Midbrain evoked potential produced by stimulation of the muscle branch of the oculomotor nerve

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Evoked potential was recorded by needle electrode from the oculomotor nucleus in decerebrate cats, following electrical stimulation of the inferior oblique nerve. The evoked potential was usually triphasic, but complex potential with the second and third negative waves, or with long latency negative waves, was incidentally recorded depending upon the position of the recording electrode. In the present paper, an attempt was made to clarify in detail, the physiological properties of the evoked complex potential. By changing the intensity or frequency of the inferior oblique nerve stimulation, the complex potentials could be classified into 2 types: (1) those produced by firing of the motoneurons by antidromically conducted impulses on the efferent fibers, and (2) those produced by transsynaptic firing of the motoneurons by orthodromically conducted impulses on the afferent fibers. As shown by the results of repeated stimulation of the trigeminal nerve and severance of the trigeminal nerve trunk in the middle cranial fossa, the inhibitory effect of the trigeminal nerve on the oculomotor nucleus was demonstrated. Also, the possible role of the trigeminal nerve in exerting an inhibitory force on the oculomotor neurons through the internuncial neurons was discussed.

Key words: oculomotor nucleus, evoked potential, complex potential, inferior oblique nerve, trigeminal nerve, midbrain, electrical stimulation, electrode placement, neuronal connections, neuronal synapse, electrical tissue inhibition, cats, inhibition, stimulus strength, stimulus frequency.

The antidromic response recorded in the rabbit oculomotor nucleus was analyzed by Lorente de Nó,1 and the electrophysiological phenomenon was made clear on the basis of the histological structure of the nucleus. Previously, Shimo-oku and Jampel2 recorded evoked potential in the cat oculomotor nucleus produced by electrical stimulation of the nerve branches to the individual extraocular muscles, and reported the propagation of excitation in the nucleus by plotting the equipotential lines of the electric fields generated by the evoked potential. The evoked potential, recorded with a needle electrode in the oculomotor nucleus, usually showed triphasic waves (positive–negative–positive) with a 0.3 to 0.4 msec. latency. But some different shapes of evoked potential—complex potential—were incidentally recorded from each of the oculomotor nuclear subdivisions depending upon the position of the recording electrode, which was characterized as having 2 or 3 negative waves,

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or having a latency of several milliseconds. Further experiments to explore the nature of the potential were not attempted.

The present paper was intended to clarify in detail, the physiological properties of the evoked complex potential produced in the oculomotor nucleus by stimulation of the inferior oblique nerve.

Methods and materials

Experiments were performed on 16 adult cats, anesthetized with an intraperitoneal injection of Nembutal (30 mg. per kilogram (13 cats), or Chloralose (40 mg. per kilogram (3 cats)). Each cat was decerebrated bilaterally by thalamocolllicular section in order to eliminate impulses from the cortex on the oculomotor nucleus. Since the inferior oblique nerve has a long course in the orbit and is easily isolated from other tissues, it has been used exclusively in the present experiment, although complex potential was evoked in the same way by stimulation of the individual oculomotor nerve branches as described in a previous paper. Therefore, the inferior oblique nerve was dissected from the orbit and detached from the muscle after lateral orbitotomy. The first and second branches of the trigeminal nerve were also dissected from the orbit. The trigeminal nerve trunk central to the semilunar ganglion was exposed in the middle cranial fossa and covered by cotton moistened with warm mineral oil, after opening the dura. By use of this procedure, it was easy to cut the trigeminal nerve trunk without affording mechanical pressure to the midbrain in case of need.

Two Teflon-coated silver wires were used as bipolar stimulating electrodes, and were placed against the inferior oblique nerve and trigeminal nerve branches. For stimulation, a square pulse of 0.01 to 0.05 msec. duration, and 1 to 30 volts intensity, was applied in the form of either single or repeated shocks. The recording electrode was a sharpened dental needle with a tip diameter of about 10 μ. With the exception of the tip, the needle was insulated. It was inserted stereotaxically into the oculomotor nucleus. As previously stated, evoked potential by stimulation of the inferior oblique nerve was usually triphasic, but in the present experiment, insertion of the recording electrode was repeated until the complex potential could be recorded. An indifferent electrode was placed on the exposed skull. During the experiment, the cat's body temperature was maintained at 37 to 38°C. by means of an abdominal heating pad.

The action potential was displayed on the cathode ray oscilloscope and photographed. At the end of each experiment, an electrolytic lesion was made by direct current, and the location of the electrode tip was verified histologically.

