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Electrical nerve stimulation method for intraoperative localization of the inferior alveolar nerve within the mandible: a pilot study in rabbits

F. Kuyumcu[1,2], **Ö.Erdogan**[2], **B. Güçlü**[3]

[1]Okmeydani Agiz ve Dis Sagligi Merkezi, Istanbul, Turkey; [2]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cukurova University, Adana, Turkey; [3]Institute of Biomedical Engineering, Boğaziçi University, Istanbul, Turkey

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Abstract. The efficacy of the electrical nerve stimulation method for localizing the inferior alveolar nerve (IAN) within the mandibular bone was evaluated. Six New Zealand rabbits were used (both sides of the mandible). The IAN was stimulated through the mandibular bone and compound action potentials (CAPs) were recorded proximally from the main trunk of the nerve. Stimulation current pulse widths were set at 0.05, 0.1, 0.3, 0.5, and 1 ms. The minimum current magnitude that generated a CAP with a criterion level (300 mV peak-to-peak amplitude) was measured in the range of 0.05–5 mA. Correlations between the distance of the IAN from the active electrode site and the minimum current magnitudes were studied for each pulse width. The correlation coefficients were 0.678, 0.807, 0.893, 0.851, and 0.890 for the pulse widths of 0.05, 0.1, 0.3, 0.5, and 1 ms, respectively. The minimum current producing the criterion CAP response in the IAN was significantly ($P < 0.0001$ for all pulse widths) and highly correlated with the distance between the stimulation site and the nerve. The results suggest that electrical nerve stimulation is a promising method that can be used for the localization of the IAN, especially during mandibular implant surgery.

Keywords: nerve location; intraoperative neurophysiological monitoring; bone; trigeminal nerve; *in vivo* study.

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Inferior alveolar nerve (IAN) injury associated with mandibular surgery is a complication contributing to altered sensation of the lower lip, chin, and buccal gingiva. The outcomes of such an iatrogenic nerve injury are usually devastating for the patient and this remains a complex clinical problem with major medico-legal implications.[1] The risk of iatrogenic IAN injury depends on the procedure performed, the technique used, and the surgeon's experience. Careful preoperative examination of the location and the course of the IAN is essential for mandibular surgeries associated with the risk of nerve injury, e.g.

impacted third molar extraction, dental implant surgery, orthognathic surgery, and excision of pathological lesions.

Current techniques used to detect the location and the course of the IAN include direct dental radiographs, panoramic radiographs, computerized radiographs, surgical navigation, and cone beam computerized radiographs. All of these techniques require additional radiation exposure (if used solely for nerve localization in addition to standard preoperative diagnostic techniques) and are associated with difficulties in the intraoperative localization of the nerve bundle. Although direct radiographs can be used intraoperatively, this is a time-consuming method and may be associated with radiographic errors due to incorrect positioning of the sensor.[2] Surgical navigation provides intraoperative detection of the location of the IAN. The disadvantages of surgical navigation include the requirement for sophisticated preoperative planning and setup, and the possibility of navigation errors.[3] Intraoperative neurophysiological monitoring (IONM) may be an additional and objective method for localization of the IAN during mandibular surgeries.

IONM has been used widely during surgical procedures since the 1970s. IONM is based on the evoked potentials that are obtained by an electrical stimulation. The electrical nerve stimulation method is considered the gold standard for locating peripheral nerves.[4] Electrical stimulation of the peripheral nerve results in muscular twitching or paresthesia of the innervated region, depending on the characteristics of the nerve.[5] By using electrical nerve stimulation, it is possible to confirm the proximity of the peripheral nerve. Despite the long history of clinical use of the electrical nerve stimulation technique, it does not appear to have been studied in the mandible for locating the IAN.

The aim of the present study was to evaluate the efficacy of the electrical nerve stimulation method for the localization of the IAN within the mandibular bone. This was achieved by stimulating the nerve passing through the mandibular canal and recording from the main trunk of the IAN.

