Magnetically-invoked motor evoked potentials (MEPs); an assessment of the errors in measuring latencies.

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Abstract

Magnetic stimulation is extensively used in research of the intra-cortical connections of the human brain, but there is relatively little evidence of its reliability in terms of generating repeatable Motor Evoked Potentials (MEPs) which are often used as a means of establishing the appropriate power output of the stimulator for an individual subject. The amplitude of cortically evoked responses has long been known to be very variable, but latency has been considered to be a reliable measure, while this measurement of latency could be subject to a number of errors; we report a total error of less than 5% of the measured latency. Although coil sizes and geometries may also affect latency, we confirm that the use of surface or needle electrodes does not appear to affect latency measurement.

Keywords: Magnetic stimulation, TMS, CMCT, reliability, EMG, cortex

1. Introduction

Early experiments with the effects of magnetic fields on the human body started in the late 19th century [1]. However, the stimulator which emerged from developments at Sheffield University in 1985 [2] was the first device which successfully evoked a response from the motor cortex, and hence found a home amongst those performing research on the brain [3] [4]. Furthermore, the ability to stimulate the motor cortex of conscious humans in a non-volitional manner is potentially of use in measuring Central Motor Conduction Time (CMCT), and hence in the diagnosis of certain central nervous system diseases [5].

Magnetic stimulation in single pulses is painless [6] [7], and because magnetic fields appear to be able to pass unhindered through skin and bone without attenuation [8] [9] it provides a unique means of stimulating neurons inside the Central Nervous System (CNS). Initially the technique was used to directly measure electromyographic activity (EMG) resulting from such stimulation, but in recent years research has moved into the psychiatric and neuroscience research arena, and it is in the area of brain research that magnetic stimulation is now most widely used.

2. Problem Formulation

A Magstim 200² monophasic magnetic stimulator was used in conjunction with a Neurosign 800 EMG recording device (Magstim, Whitland, UK). The Neurosign 800 has 8 channels which can be recorded simultaneously, so that the responses from different muscles resulting from a single stimulation could be recorded. The sampling rate is 20kHz per channel.

2.1 Comparison between surface and needle electrodes

Three 20mm uninsulated needles were inserted into the midpoint of rectus femoris, one of the four muscles making up the quadriceps. Two needles were placed 20mm apart and across the belly of the muscle, and at an angle of 30° to the skin. Two Kendal H120 surface electrodes with an electrode diameter of 10mm were placed immediately above the needle electrodes.

A third needle and surface electrode were placed about 60mm away, approximately one third of the length of the rectus femoris from the tendon attaching to the knee. Figure 1 shows the first stimulation, with traces for left and right quadriceps. The take
off point is reasonably well defined because the preceding part of the waveform is flat, indicating that there was little noise being detected by the preamplifier. Both surface and needle electrodes deviate from the flat portion of the trace at the same time, although there is a difference between the left and right limbs. The recorded latencies for each are given.

Figure 1: Cortical stimulation of the quadriceps using a double-cone coil (figure-of-eight coil shaped to fit the head); left quadriceps stimulated 1cm lateral to the right of the vertex, right side stimulated 1cm to the left of the vertex, output power of stimulator at 50%. Error bars are set at ±5%.

2.2 Morphology

Figure 1 shows there is a difference in amplitude between surface and needle electrodes. It is also clear that the shape of the traces is different. Surface electrodes collect EMG from a large number of motor units and muscle fibres, with the voltage measured effectively averaged by the varying distance of muscle fibres from the electrodes. The measured EMG is therefore of lower amplitude, because of the higher impedance of the electrodes, and has fewer negative and positive deflections, because the voltages arriving at the electrodes from different muscle fibres arrive at different times and may be of different polarities, thereby reducing the collected voltage at that time.

Figure 1 illustrates some of the pitfalls which may be encountered when recording stimulated EMG signals. It is evident that take off points for both needle and surface electrodes are similar, and that the amplitude of needle electrodes is greater than and more complex in morphology than that of surface electrodes. However, it is difficult to identify the take off point in some of the traces; the waveforms shown were obtained without multiple stimulations to obtain the ‘best’ example, so are typical of real EMG recordings. At a power of 50% with this particular coil, which is near the threshold of this subject, the take off point is open to some interpretation.

The take off point can be determined by deciding where the compound muscle action potential (CMAP) begins to deviate from the resting potential. However, this resting potential is subject to a number of variables. In order to facilitate the determination of the take off point, the following precautions were undertaken:

- The subject was asked to relax so that voluntary EMG was not present
- Electrode impedance, especially for surface type electrodes, must be low.
- The type and condition of the cables, especially those from the electrodes to preamplifier.
- EMG cables were kept away from the stimulator.
- The common mode rejection ratio (CMMR) of the preamplifier needs to be high.
- The frequency response of the preamplifier and any associated filter needs to be adequate to reproduce the EMG waveforms faithfully.
- The amplitude of the magnetic field stimulation needs to be sufficient to excite the nerve fibres.

These factors all create difficulty in determining the take off point. Some can be eliminated; cables issues, skin preparation to lower impedance, using quality amplifiers – but unless repeated stimulations are carried out to obtain the ideal EMG response, some degree of subjectivity is necessary.

