 5 kΩ, the skin areas over the electrode application sites were rubbed with an abrasive skin cleaning paste and cleaned with an alcohol pad. Electrode gel was used with all surface electrodes for good electroconductive coupling. The surface electrodes were placed over the belly of each gastrocnemius muscle, 2 cm below the insertion of the gastrocnemius on the Achilles tendon for the soleus and over the belly of the tibialis anterior. The ground electrode was placed over the tibia. Anatomical landmarks of surface electrode positions were retained during the first test session to replace the electrodes over the same muscle sites at each test.

During an experimental session, tests were done in the following order: 1) application of electrical stimulations to record H reflexes and maximal M waves at rest, 2) application of Achilles tendon taps to elicit T reflexes at rest, 3) requiring of maximal voluntary contractions under isometric conditions, 4) performance of quick-release movements to determine the musculotendinous stiffness, 5) sinusoidal per-
turbations under voluntary contractions to record stretch reflexes, and 6) sinusoidal perturbations at rest to determine the musculoarticular stiffness. Resting periods were standardized in terms of intratest (1-min) and intertest (3- to 5-min) periods. The total duration of the experimental protocol was limited to 90 min, imposed by the medical board of the missions.

Reflex Characteristics

H and T reflexes. The H reflex was elicited by a submaximal electrical stimulus (1-ms duration) to the posterior tibial nerve, with the cathode located in the popliteal fossa and the anode placed over the knee, proximal to the patella. The intensity of the electrical stimulus was progressively increased in 5-s intervals, until a maximal Sol H reflex (H\text{max}) with no (or minimal) motor direct response (M wave) was obtained. Because of the restrained total experimental time, it was impossible to repeat the H recording at stimulus intensities giving the maximal H response on each part of the TS. Thus we chose to analyze the H response of the TS muscles, zooming in on the intensity at which the reflex of the highly excitable Sol was maximal. Then the stimulus intensity was increased until the maximal motor direct (M\text{max}) response was obtained on each part of TS. The M\text{max} response was used to normalize all reflex responses and thus to take account of different conditions of skin and surface electrodes impedance in signals recorded on different days.

Finally, taps to the Achilles tendon by means of the electromagnetic hammer were applied. The hammer was positioned as to obtain optimal responses, i.e., at a right angle to the Achilles tendon, a few centimeters above the sole of the foot, where the concavity of the tendon was maximal and, at rest, to keep a distance of ~2 mm to the skin. The tendon tap corresponded to the maximal intensity delivered by the electromagnetic unit, which was the same in pre- and postflight tests. Furthermore, anatomical landmarks were carefully retained to place the hammer in the same position at each test.

Data processing consisted in averaging 10 H and T responses to get the H\text{max} and T responses. The M\text{max} response was obtained by averaging five M-wave records. Then Sol, GL, and GM EMG were rectified and the areas of the H\text{max}, T, and M\text{max} responses of each muscle were computed. Computing the area of each muscle instead of the amplitude takes into account the polyphasic response in some of the recorded H and T reflexes of the GL and GM muscles. The TS M\text{max}, H\text{max}, and T responses was obtained by summing up the corresponding Sol, GL, and GM areas. For test-to-test comparisons, H\text{max} and T responses of TS were normalized with respect to TS M\text{max} (H\text{max}/M\text{max}, T/M\text{max} Ratios). Moreover, T/H\text{max} ratios were calculated to get an index of muscle spindle sensitivity and γ-drive (31).

Stretch reflexes. Stretch reflex activities were elicited by using sinusoidal length perturbations superimposed on a voluntary contraction according to a methodology described by Rack et al. (36). First, the cosmonaut was asked to develop a maximal voluntary contraction (MVC) against the actuator while no handgrip was allowed during contraction. The MVC of the day was defined as the highest of three attempts to generate the maximal voluntary effort. Then the cosmonaut was instructed to match an oscilloscope trace, providing feedback of his level of torque, and to hold it at 50% of his MVC during the test. After the cosmonaut reached the target torque, sinusoidal length perturbations were imposed on the ankle joint. The duration of the sinusoidal perturbations was 4 s, and the displacement amplitude was 3° peak to peak around the reference position. Frequencies of 4–16 Hz were successively presented by using steps of 1 Hz, except for frequencies higher than 12 Hz, for which steps were 2 Hz. When the ankle joint is considered a priori as a linear input-output system, imposed sinusoidal perturbations in displacement result in a sinusoidally modulated torque. Because the cosmonauts were asked to maintain a target torque, this task was facilitated by low-pass filtering the torque signal, visualized on the control oscilloscope to mask the oscillations in the torque trace. Thus all cosmonauts were able to keep their level of torque at the target value without any difficulty. The cosmonaut relaxed as soon as the perturbation stopped, and a resting period was given after each sequence to prevent fatigue (see Experimental Procedure). Experiments were done in the same way on R+2/3+ and on R+5/+6 by using the 50% MVC pre-flight target torque as reference value.

