Sympathetic outflow enhances the stretch reflex response in the relaxed soleus muscle in humans

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Hjortskov, Nis, Jørgen Skotte, Christian Hye-Knudsen, and Nils Fallentin. Sympathetic outflow enhances the stretch reflex response in the relaxed soleus muscle in humans. J Appl Physiol 98: 1366–1370, 2005. First published November 12, 2004; doi:10.1152/japplphysiol.00955.2004.—Animal experiments suggest that an increase in sympathetic outflow can depress muscle spindle sensitivity and thus modulate the stretch reflex response. The results are, however, controversial, and human studies have failed to demonstrate a direct influence of the sympathetic nervous system on the sensitivity of muscle spindles. We studied the effect of increased sympathetic outflow on the short-latency stretch reflex in the soleus muscle evoked by tapping the Achilles tendon. Nine subjects performed three maneuvers causing a sustained activation of sympathetic outflow to the leg: 3 min of static handgrip exercise at 30% of maximal voluntary contraction, followed by 3 min of posthandgrip ischemia, and finally during a 3-min mental arithmetic task. Electromyography was measured from the soleus muscle with bipolar surface electrodes during the Achilles tendon tapping, and beat-to-beat changes in heart rate and mean arterial blood pressure were monitored continuously. Mean arterial pressure was significantly elevated during all three maneuvers, whereas heart rate was significantly elevated during static handgrip exercise and mental arithmetic but not during posthandgrip ischemia. The peak-to-peak amplitude of the short-latency stretch reflex was significantly increased during mental arithmetic (P < 0.05), static handgrip exercise (P < 0.001), and posthandgrip ischemia (P < 0.005). When expressed in percent change from rest, the mean peak-to-peak amplitude increased by 111 (SD 100)% during mental arithmetic, by 160 (SD 103)% during static handgrip exercise, and by 90 (SD 67)% during posthandgrip ischemia. The study clearly indicates a facilitation of the short-latency stretch reflex during increased sympathetic outflow. We note that the enhanced stretch reflex responses observed in relaxed muscles in the absence of skeletomotor activity support the idea that the sympathetic nervous system can exert a direct influence on the human muscle spindles.

Method

Subjects. Nine healthy subjects (4 men and 5 women) participated in the study. The subjects were 37.2 yr (SD 6.3) with average heights and weights of 173 cm (SD 5.3) and 71.4 kg (SD 13.1), respectively. The local ethics committee of Copenhagen approved the study. All participants gave their informed consent before their inclusion in the study.

Procedure. The protocol is illustrated in Fig. 1. When arriving to the laboratory the subjects were interviewed and the protocol was explained. Because bladder distension increases MSNA (7), the subjects voided before the experiment. Electromyograph (EMG) electrodes were placed at the right soleus muscle. Maximal voluntary contraction (MVC) was determined from the peak force of three maximal isometric efforts using a handgrip dynamometer (Bofors). From this peak force, 30% MVC was calculated. The stretch reflexes were elicited by tapping the Achilles tendon during six tapping trials, i.e., during 3 min of rest (rest 1), during 3 min of static handgrip exercise at 30% MVC followed immediately by 3 min of posthandgrip ischemia, followed by another 3 min rest (rest 2), during 3 min of mental arithmetic, and finally during 3 min rest (rest 3). The order of the static handgrip exercise/posthandgrip ischemia and mental arithmetic interventions was randomized. Tapping was started 1 min into the experimental protocol. The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

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Stretch reflexes. Subjects were seated in a chair of the Biodex System III isokinetic dynamometer (Biodex Medical, Shirley, NY) with the right leg placed on a pedal in an ankle joint position of ~90° so that a standardized relaxed position could be maintained without any muscle activity occurring. The angle of the knee joint was ~100–120°. The stretch reflexes were elicited by tapping the Achilles tendon during 90 s (50 taps). An automatic reflex hammer produced 100–120°. The stretch reflexes were elicited by tapping the Achilles tendon. The proximal electrode was located 3 cm below the insertion of the gastrocnemius muscle on the Achilles tendon. The interelectrode distance was 2 cm. The raw EMG signals were sampled with a frequency of 5,000 Hz. The data were high-pass filtered with a cutoff frequency of 10 Hz. Before additional processing of the data occurred, visual checks for noise and artifacts were performed. The onset of the short-latency stretch reflex was determined by averaging 50 reflex responses. The latency was defined as the point in time when the EMG signal exceeded a threshold level of 3 SDs of the background EMG. Tapping the Achilles tendon elicited generally an EMG response consisting of one peak named M1 (32). Mean peak-to-peak amplitudes of M1 were calculated.

