High-voltage stimulation over the human spinal cord: sources of latency variation

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SUMMARY Percutaneous electrical stimuli (up to 600 V) were applied over the cervical spinal cord to evoke responses in the biceps brachii and thenar muscles. Cathodal stimulation over the C7 spinous process was more effective than anodal stimulation or stimulation over the C5 or C3 spinous process. As the stimulus intensity was increased, the response amplitude increased and the latency decreased. When progressively higher levels of supramaximal stimuli were delivered the latency often decreased further. The shortest latencies evoked by stimulation over the C7 spinous process were close to the latencies of the responses evoked by supramaximal stimulation near Erb's point. Thus, with this type of stimulation, the site of nerve activation changes with different stimulus intensities. The variability in latency introduced by distal spread of the site of activation will affect measurements of central motor conduction time and should be considered in the diagnostic use of this technique.

Percutaneous electrical stimulation¹ is being used more commonly to evaluate the integrity of peripheral and central motor pathways.^{2,3} Voltages up to 1500 V (50–100 μ s decay) are applied over the motor cortex or spinal cord via surface electrodes placed several centimeters apart. This technique has been used to study the motor conduction times in patients with multiple sclerosis,^{2,5,7–9} motor neuron disease,^{4,6,9} cerebral haemorrhage^{2,9} and cervical spondylosis.^{2,9,10} With this technique, central motor conduction time is estimated by subtracting the response latency to stimulation over the spinal cord from the latency to stimulation of the motor cortex. Several studies using apparently similar methodologies have reported central conduction times to the thenar muscles (motor cortex to C7/T1 motor root) ranging from 5.0 ms–8.3 ms in normal subjects.^{4,6,9,11,12} In contrast, the response latencies of the thenar muscles to cortical stimulation show little variation, 19.6 ms–20.3 ms in the different reports.^{4,6,9,11,12} Therefore, the differences in apparent central conduction times must depend on variability in the latencies to spinal stimulation (range 12.1–15.3 ms).^{4,6,9,11,12} Much of this variation is due to the results of one study.⁶ The same discrepancy is evident for central conduction times to the biceps brachii.^{4,6,9,12}

Since a reported variability of over 60% in normal

central motor conduction time may limit the diagnostic value of this technique, we have investigated methodological factors that affect the latencies to percutaneous electrical stimulation over the vertebral column. Mills and Murray¹³ have shown that the site of activation by stimulation over the cervical spinal cord is the proximal motor root, a result recently confirmed for stimulation over the conus medullaris.¹⁴ The present study demonstrates that the site at which the motor axons are activated following such stimulation varies with the stimulus intensity.

Methods

Experiments were performed on seven adults who ranged in age from 22–42 years and ranged in height from 160 to 191 cm. Subjects had no history of neurological impairment and were studied in the supine position. Experimental procedures were approved by the institutional ethics committee and informed consent was obtained.

Electrical stimuli from a Digitimer D180 stimulator were applied over the spinal cord through surface electrodes (10 mm diameter) filled with conductive gel. The stimulator delivered up to 750 volts via a capacitative discharge with a 50 μ s decay. Electrodes were routinely placed at the inion and over the spinous processes of the C3, C5, and C7 vertebrae. The brachial plexus at Erb's point was also stimulated using the same equipment connected to a saddle electrode assembly (10 mm electrode diameter, interelectrode distance 6 cm). The cathode was placed over Erb's point with the anode superior and lateral to it.

Electromyographic activity (EMG) was recorded with surface electrodes from the thenar muscles with one electrode over the motor point of abductor pollicis brevis and the other

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3 cm distal to it. For biceps brachii one electrode was secured over the midpoint of the belly of the short head of the muscle and the other 4 cm distal and parallel with the muscle fibres. Arm temperature was monitored and the initial temperature of 31–33°C was maintained within 0.5° during an experimental session.

In six subjects, the cathode was initially over C7 with the anode over the inion. In one subject, the cathode was over C7 with the anode placed 6 cm cephalad. Stimuli were first applied at low levels (110–190 V) and increased until responses of maximal amplitude were recorded at more than one consecutive stimulus intensity. To minimise discomfort, the maximum stimulus intensity was limited to 600 V. For Erb's point stimulation, the stimulus intensity was adjusted to evoke a response of similar amplitude to the maximal response obtained from the C7 spinous process. Throughout the experiment, visual and auditory feedback were provided to the subjects to help them relax the muscles before each stimulus was given.

Subsequently, to evaluate the effect of different stimulation sites on the latency and amplitude of evoked responses, similar procedures were followed when the cathode was over the C5 or C3 spinous process, using stimulus intensities that previously evoked a moderate response (peak-to-peak amplitude 1–2 mV) from the C7 level. In addition, to compare cathodal and anodal stimulation, anodal stimulation at the C7 spinous process (cathode at the inion) was performed. A control study showed that responses of similar size were recorded regardless of whether the distance between the cathode and anode was 6 or 12 cm. Unless otherwise stated cathodal stimuli were delivered.

All EMG signals were filtered (32 Hz–1.6 kHz) and stored on FM tape (DC–1.25 kHz) for analysis. Latencies of the potentials and their amplitudes were measured from single unrectified trials. Because amplitudes of the first negative peak of responses and the peak-to-peak amplitude measurements showed similar changes from trial to trial, only the latter are reported. Responses of 90–100% of the largest recorded amplitude have been considered maximal. To obtain precise latency measurements, responses were measured at high gain on a fast time-base using a digital oscilloscope with cursors. Values for the latency and amplitude of all responses at a given stimulus intensity were averaged. Consecutive responses at the same stimulus intensity generally showed little variability.

Results

Latencies of EMG potentials in the upper limb to percutaneous electrical stimulation over the cervical spinal cord may diminish as the stimulus intensity increases. Figure 1 demonstrates that as the stimulus intensity was increased the latency for responses in biceps brachii decreased. This latency change was evident for responses of maximal amplitude. In an extreme instance the latency of the response to stimulation over C7 could be as short as that following stimulation at Erb's point (fig 2). As demonstrated by figs 1 and 2, the latency decreased with increased stimulus intensity whether the inter-electrode distance for the stimulating electrodes was 6 or 12 cm.

Fig 1 Superimposed EMG responses from single trials recorded from biceps brachii following cathodal stimulation over the C7 vertebral process (anode: inion) in one subject. As the stimulus intensity was progressively increased from 185 V to 525 V, the latency of the response gradually decreased (from Arrow A to Arrow B) and the amplitude of the response increased. The latency may decrease further in response to supramaximal stimuli. Vertical calibration: 1 mV.

In most subjects, biceps brachii was activated at a lower stimulus intensity than abductor pollicis brevis, regardless of whether the cathode was over C7, C5 or C3. As the stimulus intensity increased, the response amplitude increased and the latency decreased for both muscle groups (figs 3 and 4). The latencies of responses of maximal amplitude decreased on average 0.42 ms (SD 0.35 ms; range: 0.0–0.98 ms) for the thenar muscles and 0.41 ms (SD 0.28 ms; range: 0.1–0.98 ms) for the biceps brachii as intensity was raised to supramaximal levels. The greatest decrease in latency for responses to supramaximal stimulation was observed in subjects in whom responses of maximal amplitude were obtained at relatively low intensities and who thus received supramaximal stimuli over a greater stimulus range (figs 3 and 4).

In all subjects, the shortest latencies recorded with stimulation over C7 were equal or close to the latencies following stimulation of Erb's point. For the thenar muscles, the shortest latencies recorded following supramaximal stimulation over C7 were on average 0.35 ms, (SD 0.53; range: –0.50 to 1.10 ms) longer than the latencies observed with Erb's point stimulation. For the biceps brachii, this latency difference averaged 0.40 ms, (SD 0.26; range: 0.05 to 0.65 ms).

Fig 2 Single trial EMG responses recorded in the thenar muscles following cathodal stimulation over the C7 vertebral process (anode: 6 cm cephalad) at two stimulus intensities (340 and 525 V) and stimulation at Erb's point. In all subjects, as the stimulus intensity was increased sufficiently, the latency to vertebral stimulation decreased. In the case illustrated, stimulation over C7 at a supramaximal level activated a population of rapidly conducting motor axons near Erb's point. Response latencies are indicated below the responses. Vertical calibration: 2 mV.

Even latencies of *submaximal* responses evoked by stimulation over C7 sometimes fell within 0.5–1.0 ms of the latencies with Erb's point stimulation.

At the same stimulus intensity, responses (in both muscles) to cathodal stimuli over C5 and C3 were generally smaller than those to stimuli over C7. In one subject stimulation over the T1 spinous process produced larger responses at a lower stimulus intensity than stimulation over C7. When responses in biceps brachii of similar amplitude were compared, stimulation over C5 produced responses of equal or longer latency than those following stimulation over C7. This was also the case for the thenar muscles, although cathodal stimulation over C5 produced responses of less than 5% of maximal amplitude in two subjects. Stimulation over C3 usually produced little or no response, especially in thenar muscles. When responses were obtained following stimulation over C3, they were of longer latency and required higher stimulus intensities than those evoked by stimulation over C7.

The threshold for activation of both biceps brachii and the thenar muscles was higher with anodal than cathodal stimulation over C7. For potentials of moderate amplitude, anodal stimulation generally required higher stimulus intensities; but as the maximal response amplitude was approached, equal stimulus intensities of cathodal and anodal stimulation over C7 evoked responses of maximal amplitude. For responses of equal amplitude, latencies were similar with anodal and cathodal stimulation.

Discussion

Percutaneous electrical stimulation over the cervical spinal cord can evoke responses of large amplitude and short latency in the muscles of the upper limb^{2,4,6,7,9,11,12} and even the diaphragm.¹⁵ However, the present study shows that the latency of the evoked response varies as both stimulus intensity and stimulus site change.

As mentioned above, several studies have estimated the normal central motor conduction time at about 4.3 ms, (SD 0.6) for biceps brachii and 5.0 ms, (SD 0.6) for thenar muscles,^{4,5,9,11,12} while others⁶ have reported values of 6.2 ms, (SD 1.6) and 8.3 ms, (SD 2.0) ms for the same muscles. The latter control conduction times are 2–3 ms longer (and more variable) than the former values. In all of these studies, the latencies of the responses to motor cortical stimulation are similar. Therefore, differences in the latencies of responses to spinal stimulation are largely responsible for the variability in reported central conduction times.

At first glance, the methodologies used for stimulation over the spinal column in previous measurements of central motor conduction appear similar. However, there were several differences such as: (1) exact location of stimulating electrodes, (2) stimulus intensity and duration, (3) distance between stimulating electrodes, and (4) electrode size. Given the large stimulus voltages and large inter-electrode distances it is theoretically possible that any of these factors may

Fig 3 Relationship of the stimulus intensity to response amplitude (upper panel) and to the change in latency (lower panel) for the thenar muscle following cathodal stimulation over the C7 spinous process. For each subject, the largest response evoked is defined as 100% maximal amplitude. Change in latency is defined as the latency of a response minus the latency of the response at 100% maximal amplitude. Each subject reached maximal amplitude at a different stimulus intensity. There was a variable reduction in latency as the stimulus intensity reached, and then exceeded, the level required to produce a maximal response. Each symbol represents a different subject. Each value is the average of 2–4 responses.

contribute to the variation in reported latencies of evoked responses following spinal stimulation. Furthermore, subject height¹⁶ and the location of recording electrodes may affect the latencies of the responses.

The present findings show that stimulus intensity is one major source of variability in the latency to spinal stimulation: the higher the intensity the more the latency approximated the latency following stimulation at Erb's point. Even greater latency changes might have been seen if the stimulus intensity had not been limited to 600 V. The study by Ingram and Swash⁶ which reported long central motor conduction times used stimulus intensities up to 1000 V and this may have activated motor axons at a more distal site than the emerging anterior root.¹³

Fig 4 Relationship of the stimulus intensity to response amplitude (upper panel) and to the change in latency (lower panel) for biceps brachii following cathodal stimulation over the C7 spinous process. Change in latency is defined as the latency of a response minus the latency of the response at 100% maximal amplitude. See legend to fig 3 for further details. Each symbol represents a different subject. Each value is the average of 2–4 responses.

The extent of latency change with an increase in stimulus intensity varies between subjects (figs 3 and 4), thereby eliminating any simple solution to this problem. Mills and Murray¹³ suggested that the usual site of activation is at the proximal motor root about 4 cm from the anterior horn. Maertens de Noordhout and colleagues¹⁴ have reported that the effective point of stimulation for lower limb motor axons could be varied by moving the cathode from T11 to S1. However, the present study used a constant stimulus site and found that the latency of the evoked response varied with stimulus intensity. In addition, some submaximal responses were probably generated closer to Erb's point than indicated by Mills and Murray's¹³ calculations. The decrease in latency for submaximal responses may be due to recruitment of faster conducting axons, but is more likely to result from the progressive displacement of the site of activation to more distal nodes of Ranvier. This change in the site of the excitation of the motor axons has been well documented for peripheral nerve stimulation¹⁷ and has also been observed for stimulation over the thoracic cord (unpublished data, see also ref. 18).

The range of reported central motor conduction

times for the same muscle groups may limit the diagnostic use of this technique. There is no formula which will guarantee accuracy of the latencies to spinal stimulation, but some precautions may increase the reliability of the technique. The critical stimulus intensity should be 50% of that required to evoke a maximal response. This stimulus intensity is likely to activate many if not most of the fastest conduction motor axons. Theoretically it might be advisable to minimise the inter-electrode distance to limit the area of activation though we have no evidence to support this view. The phenomenon was documented for two interelectrode distances here (figs 1 and 2). When the central motor conduction time appears pathologically long, it would be prudent to reassess peripheral conduction either by stimulation at the brachial plexus or by measurement of F-wave latencies.^{19 20}

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