Journal of Neuroscience Methods 405 (2024) 110096

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Short communication

A novel method of neurophysiological brainstem mapping in neurosurgery

Enrica Fava [a,*], Davide Colistra [b], Maria Fragale [b], Marco Cenzato [b]

[a] Department of Neurosurgery, Great Metropolitan Hospital of Niguarda, University of Milano, Italy
[b] Department of Neurosurgery, Great Metropolitan Hospital of Niguarda, Milano, Italy

ARTICLE INFO

Keywords:
Intraoperative neurophysiology
Brainstem mapping
Cranial nerve
Corticospinal pathway
Corticobulbar pathway
Tongue

ABSTRACT

Background: Brainstem mapping with electrical stimulation allows functional identification of neural structures during resection of deep lesions. Single pulses or train of pulses are delivered to map cranial nerves and corticospinal tracts, respectively.
New method: We introduce a hybrid stimulation technique for mapping the brainstem. The stimulus consists of an electrical single pulse followed by a short train of 3–5 pulses at 500 Hz, at an interval of 60-75 ms. The responses to this stimulation pattern are recorded from appropriate cranial and limb muscles.
Results: Both the single pulse and the short train elicit electromyographic responses when motor fibers or motor nuclei of the cranial nerves are stimulated. Responses to the train but not to the preceding single pulse indicate activation of the descending motor tracts, in the mesencephalon and the pons. Conversely, in the medulla, limb responses to stimulation of the corticospinal tracts are elicited by a single pulse. Identification of the extra and intra-axial courses of the trigeminal motor and sensory fibers is possible by recording responses from the masseter and the tongue muscles.
Comparison with existing method(s): To date, either a pulse or a train is delivered during brainstem mapping, switching from one to the other modality according to the expected target structure. This procedure can be time-consuming and may even lead to false negative responses to the stimulation, eventually leading to inaccurate neurosurgical procedures.
Conclusions: The novel hybrid pulse-train technique enhances the advantage of brainstem mapping procedure, minimizing pitfalls and improving patient safety.

1. Introduction

The brainstem controls many vital functions, critical for survival and subserve higher integrative functions, not fully unveiled. Surgery in this crowded anatomical region, connecting the forebrain to the spinal cord, requires great attention from the neurosurgeon. Intraoperative neurophysiology has been extensively applied to assist brainstem surgery, mostly as a monitoring procedure, with continuous recording of sensory and motor evoked responses, and of electromyography from the muscles targeted by the motor cranial nerves. Neurophysiological monitoring allows recording of signals running in the ascending somatosensory system and in the descending corticospinal and corticobulbar pathways and can track a few of the countless reflex pathways involving the cranial nerves.

A valuable addition to monitoring is neurophysiological brainstem mapping, a procedure requiring direct electrical stimulation of the brainstem to identify the safest entry zone to resect intra-axial lesions. Earliest studies had focused on the mapping of the floor of the fourth ventricle, and of the corticomotor fibers in the cerebral peduncles (Deletis et al., 2000; Katsuta, 1993; Sala et al., 2007; Strauss et al., 1993; Tanaka et al., 2007). Recently, corticospinal tract mapping within the lower brainstem was reported by Li et al. (2018) and by Yang et al. (2022). Yang et al. (2022) additionally studied the relationship between the stimulation intensity and the distance of the stimulated site from the Corticospinal Tract (CST), as assessed by postoperative Diffusion Tensor Imaging and Tractography. In all these studies, direct electrical stimulation was applied by a handheld probe delivering either single pulses or short train of pulses.

In our study, we introduced a hybrid stimulation strategy, that combined both one single pulse and one short train of 3–5 pulses of the same intensity. This stimulation modality was adopted in a series of patients operated for brainstem cavernous malformations (BSCM), that usually displace neural structures around them, allowing the neurosurgeon a narrow safe corridor to reach the lesion. Our hypothesis was that

* Correspondence to: Dept.of Neurosurgery, Great Metropolitan Hospital of Niguarda, Piazza Ospedale Maggiore, 3, Milano 20162, Italy.
E-mail address: enrica.fava@gmail.com (E. Fava).

https://doi.org/10.1016/j.jneumeth.2024.110096
Received 29 September 2023; Received in revised form 3 February 2024; Accepted 22 February 2024
Available online 28 February 2024

the pulse-train stimulation strategy could identify both the cranial nerve fibers or nuclei and the descending motor tracts, eliciting structure-specific patterns of muscle responses.

2. Materials and methods

This study included 31 patients undergoing resection of Brainstem Cavernous Malformations (BSCM), at the Neurosurgical Unit of the Niguarda Hospital (Milano Italy) with intraoperative neurophysiological monitoring (ION) and brainstem mapping, in the last two years. According to the anatomical site, 14 lesions were thalamo-mesencephalic (*mes*), 12 were pontine (*pons*) and 5 medullary (*med*). All patients had had at least one haemorrhagic episode prior to surgery.

All surgeries were performed under general anaesthesia, with propofol and remifentanil, by the same senior neurosurgeon. No muscle relaxants were delivered after intubation. All patients were operated on either in the prone or lateral positions. Two systems were used for ION: NIM-Eclipse (Medtronic, USA) and ISIS Xpert IOM System (Inomed, Germany). Conventional ION monitoring procedures were adopted in all cases, by recording four limbs somatosensory evoked potentials and transcranial motor evoked potentials, transcranial corticobulbar motor evoked potentials, auditory brainstem responses, electroencephalography, free running electromyography and blink reflex.

Neurophysiological brainstem mapping was performed by a monopolar handheld probe (1.6 mm diameter; Spes Medica, Italy), delivering the pulse-train stimulation pattern, including first one single pulse (0.1–0.2–0.5 ms duration) then, after an interval of 60–75 ms, a short train of 3–5 pulses, at 500 Hz. A corkscrew reference electrode for the monopolar probe was inserted in the scalp, on the midline halfway between the vertex and the inion. In Fig. 1, top, a sketch of the stimulation pattern is drawn. Stimulus duration and current intensity were always the same for the single pulse and the train. The current intensity ranged from 0.2 to 8 mA. Stimulation started at 0.2 mA and gradually increased until a positive response was obtained to either the single pulse or the train, or the value of 8 mA was attained. The intensity of 8 mA was required only in one patient operated for a pontine BSCM where stimulus duration was 0.1 ms. No adverse effects were recorded.

Kodama et al. (2022) reported stimulation intensities from 13 to 20 mA while mapping the Corticospinal Tract from the ventral pons in a patient with BSCM. Li et al. (2018) reported intensities 1–10 mA in brainstem mapping, with a train of five pulses of 0.2 ms duration.

Muscle responses were recorded by subdermal needle electrodes from distal limb muscles (Abductor Pollicis Brevis, APB, in the hand and Abductor Hallucis, AH, in the foot) and multiple cranial muscles: Orbicularis Oculi, Orbicularis Oris, Mentalis, Masseter, Temporal, Tongue (right and left sides). Surface electrodes integrated in the endotracheal tube recorded responses from the vocal folds.

The muscle responses to neurophysiological mapping were classified as Compound Muscle Action Potentials (CMAP) when the motor fibers of the cranial nerve were stimulated, and as probe-MEP when limb responses were evoked by the pulse-train stimulation delivered by the probe. From the tongue muscles, in addition to CMAP and probe-MEP, also long-latency responses (t-LLR) were recorded (Pescador et al., 2022; Sarnthein et al., 2022; Szelényi and Fava, 2022).

The surgical strategy was affected by brainstem mapping in the search of a safe entry zone, both in telovelar and lateral surgical approaches. At the end of the surgeries, stimulations were applied by the monopolar probe within the resection cavity, to check the proximity to the descending motor tracts, cranial nerve nuclei and fibers.

The study was approved by the ethics committee of Niguarda Hospital (710–14122020).

3. Results

The workflow of brainstem mapping was different according to the site of the BSCM and the surgical approach to the lesions: telovelar approaches required firstly mapping of the floor of the fourth ventricle, then depth stimulation was applied, after lesion resection; in the lateral brainstem approaches, the neurosurgeon first sought responses after stimulation of the cranial nerve roots, then applied direct brainstem stimulation, to track the intra-axial cranial nerve fibers, the motor nuclei and the descending motor tracts. Last, deep stimulation was applied after lesion resection. In the *mes* lesions, 10/14 patients received either mapping of the floor of the 4th ventricle (2 cases) or direct brainstem stimulation in the remaining 8 cases, operated with a lateral approach. In four patients no neurophysiological mapping was applied.

In the *pons* lesions, 12/12 patients received either mapping of the floor of the 4th ventricle (4 cases) or antero-lateral brainstem stimulation in the remaining 8 cases, operated with a lateral approach. In the *med* lesions, brainstem mapping was applied only in 3/5 patients.

The standard method for brainstem mapping adopts either a single pulse while mapping of the floor of the fourth ventricle (see Morota

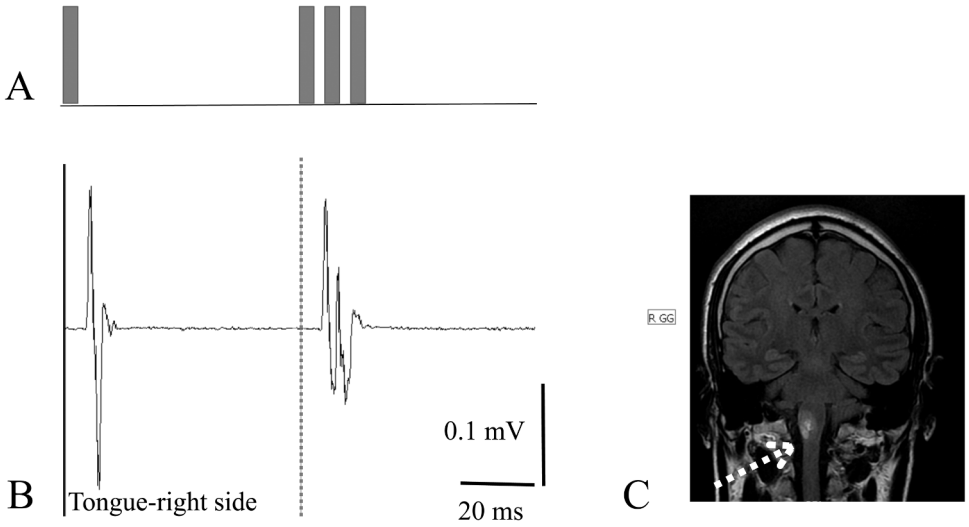

Fig. 1. Intra-axial probe stimulation of the right hypoglossal nucleus in a patient operated for a medullary BSCM. A: the pulse-train stimulation pattern. Stimulus duration 0.1 ms, 75 ms between the single pulse and the train of three pulses, at 500 Hz. B: the muscle responses (CMAP) recorded from the right side of the tongue to both the single pulse and the train. The vertical grey line marks the single pulse onset. The vertical dotted line marks the train onset. Onset latency of the CMAP is 6.7 ms after the single pulse. C: Coronal T2 FLAIR MRI showing the lesion. The white arrow points to the right medullary stimulation site.

et al., 2023 for a review), or a train of pulses when tracking the corticomotor tracts (Sala et al., 2007, 2015; Tanaka et al., 2007). The neurophysiologist in charge of delivering the stimulation to the probe held by the neurosurgeon must choose the correct stimulus modality to avoid false negatives, as expected in case a single pulse were delivered with the goal to map the corticospinal tracts. In our study, we joined the two types of stimulation, by delivering them in a sequence, called pulse-train paradigm.

The muscle responses evoked by the pulse-train paradigm fell into four categories:

1. *CMAPs to stimulation of the motor cranial nerve fibers and nuclei*, appearing after single pulse and after train stimulation in all patients operated for lesion within the pons and the medulla, as illustrated in Fig. 1 for intramedullary stimulation of the right hypoglossal nucleus. With subthreshold stimulation intensity, train stimulation only evoked CMAPs, as shown in Fig. 2 (A, top trace) for stimulation of the motor fibers in the right trigeminal root. CMAPs were evoked from stimulation of the extra and intra-axial cranial nerve fibers (Fig. 2 A and B, top traces) and from the motor nuclei (Fig. 1).