Results

Effects of stimulus strength. As shown in Fig. 1, A, 1, stimulation 0.05 msec. in duration, and one volt in strength, given to the inferior oblique nerve, did not evoke any potential in the nucleus. A triphasic potential with a latency of approximately 0.4 msec. was recorded by a slightly stronger stimulus such as 0.05 msec. in duration, and 2 volts in strength (Fig. 1, A, 2). Moreover, the second wave with a latency of 1.8 msec., and the third wave with a latency of 2.6 msec. were recorded with increasing stimulus strength (Fig. 1, A, 3, 4, and 5).

Fig. 1, B, shows another example of evoked potential records. In this case, the evoked response which combined a small diphasic wave with a 0.3 msec. latency, and the second negative wave with a 2.2 msec. latency, appeared by stimulation of 0.05 msec. in duration, and 4 volts in

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Fig. 1. Effects of stimulus strength. Numbers on the left side indicate stimulus strength: 1 = 1 volt, 2 = 2 volts, 3 = 4 volts, 4 = 5 volts, and 5 = 6 volts. In column A, the second and third waves appeared by increasing the stimulus strength (traces 3, 4, and 5). In column B, the second negative wave appeared coincidentally with the first wave by 4 volts stimulus strength (trace 3). Downward deflection shows a negative trend in this and subsequent figures.
strength, as shown in Fig. 1, B, 3. In a different experiment with the minimal stimulus strength inducing the usual first wave, the second wave was followed inseparably as shown in Fig. 2, A, left column. Increasing the stimulus strength to 2 times (Fig. 2, B), and 3 times (Fig. 2, C) the minimal stimulus strength, the third wave with a latency of approximately 5 msec. appeared.

In view of the results obtained with various stimulus strengths, it might be reasonable to classify the complex potential into 2 types: one which was not evoked until a stimulus was applied that was stronger than those which evoked the usual first wave, and another, in which evoked potential with more than 2 peaks was caused by threshold stimulation.

**Effects of repeated stimulation of the inferior oblique nerve.** A possible modification of the evoked potential to repeated minimal stimulation of the inferior oblique nerve was examined. In certain instances the pattern of the evoked potential was not changed by repeated stimuli of 10 pulses per second or 100 pulses per second, as shown in the first and third negative waves in Fig. 2. On the other hand, disappearance of the evoked negative wave occurred even at a rather low frequency stimulation such as 10 pulses per second, as seen in the second negative wave of Fig. 2. In another instance (Fig. 3, A and C), an inconstant disappearance of the negative wave by increasing the stimulus frequency to 100 pulses per second was observed, although there was no change in the pattern of the evoked potential of 10 pulses per second stimulation. Furthermore, contrary to the disappearance of the evoked potential by repeated stimulation, the appearance of a new component took place by increasing the stimulation frequency from one pulse per second to 10 pulses per second, as shown in Fig. 3, B.

From these results it would be reasonable to classify the evoked potential into different types according to the attitude toward repeated stimulation of the inferior oblique nerve, namely, those which could follow the high frequency of repetition, those which could not, and those
which could easily appear or disappear at low frequency of repetition.

**Effects of the trigeminal nerve activity.**

a. *Effects of severance of the trigeminal nerve.*** Fig. 5 shows a coordinated mapping on the midsagittal plane of the evoked potential in the oculomotor nucleus, produced by inferior oblique nerve stimulation. The coordinate system in the figure was based upon the atlas by Snider and Niemer as shown in Fig. 4. An imaginary fixed rectangular coordinate system was set up within the midbrain parenchyma. The origin of the coordinate system was at the junction of 3 perpendicular planes: the midsagittal plane, the vertical interaural plane (located by the position of the ear plugs), and the horizontal plane (parallel with the horizon, and located 10 mm. above the interaural line). In each pair of the traces in Fig. 5, the upper record shows the evoked potential produced by stimulus strength which was minimal, but enough to evoke the first wave, while the lower one is a response to threelfold stimulus strength of the minimal one. As seen in Fig. 5, the complex potential was recorded only near the area of A 1, H 0 to H -1. Using the same cat, the evoked potential by inferior oblique nerve stimulation was reexamined immediately after severance of the trigeminal nerve trunk.
Fig. 5. A coordinate mapping of the evoked potential in the oculomotor nucleus and its adjacent area on the midsagittal plane by inferior oblique nerve stimulation. The coordinates are shown in Fig. 4. The left side of the figure is rostral. Each potential is indicated by superimposition.