Blood pressure and heart rate. Noninvasive continuous beat-to-beat changes in heart rate (HR, beats/min) and systolic (SBP, mmHg), diastolic (DBP, mmHg), and mean arterial (MAP, mmHg) blood pressures were measured with an inflatable cuff placed over the proximal portion of the middle finger connected to a Finometer device (Finapres Medical Systems BV-TNO TPD Biomedical Instrumentation) and recorded by a computer. The HR and blood pressure data were analyzed by use of BeatScope software package version 1.1 (TNO TPD Biomedical Instrumentation). The blood pressure was automatically corrected for hydrostatic pressure to compensate for vertical movements of the hand with respect to heart level and the concomitant pressure changes in the finger blood pressure.

Subjective experience of stress. The participants reported subjective experiences of stress just after rest 1 and after mental arithmetic.

Maneuvers to induce muscle sympathetic activation in the lower leg. Three maneuvers inducing substantial elevations in MSNA in the lower leg (1, 4, 31, 33) were used, i.e., static handgrip exercise, posthandgrip ischemia, and mental arithmetic. The subjects performed 3 min of static handgrip exercise at 30% MVC with their dominant arm. The upper arm was kept vertical with a 90° flexion in the elbow, and the subjects received auditory feedback of the handgrip force. Just before the end of exercise (1–2 s), the circulation to the forearm was occluded by inflation of a pneumatic cuff on the upper portion of the exercising arm to above systolic blood pressure (250 mmHg). Posthandgrip ischemia was maintained for 3 min. Mental stress was elicited by 3 min of mental arithmetic. The arithmetic task involved having subjects subtracting a two-digit number from a four-digit number orally, starting with subtracting 17 from 2,013. The subjects were informed about their performance in nonsupportive language during the task.

RESULTS

The cardiovascular data are presented in Table 1. SBP, DBP, and MAP were significantly elevated during static handgrip exercise (P < 0.001), posthandgrip ischemia (P < 0.001), and mental arithmetic (P < 0.05) compared with rests 1–3. HR was significantly elevated during static handgrip exercise and men-
tal arithmetic compared with *rests 1-3* and posthandgrip ischemia ($P < 0.05$). Furthermore, SBP, DBP, MAP, and HR during *rests 1-3* did not differ, indicating a stable baseline. Finally, no differences were observed between static handgrip exercise, posthandgrip ischemia, and mental arithmetic for SBP, DBP, and MAP. The time course for HR and MAP along with superimposed stretch reflexes during *rest 1*, mental arithmetic, static handgrip exercise, and posthandgrip ischemia for one subject are illustrated in Fig. 2. The changes expressed as percent change from *rest 1* in MAP and HR are illustrated in Fig. 3. The participants reported significantly more stress [6.9 (SD 2.4) vs. 0.6 (SD 0.9)] and tenseness [5.4 (SD 2.1) vs. 0.9 (SD 1.1)] during mental arithmetic compared with *rest 1* ($P < 0.001$). Furthermore, no changes were found for exhaustion [1.6 (SD 2.3) vs. 0.2 (SD 0.4)] and concentration [6.2 (SD 2.9) vs. 5.3 (SD 2.5)] between mental arithmetic and *rest 1*.

No changes in tapping characteristics and background EMG activity were observed in the different tapping sessions (Table 2). The quiescence of the soleus muscle was confirmed by the EMG analysis. Furthermore, no changes were observed in the mean EMG onset latency of the stretch reflex between the different tapping sessions (Table 2). The peak-to-peak amplitude of the short-latency stretch reflex was significantly increased during mental arithmetic ($P < 0.05$), static handgrip exercise ($P < 0.001$), and posthandgrip ischemia ($P < 0.005$) compared with *rests 1-3* (absolute values of the peak-to-peak amplitude expressed in $\mu$V are shown in Table 2). The relatively large SD of the reflex amplitudes reflects relatively large intersubject variability. When expressed in percent change from *rest 1*, the mean peak-to-peak amplitude increased by 111 (SD 100)% during mental arithmetic, by 160 (SD 103)% during static handgrip exercise, and by 90 (SD 67)% during posthandgrip ischemia (Fig. 3). The peak-to-peak amplitude increased 2.2 (SD 17)% during *rest 2* and decreased by 9.5 (SD 17)% during *rest 3*.