2 A. *Mesencephalic and pontine probe-MEPs,* evoked only by train stimulation and never by a single pulse (Fig. 3, A and B). Mesencephalic probe-MEPs showed mean latencies of 22.9 ms for the APB (range 15.2–26.6), 42.5 ms for the AH (range 35.1–48.29), 13.4 ms for the Mentalis (range 8.5–16.6) and 13.8 ms (range 9.2–16.4) for the Tongue muscles. Pontine probe-MEPs showed mean latencies of 22.1 ms for the APB (range 21.2–23.2), 38.8 ms for the AH (range 34.7–47.5); 10.2 ms for the Mentalis (range 9.8–10.6) and 10 ms in the only patients showing probe-MEP from the Tongue muscles.

2B. *Medullary limb probe-MEPs,* obtained in all patients in whom probe mapping was achieved (3/5). In all three cases limb MEPs could be obtained with either the single pulse and the train or the single pulse only (Fig. 4). Both ipsilateral and contralateral probe-MEPs were recorded in one patient. Medullary probe MEPs showed mean latencies of 21.2 ms for the APB (range 19–22.8), 41.1 ms for the AH (range 38–42.2).

3. *Long-latency tongue responses (t-LLRs)*, recorded from the tongue after stimulation of the trigeminal root and of the intra-axial trigeminal sensory fibers (Fig. 2 A and 2 C, bottom traces). At lower intensities only train evoked t-LLR, while at higher intensities both single pulse and train proved effective.

4. Discussion

Brainstem Cavernous Malformations (BSCMs) represent challenging lesions due to the complex anatomy of the brainstem and the unpredictable displacement of densely packed peri-lesional neural systems. The high concentration of eloquent structures within the space of a thumb (Rushmore et al., 2020) makes the resection of BSCMs at high risk of peri-operative morbidity. The arsenal of tools of the intraoperative neurophysiology can reduce the intra-operative morbidity, and the technique of neurophysiological brainstem mapping was developed to allow the identification of the eloquent structures most closely related to the surgical field, as cranial nerve fibers, nuclei and descending motor fibers. Brainstem mapping started in 1993 with electrical stimulation of the floor of the fourth ventricle and recording the electromyographic responses of the facial muscles (Katsuta et al., 1993) and of the facial and tongue muscles (Strauss et al., 1993) to identify the facial nerve fibers and the hypoglossal nuclei in the rhomboid fossa in patients with intrinsic brainstem lesions. These Authors applied single pulse stimulation. Direct stimulation was then applied to the cerebral peduncles, to identify the descending motor fibers of the Corticospinal Tract (CST), with single pulses and direct recording of the D-wave from the spinal