Materials and methods

Subjects and anaesthesia

The study was reviewed and approved by the Institutional Ethics Committee for the Local Use of Animals in Experiments of Boğaziçi University. Six skeletally mature male New Zealand white rabbits, weighing between 2.1 and 3.7 kg (mean 2.69 ± 0.46 kg), were used. Preoperatively, all rabbits were monitored daily for 2 weeks with regard to their general health and food intake. All rabbits survived this phase without any significant systemic or local pathology or impairment in their general health. Each rabbit underwent the same surgical procedure and the electrical nerve stimulation method.

The rabbits were anaesthetized with 35 mg/kg ketamine (Alfamyne; Egevet, Izmir, Turkey) and 5 mg/kg xylazine (Rompun, Bayer, Istanbul, Turkey), initially via intramuscular route. After induction, the anaesthesia level was maintained with 2% isoflurane (Forane; Abbott, Istanbul, Turkey) in oxygen. The surgical site was shaved and prepared with 10% povidone–iodine solution. After securing the animal in a supine position, the submandibular region was prepared and draped under aseptic conditions. The inferior border of the mandible was approached via submandibular incision. Vital signs of the rabbits were monitored continuously during the operation.

Surgery and identification of related structures

A skin incision of approximately 2 cm in length was made parallel to the inferior–lateral surface of the mandible. After incising the skin and the platysma muscle, the overlying fascia was dissected. The facial artery and vein were ligated. The periosteum was reflected and the inferior border of the mandible was exposed. The medial pterygoid muscle was dissected bluntly and the lingual and the inferior alveolar nerves were approached at the posterior aspect. The periosteal dissection was continued anteriorly and the mental nerve bundle identified. Finally, the IAN, the mental nerve, and the inferior border of the mandible were exposed.

Nerve stimulation and recording setup

A commercially available nerve stimulator device (Tracer III Portex; Smiths Medical, Kent, UK) was used to electrically stimulate the IAN. The device delivers electrical current between 0.05 and 5 mA at 0.05–1 ms pulse widths and at 1 or 2 Hz pulse frequency. The current output, pulse width, and pulse frequency are selectable and can be controlled with a foot pedal. Initially, the output of the device was attached to the mental nerve bundle via stainless steel needle electrodes (30 AWG) to check that the entire stimulation and recording system was working properly. On the posterior aspect, stainless steel hook electrodes (diameter 0.254 mm) were attached to the IAN (1 cm distance between recording electrodes) and the evoked potential signals were amplified by a custom-made differential AC amplifier (gain 100/1000, low-pass filter cut-off frequency 5 kHz). The ground electrode was placed under the skin away from the surgical site. The voltage across the stimulation electrodes and the evoked-potential amplifier output were monitored with an oscilloscope (TDS 220; Tektronix, Wilsonville, OR, USA). For some trials, the digitized data of triggered oscilloscope channels were saved directly to a USB memory stick. Since this took a considerable amount of time (sometimes several minutes), the digitized data were not saved in every trial to avoid delays during the experiment.

After initial testing, the IAN stimulation was performed through the mandibular bone between the mental foramen and foramen linguae. For this purpose, an annealed stainless steel wire (diameter 0.254 mm) was insulated with capillary glass (outer diameter 1.0 mm) using cyanoacrylate glue and acted as the cathode. The stimulating metal end was cut flush with the glass, and depth markings were made. The anode was a stainless steel needle (30 AWG) placed anteriorly at the mental nerve. Figure 1a shows a diagram of the IAN stimulation and recording setup.