3. Problem Solution

An alternative method of estimating uncertainties in a measured quantity is to measure it repeatedly a large number of times and to calculate the spread in the results. To investigate whether a determination of the take-off point by eye could be achieved consistently, 25 random stimulus evoked muscle potentials were chosen from those used to measure Central Motor Conduction Time in a separate experiment. The take-off point was determined by eye and recorded; this was repeated 10 times over a period of several days, with the results passed to a colleague each time for recording so that the author did not have access to previously measured data.

The waveforms were divided into 3 groups based on how easy it was to clearly identify the take-off point.
for the muscle action potential, A, B and C. The A group contained waveforms where the take off point was well defined with a flat line preceding the take off point; those in group B had take off points which were clear but were not well defined in that a degree of judgement was required, often because of 50Hz electrical noise; and those in group C had poorly defined take off points where it was difficult to determine. As there were only 3 waveforms which were included in group C, groups B and C were merged. Examples of waveforms from Groups A and B are shown in Figure 2.

![Waveform Example](image)

Figure 2: examples of take off points; A is well defined with a flat line before a clear take off point, indicated at 20.55ms; B does not have a flat line before the take off point, nor is there any sudden deviation to indicate it; the circle shows the approximate position of the take off point

The 95% confidence limits for each waveform and the percentage from the arithmetic mean were calculated. The mean of all waveforms in group A was 1.77% and that for all waveforms in group B was 4.69% or ±2.35% around the mean, although this error was magnified by 2 of the readings which resulted in disproportionate errors of 15% and 16%; without these 2 readings, the percentage error for group B would have been 3.73% or ±1.865%.

The errors contributing to the uncertainty in the measurement of latencies can be itemised as shown in Table 1.

<table>
<thead>
<tr>
<th>Source of error</th>
<th>Percentage or absolute error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recording equipment error</td>
<td>±2%</td>
</tr>
<tr>
<td>Screen error</td>
<td>±0.125%</td>
</tr>
<tr>
<td>Rounding errors</td>
<td>±0.01ms</td>
</tr>
<tr>
<td>Total error</td>
<td>±2.125% (plus 0.01ms absolute error)</td>
</tr>
</tbody>
</table>

Table 2: gives the 5-number summaries for the absolute uncertainties and the percentage uncertainties in the latency measurement.

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>1st Quartile</th>
<th>Median</th>
<th>3rd Quartile</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute uncertainties (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All latencies</td>
<td>0.02</td>
<td>0.105</td>
<td>0.205</td>
<td>0.266</td>
<td>0.675*</td>
</tr>
<tr>
<td>Group A latencies</td>
<td>0.02</td>
<td>0.0775</td>
<td>0.14</td>
<td>0.23</td>
<td>0.36</td>
</tr>
<tr>
<td>Group B and C latencies</td>
<td>0.02</td>
<td>0.155</td>
<td>0.24</td>
<td>0.32</td>
<td>0.675*</td>
</tr>
<tr>
<td>Percentage uncertainties (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All latencies</td>
<td>0.06</td>
<td>0.58</td>
<td>1.21</td>
<td>1.87</td>
<td>8.21*</td>
</tr>
<tr>
<td>Group A latencies</td>
<td>0.06</td>
<td>0.41</td>
<td>0.92</td>
<td>1.45</td>
<td>1.87</td>
</tr>
<tr>
<td>Group B and C latencies</td>
<td>0.06</td>
<td>1.08</td>
<td>1.83</td>
<td>2.92</td>
<td>8.21*</td>
</tr>
</tbody>
</table>
Table 3: gives the mean absolute uncertainty (±SD) and percentage uncertainty (±SD) for the latency measurements, Group A and Group B/C shown separately

<table>
<thead>
<tr>
<th></th>
<th>Mean absolute uncertainty (ms)</th>
<th>Mean percentage uncertainty (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>0.157±0.098</td>
<td>0.88±0.57</td>
</tr>
<tr>
<td>Group B/C</td>
<td>0.253±0.142</td>
<td>2.35±2.00</td>
</tr>
</tbody>
</table>

An independent-samples t-test conducted on the absolute uncertainties for Groups A and B/C showed a significant difference in the uncertainties (n₁=23, n₂=25, p<0.01). A similar result was also found when the t-test was conducted on the percentage uncertainties in the latency measurements for these two groups.

4. Conclusion

The accuracy of latency measurements is not usually stated in literature. Instead, a range of normal values is often used, but it is not clear from these ranges whether allowances have been made for errors inherent in the recording method, or whether the range relates only to the inter-subject physiological variation. The data presented here shows that latency measurements can be made with a degree of accuracy better than ±5%. If care is taken in skin preparation and good practice observed when using electronic equipment, then this degree of accuracy can be improved to better than ±2%.

There are a number of errors inherent in any form of measurement, and it is important to understand these potential errors so that experiments can be appropriately designed, a protocol designed to reduce variability, equipment properly used, and results correctly interpreted. Reliance on automatic latency measurement may lead to inconsistent errors, whereas an understanding of the errors can provide confidence that the results are within acceptable limits. The results presented here show that an MEP can be generated, recorded and the latency measured with an accuracy of better than 5%.

References: