

Blink synkinesis monitoring during microvascular decompression for hemifacial spasm

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Abstract

Background: In the present study, we investigated whether blink synkinesis monitoring during microvascular decompression (MVD) is effective for predicting long-term outcomes in patients with hemifacial spasm (HFS).

Methods: This retrospective study included 69 patients who had undergone MVD for HFS at a tertiary hospital. All patients underwent intraoperative monitoring of blink synkinesis, lateral spread responses (LSRs), and facial nerve motor-evoked potentials (FNMEPs). Baseline signals were compared to those obtained following decompression with Teflon, and postoperative outcomes were recorded.

Results: A total of 65 patients were observed with complete relief of symptoms after 1 year after MVD, while 61 patients were observed with initial disappearance of blink synkinesis, 57 patients were observed with initial elimination of the LSR, and 45 patients with initial decreases in FNMEP amplitude (>50%). The highest sensitivity and accuracy values were observed for blink synkinesis. Chi-square tests comparing the sensitivity of the three methods revealed that FNMEP monitoring was associated with significantly lower sensitivity values than the remaining methods. Combined use of blink synkinesis and LSRs did not significantly increase sensitivity (61/65 vs 62/65) or accuracy (62/69 vs 63/69).

Conclusion: Our results demonstrate that blink synkinesis monitoring is safe during MVD for HFS. Furthermore, blink synkinesis was associated with the highest sensitivity and predictive values among the three methods evaluated. These findings suggest that blink synkinesis can be regarded as the first choice for intraoperative monitoring during MVD. Concurrent use of blink synkinesis and LSR monitoring may maximize the ability to predict patient prognosis and determine the extent of decompression.

Keywords: Blink synkinesis; Hemifacial spasm; Intraoperative monitoring; Lateral spread response; Microvascular decompression

1. INTRODUCTION

Hemifacial spasm (HFS) is a chronic movement disorder characterized by the tonic-clonic contraction of the facial muscles, typically beginning with the orbicularis oculi and progressing to the frontalis, orbicularis oris, and platysma muscles.^{1,2} The symptoms of HFS may be aggravated by emotional changes as well as voluntary movement.³ Although HFS is nonlife-threatening, affected patients often experience social embarrassment, difficulties with social interaction, visual and verbal impairments, and poor health-related quality of life.^{4,5}

While it is widely accepted that HFS is associated with the breakdown of myelin within the facial nerve root entry zone and abnormal ephaptic transmission, the precise mechanisms underlying the development of the disorder remain unknown.⁶ Indeed,

surgical approaches during microvascular decompression (MVD) are based on this fundamental theory. Previous researchers have proposed two main pathophysiological hypotheses to explain the changes that occur following vascular compression. The peripheral theory states that ectopic impulses from the compression site induce abnormal muscle responses.⁷⁻⁹ In contrast, the central theory argues that HFS is induced by hyperexcitability of the facial nucleus and reorganization of facial nuclei or interneurons.¹⁰⁻¹² However, the precise association between facial nerve compression and central changes remains to be elucidated.

While numerous studies have demonstrated that MVD is effective in relieving such symptoms, emerging modifications have been proposed to improve outcomes and minimize complications.¹³

Electromyography studies have revealed that lateral spread of the supraorbital nerve reflex (ie, blink synkinesis) can be observed in patients with HFS. In healthy controls, the blink reflex is limited to the bilateral orbicularis oculi muscle.¹⁴ Stimulation of the supraorbital nerve, a branch of cranial nerve V, induces a trigeminal-facial inhibitory reflex that suppresses activity in the lower facial muscles.¹⁵ However, such stimulation results in abnormal synkinetic contraction of the orbicularis oculi and oris muscles in patients with HFS, which is similar to the response in lateral spread response (LSR). Møller et al demonstrated that decompression of the facial nerve leads to the

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Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2019) 82: 519-523.

Received February 22, 2019; accepted February 26, 2019.

doi: 10.1097/JCMA.000000000000106.

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resolution of both LSR and blink synkinesis, and he suggested that the mechanisms underlying this phenomenon are related to hyperexcitability of the facial nucleus.¹⁶

Currently, most evidence-based methods for intraoperative neurophysiological monitoring (IONM) during MVD are based on the LSR,¹⁷ facial nerve motor-evoked potentials (FNMEPs),¹⁸ and brainstem auditory-evoked potentials (BAEPs).^{19,20} However, the prognostic value of the LSR remains debatable due to concerns regarding false-negative and false-positive results. Although one recent study aimed to improve the efficacy of the LSR during IONM,²¹ no studies have investigated the usefulness of blink synkinesis during HFS surgery. Therefore, in the present study, we evaluated the clinical utility of blink synkinesis for intraoperative neurophysiological monitoring (IONM) during MVD for HFS, relative to that of the current monitoring methods.

2. METHODS

The present study included 69 patients with HFS who had been referred by neurologists or had directly visited the neurosurgery clinic at a tertiary hospital. The clinical characteristics of the patient population (age, gender, lesion side, duration of HFS, previous history of botulism toxin A injection, follow-up duration, offending vessels) are described in Table 1.

All patients underwent MVD with IONM. Before surgery, all patients underwent brain MRI to exclude other etiologies. Diagnoses were verified via electrophysiological analyses of the LSR and blink synkinesis, while each patient's clinical characteristics and history were recorded prior to surgery. Intraoperative neurophysiological findings and the affected arteries were recorded by the same experienced physician in all cases. Prognosis and complications were recorded during follow-up visits, during which patients provided subjective assessments of the extent of relief, which was classified as follows: complete relief, >90%; partial relief, 50% to 90%; no response, <50%. The accuracy of each monitoring method was determined based on the true positive and negative rates among all patients. The present study was approved by the local institutional review board.

2.1. Intraoperative monitoring

Blink synkinesis, LSRs, and FNMEPs were monitored and used for surgical guidance during MVD. Total intravenous anesthesia was administered throughout the course of the procedure,

Table 1
Demographic characteristic of enrolled patients

Variable	Value
Age	50.2 ± 11.6 y (28-80)
Sex	
Male	25
Female	44
HFS side	
Right	31
Left	38
Duration of HFS	4.9 ± 4.2
Follow-up period	34.8 ± 15.3
Offending vessel	
AICA	38
BA	1
PICA	13
VA	16
PICA + VA	1
Previous Botox	5 ± 9.4 times

AICA = anterior inferior cerebellar artery; BA = basilar artery; HFS = hemifacial spasm; PICA = posterior inferior cerebellar artery; VA = vertebral artery.

during which no muscle relaxants were used, with the exception of a single dose during induction. Following anesthesia, two subdermal needles were placed over the ipsilateral orbicularis oculi and mentalis for simultaneous recording of blink synkinesis responses to supraorbital nerve stimulation and LSRs to stimulation of the zygomatic and marginal mandibular branches of the facial nerve. Baseline thresholds for eliciting blink synkinesis and LSRs were defined prior to opening of the dura. Postdecompression thresholds were determined after separating the facial nerve from the offending vessel using Teflon. Disappearance of or increases in blink synkinesis or LSR thresholds were regarded as positive prognostic indicators of surgical outcomes. BAEPs and FNMEPs were elicited via C5 or C6/Cz montage for additional intraoperative monitoring, in accordance with standard procedures. FNMEP amplitude was defined as the difference between the peak positive and negative values of the waveform. Decreased amplitude was defined as a >50% reduction in the mentalis muscle.

A Cadwell Cascade workstation was used for intraoperative monitoring. Electrical stimulation for blink synkinesis and LSRs was applied as square-wave pulses (intensity: beginning at 1 mA and increasing thereafter; duration: 0.1 ms; cathode proximal), and all electromyographic recordings were bandpass-filtered from 10 Hz to 5 kHz (gain: 200 mV/division; duration of analysis: 50 ms).

2.2. Statistical analysis

Statistical analyses were performed using SPSS (Version 23, IBM Corporation, Armonk, NY). The level of statistical significance was set at $p < 0.05$. Demographic characteristics were summarized using descriptive statistics. Continuous variables are presented as the mean ± SD. Chi-square tests were used to compare sensitivity among the various monitoring methods. Spearman's correlation analyses were used to evaluate the correlation between individual IONM methods and related factors (age, gender, duration since onset).

3. RESULTS

Table 2 lists the postoperative outcome at 1 week, 3 months, and 1 year after the surgery according to the results of each intraoperative monitoring method. At 1 year after MVD, disappearance of blink synkinesis was observed in 61 patients, elimination of the LSR was observed in 53 patients, and decreases in FNMEP amplitude (>50%) were observed in 37 patients. The number of patients with complete response increased over time in all groups.

Table 3 presents a comparison of relief rates at different stages of follow-up for patients with initial disappearance of blink synkinesis/LSR or decreased FNMEP amplitude during surgery. Relief rates increased over time, and the final relief rate was approximately 95% at the 1-year follow-up.

The sensitivity, specificity, positive and negative predictive values, and accuracy of each IONM method are listed in Table 4. The highest sensitivity and accuracy values were observed for blink synkinesis. Chi-square tests comparing the sensitivity of the three methods revealed that FNMEP monitoring was associated with significantly lower sensitivity values than the remaining methods. We then examined whether combined use of blink synkinesis/LSR could improve these results (Tables 3 and 4); however, no significant increases in sensitivity (61/65 vs 62/65) or accuracy (62/69 vs 63/69) were observed.

Correlations between each pair of IONM methods were as follows: MEP and LSR ($r = 0.842$, $p = 0.024$); MEP and blink synkinesis ($r = 0.18$, $p = 0.14$); blink synkinesis and LSR ($r = 0.556$, $p < 0.001$). No significant correlations were observed between any method and the duration of onset, age, or gender.

Table 2**Clinical outcome according to IONM results after MVD at 1 week, 3 months, and 1 year**

	1 week			3 months			1 year		
	CR	PR (50%-90%)	NR (<50%)	CR	PR (50%-90%)	NR (<50%)	CR	PR (50%-90%)	NR (<50%)
BS									
-	49	13	2	58	4	2	61	1	2
+	4	0	1	4	0	1	4	0	1
LSR									
-	46	12	2	54	4	2	57	1	2
+	7	1	1	8	0	1	8	0	1
FNMEP									
-	36	10	2	43	3	2	45	1	2
+	17	3	1	19	1	1	20	0	1

BS = blink synkinesis; CR = complete relief; FNMEP = facial nerve motor-evoked potential; IONM = intraoperative neurophysiological monitoring; LSR = lateral spread response; MVD = microvascular decompression; NR = no response; PR = partial relief.

Among all 69 patients, four reported transient hearing impairment (5.8%), three reported permanent hearing loss (4.3%), and two reported transient dizziness (2.9%). No cases of infection, bleeding, cerebrospinal fluid (CSF) leakage, or death were observed.

4. DISCUSSION

In the present study, we compared the usefulness of blink synkinesis monitoring during MVD for HFS with that of the currently used methods. While our findings demonstrated that IONM of blink synkinesis is both sensitive and safe, we observed no significant differences in the prognostic value of the three IONM methods.

Blink synkinesis and LSRs exhibited higher sensitivity and accuracy values than FNMEPs, which may be explained by the potential mechanisms underlying HFS. Previous studies have suggested that HFS is associated with hyperactivity of the facial muscles and/or ephaptic transmission to other branches of the facial nerve. FNMEPs are used to monitor the integrity of the motor cortex, corticobulbar tract, facial nucleus, and facial nerve.²² Blink synkinesis involves a polysynaptic pathway that receives afferent input from the supraorbital nerve, projections from the trigeminal nucleus to the facial nerve, and the induction of motor responses in the orbicularis oculi muscle.¹⁴ In contrast, LSRs rely on cross-transmission among the different branches of the facial nerve.

Unlike other IONM methods, FNMEPs are associated with several neuroanatomical pathways involving the motor cortex. Our findings support the notion that HFS-related abnormalities can be observed in various anatomical regions of the cortex. One previous resting-state functional MRI study revealed that HFS is associated with hyperexcitability of the facial nucleus and motor cortex, as well as dysfunction of the facial motor inhibitory cortex.²³ The involvement of multiple areas may explain the poor

sensitivity of FNMEPs. However, it remains unclear whether successful MVD results in normalization of these phenomena.

Although we observed similar sensitivity and accuracy values for blink synkinesis and LSRs, slightly better results were observed for blink synkinesis monitoring. This finding is in accordance with the stronger correlation observed between blink synkinesis and LSRs than between FNMEPs and LSRs, indicating that the mechanisms underlying blink synkinesis and LSRs may be similar in patients with HFS. A recent pilot study investigating the origin of HFS used diazepam to suppress the facial motor nucleus, but was unable to exclude either the central or peripheral hypothesis when examining blink synkinesis. However, their results suggested that the LSR is more likely to be associated with a peripheral origin.²⁴ Given a central origin specific to the facial nucleus, blink synkinesis responses involving the facial nucleus should be similar to those for FNMEPs. However, in the present study, we observed no correlation between FNMEPs and blink synkinesis.

Although we observed slightly better results for blink synkinesis than for LSRs, the reason for this difference is not fully understood. Theoretically, the disappearance of the LSR reflects peripheral changes, while the disappearance of blink synkinesis suggests either peripheral or central changes. However, studies regarding the mechanisms underlying HFS remain inconclusive, and each potential mechanism is not universally applicable to individual methods of evaluation. Hence, it is not surprising that discrepant results among the three IONM methods were observed in the same patient. These findings suggest that HFS may be associated with heterogeneous peripheral and central mechanisms in each patient. As changes in either peripheral or central components may explain blink synkinesis responses, these responses may be slightly more sensitive than LSRs.