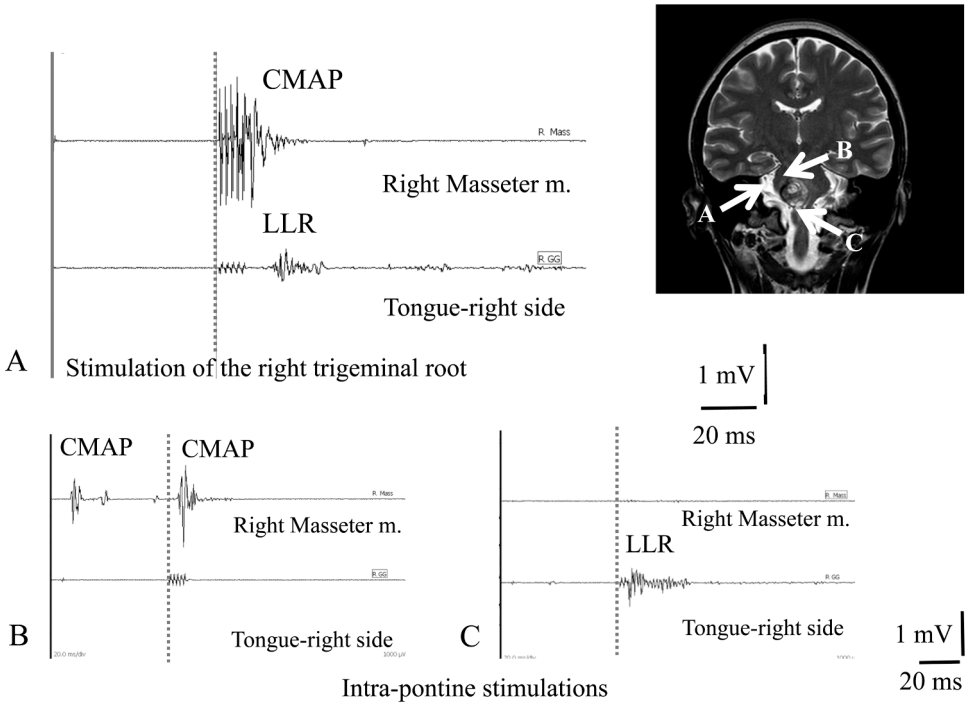

Fig. 2. Probe stimulation of the trigeminal fibers in a patient operated for a pontine BSCM. Pulse-train stimulation, 60 ms between the single pulse and the train of five pulses. The vertical grey line marks the single pulse onset.The vertical dotted lines marks the train onset. On the right:T2W-TSE MRI. The white arrows point to the stimulation sites. A: Left. Extra-axial stimulation of the sensory and motor fibers in the trigeminal root, 0.9 mA. The Masseter motor response (CMAP, top) is evoked by the train and not by the single pulse, due to low intensity, subthreshold stimulation. The ipsilateral long-latency tongue response (LLR, bottom) to the sensory fibers is simultaneously elicited by the train, with a latency of 18 ms. The onset of the Masseter muscle response overlaps the train stimulus artefact. B and C: Intra-axial stimulations of the trigeminal fibers, at different sites, 2.5 mA. In B the motor fibers and in C the sensory fibers were separately met by the probe, that elicited a double CMAP at 5 ms latency from the Masseter muscle (B, top; in the bottom trace only the stimulus artefact is visible), and a tongue long-latency response (C, bottom), only to train, with a shorter latency than in A, due to more proximal stimulation, and partially overlapping the train stimulus artefact.

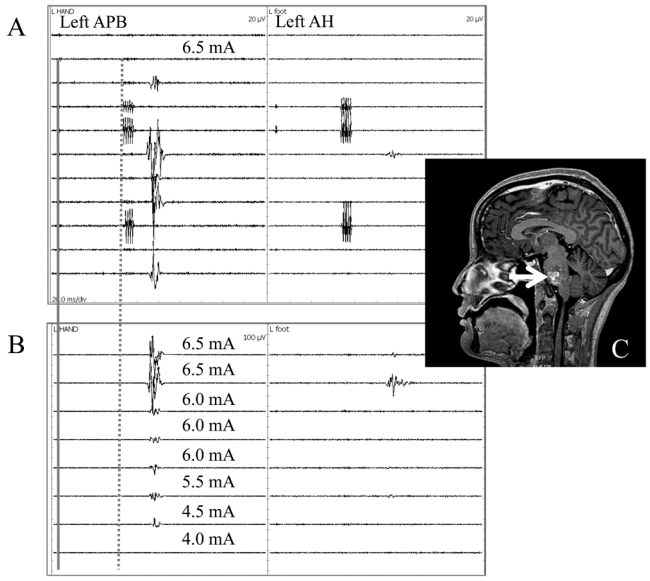

Fig. 3. Same patient as in Fig. 2, pontine BSCM. Probe mapping on the ventral pons, at level of the right trigeminal root, before incision. A single pulse (grey line) is followed by a train of five pulses (dotted grey line). Train stimulus artefact is visible only when the probe isn't in contact with the pons. Stimulation intensities are reported. Probe-MEPs are evoked from the right corticospinal tract and are recorded in the contralateral hand (APB) and foot (AH) muscles, only by train stimulation. A minimum intensity of 4.5 mA is required. A.The neurosurgeon is stimulating on different spots, with a fixed intensity of 6.5 mA. B.In the best spot, stimulation intensity is reduced from 6.5 to 4.0 mA. Threshold intensity is 4.5 mA. C. MRI showing the stimulated site (white arrow).

cord (Deletis et al., 2000), or with trains of pulses and recording of muscle MEPs (Sala et al., 2007). Tanaka et al. (2007) first applied train stimulation to the surface of the brainstem to get continuous limb MEPs during posterior fossa surgery. Brainstem mapping within the pons and the medulla is a recent advance (Li et al., 2018; Yang et al., 2022), mostly aimed to identification of the corticospinal tracts.

