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Is hemifacial spasm a phenomenon of the central nervous system? – The role of desflurane on the lateral spread response

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HIGHLIGHTS

- During surgery for hemifacial spasm, the lateral spread response (LSR) is suppressed by 43% by desflurane (+total intravenous anesthesia, TIVA) compared to TIVA alone.
- During LSR acquisition neither the order of drug administration, EEG state or mean arterial blood pressure were responsible for the suppression observed with desflurane.
- These data provide direct evidence that a central mechanism of action is involved in the genesis of the LSR.

ABSTRACT

Objective: A signature EMG feature of hemifacial spasm (HFS) is the lateral spread response (LSR). Desflurane is a common anesthetic with potent effects on synaptic transmission. We tested the hypothesis that the LSR is mediated by corticobulbar components by comparing the LSR during total intravenous anesthesia (TIVA) or TIVA plus desflurane during microvascular decompression (MVD) surgery.
Methods: 22 HFS patients undergoing MVD surgery participated in this prospective study. The LSR data was recorded from the o. oculi, o. oris and mentalis muscles prior to opening dura. LSR onset latencies and amplitudes were determined under TIVA and TIVA/desflurane (0.5 and 1 MAC). Facial muscle LSRs and EEG were analyzed.
Results: Desflurane (1 MAC) significantly decreased the LSR amplitude in all 3 facial muscles ($p < 0.01$). Pooled LSR data from all facial muscles showed desflurane inhibited the LSR amplitude by 43% compared to TIVA ($p < 0.001$). No effects on the latency of the LSR or on EEG state were observed.
Conclusions: LSR inhibition by desflurane suggests a central mechanism involvement in the genesis of this signature HFS response.
Significance: This study demonstrates that facial nerve vascular compression and plastic changes within the CNS are part of the pathophysiology of HFS.

1. Introduction

Hemifacial spasm (HFS) is a unilateral, involuntary and irregular twitching of the facial muscles. HFS can be managed clinically using serial botulinum toxin (Botox) injections into the affected muscles or surgically treated with microvascular decompression (MVD) of the facial nerve. The etiology of HFS was originally suggested by Gardner and Sava (1962) and subsequently refined to include vascular (arterial or venous) compression of the facial nerve at the root entry/exit zone (Jannetta et al., 1977; Moller and Jannetta, 1985, 1986, 1987). It remains unclear how the chronic neurovascular contact can lead to a hyperactivity disorder manifested as facial twitching.

A hallmark feature of HFS is the ability to evoke the lateral spread response (LSR). The LSR occurs when electrical stimulation of one branch of the facial nerve produces an evoked electromyography (EMG) response in facial muscles innervated by a different branch of the facial nerve. By way of example, stimulation of the

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zygomatic branch of the facial nerve will result in LSR from the orbicularis oris and/or the mentalis muscles and stimulation of the mandibular branch of the nerve can generate LSR from the orbicularis oculi.

The mechanism of the LSR remains controversial but there are two competing hypotheses: (1) a peripheral hypothesis, whereby ephaptic transmission, presumably at the site of neurovascular compression produces spasms (Nielson, 1984a,b; Tankere et al., 1998; Yamashita et al., 1986); and (2) excitability changes within the facial motor nucleus causing generalized hyperactivity in the facial nerve pathways (reviewed in Moller, 1998; Kaufmann and Wilkinson, 2006). Peripheral ephaptic transmission, and contingent facial nerve de-myelination at the site of neurovascular compression, has been strongly argued as a sufficient explanation for the LSR remain indirect and inconclusive (Nielson, 1984a,b; Ravits and Hallett, 1986). For example, blink reflex R1 latencies should provide consistent evidence for a facial nerve demyelinated segment in HFS patients but there is no consensus in the literature for this (Nielson, 1984a; Eekhof et al., 1995, 2000; Montero et al., 2007).

Evidence for a central mechanism was first suggested by Moller and Jannetta (1985, 1986, 1987). It is well established that transcranial, electrically stimulated, motor evoked potentials (MEP) are mediated by corticospinal or corticobulbar pathways (Dong et al., 2005). We and others have observed, during MVD operations, the amplitude of facial motor evoked potentials (MEP) to decrease (or threshold to increase) following MVD similar to the LSR (Wilkinson and Kaufmann, 2005; Fukuda et al., 2010, 2012; Fernandez-Conejero et al., 2012). Facial MEP in HFS patients demonstrate low activation thresholds and responses to single pulse transcranial electric stimulation suggesting elevated excitability of the facial motor neuron pool and/or the motor cortex. Facial MEP activation threshold increases and the responses to single pulse stimulation decrease following MVD (Wilkinson and Kaufmann, 2014). These findings suggest altered excitability in the corticobulbar pathway of HFS patients which may help explain the mechanism of the LSR and spasm etiology.