Experimental procedure

After confirming compound action potentials (CAPs) at the IAN by stimulating the mental nerve, five osteotomy points were marked along the inferior border of the mandible. A 1.1-mm diameter cylindrical implant drill was used to make the osteotomies, which were performed vertically from the inferior border of the mandible towards the IAN under copious irrigation and at a speed of 600 r.p.m. (Fig. 1b). The first osteotomy was prepared with 1-mm depth at the most distal point. The stimulation was applied at different pulse widths (0.05, 0.1, 0.3, 0.5, and 1 ms) by the glass-insulated cathode at the deepest point of the osteotomy cavity. The minimum current magnitude that generated a CAP peak-to-peak amplitude of 300 mV (criterion level) was recorded for each pulse width (Fig. 2a). Successive osteotomies were performed at 1-mm depth intervals up to 5 mm and the stimulation/recording protocol was repeated. If the criterion could not be reached within the range of the stimulator, no recording was made and

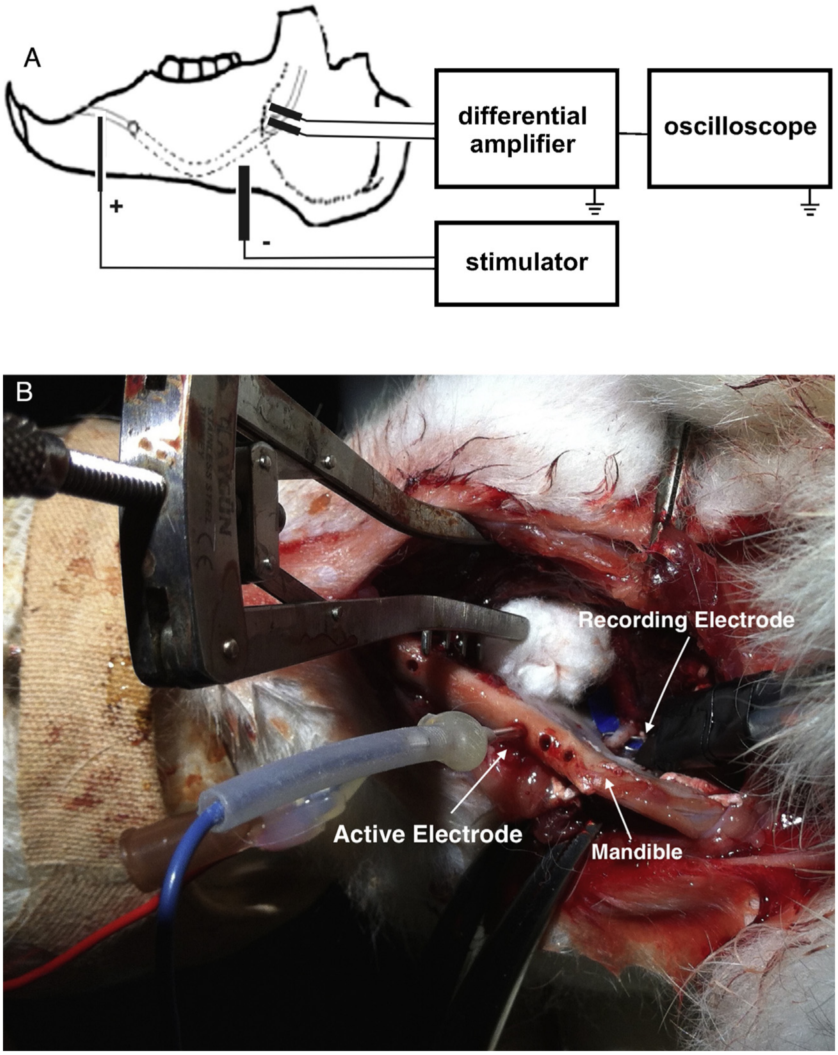

Fig. 1. (a) Diagram of the IAN stimulation and recording setup. The glass-insulated wire electrode (cathode) of the stimulator was placed within the mandibular osteotomy cavity. The anode was a needle electrode placed anteriorly at the mental nerve. The recording was performed proximally from the main trunk of the IAN using hook electrodes. The compound action potentials (CAPs) were amplified and monitored on an oscilloscope. (b) Intraoperative photograph showing the stimulation of the nerve through an osteotomy on the exposed mandibular surface using the glass-insulated cathode (active electrode). The two hook electrodes placed under the main IAN trunk for recording are seen on the right of the photograph.

the next osteotomy point was tested. If the drill penetrated the IAN canal inadvertently, the remaining protocol for the particular osteotomy point was terminated and the ipsilateral side of the mandible was excluded from further recordings. The same protocol was applied to all osteotomy points and both sides of the mandible. At the end of the experiment, the animal was euthanized with an intraperitoneal injection of 100 mg/kg thiopental (Pental; IE Ulagay, Istanbul, Turkey). The mandibles were harvested and prepared for radiographic evaluation. Figure 2b shows a harvested specimen that was sectioned at two osteotomy points sagittally.