Brainstem mapping started as a method to identify a safe entry zone and developed into a method to guide the neurosurgeon throughout the resection of intra-axial lesions, even affecting the surgical strategy, when sites positive to mapping are encountered. Electrical stimulation was adapted to the surgical needs, with the goal of identifying more and more complex structures, as the corticospinal and corticobulbar tracts. Under anaesthesia, a train of stimuli is required to elicit muscle responses from polysynaptic neural pathways, including the descending motor tracts and reflex circuits. Deletis et al. (2009) demonstrated that a train of stimuli is needed to elicit the early response of the blink reflex, R1, to monitor the trigemino-facial circuit in the pontine region during surgery. In brainstem mapping, cranial nerves fibers and descending motor tracts can be stimulated in a narrow space, with differential propensity to respond to either a single pulse or to short trains of pulses. At threshold intensity, the cranial motor nuclei and fibers are stimulated by both single pulses and by trains. We noted that at subthreshold stimulation intensity, the train modality is more effective than single pulse for trigeminal motor fibers (see Fig. 2A), as already reported by Tellez et al. (2016), in the peripheral facial nerve. If we pay attention also to responses of the tongue muscles while stimulating the peritrigeminal pontine region, we can record long latency responses, evoked by a single pulse or a train of pulses hitting the intracranial trigeminal sensory fibers, as demonstrated by Szelényi and Fava (2022) and Pescador et al. (2022). Selective identification of motor and sensory trigeminal fibers is then possible by recording CMAPs from the masticatory muscles and t-LLR from the tongue muscles, and this was obtained from both extra- and intra-axial stimulations (Fig. 2).

The peritrigeminal pontine region is a frequent site of BSCMs (Catapano et al., 2022) and mapping is mandatory to identify a safe entry zone. The corticomotor tracts run a few millimeters anterior to the trigeminal root fibers. They were identified in all our patients by train stimulation. Even with suprathreshold stimulus intensity, we never got