**DISCUSSION**

The present study examined the influence of sympathetic outflow on the stretch reflex in human soleus muscles. We demonstrated an enhanced reflex response irrespective of the kind of maneuver used to increase the muscle sympathetic outflow to the leg despite differences in the magnitude of the response.
Static handgrip, posthandgrip ischemia, and mental stress all increased the amplitude of the short-latency stretch reflex in the soleus muscle. Interestingly, the internal relationship between the magnitudes of the responses elicited by the three interventions may reflect differences in their ability to increase muscle sympathetic outflow.

Static handgrip exercise at 30% MVC elicits a marked increase in MSNA in the nonexercising legs. Mark et al. (18) demonstrated a 193% increase in MSNA recorded from the peroneal nerve during static handgrip exercise at 30% MVC, Scherrer et al. (30) demonstrated a 431% increase, whereas Vissing et al. (33) demonstrated a 273% increase in the second minute of static handgrip exercise. During posthandgrip ischemia, the MSNA remains elevated above baseline level and in some studies (18, 33) it is maintained at a level comparable to the exercise recordings. In most studies, however, there is a decline in MSNA in the occlusion period (21, 25, 30), and Kamiya et al. (14) found a reduction of ~40% when handgrip exercise was compared with posthandgrip ischemia. In mental stress experiments, increases of 43 to 367% in MSNA, with a relatively large variability between subjects, have been reported. When stress is compared directly with handgrip exercise in the same experimental series, the MSNA is consistently larger during static handgrip than during mental stress [Peak changes in MSNA during handgrip and mental arithmetic, 188 and 51%, respectively (34)]. Seemingly, the relative ranking of enhanced stretch reflex responsiveness in the present study fits nicely with the previously reported magnitude of peak changes in MSNA during handgrip, posthandgrip ischemia, and mental stress. Additionally, consistent with the large variability in MSNA during mental stress compared with handgrip exercise in the literature, the variability in the enhancement of the stretch reflex in our study is greater in the mental task (coefficient of variation = 0.90) than in the static handgrip exercise (coefficient of variation = 0.64) and posthandgrip ischemia (coefficient of variation = 0.74).

### Table 2. Stretch reflex characteristics

<table>
<thead>
<tr>
<th></th>
<th>EMG Background Activity, µV</th>
<th>Tapping Depth, mm</th>
<th>Tapping Duration, ms</th>
<th>EMG Onset Latency, ms</th>
<th>Peak-to-Peak Amplitude, µV</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1</td>
<td>0.3 (0.3)</td>
<td>5.0 (1.0)</td>
<td>4.8 (1.7)</td>
<td>38.8 (2.9)</td>
<td>266.8 (214.4)</td>
</tr>
<tr>
<td>R2</td>
<td>0.3 (0.3)</td>
<td>5.0 (0.9)</td>
<td>4.8 (1.7)</td>
<td>39.2 (3.2)</td>
<td>261.7 (205.8)</td>
</tr>
<tr>
<td>R3</td>
<td>0.3 (0.2)</td>
<td>5.1 (1.0)</td>
<td>4.8 (1.8)</td>
<td>39.1 (3.2)</td>
<td>240.6 (1842)</td>
</tr>
<tr>
<td>SHG</td>
<td>0.9 (0.8)</td>
<td>5.0 (1.0)</td>
<td>4.9 (1.8)</td>
<td>38.8 (2.7)</td>
<td>556.6 (359.4)*</td>
</tr>
<tr>
<td>PHI</td>
<td>0.7 (0.8)</td>
<td>5.1 (1.0)</td>
<td>4.9 (1.7)</td>
<td>39.0 (2.7)</td>
<td>473.0 (375.6)†</td>
</tr>
<tr>
<td>MA</td>
<td>0.7 (1.0)</td>
<td>5.1 (1.0)</td>
<td>4.9 (1.8)</td>
<td>39.2 (2.8)</td>
<td>422.3 (240.7)‡</td>
</tr>
</tbody>
</table>

Values are means (SD). *P < 0.001 vs. R1–3. †P < 0.005 vs. R1–3. ‡P < 0.05 vs. R1–3.