With regard to the processing procedure, data were first inspected visually to keep a number of successive periods where the required voluntary torque remained almost constant. It was also verified that TA antagonist activity, which can contaminate the agonist EMG by a cross-talk phenomenon, remained low whatever the timeline of data collection (BCD1, BCD2, R+2/3+, and R+5/6). After this windowing, the EMG of Sol, GL, and GM were averaged over the remaining periods and then rectified and summed up to express the TS activity. This method is particularly adequate at relatively high frequencies (>6 Hz) at which the stretch reflex may consist in a more synchronous burst and the voluntary background EMG activity is low in relation to the reflexly evoked EMG response. At the lowest frequencies (4 and 5 Hz), reflex activities of the averaged and then rectified EMG signals were seldom detectable (see Fig. 1). Because the present study mainly concerned the analysis of the early, monosynaptic component of the stretch reflex, averaging before rectification favored the delineation of such time-locked, periodic EMG signals (13). Moreover, because the EMG of Sol, GM, and GL were first averaged and then rectified, no correction of the voluntary background EMG activity was necessary (see also Fig. 1). Thus data processing was conducted over frequencies ranging from 6 to 16 Hz. A mean stretch reflex amplitude (SRA), expressed by the ratio between stretch reflex area and duration, was normalized with respect to mean M\text{max} (M\text{max} = M\text{max} area/M\text{max} duration) and related to each frequency of the imposed perturbation. The area under the SRA/M\text{max}-frequency curve obtained was defined as the frequency distribution of the SRA (FD-SRA). This parameter was validated to express changes in TS stretch reflex excitability (25).

Elastic Characteristics

Detailed information about the experimental protocol and the data processing have already been reported elsewhere (26) but will be reviewed briefly here.

Elastic properties of the musculoarticular system were determined by using sinusoidal perturbations with no participation of the cosmonaut (i.e., 0% of MVC). Sinusoidal perturbations (3° peak to peak) were imposed over frequencies ranging from 4 to 16 Hz and were used to construct frequency-response functions (i.e., Bode diagrams). To do so, averaged displacement-to-torque ratios and the phase shift between displacement and torque were plotted against the imposed frequency. Such a Bode diagram reflects the mixed mechanical contribution of inertia (I), viscosity (B), and elasticity (K) according to the formula

\[ T(t) = I \frac{d^2\Theta(t)}{dt^2} + B \frac{d\Theta(t)}{dt} + K\Theta(t) \]
where $T$ is the torque, $\Theta$ is angular displacement, $t$ is time, $d\Theta/dt$ is angular velocity, and $d^2\Theta/dt^2$ is angular acceleration. Because measurements were performed in passive conditions, musculoarticular stiffness was expressed as $K_n$.

These sinusoidal perturbations were performed once in BDC1 or BDC2 and on R+2/+3. Because of the restrained time schedule of the cosmonauts, we could not conduct this part of the experiment on R+5/+6.

Elastic properties of the musculotendinous complex were evaluated by means of a quick-release technique (18) to determine the characteristics of the so-called series elastic component (SEC). Briefly, the cosmonaut maintained an isometric target torque (25, 50, and 75% MVC), and a quick-release movement was achieved by a sudden releasing of the footplate of the ankle ergometer. SEC characteristics were measured at the beginning of the quick-release movement, when the elastic elements are supposed to recoil and before any reflex changes in muscle activation are possible, i.e., when acceleration is maximal ($\dot{\theta}_{\text{max}}$). This was confirmed by inspecting visually the recorded EMG. SEC stiffness ($S$) was calculated as the ratio between variations in angular acceleration (as a derivative of angular velocity) and angular displacement, multiplied by the corresponding inertia value. Inertia was calculated by considering the equality between the initial target torque and the dynamic torque $1\cdot\dot{\Theta}_{\text{max}}$ at the release, when acceleration is maximal ($\dot{\Theta}_{\text{max}}$) (see also Ref. 26). Then the slope of the linear relationship between stiffness and the isometric torque initially exerted by the cosmonaut was defined as the stiffness index of the musculotendinous complex ($S\text{I}_{\text{MRT}}$).