One may debate the usefulness of blink synkinesis for INOM during HFS surgery. However, it is not always easy to identify the zygomatic branch of the facial nerve for stimulation of LSR in the operating room. The use of blink synkinesis does not

Table 3**Comparison of MVD outcomes in patients with initial disappearance of BS/LSR or improvements in FNMEP during IONM**

	1 week			3 months			1 year		
	HFS (-)	HFS (+)	Relief rate	HFS (-)	HFS (+)	Relief rate	HFS (-)	HFS (+)	Relief rate
BS	49	15	76.6	58	6	90.6	61	3	95.3
LSR	46	14	76.7	54	6	90.0	57	3	95.0
FNMEP	36	12	75	43	5	89.6	45	3	93.8
BS + LSR	50	15	76.9	59	6	90.8	62	3	95.4

BS = blink synkinesis; FNMEP = facial nerve motor-evoked potential; HFS = hemifacial spasm; IONM = intraoperative neurophysiological monitoring; LSR = lateral spread response; MVD = microvascular decompression.

Table 4**Comparison of sensitivity, specificity, and predictive values among the three monitoring methods**

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
BS	61/65	¼	61/64	1/5	62/69
LSR	57/65	¼	57/60	1/9	59/69
FNMEP	45/65	¼	45/48	1/21	46/69
BS + LSR	62/65	¼	62/65	1/4	63/69

BS = blink synkinesis; FNMEP = facial nerve motor-evoked potential; LSR = lateral spread response.

require localization of the nerve via stimulation, as the supra-orbital notch can be palpated to access the supraorbital nerve, which may also decrease the duration of the procedure.

We aimed to determine whether interindividual differences in IONM results were associated with long-term outcomes. However, no significant differences were observed. Similarly, previous studies that have examined correlations between IONM changes and long-term outcomes have reported controversial results. Some authors have suggested that the persistence of LSRs or absence of FNMEP changes is correlated with poor long-term outcomes. However, further studies involving larger sample sizes have questioned the utility of IONM for determining long-term outcomes of HFS surgery.²⁵ Indeed, it remains difficult to discriminate delayed signal changes (false negative) and the persistence of symptoms despite signal changes (false positive), as the latter is not always indicative of incomplete or failed surgery.^{26,27} Moreover, persistent symptoms are not always correlated with the duration of onset to symptom relief after surgery. Rather, delayed recovery may be related to the delayed normalization of central hyperexcitability.^{28,29} However, no studies have examined neurophysiological patterns in patients with initially unchanged IONM and delayed resolution of clinical symptoms. Future studies should evaluate such patients in order to develop more accurate methods of predicting long-term prognosis and determine the usefulness of IONM in this population.

Because we suspected that HFS may be associated with both central and peripheral mechanisms, we evaluated the combined use of blink synkinesis and LSRs (Tables 3 and 4). Although we observed no significant differences between combined use of blink synkinesis/LSRs and individual application of blink synkinesis or LSRs, the concurrent use of the two methods may cover different mechanisms in each patient, providing greater confidence during surgery. However, given the complexity and sensitivity of these techniques, blink synkinesis may represent the superior choice if only one IONM method can be used.

A previous study by Wei et al reported no significant differences in MVD outcomes between patients treated with and without IONM.²⁵ While similar clinical outcomes were observed for blink synkinesis monitoring in the present study, IONM is still recommended when available. IONM not only provides an indicator of successful decompression based on signal changes but can also act as a warning sign of insufficient decompression.^{25,30} Although further exploration may be warranted in some cases, surgeons should not pursue the elimination of blink synkinesis, LSRs, or decreases in FNMEP amplitude in patients with complete decompression, as persistent neurophysiological abnormalities are not always correlated with poor prognosis. Future studies should aim to determine the role of central hyperexcitability in HFS, which may help to determine the appropriate IONM protocol.

Our results are in accordance with those of the previous studies, which have reported sensitivity values ranging from 42% to 94% for LSRs.³¹ However, such studies failed to compare these values among different methods in individual patients. Our study is advantageous in that we have compared the sensitivity and predictive value of three IONMs for MVD, observing that sensitivity, positive predictive value, and accuracy were greater

for blink synkinesis than for other methods. Such findings suggest that blink synkinesis may be the most sensitive and easily reversible neurophysiological parameter during MVD.

The present study possesses several limitations of note, including its retrospective design and small sample size, thus selection and recall bias are possible concerns. Moreover, the IONM was performed before and after MVD, rather than during each procedure (eg, CSF drainage or arachnoid membrane dissection). Thus, we were unable to determine whether individual steps of the procedure influence clinical outcomes.

In conclusion, based on the available neurophysiological evidence, our results demonstrate that blink synkinesis monitoring is safe during MVD for HFS. Furthermore, blink synkinesis was associated with the highest sensitivity and predictive values among the three methods evaluated. These findings suggest that blink synkinesis can be regarded as the first choice for IONM during MVD. Concurrent use of blink synkinesis and LSR monitoring may maximize the ability to predict patient prognosis.

ACKNOWLEDGMENTS

This study was supported by a grant from Taipei Veterans General hospital (V107C-006).

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