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Intraoperative spinal cord monitoring using low intensity transcranial stimulation to remove post-activation depression of the H-reflex

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HIGHLIGHTS

- A spinal cord monitoring technique was tested during spinal deformity correction surgery.
- Low intensity TES removed post-activation depression of the H-reflex in 20/20 patients.
- The interaction did not diminish with time and produced minimal movement within the surgical field.

ABSTRACT

Objective: To investigate whether low intensity transcranial electrical stimulation (TES) can be used to condition post-activation depression of the H-reflex and simultaneously monitor the integrity of spinal motor pathways during spinal deformity correction surgery.
Methods: In 20 pediatric patients undergoing corrective surgery for spinal deformity, post-activation depression of the medial gastrocnemius H-reflex was initiated by delivering two pulses 50–125 ms apart, and the second H-reflex was conditioned by TES.
Results: Low intensity TES caused no visible shoulder or trunk movements during 19/20 procedures and the stimulation reduced post-activation depression of the H-reflex. The interaction was present in 20/20 patients and did not diminish throughout the surgical period. In one case, the conditioning effect was lost within minutes of the disappearance of the lower extremity motor evoked potentials.
Conclusion: Post-activation depression was used to detect the arrival of a subthreshold motor evoked potential at the lower motor neuron. The interaction produced minimal movement within the surgical field and remained stable throughout the surgical period.
Significance: This is the first use of post-activation depression during intraoperative neurophysiological monitoring to directly assess the integrity of descending spinal motor pathways.

1. Introduction

Monitoring of transcranial motor evoked potentials (MEPs) is currently the preferred technique for assessing the integrity of motor pathways during spine surgery (Kothbauer et al., 1998; MacDonald et al., 2013). The presence of an MEP represents intact motor pathways (Kothbauer et al., 1998). In 1993, Taniguchi and colleagues introduced the technique of high-frequency (300–500 Hz) multi-pulse transcranial electrical stimulation (TES) to more consistently bring lower motor neurons (LMN) to firing threshold and produce a muscle MEP. This approach helps overcome the suppressive effects of anesthesia (Erickson, 1949; Wood et al., 1988; Sloan, 1998; MacDonald et al., 2003) and has been essential to current intraoperative neurophysiological moni-

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toring (IONM) practices. Multi-pulse TES has been used to detect iatrogenic motor tract injury with the overall goal of reducing the incidence of post-operative neurological deficits. However, pre-existing neurological conditions (Langeloo et al., 2001) and the immature central nervous system of young children (Andersson and Ohlin, 1999; Erb et al., 2005) can affect the production of an MEP (Chen et al., 2007; Master et al., 2008; Sloan et al., 2008). Double trains are often used to enhance low amplitude responses (Journée et al., 2004, 2007). Likewise, complementary techniques including the use of multiple trains of TES (MacDonald et al., 2003; Tsutsui et al., 2015), afferent facilitation (Taniguchi et al., 1991; Andersson and Ohlin, 1999) and post-tetanic facilitation (Hayashi et al., 2008) have been shown to enhance the depolarization of LMN thereby augmenting leg MEPs.

As an adjunct to multi-pulse TES, intraoperative recording of the Hoffmann (H)-reflex can be used to monitor sensorimotor pathways (Leppanen et al., 1993, 1995). Reflex monitoring not only enables the assessment of a large portion of the output from the motor pool (20–100%; Leis et al., 1996), but can also be applied continuously throughout surgery with little to no disruptive patient movement (Leppanen, 2006). A change in reflex amplitude may directly signify a compromise to segmental motor pathways (reviewed in Leppanen, 2006). Reflex monitoring remains limited, however, as it only provides indirect information about pyramidal and extrapyramidal connectivity, such as during spinal shock (Calancie et al., 1993). To provide a more direct measure of descending motor function, the H-reflex can be paired with an MEP (Cowan et al., 1983, 1986; Taniguchi et al., 1991). While the spatio-temporal summation of these responses has been described as an effective way of enhancing low amplitude MEPs without increasing patient movement (Journée et al., 2007), accurate assessment of the interaction requires baseline values of the H-reflex and the MEP as well as continuous knowledge of the combined, composite response. This added complexity may have limited its clinical acceptance.

Following the production of an H-reflex, a subsequent reflex induced along the same pathway can be reduced for up to 10 s at rest (Andrews et al., 2015a; Crone and Nielsen, 1989; Pierrot-Deseilligny and Burke, 2005). This phenomenon, known as post-activation depression or homosynaptic depression, has been characterized in humans following peripheral nerve stimulation (Magladery et al., 1952; Paillard, 1955; Rothwell et al., 1986) and has been associated with changes in presynaptic inhibition (Crone and Nielsen, 1989; Schieppati, 1987) and/or changes in the amount of neurotransmitter released from the Ia terminal (Hultborn et al., 1996). Transcranial magnetic stimulation (TMS) can remove post-activation depression in awake individuals (Roy et al., 2014; Andrews et al., 2015b) and the strength of the interaction is graded as a function of the stimulus intensity. The presence of an interaction likely confirms the preservation of descending corticospinal pathways in the spinal cord. It has not yet been shown whether the interaction is preserved under general anesthesia; a condition of increased spinal inhibition. The aim of this study is first to investigate the effect of corticospinal excitation on post-activation depression under general anesthesia, and secondly, to examine the stability of this interaction during routine IONM taking place during spinal deformity correction surgery.

2. Methods

2.1. Patients

Twenty pediatric patients (three male) aged 10–17 years (mean age, 14.1 ± 0.4 years) undergoing corrective surgery for spinal deformity were recruited from a single clinical site to participate in this study. Inclusion criteria were pediatric patients with spinal deformity, requiring surgical correction with routine IONM. In 17 patients, the primary diagnosis was adolescent idiopathic scoliosis; 2 had a congenital form of scoliosis, and one was diagnosed with kyphosis. One patient with congenital scoliosis was also diagnosed with Sotos syndrome (i.e. cerebral gigantism). The rostral and caudal end vertebrae targeted for instrumentation were respectively between T2–T9 and L1–S2. Patients and/or their guardians assented/consented to the experimental protocol as approved by the Human Health Research Ethics Board at the University of Alberta.

2.2. Anesthetic regime

General anesthesia was maintained with propofol, ketamine, and remifentanil in 18 patients. Sevoflurane (0.2–0.5 MAC or minimum alveolar concentration), propofol and sufentanil was used in 2 of the patients. No muscle relaxants were used during the procedure.

2.3. Recording and stimulation

Data were collected during multimodal IONM using a Cadwell Elite neuromonitoring system (Kennewick, WA USA). For the study, MEP recordings were evaluated in the right medial gastrocnemius (MG), tibialis anterior (TA) and abductor hallucis (AH) using a pair of subdermal needle electrodes. The H-reflex was elicited in the MG following stimulation of the tibial nerve (TN) using a constant-current stimulator (Digitimer DS7A; Digitimer Ltd., Welwyn Garden City, UK) with the cathode on the popliteal fossa and the anode 4 cm more proximal (see Andrews et al., 2015b). The conditioning MEP was delivered using a constant-voltage stimulator (Digitimer D185) with a pair of bent needle electrodes placed at C1–C2. Anodal TES was provided using a train of 1–5 monophasic pulses (50 μs duration) using an interstimulus interval of 1.1 ms. The peripheral and central stimulators were triggered using custom-written MATLAB (MathWorks, Natick, MA) software. Experimental testing was performed intermittently throughout the surgical procedure.

2.4. Parameter optimization

The TES intensity was initially adjusted to elicit a muscle MEP that was conducive for routine IONM (i.e. ~275 V; 5 pulses; 1.1 ms ISI). The H-reflex intensity was adjusted to produce a response that was 50–100% of its maximum. The intensity was periodically adjusted to maximize the H-reflex/M-wave ratio. Post-activation depression was induced by two TN stimuli 100 ms apart, as this interval typically resulted in a small amount of recovery of the second H-reflex (H2; see top trace Fig. 1A; see Andrews et al., 2015b). Three steps were taken to maximize the influence of the MEP on post-activation depression. First, the delay between TES and the second TN stimulus (i.e. TES/TN delay) was varied from 0 to 20 ms (see Roy et al., 2014). Once the optimal delay was determined, the interpulse interval (IPI) of the two TN stimuli was systematically increased from 10 to 150 ms. Each condition was repeated without TES for comparison. The IPI that produced the greatest increase in H2 with TES (conditioned) relative to H2 without TES (unconditioned) was chosen and fixed for the duration of the procedure. Lastly, the number of TES pulses was varied from 0 to 5 to evaluate the strength of the effect as a function of the TES intensity. The number of TES pulses was chosen based on the presence of appreciable recovery of H2 while minimizing patient movement caused by the MEP. Note that while the H-reflex generated plantarflexion, this movement was far away from the surgical field and caused minimal interference. Patient movement refers to visible activity within or around the surgical