Spinal and pudendal nerve modulation of human corticoanal motor pathways

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1University Department of Gastroenterology, Hope Hospital, Salford M6 8HD; 2Medical Research Council Human Movement and Balance Unit, Institute of Neurology, Queen Square, London WC1N 3BG, United Kingdom; and 3Department of Gastroenterology, Heinrich Heine University, 40225 Dusseldorf, Germany

Hamdy, Shaheen, Paul Enck, Qasim Aziz, John C. Rothwell, Samet Uengoergil, Anthony Hobson, and David G. Thompson. Spinal and pudendal nerve modulation of human corticoanal motor pathways. Am. J. Physiol. 274 (Gastrointest. Liver Physiol. 37): G419–G423, 1998.—We investigated the effects of lumbosacral and pudendal nerve stimulation on the corticofugal pathways to the human external anal sphincter. In 11 healthy subjects, anal sphincter electromyographic responses, evoked to transcranial magnetic stimulation of the motor cortex, were recorded 5–500 ms after lumbosacral root or pudendal nerve stimulation. Lumbosacral and pudendal nerve stimulation alone evoked responses with amplitudes of 293 ± 73 and 401 ± 153 µV and latencies of 3.2 ± 0.2 and 2.2 ± 0.2 ms, respectively. Cortical stimulation also evoked responses with amplitudes of 351 ± 104 µV and latencies of 20.9 ± 1.1 ms. When lumbosacral or pudendal nerve stimulation preceded cortical stimulation, the cortically evoked responses were facilitated (P < 0.01), with the effect appearing greatest at 5–20 ms after both lumbosacral and pudendal excitation and at 50–100 ms after lumbosacral excitation alone. Our results demonstrate that cortical pathways to the external anal sphincter are facilitated by prior lumbosacral and pudendal nerve stimulation, indicating that sensorimotor interactions are important in the central neural control of sphincter function.

The importance of cortical influences in the control of the external anal sphincter is well recognized. Direct repetitive stimulation of the most medial motor cortex, adjacent to the interhemispheric fissure, will induce anal sphincter contractions (14, 26). More recent experiments in humans have shown that the corticofugal pathways to the external anal sphincter can be studied noninvasively by recording the electromyographic (EMG) or manometric responses evoked in response to transcranial electrical and magnetic stimulation of the motor cortex (8–10, 15, 17, 18, 25). Furthermore, direct stimulation of the lumbosacral motor roots and of the pudendal nerve has been used to assess the peripheral efferent innervation of the anal sphincter both in healthy individuals (9, 15, 18, 23) and in patients with fecal incontinence (12, 13, 20, 21, 22). However, although it is known that neural input from both the cerebral cortex and spinal cord is important in the regulation of anal continence, no data exist on their central-peripheral interactions in humans. The aim of our study was therefore to explore how the cortical pathways to the external anal sphincter are influenced by spinal root and pudendal nerve excitation.

METHODS

Subjects

Healthy adult volunteers (n = 11, 8 males and 3 nulliparous females, mean age 33 yr, age range 26–45 yr) were recruited from personnel affiliated with the research units involved in the project. None of the volunteers reported any gastrointestinal, pelvic floor, or anorectal problems, and all gave informed written consent before the study.

Magnetic Stimulation

Magnetic stimulation of the cerebral cortex and the lumbosacral roots was performed using commercially available magnetic stimulators (Magstim 200; MAGSTIM, Whitland, UK).

Cortical stimulation. Motor cortex stimulation was performed using a magnetic stimulator connected to a 110-mm-diameter double cone coil (type 9920; MAGSTIM), which, when positioned over the vertex of the cranium, induces currents along the interhemispheric fissure, thereby stimulating the region of the motor cortex innervating the pelvic and lower limb musculature (10).

Peripheral neural stimulation. Peripheral neural stimulation was performed using a magnetic stimulator connected to a 90-mm-diameter, figure-eight coil, which provided focal stimulation of an area of tissue ~2 cm² beneath its central bifurcation.

Lumbosacral root stimulation was achieved by discharging the coil over the right lumbosacral region. The center of the coil bifurcation was positioned 3–5 cm right of the midline, between the third and fifth lumbar vertebrae (9, 15).

Common peroneal nerve stimulation was performed to control for any nonspecific effects of peripheral neural excita-
tion by positioning the coil over the lateral aspect of the neck of the right fibula (3).

Combined peripheral and cortical stimulation. Combined peripheral and cortical stimulation was performed using two magnetic stimulators connected to a timing device (Bistim Module; MAGSTIM), programmed to discharge both stimulators at intervals varying from 5 to 500 ms.

Electrical Stimulation

Pudendal nerve stimulation. Electrical stimulation of the right pudendal nerve was performed using the St. Mark's glove electrode (model 13L40; Dantec, Skovlunde, Denmark). The stimulation electrode pair was positioned over the tip of the operator's index finger and then inserted intrarectally to the ischial spine adjacent to the pudendal nerve (13). The electrode pair (distance between electrodes = 1.5 cm) was connected to an electrical stimulator device (model DS7; Digitimer, Welwyn Garden City, UK) via a trigger generator (Neurolog System; Digitimer) that delivered single stimuli (pulse duration 0.1 ms, voltage 280 µV) at a standard, supramaximal intensity of 15 mA.

Combined pudendal and cortical stimulation. Combined pudendal and cortical stimulation was performed by connecting both the magnetic stimulator and the electrical stimulator to a timing device (Neurolog System, Digitimer), the output of which was programmed to discharge the magnetic stimulator at intervals of 5–500 ms after the electrical stimulus.

EMG Recording

EMG responses were detected from the striated muscle of the external anal sphincter using the St. Mark's glove electrode. The recording electrode pair (distance between electrodes = 1 cm) was positioned over the base of the operator's index finger, which, when inserted intrarectally, made direct contact with the external anal sphincter.

The electrode pairs were connected to a preamplifier (CED 1902; Cambridge Electronic Design, Cambridge, UK) with filter settings of 5–2,000 Hz. Response signals were then collected through a laboratory interface (CJD 1401 Plus; Cambridge Electronic Design) at a sampling rate of 4–8 kHz and fed into a 486 Sx desktop computer for immediate display, data collection, and averaging. During each study, electrode contact was monitored at 10-min intervals by observing the real-time EMG responses to voluntary anal sphincter contractions.

Experimental Protocol

The protocol described below was presented to, and approved by, the Salford Health Authority Ethics Committee. Throughout each study, the volunteer, having previously emptied his rectum by defecation, lay comfortably on a couch in the left lateral position, and the vertex of the cranium was identified according to the International 10–20 system (11). Then, after a digital examination to ensure that the rectum was empty, the St. Mark's glove electrode was inserted.

Effect of lumbosacral and pudendal nerve stimulation on the cortically evoked anal EMG response. First, to ensure that the optimal stimulation position for evoking anal responses was achieved at each site, the position of the stimulators was adjusted locally until those points that produced the shortest latency and largest amplitude responses were determined. The figure-eight coil was then discharged over the right lumbosacral roots at an intensity of 0.6 T, which was increased by steps of 0.1 T until EMG responses were evoked in the anal sphincter. The lowest intensity that induced these responses was then defined as the threshold stimulus intensity.

Next, two stimuli 15 s apart were delivered to each of the following three sites, in random order: 1) the right lumbosacral roots, at 0.4 T above the threshold intensity; 2) the right common peroneal nerve, at an intensity identical to that used for the lumbosacral roots; and 3) the right pudendal nerve, at a supramaximal intensity of 15 mA (12). After each stimulation, the anal sphincter EMG responses were recorded. Next, the cerebral cortex of each subject was stimulated, at an initial discharge intensity of 0.6 T, which was increased by steps of 0.1 T until anal sphincter EMG responses were obtained at least 50% of consecutive trials, this being defined as the threshold intensity. Three stimuli, 15 s apart, were then delivered at 0.4 T above the threshold intensity, and the EMG responses to each were recorded.

Finally, a series of stimuli were delivered to the lumbosacral spine, pudendal nerve, and common peroneal nerve, in random order, at the intensities and positions described above. Each stimulus was followed by stimulation of the cortex, at 0.4 T above threshold intensity, at intervals of 5, 10, 20, 30, 50, 100, 200, 300, and 500 ms. Three stimulations, each 15 s apart, were delivered for each interval, and the anal sphincter EMG responses were recorded.

Definition of Terms

For the purposes of our study, response latency is the interval between the onset of the stimulus and the onset of the EMG response, expressed in milliseconds. Response amplitude is the maximum peak to peak voltage of the EMG response, expressed in microvolts. Response facilitation is the enhancement of the EMG response by either a reduction in the response latency or an increase in the response amplitude.

Data Analysis

For each subject, the mean value of the three EMG responses evoked was calculated and used for analysis. The
group mean cortically evoked anal EMG responses after lumbosacral and pudendal nerve stimulation were compared with the responses after common peroneal nerve stimulation.

Statistical Tests

The normality of the data was first assessed using the Shapiro-Wilks test (1). Where the correlation obtained was consistent with normality, the paired two-tailed Student’s t-test was applied. Where the correlation obtained was not consistent with normality, natural logarithms of the data were calculated and the Shapiro-Wilks test was reapplied. If normality of distribution was obtained, then the paired two-tailed Student’s t-test was applied to the transformed data; if not, Wilcoxon’s signed-rank sum test was used on the untransformed data. Results are expressed in the text as means ± SE unless stated otherwise. A P value of 0.05 or less was taken to indicate that any observed differences were unlikely to have occurred by chance.

RESULTS

Effect of Lumbosacral and Pudendal Nerve Stimulation

Stimulation of either the lumbosacral roots (mean threshold intensity 1.1 ± 0.1 T) or the pudendal nerves always evoked a biphasic or triphasic anal sphincter EMG response (Fig. 1). Although the response amplitudes to stimulation of either site were similar, as expected, response latencies were shorter after pudendal nerve stimulation (Table 1).

Table 1. External anal sphincter EMG response characteristics after peripheral and cortical stimulation

<table>
<thead>
<tr>
<th></th>
<th>Response Latency, ms</th>
<th>Response Amplitude, µV</th>
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<tbody>
<tr>
<td>Pudendal nerve stimulation</td>
<td>2.2 ± 0.2</td>
<td>401 ± 153</td>
</tr>
<tr>
<td>Lumbosacral spine stimulation</td>
<td>3.2 ± 0.2</td>
<td>293 ± 73</td>
</tr>
<tr>
<td>Cortical stimulation</td>
<td>20.9 ± 1.1</td>
<td>351 ± 104</td>
</tr>
</tbody>
</table>

Data are means ± SE. EMG, electromyographic.

![Fig. 2](http://example.com/f2.png)

Fig. 2. Cortically evoked external anal sphincter EMG responses in 1 individual are shown before (cortical stimulation alone) and after conditioning pudendal, lumbosacral, and common peroneal nerve stimulation at interstimulus intervals (ISI) of 5, 20, 100, and 500 ms. Three traces are superimposed to show reproducibility. Cortical stimulus occurred at 0 ms; arrows indicate onset of EMG response. It can be seen that at intervals of 5 and 20 ms, both lumbosacral and pudendal nerve stimulation facilitate cortically evoked responses compared with common peroneal nerve stimulation.

![Fig. 3](http://example.com/f3.png)

Fig. 3. Effects of prior lumbosacral (●), pudendal (○), and common peroneal (□) nerve stimulation on amplitudes and latencies of cortically evoked anal EMG responses at increasing interstimulus intervals. Vertical axes show percentage of response to cortical stimulation alone; horizontal broken line indicates 100%. Prior lumbosacral and pudendal nerve stimulation increases amplitude and shortens latency of cortically evoked responses compared with common peroneal nerve stimulation. After lumbosacral stimulation, a second increase in response amplitude is observed at 50–100 ms. *† P < 0.01.
nal nerve stimulation compared with lumbosacral root stimulation (Table 1). Common peroneal nerve stimulation never evoked responses in the anal sphincter.

Effect of Cortical Stimulation

Cortical stimulation (mean threshold intensity 1.3 ± 0.1 T) always evoked biphasic or triphasic responses in the anal sphincter (Table 1, Fig. 1). When either lumbosacral or pudendal nerve stimulation preceded cortical stimulation, the cortically evoked anal responses were facilitated (Figs. 2 and 3), whereas prior common peroneal nerve stimulation (mean intensity 1.1 ± 0.1 T) had no effect.

Effect of Lumbosacral and Pudendal Nerve Stimulation on the Cortically Evoked Anal EMG Response

Response amplitude. Prior lumbosacral stimulation increased the corticoanal response amplitudes (P < 0.01), with the maximal effect appearing biphasic, at interstimulation intervals of 5–20 ms and 50–100 ms (Fig. 3).

Pudendal nerve stimulation also increased the response amplitudes (P < 0.01), although, in contrast to lumbosacral stimulation, the maximal effect appeared at intervals of 5–20 ms (Fig. 3).

Response latency. Both lumbosacral and pudendal nerve stimulation shortened the latency of the corticoanal responses, at intervals of 5–20 ms (P < 0.01; Fig. 3).

DISCUSSION

Our study demonstrates that the cortical pathways to the human external anal sphincter can be modulated by applying conditioning stimuli to nerves innervating the pelvic musculature. The observation that both lumbosacral and pudendal nerve stimulation facilitated the corticoanal responses at an interval of 5–20 ms is consistent with a direct antidromic excitation of the sacral motoneurons innervating the external anal sphincter and is similar to the increased excitability induced by voluntary contraction of the sphincter (15). Moreover, the duration of the facilitation also suggests that the time course of the decay of the excitatory postsynaptic potentials (EPSPs) induced within these motoneurons is in the order of 20 ms.

The further observation that lumbosacral but not pudendal nerve stimulation induced a second, delayed rise in the corticoanal response amplitudes, without concurrent reduction in latency, is interesting. Such a pattern might occur if the cortex was excited after the motoneuron EPSPs had returned to resting levels, and could be explained by the activation of ascendingafferent pathways, which would increase cortical excitability while leaving the motoneurons unaltered (5, 19). Repeated sensory stimulation of the anal canal or lumbosacral roots has been shown to induce cerebral evoked potentials with onset latencies of ~30–40 ms (7, 15, 18, 24); thus it could be argued that the late facilitation effect seen in our study (maximal at ~100 ms) occurred during a phase of cortical excitation induced by stimulation of pelvic afferent fibers. A cortical stimulus applied during this phase would therefore evoke a greater number of descending volleys to the motoneurons and would by spatial summation induce a larger response amplitude, without a corresponding reduction of the response latency (19).

The fact that the later facilitation was seen with lumbosacral but not pudendal nerve stimulation, despite their common efferent pathway, suggests that lumbosacral stimulation must have led to greater induction of afferent fiber excitation, a likely consequence of the different stimulation methods used. Thus, whereas the pudendal nerve electrical stimulus is very localized, exciting only fibers in the nerve itself, the lumbosacral magnetic stimulus is more diffuse and activates a greater area of neural tissue. It is therefore likely that the lumbosacral stimulus excited more pelvic afferents than the pudendal stimulus, so that a biphasic facilitation pattern was observed after lumbosacral but not pudendal nerve stimulation.

Our observations may have relevance in the functional assessment of the neural pathways involved in the extrinsic control of the anal sphincter, where the relative motor and sensory contributions of both the motor cortex and pelvic nerves in the control of anal continence can now be explored in greater detail. Thus future clinical studies comparing the degree of corticoanal facilitation to pudendal and lumbosacral nerve stimulation in patients with central and peripheral nervous system injury, both with and without anal incontinence, should provide greater insight into the pathophysiology of fecal incontinence after cerebral and pelvic sensorimotor damage.

Lumbosacral and pudendal nerve stimulation facilitates human cortical motor pathways to the external anal sphincter. These findings indicate that sensoriotor, peripheral-central neural interactions are important in the volitional control of anal continence.

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