**Statistics**

Differences in the parameters observed between the different time schedules of data collection were analyzed by using a two-way ANOVA for repeated measurements with main effects of cosmonaut and spaceflight. A post hoc Fisher’s least significant differences test was then applied to determine the significance of the differences. Linear regression analyses were used to check whether changes in reflex values correlated with the corresponding changes in stiffness values. Possible outliers were identified by Studentized residuals and significance was attested by Grubbs’ test (Statgraphics). Data are presented as means ± SE. The level of significance was set to $P < 0.05$.

**RESULTS**

**Reflex Characteristics**

No significant differences were found between the two baseline measurements (BDC1, BDC2) for all parameters, so that they were averaged to get BDC data. Moreover, no significant changes in TS $M_{\text{max}}$ area were found whatever the tested timeline (BDC, R+2/+3, R+5/+6). The outlier identification analyses for each parameter indicated that cosmonauts C1 and C2, who spent 90 days in space, presented no significant departures from the other cosmonauts. Thus they were included in the population.

Mean $H_{\text{max}}/M_{\text{max}}$ slightly increased between BDC and R+2/+3 from 30.0 ± 3.6 to 34.1 ± 3.7% and was 32.6 ± 5.9% on R+5/+6. The ANOVA indicated no significant main effect of spaceflight [$F(2,22) = 0.77; P > 0.05$] but a significant variability between the cosmonauts [$F(11,22) = 3.79; P < 0.05$].

Significant main effects of spaceflight were found for differences in $T/M_{\text{max}}$ [$F(2,22) = 4.73; P < 0.05$], whereas ANOVA indicated no significant main effect of cosmonaut [$F(11,22) = 0.49; P > 0.05$]. Mean $T/M_{\text{max}}$ increased significantly between BDC (9.6 ± 2.1%) and R+2/+3 (15.1 ± 3.9%) by 57% but decreased significantly between R+2/+3 and R+5/+6 (11.9 ± 2.8%) by 21%. No significant differences were found between BDC and R+5/+6.

As for $T/H_{\text{max}}$, this parameter changed from 33.5 ± 7.2% on BDC to 43.7 ± 9.1% on R+2/+6 and was still...
Increased on R+5/+6 (46.5 ± 8.1%). The ANOVA indicated no significant main effect of spaceflight \( F(2, 22) = 0.47; P > 0.05 \) but a significant main effect of cosmonaut \( F(11,22) = 2.34; P < 0.05 \).

Significant main effects of spaceflight were found for FD-SRA differences \( F(2,22) = 4.87; P < 0.05 \), whereas the ANOVA indicated no significant main effect of cosmonaut \( F(11,22) = 0.45; P > 0.05 \). Thus mean FD-SRA increased significantly by 31% between BDC (0.29 ± 0.03 s\(^{-1}\)) and R+2/+3 (0.38 ± 0.06 s\(^{-1}\)) but decreased significantly by 29% between R+2/+3 and R+5/+6 (0.27 ± 0.02 s\(^{-1}\)). No significant differences were found between BDC and R+5/+6. A summary is given in Table 1.

**Stiffness-Reflex Relationships**

The results of microgravity-induced changes in mechanical properties of the human ankle plantarflexor muscles will be reviewed briefly, because they have been reported in detail elsewhere (26, 27). Maximal torque during MVC decreased significantly by 17% when tested on R+2/+3, whereas no significant changes were observed between R+2/+3 and R+5/+6 or between BDC and R+5/+6. Significantly lower \( K_p \) values were reported when measured after spaceflight on R+2/+3, leading to a mean decrease of 11%. On the other hand, \( S_I_{MRT} \) increased significantly by 25% between BDC and R+2/+3 and by 54% between BDC and R+5/+6. When compared between R+2/+3 and R+5/+6, \( S_I_{MRT} \) still showed a significant increase of 24% compared with R+2/+3. A summary is given in Table 2.

The relationships between individual changes in the elastic properties and the mechanically elicited reflex activities at rest and under voluntary contractions were constructed for the nine cosmonauts for whom all reflex and mechanical data sets were available. Thus changes in the mechanically elicited reflex activities at rest (TS T/M\(_{max}\)) were related to changes in \( K_p \), whereas changes in stretch reflex activities under voluntary contraction (TS FD-SRA) were related to changes in \( S_I_{MRT} \).