The consistent enhancement of stretch reflex responsiveness we found contrasts with animal data reporting a decrease in static and dynamic muscle spindle sensitivity during stimulation of the cervical or lumbar sympathetic chain (10, 24, 27). However, the results from human studies are ambiguous and there may be methodological or species differences. In a study by Macefield et al. (17), microneurographic recordings from muscle spindles showed no changes in discharge frequency of either primary or secondary muscle spindle afferents during a strong and sustained physiological activation of muscle sympathetic outflow. However, the study investigated only static sensitivity of the muscle spindles and not the dynamic sensitivity of the muscle spindles exposed to controlled stretch.

A mental computation task (28) and unpleasant picture viewing (3) both clearly facilitated the stretch reflex in the soleus muscle. An increased firing rate from primary muscle spindle afferents and increased stretch sensitivity during mental computation have also been demonstrated (26). In a study of a mental computation task, Rossi-Durand and colleagues (28) observed that the increases in stretch reflex amplitude occurred without H-reflex changes, indicating changes in muscle spindle sensitivity rather than changes in α-motoneuron excitability or presynaptic inhibition on Ia afferents. They ascribed the increased stretch sensitivity during mental computation to a fusimotor sensitization of muscle spindles and suggested that, in relaxed subjects performing mental computation, the presetting of the fusimotor activation in priming spindle sensitivity could prepare the muscle spindles to better play their role in proprioception and motor control.

Activation of fusimotor neurons during mental stress seems feasible because mental tasks activate the same cortical areas that are involved in movement and motor tasks (9). Nevertheless, although animals can activate their fusimotor neurons independently of the skeletomotor system (α-motor), this has not been found in humans despite intensive search (8, 9, 13). The observation of an increased stretch reflex in relaxed muscles with no skeletomotor activity during mental computation tasks and in all three tests conditions in the present study thus supports the idea of a direct modulation of muscle spindle sensitivity via the sympathetic nervous system.

It could be argued that although the soleus muscle remains inactive during all three maneuvers used to increase MSNA, the handgrip and mental stress situation involve a central command component that at least in theory could influence the fusimotor system. The enhancement of the stretch reflex response during posthandgrip ischemia, however, persists in a situation in which the central command component is eliminated, as evidenced in the return of HR to baseline levels (29). In this case, modulation of spindle sensitivity seems to rely on the influence of a peripheral sympathoexcitatory reflex elicited via metabolites trapped in the occluded muscle and resulting in an increased muscle sympathetic outflow. However, because we tested only the contribution from the muscle spindle, we cannot exclude the possibility of a reflex reinforcement via presynaptic disinhibition acting at the Ia motoneuron synapse.

The enhanced stretch reflex sensitivity during posthandgrip ischemia could originate from a residual effect from static handgrip exercise. However, because Enoka et al. (6) demonstrated a quick T reflex recovery (within seconds) after static exercise, and we started Achilles tendon tapping 60 s after static handgrip exercise, this indicates that the enhanced sensitivity was related to posthandgrip ischemia.

Gregory et al. (12) studied the mechanisms of the potentiation of the stretch reflex during the Jendrassik maneuver,
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corresponding to the static handgrip exercise in the present study. They demonstrated that the fusimotor system is not involved in the reinforcement and neither is direct excitatory or presynaptic disinhibitory effects on motoneurons. As an alternative, they proposed that oligosynaptic neurons might contribute to the tendon stretch reflex, which may not be strictly monosynaptic. Taking the findings of the study by Gregory et al. and the findings from our study into account, the stretch reflex may be enhanced via sympathetic modulation during static handgrip exercise.

When considering the functional implication of an increased stretch reflex gain during states of high MSNA, such as during mental stress, the potency of the reflex system could tune the system to a more powerful and appropriate reaction. However, the increased stretch reflex sensitivity during increased MSNA may have potentially adverse effects. Interestingly, increased spine loading was observed during a stressful standardized lifting task compared with nonstressful conditions (5, 19). The authors suggest that the demonstration of an increased stretch reflex of the musculoskeletal system, manifesting itself through less lifting task compared with nonstressful conditions (5, 19). The increased stretch reflex sensitivity during increased MSNA system to a more powerful and appropriate reaction. However, mental stress, the potency of the reflex system could tune the stretch reflex gain during states of high MSNA, such as during static handgrip exercise.

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