It is well known that inhalational anesthetics, such as desflurane, act within the central nervous system to produce analgesia and amnesia. This action is likely multifactorial but a mechanism involving inhibition of synaptic transmission is certainly included (Jameson and Sloan, 2012). We reasoned that if the LSR is centrally generated then desflurane should have an inhibitory effect on this response. In this study we compared LSR during total intravenous anesthesia (TIVA) versus TIVA plus desflurane (at two concentrations) in patients undergoing MVD for relief of their HFS.

2. Methods

After approval from the institutional ethics committee, patients were recruited into this prospective study. Signed, informed consent was obtained from all the participants. In addition to our routine study protocol cranial nerve VIII monitoring was continuously performed on all patients (Kaufmann and Wilkinson, 2006).

Inclusion criteria: patients, of either sex, between 18 and 75 years, otherwise normal neurological exam and an ASA grade of 1 or 2. Exclusion criteria: existing neuromuscular disease, previous surgery with facial nerve involvement, pre-existing significant medical disease, clinically detectable facial neuropathy (House–Brackmann $\geqslant 2$) and Botox treatment <6 months prior to pre-operative evaluation.

2.1. Neurophysiology

On the patient's spasm side, facial muscle EMG was recorded with paired subdermal needles (Medtronic/Xomed, Minneapolis, MN, USA) inserted into the orbicularis oculi, orbicularis oris and mentalis muscles. Impedances were below 5 kΩ. The signals were amplified, filtered (30–3000 Hz) and displayed using a commercial neuromonitoring workstation (Cadwell Cascade; Cadwell Laboratories, Kennewick, WA, USA).

The LSR was evoked using a pulse duration of 200 μs and stimulus strength between 6 and 40 mA with electrodes positioned over the mandibular and zygomatic branches of the facial nerve. Stimuli were delivered through 2 cm adhesive disc-type electrodes (Cadwell Laboratories, Kennewick, WA, USA). Stimulation of the mandibular branch of the facial nerve evoked the LSR from the o. oculi and zygomatic stimulation produced LSR from the o. oris and/or the mentalis muscles. All LSR data for the study protocol, were obtained prior to dural opening.

A two channel EEG was monitored in all patients using 25 gauge subdermal needles (Chalgren Gilroy, CA, USA) positioned at F3 and F4 referenced to Cz. The records were amplified and displayed using a 5 s sweep and band pass filtered from 1 to 70 Hz. Digital analysis of the records was continuously performed and displayed as a density spectral array (DSA) for quantification of the EEG over time.

2.2. Anesthesia protocol

All standard monitors were applied and dependent radial artery cannulation was performed, pre-induction, in all patients. Patients were induced with a remifentanil bolus (1 μg/kg), propofol bolus (2–3 mg/kg) and depolarizing muscle relaxant succinylcholine 1.5 mg/kg) and the trachea was intubated using an appropriately sized flexometallic tube. No neuromuscular blockade was used thereafter. The restoration of neuromuscular function was assessed using the train of four methods when stimulating the mandibular branch of the facial nerve and recording the mentalis muscle M wave.

Anesthesia was maintained on propofol infusion (100–300 μg/kg/min) and remifentanil infusion (0.05–0.2 μg/kg/min). Total fresh gas flow was maintained at 2 l with 40% oxygen in air and end tidal CO_2 was maintained between 30 and 35 mm Hg. For the study period desflurane was initiated at 8% (flow increased to 8 l) to rapidly achieve 0.5 MAC and/or 1.0 MAC. Mean arterial blood pressure was kept between 70 and 90 mm Hg using phenylephrine (100 μg)/ephedrine (5–10 mg) boluses as necessary. Normothermia was maintained throughout the procedure. Following the completion of the study protocol desflurane was reduced to $\leqslant$0.5 MAC throughout the procedure. At the conclusion of surgery all infusions/desflurane were stopped, the trachea extubated and the patient transferred to the post anesthesia care unit.

2.3. Study protocol

LSR was compared under conditions of TIVA versus TIVA plus 0.5 or 1 MAC desflurane. Half the patients first received TIVA followed by the addition of desflurane to 1 MAC and the other half first received TIVA plus 1 MAC desflurane followed by TIVA alone, all prior to opening of the dura. At least 10 min was allowed for equilibration following the introduction of desflurane and often 20 or more minutes were required for the elimination of desflurane when switching to TIVA alone.

2.4. Data analysis

Individual LSR peak-to-peak amplitudes (μV) and onset latencies (ms) were averaged from 10 consecutive single sweep responses at each anesthetic condition (TIVA only versus TIVA plus desflurane (0.5 MAC and/or 1.0 MAC)). We chose to obtain LSR averages to remove the influence of response fluctuations and