### Table 1. Electrically and mechanically elicited reflex responses of the triceps surae at rest and during voluntary contractions before long-term spaceflight, after landing, and some days later

<table>
<thead>
<tr>
<th></th>
<th>BDC</th>
<th>R+2/+3</th>
<th>R+5/+6</th>
</tr>
</thead>
<tbody>
<tr>
<td>( H_{max}/M_{max}, % )</td>
<td>30.9 ± 3.6</td>
<td>34.1 ± 3.7</td>
<td>32.6 ± 5.9</td>
</tr>
<tr>
<td>T/M(_{max}, % )</td>
<td>9.6 ± 2.1</td>
<td>15.1 ± 3.9</td>
<td>11.9 ± 2.8</td>
</tr>
<tr>
<td>T/H(_{max}, % )</td>
<td>33.5 ± 7.2</td>
<td>43.7 ± 9.1</td>
<td>46.5 ± 8.1</td>
</tr>
<tr>
<td>FD-SRA, s(^{-1})</td>
<td>0.29 ± 0.03</td>
<td>0.38 ± 0.06</td>
<td>0.27 ± 0.02</td>
</tr>
</tbody>
</table>

Values are means ± SE of the normalized H and T reflexes (\( H_{max}/M_{max}, T/M_{max} \)) and T to \( H_{max} \) ratio (T/M\(_{max}\)) at rest and stretch reflex (FD-SRA) of voluntarily activated muscles before (BDC), 2 or 3 days (R+2/+3) after spaceflight, and 5 or 6 days (R+5/+6) after spaceflight. *Significant differences at the P < 0.05 level.

### Table 2. Mechanical properties before long-term spaceflight, after landing, and some days later

<table>
<thead>
<tr>
<th></th>
<th>BDC</th>
<th>R+2/+3</th>
<th>R+5/+6</th>
</tr>
</thead>
<tbody>
<tr>
<td>( K_p, N\cdot m\cdot rad^{-1} )</td>
<td>39.12 ± 1.19</td>
<td>34.78 ± 1.27</td>
<td></td>
</tr>
<tr>
<td>( S_I_{MRT}, rad^{-1} )</td>
<td>3.38 ± 0.13</td>
<td>4.21 ± 0.11</td>
<td>5.21 ± 0.33</td>
</tr>
<tr>
<td>MVC, N-m</td>
<td>108.9 ± 5.6</td>
<td>90.9 ± 7.3</td>
<td>94.9 ± 6.2</td>
</tr>
</tbody>
</table>

Values are mean ± SE of passive musculoarticular stiffness (\( K_p \)), musculotendinous stiffness (\( S_I_{MRT} \)), and maximal voluntary contraction (MVC) at BDC, R+2/+3, and at R+5/+6. Changes in \( K_p \) at R+5/+6 are missing because no measurement was made on day R+5/+6. *Significant differences at the P < 0.05 level.

Figure 2 illustrates paired changes between T/M\(_{max}\) and \( K_p \) for each cosmonaut in postflight conditions. This figure reveals that changes in T/M\(_{max}\) were related to changes in \( K_p \) for eight of nine cosmonauts. Indeed, the Studentized residual of cosmonaut C7 was 4.96, and Grubbs’ test indicated that this value represents a significant outlier (P < 0.05). Figure 3 depicts the results of paired changes between FD-SRA and \( S_I_{MRT} \) for each cosmonaut in postflight conditions (Fig. 3A) and in early recovery conditions (Fig. 3B). As shown in Fig. 3A, the increase in FD-SRA did not correlate with the increase in \( S_I_{MRT} \) in postflight conditions. On the other hand, Fig. 3B reveals that the opposite changes in FD-SRA and \( S_I_{MRT} \) during the early recovery period were correlated when considering individual data (see Fig. 3 legend).

**DISCUSSION**

Removal of gravitational environment gives the ability to understand how earth’s gravity has shaped the evolution of the neuromuscular system to control posture and movement. The present study examines...
changes in reflex excitability after long-term spaceflight and analyzes how central processes and peripheral mechanisms, like muscle and joint stiffness (26), interfere in the reflex changes found after spaceflight.

Central Adaptive Processes

Two or three days after landing, an increase in reflex excitability was assessed by the trend of higher H reflexes and by the significant increase in T and stretch reflexes. One possible mechanism to explain changes in reflex excitability can be an adaptive response at the level of the motor units. This adaptation was expected, because after exposure to a microgravity environment (real or simulated), an increase in the postural muscle content in fast type fibers is usually reported (for review, see Ref. 14). By analogy with studies about strength training effects (2, 8, 16, 28, 33, 34), lower reflexes were expected for muscles with a higher content of fast fibers. Thus the reverse changes reported in the present study cannot be explained by a fiber-type transition phenomenon. This does not mean that this fiber transition was not present (the cosmonauts were not submitted to muscular biopsies), but, if present, the influence of this phenomenon on the reflex changes was masked by more apparent adaptive processes. When H reflexes were tested in a lying position, Duchateau (11) suggested that the higher H reflexes recorded after a 150-day bed-rest case study were due to an increase in synaptic efficacy on the unloaded motoneurons by a partial removal of presynaptic inhibitory phenomena. Indeed, Gallego et al. (15) demonstrated in animals that disuse enhanced the synaptic efficacy in spinal motoneurons. This increase in synaptic efficacy can mainly explain the trend for higher reflexes found after spaceflight. The reason for observing a trend but not a significant increase in H reflex amplitude like after bed rest could be that, in the space station, the concerned muscles remained active by the daily tasks and exercises performed by the cosmonauts. Thus the muscle unloading was less pronounced than in the case of a long-term bed rest. These in-flight activities probably varied in type and intensity from one cosmonaut to another, contributing to the large intersubject variability in the reflex changes. It must also be recalled that reflexes were tested 2 or 3 days after landing, i.e., when the recovery to a gravitational environment was already in progress. Unfortunately, it was not possible to apply the present protocol sooner and to analyze reflexes just after landing, but if such measurements were authorized, the H reflex changes probably should differ in intensity.

With regard to the T reflex, Russian studies (cited in the review of Ref. 12) reported opposite changes in nonnormalized patellar or Achilles tendon reflexes, measured on a few members of different missions. In the present study, the increase in normalized T reflexes can also reflect the increase in synaptic efficacy. However, T and H responses cannot be compared directly, because they differ, notably in the composition and/or temporal dispersion of the involved afferent volleys (6, 32). Furthermore, T responses were, for all subjects, lower than the H reflexes, and it is well known that small reflexes are more sensitive to excitatory and inhibitory influences than reflexes of greater amplitudes (9). Thus the increase in synaptic efficacy can be more effective on the smaller T reflexes than on the maximal H reflexes.

In the same way, the higher FD-SRA values, found at R+2/+3, can also reflect changes in synaptic efficacy, such changes being susceptible to be influenced under voluntary contractions. Further analyses of which mechanism, supraspinal and/or peripheral (e.g., coming from cutaneous or tendinous afferents), would be responsible for the origin of these changes in synaptic efficacy go beyond the scope of the present study. However, it seems that this central adaptive process plays a large part in the changes of reflex excitability, observed 2 or 3 days after landing.

The decrease in all reflex responses at R+5/+6 compared with R+2/+3 comports with the hypothesis that the higher synaptic efficacy was mainly responsible for the reflex changes at R+2/+3. At R+5/+6, the muscle reloading is more effective, and a return to normal synaptic efficacy is probably in progress and contributes to the reflex decrease at that time. An increase in \( \gamma \)-motoneuron drive can also contribute to the changes...
in the reflex mechanically induced, as indicated by the trend for higher T-to-H ratios at R+2/+3 and R+5/+6. These changes affecting muscle spindle sensitivity to stretch have been reported as a result of postural instability (39) to which cosmonauts are subjected on their return to Earth. If present, this mechanism will be more pronounced in active muscles than at rest and thus will affect the FD-SRA more profoundly than the T reflex.