Radiographic evaluation

The mandibles were split at the midline with the aid of a scalpel. Digital radiograms of the hemimandibles were obtained from the lateral aspect, with a 1-cm long orthodontic wire attached to the sensor of the digital radiography device (RVG; Trophy Radiologie, Vincennes, France). The X-ray unit (Densomat; Philips, Eindhoven, Netherlands) was set at 65 kVp, 300 mA, and 0.12 ms. The X-ray cone was directed perpendicular to the sensor from a distance of 40 cm. Digital images were converted to TIFF format and stored on the hard drive of a personal computer. The images were processed using standard software (ImageJ v.1.23; Wayne Rasband, National Institutes of Health, Bethesda, MD, USA). The lengths on the images were calibrated based on a 1-cm long orthodontic wire. The actual distances between the inferior alveolar canal and the particular osteotomy depths (1–5 mm as determined by the drill bit and the glass-insulated electrode) were measured on the radiographs. Figure 2c shows an example of a radiographic image.

Statistical analysis

The association between the current magnitude (for the criterion CAP level) and the distance from the IAN was studied using Pearson's correlation. In addition, the Pearson's correlation between the CAP latency and the IAN distance was calculated to further validate stimulation through the mandibular bone. The significance level of the correlation was set at $P = 0.05$. The data were analyzed in SPSS 15.0 software for Windows (SPSS Inc., Chicago, IL, USA).

Results

The minimum, maximum, and mean current magnitudes that generated a CAP peak-to-peak amplitude of 300 mV (criterion level) are shown in Table 1. The number of valid recordings ranged from 45 to 75; these were mainly reduced due to inadvertent penetration of the drill bit into the mandibular canal and out-of-range current magnitudes. Table 1 includes data for all IAN distances calculated after the experiment.

The strength–duration curves from a representative IAN (rabbit number 2, left side) are given in Fig. 3a. As the stimulus pulse width increased, the current magnitude required for excitation decreased and approached the rheobase. On the other hand, high currents were required for short pulse widths. Figure 3a includes data from different osteotomy points (O1, O3, O5) and different IAN distances (indicated in millimetres in the figure legend). Regardless of the osteotomy point, the strength–duration curves shifted upwards with increasing IAN distance, as expected. To further validate excitation through the mandibular bone, the CAP latencies calculated from the available digitized data set (see Materials and methods) were plotted against IAN distances. There was a moderate, but significant positive correlation ($r = 0.476$, $P = 0.014$) between latency and distance.

Fig. 2. (a) A representative compound action potential (CAP; upper trace, amplifier gain 100) is plotted using the digitized data (see text). The IAN was stimulated through the mandibular bone with a 3.0-mA, 0.1-ms current pulse applied from an approximate distance of 1.8 mm. The lower trace is the voltage (in arbitrary units) across the stimulation electrodes and was used to trigger the oscilloscope. (b) Photograph showing a specimen sectioned sagittally at two osteotomy points. Note that the inferior alveolar canal has been penetrated by the osteotomy on the left side. (c) Digital dental radiograph showing the osteotomies prepared on the inferior border of the mandible. An orthodontic wire (1 cm) was attached to calibrate for length in the image analysis software (IAN, inferior alveolar nerve; Inf. B. of M., inferior border of the mandible).

Table 1. The minimum, maximum, and mean current magnitudes that generated a compound action potential (CAP) with peak-to-peak amplitude of 300 mV (criterion level), are given for each pulse width in the stimulation protocol. The mean and the minimum current magnitudes evoking a CAP (at the criterion level) decreased at longer pulse widths.