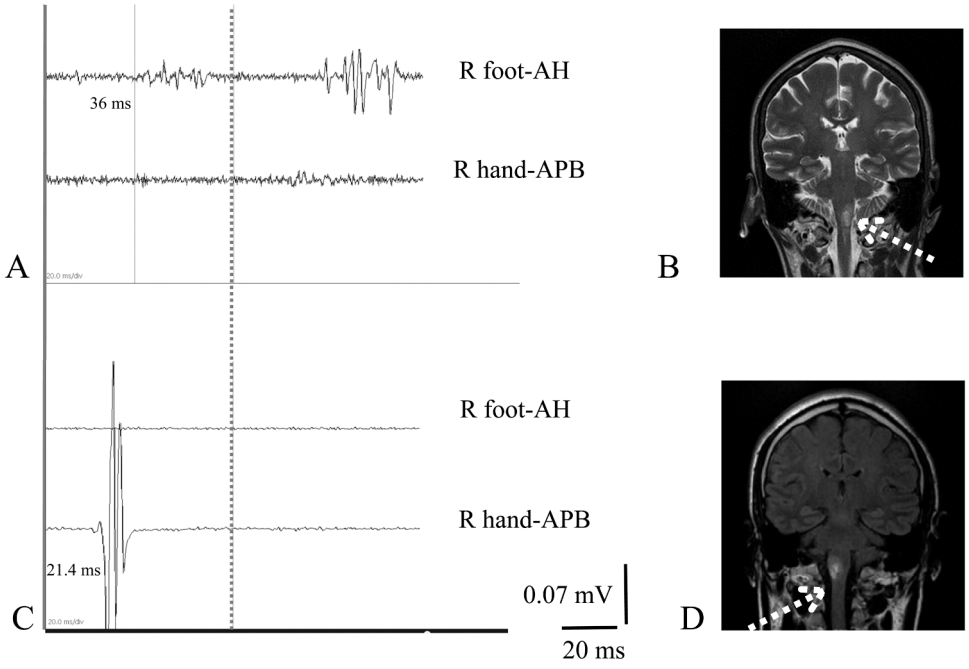

Fig. 4. Probe-MEPs from stimulation of the corticospinal tracts in the medulla, in two patients. A single pulse (grey line) is followed by a train of pulses (dashed grey line). A: Left lateral medullary stimulation, 3.9 mA, 0.2 pulse duration. A double probe- MEP is evoked on the R foot by both the single pulse (left, latency 36 ms) and the train of pulses (right). B: T2 MRI showing the left medullary BSCM. The white arrow points to the stimulation site. C: Right antero-lateral stimulation, 6 mA, 0.1 ms pulse duration. A probe-MEP is evoked on the right hand (APB) by the single pulse only (left, latency 21.4 ms). Same patient as in Fig. 1. D: T2 FLAIR MRI showing the right medullary BSCM. The white arrow points to the stimulation site.

probe-MEPs after single pulse stimulation, as illustrated in Fig. 3.

Limb probe-MEPs to a single pulse were indeed recorded in 3/3 patients when the medulla was stimulated, as if a higher excitability of the corticospinal tract were present in the medullary region. In the paper by Yang et al. (2022), probe-MEPs to a single pulse were obtained by stimulation in the medullary region, on the floor of the fourth ventricle, in four patients operated for brainstem neoplasms. This result deserves further research.

5. Conclusion

In this series of patients operated for BSCM with neurophysiological mapping and monitoring, we demonstrated that the pulse-train technique of stimulation can extend the yield of brainstem mapping. It is mandatory that a high number of muscle channels are recorded, including bilateral tongue muscles and distal limb muscles. The different patterns of muscle responses must be critically interpreted according to the surgical anatomy and the stimulation sites. We suggest that our hybrid stimulation strategy can also minimize the technical pitfalls, that may lead to a falsely negative mapping due to an inadequate stimulation modality.

6. Limitations

In this study, brainstem neurophysiological mapping guided the surgeon in the search of a safe entry zone. The stimulations applied in the depth after resection were retrospectively reviewed. No fiber tractography was obtained. A small number of patients were studied.

Funding

This work was supported by the University of Milano, Italy, PSR2021-C to EF.

CRediT authorship contribution statement

Enrica Fava: Writing – original draft, Methodology, Conceptualization. **Marco Cenzato:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Investigation. **Davide Colistra:** Writing – review & editing, Supervision, Project administration, Investigation. **Maria Fragale:** Writing – review & editing, Project administration, Investigation, Conceptualization.

Declaration of Competing Interest

None.

Data availability

Data will be made available on request.

Acknowledgments

We would like to thank the operating theater staff for their excellent cooperation.

References

Catapano, J.S., Rumalla, K., Srinivasan, V.M., Lawrence, P.M., Keil, K.L., Lawton, M.T., 2022. A taxonomy for brainstem cavernous malformations: subtypes of pontine lesions. Part 1: basilar, peritrigeminal, and middle peduncular. J. Neurosurg. 137 (5), 1462–1476. https://doi.org/10.3171/2022.1.JNS212690.

Deletis, V., Sala, F., Morota, N., 2000. Intraoperative neurophysiological monitoring and mapping during brain stem surgery: a modern approach. Oper. Tech. Neurosurg. 3 (2), 109–113. https://doi.org/10.1053/oy.2000.6562.

Deletis, V., Urriza, J., Ulkatan, S., Fernandez-Conejero, I., Lesser, J., Misita, D., 2009. The feasibility of recording blink reflexes under general anesthesia. Muscle Nerve: Off. J. Am. Assoc. Electrodiagn. Med. 39 (5), 642–646. https://doi.org/10.1002/mus.21257.

Katsuta, T., 1993. Physiological localization of the facial colliculus during direct surgery on an intrinsic brain stem lesion. Neurosurgery 32 (5), 861–863.