**Peripheral Adaptive Processes**

In addition to central mechanisms, peripheral components, like tendon stiffness and/or muscle spindle responsiveness, may also influence the reflex responses mechanically elicited. Indeed, the T reflex activates the reflex pathway from the muscle spindles up to the motoneurons, whereas the H reflex bypasses the spindles. Furthermore, besides the possible changes in γ-drive, a comparison between changes in T and H reflex could also indicate that an externally applied stretch comes to the muscle spindles through more or less compliant musculotendinous structures. Such a link between muscle spindle activation and tendon stiffness can be expected, because, for example, in a long and relatively more compliant tendon some of the imposed movement is taken up in the tendon, and less of the imposed movement is transmitted to the muscle spindles (36). For instance, some studies suggested that alterations in T/H ratio values should be partly attributed to changes in tendon stiffness (2, 3). In the present study, the expected link between changes in T reflex and changes in passive stiffness failed to be observed at R+2/+3 by considering changes in mean TS T reflex (57%) and in $K_p$ ($-11\%$). However, an individual analysis of changes in T/M max and in $K_p$ reveals that changes in passive stiffness had an influence on the T reflex for the majority of the cosmonauts (see Fig. 2). The highest changes in T reflex were found for the cosmonauts who showed an increase in $K_p$ values, and reversibly a strong decrease in $K_p$ values led to a decrease in the T reflex. This supports the idea that peripheral mechanisms contribute to the changes in reflex excitability as a result of spaceflight.

Adaptation of the muscle spindles themselves can be proposed to contribute to T reflex changes. Some data are in favor of an increase in spindle sensitivity after disuse. For example, after immobilization, passive stretch led to higher static and dynamic indexes of primary endings in the cat peroneus longus (17). Morphological and histochemical alterations in muscle spindles of disused muscles were suspected to affect the elastic properties of muscle spindles (10, 20). Furthermore, Zelena and Soukup (43) reported an increase in the number of intrafusal fibers within the spindles of soleus muscles unloaded by deafferentation. However, for instance, the hypothesis of a spindle adaptation due to unloading by spaceflight remains entirely prospective, studies about this adaptive phenomenon are in progress.

Because contraction may improve the mechanical linkage between muscle and joint, changes in the elastic properties of the musculotendinous complex can also influence stretch reflex activities. When a muscle contracts, the stiffness of both tendon and muscle fibers increases, but not by the same amount, because a tendon acts like a spring with a constant stiffness from 20–30% of MVC and higher (for a review, see Ref. 35). The distribution of the externally imposed perturbation then depends on the relative stiffness between tendon and muscle fibers (37) so that it may become difficult to estimate how much of the external perturbation will be “seen” by the muscle spindles (36). Whatever the case, it is conceivable that an increase in musculotendinous stiffness should lead to higher muscle spindle activation. The increases in both $S_{MT}$ and FD-SRA in postflight conditions seemed to support this hypothesis. However, the reported increase in stretch reflex and musculotendinous stiffness (31% in FD-SRA vs. 25% in $S_{MT}$) failed to show any correlation when individual data were considered (see Fig. 3A). This lack of correlation shows, once again, the prospect for multiple origin of the adaptive response of the stretch reflex, with the ensemble of central and peripheral factors contributing to the enhancement of the stretch reflex 2 or 3 days after spaceflight. On the other hand, data collected at R+5/+6 improved the correlation between changes in FD-SRA and changes in $S_{MT}$ of individual data (see Fig. 3B). Thus it appears that the stretch reflex was related to musculotendinous stiffness at a stage when return to a normal synaptic efficacy was suspected to be in progress.

In conclusion, this study where reflexes were elicited in different ways gives a better understanding of neuromuscular adaptations due to microgravity. Furthermore, changes in mechanically elicited reflexes were related to changes in the corresponding elastic properties. From this multiparametric approach, it appears that, soon after landing (R+2/+3), the increase in the tested reflexes could be due essentially to a higher synaptic efficacy. Other mechanisms are suspected to reinforce or counteract this main central influence on the reflexes, notably the changes in elastic properties, in motoneuronal excitability, and in muscle spindle sensitivity. When synaptic efficacy was suspected to be in the way to return to a normal level, an improved correlation between changes in reflexes and elastic properties illustrated the important role of peripheral components such as the elastic properties of muscle and tendon.

These multiple influences on the reflex excitability contribute to the large variability found in the reflex changes from one subject to another. This variability may also be due to the tasks and exercises practiced on board. One of the difficulties to interpret some of the results comes from the impossibility to be informed about the type, duration, and intensity of the exercises practiced by each cosmonaut. Despite these activities, reflex and mechanical functions of muscles unloaded by microgravity remained affected. In the future, it will
be necessary to be better informed about the in-flight exercises. In these conditions, the testing protocol developed for the present study could be useful to attest the efficacy of new countermeasure programs, devoted to limit muscle atrophy and neuromuscular changes due to longer spaceflights.

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