Pulse width, ms	*n*[*]	Current magnitude, mA			
		Minimum	Maximum	Mean	SD
0.05	45	0.60	5.00	3.32	1.45
0.1	71	0.34	5.00	3.03	1.40
0.3	75	0.15	5.00	2.57	1.32
0.5	75	0.09	5.00	2.37	1.30
1	71	0.05	4.70	2.25	1.22

SD, standard deviation.

[*] The number of valid recordings for each pulse width.

For the pulse width of 0.05 ms, there were 45 valid recordings. The mean current magnitude that generated a CAP at the criterion level was 3.32 mA. There was a strong positive correlation between the current magnitude and the distance of the stimulation site from the IAN (Fig. 4a; $r = 0.678$, $P < 0.0001$).

For the pulse width of 0.1 ms, there were 71 valid recordings. The mean current magnitude that generated a CAP at the criterion level was 3.03 mA. There was a strong positive correlation between the current magnitude and the distance of the stimulation site from the IAN (Fig. 4b; $r = 0.807$, $P < 0.0001$).

For the pulse width of 0.3 ms, there were 75 valid recordings. The mean current magnitude that generated a CAP at the criterion level was 2.57 mA. There was a very strong positive correlation between the current magnitude and the distance of the stimulation site from the IAN (Fig. 4c; $r = 0.893$, $P < 0.0001$).

For the pulse width of 0.5 ms, there were 75 valid recordings. The mean current magnitude that generated a CAP at the criterion level was 2.37 mA. There was a very strong positive correlation between the current magnitude and the distance of the stimulation site from the IAN (Fig. 4d; $r = 0.851$, $P < 0.0001$).

For the pulse width of 1 ms, there were 75 valid recordings. The mean current magnitude that generated a CAP at the

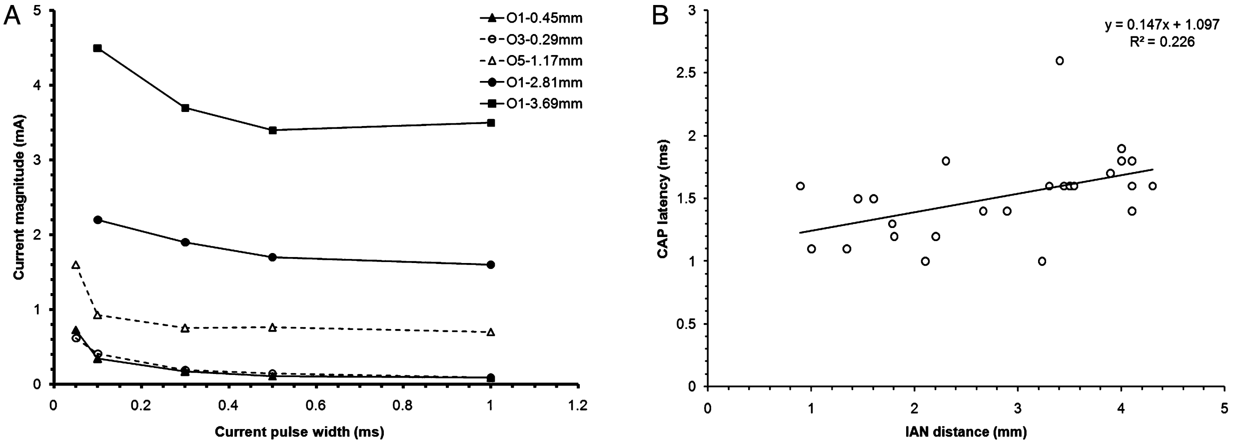

Fig. 3. (a) Representative strength–duration curves for excitation of the left IAN of rabbit number 2. The plots include data from different osteotomy points (O1, O3, O5) and different IAN distances (indicated in millimetres in the figure legend). The curves are typical for nerve excitation and shift upwards at increasing distances. (b) Compound action potential (CAP) latencies plotted against IAN distances using the available digitized data set. There is a moderate significant correlation, and excitation in the nerve occurs approximately 1 ms later for the most distant stimulation sites.

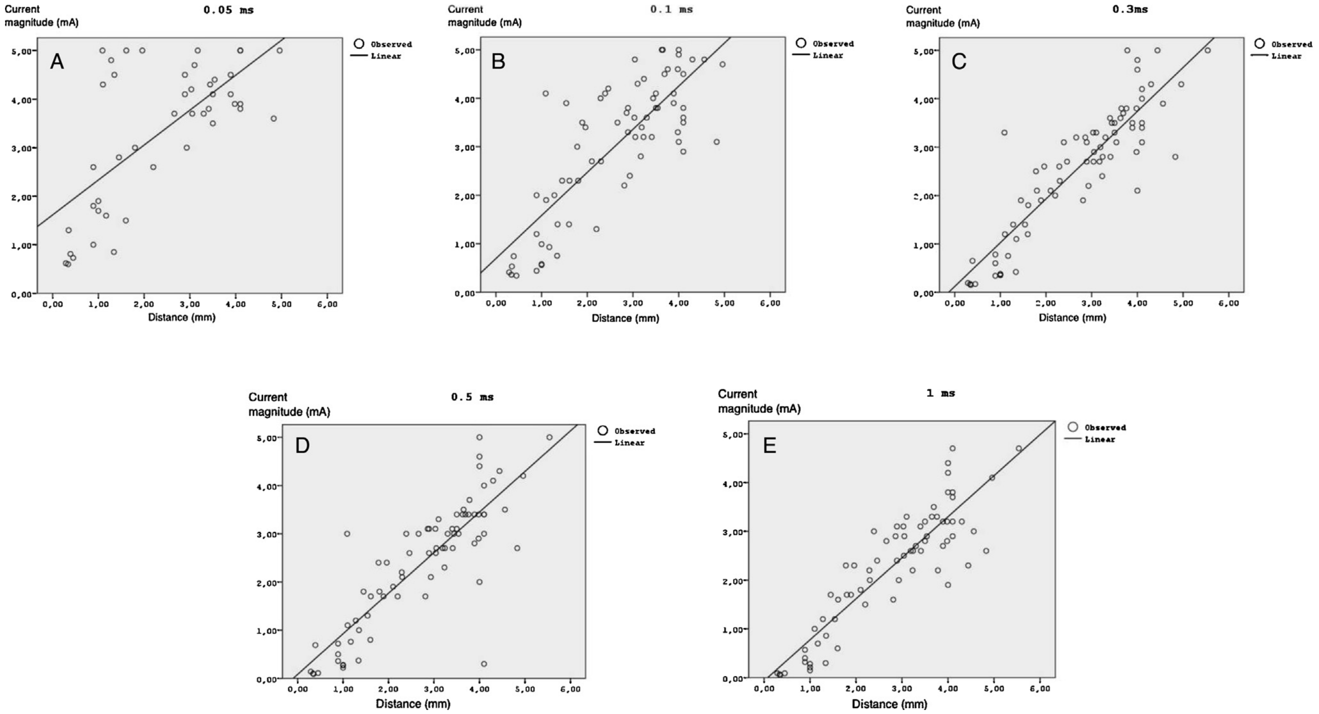

Fig. 4. The current magnitudes generating a compound action potential (CAP) at the criterion level are plotted against the distance between the stimulation site and the IAN. Current pulse width: (a) 0.05 ms; (b) 0.1 ms; (c) 0.3 ms; (d) 0.5 ms; (e) 1 ms.

criterion level was 2.25 mA. There was a very strong positive correlation between the current magnitude and the distance of the stimulation site from the IAN (Fig. 4e; $r = 0.890$, $P < 0.0001$).

In brief, the minimum current producing the criterion CAP response in the IAN was highly and significantly ($P < 0.0001$ for all pulse widths) correlated with the distance between the stimulation site and the nerve. The positive correlation shows that higher currents are required to produce the same criterion response if the stimulation is performed at a site further away from the IAN.

Discussion

This study demonstrated that the non-contact electrical stimulation of the IAN through the mandibular bone evokes a robust CAP in the nerve. It is known that localizing peripheral nerves is possible with the aid of electrical nerve locators,[6] but thus far they have been intended for use within the soft tissue. There appears to have been no study evaluating the effectiveness of electrical nerve locators for nerves stimulated within the bone.

Localization of the IAN is essential for surgeries involving the mandible. Although the IAN is a sensory nerve and its injury does not cause the loss of motor function or the impairment of facial expression, iatrogenic IAN injury may still have devastating outcomes for the patient, especially regarding dysesthesia.[7] Currently available techniques for the intraoperative localization of the IAN are mostly associated with complicated preoperative setups, the possibility of contamination of the surgical site, and unacceptable imaging errors. The aim of this study was to evaluate whether electrical nerve locators can be used to locate the IAN by intraoperative stimulation of the nerve through the mandible.

Intraoperative monitoring of the function of the IAN during orthognathic surgery has been evaluated in previous studies.[8,9] In these studies, to evaluate the impairment of electrical conduction in the IAN, the nerve was stimulated at the mental foramen, and the orthodromic sensory potentials of the IAN were recorded near the oval foramen or on the scalp. All previous studies have suggested that intraoperative monitoring of the IAN via electrical stimulation is a feasible and promising tool for the objective evaluation of intraoperative events and for the prevention of nerve injury during mandibular orthognathic surgery. The present study differs from these studies since the IAN was stimulated through the bone, which may have practical benefits during surgery. The assessment of the evoked potential, however, was conducted in a similar manner. Previous studies have evaluated the changes in IAN conduction during surgical manipulations, such as bone corticotomy, flap elevation, and segmental movements. Another use of the trigeminal somatosensory evoked potential technique in the area of oral and maxillofacial surgery is for determining the level and type of iatrogenic nerve injury following orthognathic surgery.[10–12]

Electrical nerve locators are used widely to verify peripheral nerve blocks for the purpose of intraoperative and postoperative analgesia. In order to generate a CAP in the nerve, a minimum threshold level of stimulus current should be exceeded.[5] Therefore, the amplitude and the width of the current pulse, and the distance between the stimulation site and the nerve, are three determining factors for nerve excitation. The relationship between these factors can be expressed as $E = K(Q/r^2)$, an inverse-square law similar to Coulomb's law in physics, but different in interpretation. In this equation, E is the threshold current for nerve excitation at a given pulse width, K is a constant, Q is the minimum current required at the stimulation site, and r is the distance between the stimulation site and the nerve. The equation implies that to cause nerve excitation at a distance, the minimum current applied with the stimulator should increase as the squared distance. Although there are even more detailed models for nerve excitation, it is generally accepted in the clinical setting that if the nerve can be excited by a current amplitude of 0.05 mA, the needle electrode is in direct contact with the nerve.[13] In the present study, it was found that the minimum current required to evoke a CAP (at the criterion level) was higher when the distance between the glass-insulated cathode and the nerve increased, as expected. Based on the results of the present study, it is possible to determine the proximity of the IAN for a particular pulse width. However, this requires computational modelling, which is outside the scope of this article.

It is important to note that since the stimulation anode was placed at the mental nerve, it could have been excited at the termination of the pulse in certain trials. There are two possible scenarios regarding this when the pulse is suprathreshold for the IAN. If the pulse width is relatively short and the distance between the stimulation electrodes is not long enough, the secondary excitation at the mental nerve would not propagate due to the refractoriness of the main excitation. If this were not the case, then the secondary excitation would reach the recording setup later. Since the oscilloscope was triggered with the initial slope of the pulse, data were recorded only due to the main excitation, even in those cases in which the secondary excitation could have occurred. The latency of the main excitation does not change much due to the IAN distance (see Fig. 3b). Therefore, the present results were not confounded by any possible secondary excitations. There is also the possibility of mental nerve excitation exclusively if the stimulation pulse is subthreshold for the IAN, especially at higher IAN distances. It was attempted to avoid this by recording CAPs at a criterion level much higher than the threshold that facilitated the excitation of the IAN. The reason for using the mental nerve location instead of a large and remote anode was to be able to specify an easily accessible, standardized, and mechanically stable location, and therefore, to control the current flow through the surrounding tissues while staying close to the IAN at the same time. If a remote anode were used, the local currents might be low or high near the IAN, depending on the direction between the anode and the cathode. It is preferable to use focal stimulation with very short electrode distances, but this was not practical for the purpose of the present study.

