Sensory evoked response to electrical stimulation of the trigeminal nerve in humans

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Electrical stimulation of the upper and lower lips of normal subjects evoked a consistent response recorded from over the face area of the ipsi- and contralateral hemispheres. This response consisted of seven discrete waves. Peak latencies ranged from as early as 8 msec to 115 msec. Stimulation of the lower lip evoked a response of lower amplitude and reversed polarity, as compared to the upper lip stimulation response. The data support the validity of the trigeminal sensory evoked response in the evaluation of the trigeminal pathways. Previously reported methods are reviewed and compared.

KEY WORDS • trigeminal nerve • electrical stimulation • sensory evoked response

LARSSON and Prevec were the first to record trigeminal sensory evoked responses (TSER's) in humans by mechanical stimulation of the face. Since then, several reports have described different methods of eliciting TSER's, the eventual goal of which has been to achieve an objective, quantifiable, nonverbal test associated with the perception of pain. Also, an attempt has been made to find correlation of the response with pathological conditions of the central nervous system, especially with trigeminal neuralgia. Different stimulation and recording techniques have resulted in remarkable variations of the TSER's, however, and contamination of the response by artifacts and muscle activity has contributed to this variability. Accordingly, conclusions concerning the validity and clinical implication of the TSER have varied from "suitable for electro-physiological testing of the fifth nerve function in routine clinical applications" to "the TSER in relation to qualitatively different modalities of perception is an unspecific response." The method we are reporting here has proven to be simple and reliable for TSER recording.

Materials and Methods

Thirteen healthy volunteers underwent 63 sessions of TSER. Six were male and seven female; their ages ranged from 13 to 62 years, with a mean of 34 years. Ten subjects were right-handed. All had a neurological examination and received a thorough explanation prior to the test. Each session lasted approximately 25 minutes, with a 20-minute interval between two consecutive sessions.

The subjects were comfortably reclining in complete relaxation and with closed eyes. The room was dimly illuminated. Dermal platinum-alloy needle recording electrodes* were applied to the C5 and C6 areas (low parietal region) with an Fpz reference electrode. The right ear lobe served for grounding.

Gold-plated stimulating electrodes with a 3-mm contact surface and an interelectrode distance of 10 mm were lightly applied to the lips. They were held in place by a flexible arm, thus avoiding muscle activity of the subject. No paste was necessary, as the subjects were asked to lightly moisten their lips prior to stimulation. Before each session, a baseline recording was obtained by reducing the stimulus intensity much below the subject's sensitivity threshold (0.09 mA).

Each half of the upper and lower lip was then stimulated in turn by an electrical impulse of 20 mA intensity and 20 msec duration, at a rate of two/second. Each half of a lip received 200 stimuli, with the polarity of the stimulating electrodes being reversed following the first 100 stimuli to eliminate

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* Dermal platinum-alloy needle recording electrodes, No. E2B, manufactured by Grass Instruments, 101 Old Colony Avenue, Quincy, Massachusetts.
FIG. 1. Trigeminal somatosensory evoked responses (TSER's) obtained from the upper (both upper graphs) and lower (both lower graphs) lips of a healthy 27-year-old woman. The left graphs of both upper and lower lip recordings show the early waves obtained on a time base of 50 msec. These were obscure on the 250-msec time base recording due to differences in the amplifier bandpass (see Materials and Methods section). Left (LT) and right (RT) refer to hemispheres. In both recordings, the right side of the lips was stimulated. Negative deflection is upward. $S =$ stimulation.

In a few subjects, stimulus intensity was reduced to 17 mA to avoid unpleasant sensation or lip contraction. This did not affect the amplitude or peak latencies of the response. As the lower lip was found to be less sensitive to the electrical stimuli than the upper lip, it served as the first stimulation site, allowing the subject to become familiar with the stimulus. 

The responses were analyzed and plotted by a Nicolet CA-1000 signal averaging system,† which also generated the pulses. Analysis time, which was triggered by the stimulus, was set to 50 and 250 msec. Responses from both hemispheres were recorded simultaneously. The amplifier bandpass for the early waves was set between 1 and 3000 Hz, and between 1 and 30 Hz for the late potentials. Filter sensitivity was 50 $\mu$V. Interelectrode impedance varied between 5 and 10 kOhm. The response's gain was set at 8. Calibration wave was standardized for all responses.

† Nicolet CA-1000 signal averaging system manufactured by Nicolet Instrument Corp., 5225 Verona Road, Madison, Wisconsin.

Results

Figure 1 displays a TSER obtained from the upper and the lower lips of a 27-year-old right-handed woman. Each complex consisted of seven to nine waves. The peak latencies and standard deviations of the consistent waves in both ipsi- and contralateral recordings are given in Table 1. The mean peak latencies of the waves obtained by stimulating the upper lip are compared to those obtained from stimulation of the lower lip (Table 2). The waves in both responses show almost equal peak latencies, but have reversed polarities. Various late (> 200 msec) deflections have been recorded, but were not of consistent appearance.

Amplitudes showed considerable variation among the subjects, and were not of statistical significance. However, a few observations have been possible: 1) responses from both sides of a lip had identical amplitudes; 2) amplitudes of TSER's obtained from the upper lip were higher than those obtained from the lower lip; and 3) amplitudes were higher in younger subjects.
Trigeminal sensory evoked responses

**TABLE 1**

<table>
<thead>
<tr>
<th>Area Tested</th>
<th>N₁</th>
<th>P₁</th>
<th>N₂</th>
<th>N₃</th>
<th>N₄</th>
<th>P₂</th>
<th>N₅</th>
<th>N₆</th>
</tr>
</thead>
<tbody>
<tr>
<td>upper lip</td>
<td>7.6 ± 0.5</td>
<td>13.75 ± 0.8</td>
<td>17.5 ± 0.8</td>
<td>22.12 ± 2.68</td>
<td>38.40 ± 2.14</td>
<td>43.64 ± 2.01</td>
<td>56.32 ± 2.70</td>
<td>91.08 ± 4.28</td>
</tr>
<tr>
<td>lower lip</td>
<td>8.25 ± 0.8</td>
<td>12.25 ± 0.82</td>
<td>18.16 ± 0.6</td>
<td>24.05 ± 3.64</td>
<td>32.27 ± 4.78</td>
<td>44.22 ± 4.29</td>
<td>54.33 ± 2.15</td>
<td>100.05 ± 2.41</td>
</tr>
</tbody>
</table>

* Peak latencies and standard deviations of the consistent waves. N₁, P₁, N₂ are early potentials obtained on the 50-msec time base. “Ipsi” and “contra” refer to the side of the lip stimulated as compared to the side of the recording electrode.

**TABLE 2**

<table>
<thead>
<tr>
<th>Area Stimulated</th>
<th>Mean Peak Latencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>upper lip</td>
<td>N₁, P₁, N₁₆, N₂₃, P₂₆, N₄₄, P₅₆, N₆₉, N₁₄</td>
</tr>
<tr>
<td>lower lip</td>
<td>P₈, N₁₂, P₁₈, P₂₄, N₃₉, P₄₀, N₅₀, N₁₀₁, N₁₂₀</td>
</tr>
</tbody>
</table>

* A comparison of the waves obtained by stimulation of the upper and lower lips shows almost equal peak latencies. However, the polarity of the response from the upper lip is reversed as compared to the polarity of the lower lip.

**Discussion**

Different methods have been used by various authors to evoke TSER’s. These include mechanical stimulation by manually delivered light taps over the face and air puffs to the cornea and nostril, as well as electrical stimulation of the gums, tooth pulp, chin, and lips. Mechanical stimulation of the face evoked long-latency waves only, heavily contaminated by blink reflexes and muscular activity; the stimulation technique was also quite complicated.

Electrical stimulation of the various trigeminal divisions seemed to provide the best responses. However, stimulation of the skin innervated by the ophthalmic division in our subjects either produced significant muscle activity and blink reflexes or was accompanied by pain. Thus, we chose the second and third trigeminal divisions for stimulation. Tooth pulp stimulation, advocated by Chatrian, et al., seemed to involve complicated preparation and to evoke unpleasant and at times painful sensation, and hence could not be applied for routine examination. Electrical stimulation of the gum, as used by Bennett and Jannetta, involved active participation of the subjects in holding the stimulating electrodes, and at times elicited pain. They also reported a 10% to 15% rate of failure to evoke the responses.

We found lip stimulation, first suggested by Matsumiya and Mostofsky, and largely used by Stöhr and Petruch, was the best method to use for both examiner and subject. The lips are highly sensitive, but, unlike the gums and tooth pulp, their stimulation does not provoke severe pain or unpleasant sensation. Clear responses with a high degree of bilateral cortical representation have been the rule with electrical stimulation of the lips. No special preparation was necessary, and each session was of relatively short duration, thus enabling repeat tests in the same subject.