Kodama, K., Kothbauer, K.F., Deletis, V., 2022. Mapping and monitoring of brainstem surgery. Handbook of Clinical Neurology, 186. Elsevier, pp. 151–161.

Li, Z., Wang, M., Zhang, L., Fan, X., Tao, X., Qi, L., Ling, M., Xiao, X., Wu, Y., Guo, D., et al., 2018. Neuronavigation-guided corticospinal tract mapping in brainstem tumor surgery: better preservation of motor function. World Neurosurg. 116, e291–e297. https://doi.org/10.1016/j.wneu.2018.04.189.

Morota, N., Deletis, V., 2023. Brainstem Surgery: Functional Surgical Anatomy with the Use of an Advanced Modern Intraoperative Neurophysiological Procedure. In: Advances and technical standards in Neurosurgery, Vol. 48. Springer Nature,, pp. 21–55.

Pescador, A.M., Téllez, M.J., Sánchez Roldán, M. de los Á., Samusyte, G., Lawson, E.C., Coelho, P., Lejarde, A., Rathore, A., Le, D., Ulkatan, S., 2022. Methodology for eliciting the brainstem trigeminal-hypoglossal reflex in humans under general anesthesia. Clin. Neurophysiol. 137, 1–10. https://doi.org/10.1016/j.clinph.2022.02.004.

Rushmore, R.J., Wilson-Braun, P., Papadimitriou, G., Ng, I., Rathi, Y., Zhang, F., O'Donnell, L.J., Kubicki, M., Bouix, S., Yeterian, E., et al., 2020. 3D exploration of the brainstem in 50-micron resolution MRI. Front. Neuroanat. 14, 40. https://doi.org/10.3389/fnana.2020.00040.

Sala, F., Coppola, A., Tramontano, V., 2015. Intraoperative neurophysiology in posterior fossa tumor surgery in children. Child's Nerv. Syst. 31, 1791–1806. https://doi.org/10.1007/s00381-015-2893-1.

Sala, F., Manganotti, P., Tramontano, V., Bricolo, A., Gerosa, M., 2007. Monitoring of motor pathways during brain stem surgery: what we have achieved and what we still miss? Neurophysiol. Clin. /Clin. Neurophysiol. 37 (6), 399–406. https://doi.org/10.1016/j.neucli.2007.09.013.

Sarnthein, J., Albisser, C., Regli, L., 2022. Transcranial electrical stimulation elicits short and long latency responses in the tongue muscles. Clin. Neurophysiol. 138, 148–152. https://doi.org/10.1016/j.clinph.2022.03.016.

Strauss, C., Romstöck, J., Nimsky, C., Fahlbusch, R., 1993. Intraoperative identification of motor areas of the rhomboid fossa using direct stimulation. J. Neurosurg. 79 (3), 393–399. https://doi.org/10.3171/jns.1993.79.3.0393.

Szelényi, A., Fava, E., 2022. Long latency responses in tongue muscle elicited by various stimulation sites in anesthetized humans – new insights into tongue-related brainstem reflexes. Brain Stimul. 15 (3), 566–575. https://doi.org/10.1016/j.brs.2022.03.003.

Tanaka, S., Takanashi, J., Fujii, K., Hiroshi, U., Hori, T., 2007. Motor evoked potential mapping and monitoring by direct brainstem stimulation. J. Neurosurg. 107 (5), 1053–1057. https://doi.org/10.3171/jns-07/11/1053.

Téllez, M.J., Ulkatan, S., Urriza, J., Arranz-Arranz, B., Deletis, V., 2016. Neurophysiological mechanism of possibly confounding peripheral activation of the facial nerve during corticobulbar tract monitoring. Clin. Neurophysiol. 127 (2), 1710–1716. https://doi.org/10.1016/j.clinph.2015.07.042.

Yang, Y., Neidert, M.C., Velz, J., Kälin, V., Sarnthein, J., Regli, L., Bozinov, O., 2022. Mapping and monitoring of the corticospinal tract by direct brainstem stimulation. Neurosurgery 91 (3), 496–504. https://doi.org/10.1227/neu.0000000000002065.