As the IAN is a sensory nerve, it is not possible to detect any muscular twitches when the nerve is stimulated. Therefore, the status of the stimulated nerve has to be confirmed by measuring the CAP at the proximal part of the nerve, as was applied in the present study. It might also be done by recording the antidromic action potentials from the distal end of the IAN, i.e. the mental nerve, if the stimulation electrodes are modified (see above). When designing the current study, the purpose was to assess if the IAN could be stimulated through the bone tissue and to determine the minimum current parameters required at distant sites.

The application of this method to human subjects may have some limitations. It is proposed that this technique is used specifically for dental implant surgery. For procedures performed under standard local anaesthesia, such as dental implant surgery, the placement of recording electrodes at the proximal part of the IAN may be painful for the patient and would be considered an invasive intervention. Moreover, when such local anaesthesia is applied, the nerve stimulator will not function, as nerve conduction is blocked. To overcome these limitations, one can perform supraperiosteal infiltration anaesthesia instead of an IAN block for dental implant surgery, in which both stimulation and recording electrodes are placed distal to the infiltration site. Previous studies have shown that supraperiosteal infiltration anaesthesia can be used effectively for posterior mandibular implant surgery, thus IAN block can be avoided.[14,15] It is important to note that asking the patient if he/she feels the effect of electrical stimulation may also not work during infiltration anaesthesia because of the difficulty of establishing an objective response criterion. However, a computational model based on the current results may be useful to automate the procedure and render the use of the entire recording apparatus unnecessary.[16] Another limitation of this method for human subjects is the possible presence of accessory branches of the IAN, which may result in an underestimation of the distance to the main nerve trunk. Therefore, any radiographic evidence of the accessory nerve branches should be examined preoperatively. In the present study, gross examination of the specimens and radiographic images revealed consistent mandible anatomies and the lack of accessory IAN branches in the rabbits (see Fig. 2b).

Potentially, the most effective use of this technique would be for mandibular dental implant installations under general anaesthesia. Previous studies have confirmed that CAPs can be recorded from the IAN during general anaesthesia.[8,9,17] Peripheral nerve conduction, neuromuscular function, and the generation of impulses in cutaneous receptors have also been found not to be significantly affected by volatile anaesthetics at standard anaesthetic concentrations.[18,19] As the implant surgery can be performed without the administration of an IAN block, the function of the nerve stimulator would not be compromised, and the recording electrodes could be placed at a more proximal part of the IAN with particular care to prevent the risk of nerve damage. However, the relationship between the stimulus parameters and the proximity of the IAN should be investigated in further human studies.

In conclusion, the results of this study show that the IAN can be stimulated through the mandibular bone and a compound action potential can be recorded at the proximal part of the IAN. The high correlation between the required current amplitudes and the electrode distances suggests that electrical nerve stimulation is a promising method that can be used for the localization of the IAN, especially during mandibular implant surgery. In order to obtain the most accurate and precise localization, the operation should be performed under general anaesthesia. However, it can also be used under local anaesthesia when supraperiosteal infiltration anaesthesia is applied for mandibular implant surgery.

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Competing interests

All authors of the manuscript declare that they have no conflict of interest.

Ethical approval

The study was reviewed and approved by the Institutional Ethics Committee for the Local Use of Animals in Experiments of Boğaziçi University (reference number 2012-11-27/24.12.2012).

Patient consent

Not applicable.

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Address:
Özgür Erdogan
Cukurova University Faculty of Dentistry
Department of Oral and Maxillofacial Surgery 01130
Balcali
Adana
Turkey
Tel. : +90-322-3387330
Fax: +90-322-3387331.
E-mail: ozgerdogan@yahoo.com