Unlike Stöhr and Petruch, who stimulated both lips simultaneously, we elected to stimulate each lip separately. In this way, we could test and compare the response of the second and third trigeminal divisions to each other. Moreover, by stimulating each half of a lip in turn, the responses of the same divisions on both sides could be compared to each other. In normal subjects, these were found to be identical.

Areas C₅ and C₆ (left and right low parietal regions, respectively) proved satisfactory in providing a reliable response. Using needle electrodes for recording eliminated the difficulties associated with fixation of surface electrodes over the hair, and reduced the electrode impedance significantly. No discomfort was reported by the subjects. Local anesthetic (lignocaine 1%, injected to the stimulated area), also used by Chatrian, et al., to abolish the response, resulted in diminishing amplitudes and prolonged peak latencies in one of our subjects. The same authors stimulated a non-vital tooth pulp in a healthy subject and also a vital tooth pulp in a patient with congenital insensitivity to pain, neither of which elicited any response. They also stimulated the tooth pulp of a patient who had undergone mandibulectomy (including the dental nerve) for malignancy, without evoking any response. These data provide evidence for a trigeminal nerve origin of the response.

Unlike previous observations, the latencies in the TSER’s of our subjects did not change by reducing the intensity of the stimulus, did not increase with age, and were not shorter in females. Differences in
latencies of contralateral responses as compared to ipsilateral ones, which have been noted by others,2,3 were not confirmed by us, although the waveform of the contralateral response has usually been more clearly defined. This was most prominent in the responses obtained from the lower lip.

The phenomenon of reversed deflections in the response from stimulating the lower lip as compared to that from the upper lip is interesting though of obscure origin. However, peak latencies are almost identical (Table 2). This observation has been indirectly supported by two other investigators. The triphasic wave reported by Bennett and Jannetta2 obtained by stimulating the second division of the trigeminal (the upper gum) is similar in latencies and polarity to the waves obtained by stimulating the same nerve division in our subjects. Further, the response reported by Drechsler,4 who stimulated the third division of the trigeminal nerve, is almost identical in form and peak latencies to that obtained by stimulating the lower lip in our subjects (Table 3).

A possible explanation of the reverse phenomenon is based on a similar experience (although relative to the somatosensory response) reported by Goff, et al.9 It is likely that the cells that receive signals from the third division are so located as to face the active scalp electrode from an opposite direction, as compared to the cells which receive their signals from the second division. The association sensory centers may have lost this specific structural difference, hence the similarity in deflections of the late waves.

The origin of each wave in the TSER's could only be assumed at this point. It has been suggested that the early N1 wave is of Gasserian ganglion origin, N14 is of primary sensory cortex origin, and N14 and P150 have been attributed to secondary cortical sensory areas.7 The late waves of inconsistent pattern have been considered rhythmic oscillation of alpha frequency.4,11 This assumption gains support from parallel data obtained in the somatosensory response, where the earliest wave, N9, is believed to originate in the brachial plexus and upper cord. The following waves, up to N20, are related to subcortical centers. The N20 wave is believed to represent the earliest cortical event, its origin being the postcentral gyrus. The P45 wave is thought to arise from a separate generator, situated somewhat further back in the parietal region.13

Also, the earliest waves in the auditory evoked potentials (AEP's), with peak latencies between 2 and 8 msec, have been related to the brain stem. Latencies between 8 and 80 msec are thought to arise from the thalamus (medial geniculate body) and from the primary auditory cortex. The late components, ranging from 100 to 300 msec, are thought to represent a widespread activation of the frontal cortex.8 The amplitude of AEP's, like that of the TSER's obtained in our subjects, has been noted to be much larger in young children.8

Further studies of TSER's in animals with applied lesions and in patients with known lesions along the trigeminal sensory pathways and in the central nervous system may supply the clue for the origin of the TSER waves.

Summary

Electrical stimulation of the lips in normal healthy subjects elicited a constant TSER from sensory centers over both hemispheres. The method described here proved to be a simple and accurate one. The TSER's thus obtained consist of seven to nine waves with constant, repeatable peak latencies. The waves showed inversion of their polarity in the responses obtained by stimulating the third trigeminal division as compared to those obtained by stimulating the second division. The responses over both hemispheres were rather similar in their latencies and amplitudes, but had a more clearly defined form over the contralateral hemisphere. Contrary to the latencies of the waves, their amplitudes showed considerable variations. The amplitude of responses obtained in young subjects was higher than that obtained from adults, probably due to a thinner scalp. The origin of each wave in the TSER must still be determined; however, the test probably has clinical importance and may be applied as a diagnostic tool in the evaluation of pathological conditions of the trigeminal nerve and the central nervous system.

References

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