Fig. 6. A coordinate mapping of the evoked potential after severance of the trigeminal nerve trunk using the same cat as in Fig. 5. The complex potential was recorded from a more extensive area in the nucleus than those in Fig. 5.
Fig. 7. The role of the first and second branches of the trigeminal nerve in inducing the complex potential in 2 different materials (A and B). Trace 1: Control evoked potential. Trace 2: Effect of severance of the first branch alone. Trace 3: Effect of severance of the first and the second branches successively. After cutting of the first branch, the amplitude of the third wave increased (A, 2), and the nature of the complex potential became more definite than the control (B, 2).

close to the semilunar ganglion with minimum movement of the cat's brain (Fig. 6). This results in expansion of the area from which the complex potential was recorded, i.e., the recordable area expanded anteroposteriorly from A 0.5 to 2.0, and from H 0 to -1.

In order to evaluate the role of the first and the second branches of the trigeminal nerve regarding the appearance of the complex potential, the first branch alone, or the first branch and then the second branch in succession, were severed at the point just distal to the semilunar ganglion. Fig. 7, A, I, and B, I, are control records in 2 different materials (A and B), in which complex potential was observed in both cases. After the cutting of the first branch, augmentation in amplitude of the third wave appeared in one instance (Fig. 7, A, 2), and the nature of complex potential became more definite than the control in another (Fig. 7, B, 2).

In Fig. 7, B, 3, after severing the first branch, the second branch was also cut in succession. In this case, however, there was no noticeable change in the pattern of complex potential.

The attitude of the complex potential, by changing the stimulus strength and frequency to the inferior oblique nerve, was examined after severance of the trigeminal nerve trunk in the proximity of the semilunar ganglion (Fig. 8). Complex potential by minimal stimulus strength for the first wave was shown in the upper trace of the left column in Fig. 8. As the stimulus strength was increased to 2 and 3 times the minimal strength, the components of complex potential increased, as shown in the middle and lower traces of the left column respectively, in which there were 4 negative waves. By repeated stimulation of 10 pulses per second to the inferior oblique nerve, the negative waves appeared with different latencies from those in the left column, as shown in the right column.

b. Effects of repeated stimulation of the trigeminal nerve. The complex potential was also examined with repeated stimulation at 100 pulses per second of the supraorbital nerve. The amplitude of the complex potential with different latency did not change with trigeminal stimulation as indicated in Fig. 9, A and B. In Fig. 9, C, however, the amplitude of the evoked potential showed a decrease of 15 per cent against the control with repeated trigeminal stimulation, and a reduction in the amplitude retained after cessation of repeated trigeminal stimulation with an extensive decrease of 55 per cent against the control. In another instance, as shown in Fig. 9, D, the amplitude of the third wave showed a remarkable increase after cessation of the trigeminal stimulation, although the amplitude of the evoked potential did not change during the repeated stimulation.

Discussion

There are several reports concerning fiber diameters in the oculomotor nerve. Although the spectrums of the fiber diameter are somewhat varied among authors because of the different staining methods used, they are widely distributed from the...
Fig. 8. Effects of changing stimulus strength and frequency to the inferior oblique nerve after severance of the trigeminal nerve trunk. Trace 1: Evoked potential obtained by the minimal strength to the first wave. Traces 2 and 3 are evoked potentials obtained by the 2 and 3 times the minimal stimulus strength, respectively. In the left column, the components of complex potential increased with the strong stimuli. In the right column, the negative waves with different latency from those in the left column appeared by the repeated stimulation of 10 pulses per second.

Fig. 9. Effects of repeated trigeminal nerve stimulation. Although the amplitude of the evoked potential shows no change by repeated stimulation in 2 cases (A and B), the amplitude decreased by repeated stimulation (C), or increased after cessation of the stimulation (D). In the middle trace, irregularly appearing signals (indicated by dots) different from those by the oculomotor nerve stimulation are artifacts caused by the trigeminal nerve stimulation. Abbreviations in the left column are as follows: C = control obtained by the inferior nerve stimulation, Trig = trigeminal nerve stimulation of 100 pulses per second, Off = after cessation of the trigeminal stimulation.

small diameter fibers (1 to 3 μ) to the larger ones (16 to 18 μ). Accordingly, the conduction velocity of the oculomotor nerve varies, ranging from the slowest, 6 m. per second, to the fastest, 120 m. per second. The former belongs to a range of the afferent fiber, and the latter belongs to a range of the somatic efferent fiber.

When one takes into account the histological evidence of the fiber composition of the oculomotor nerve, the complex potential which appears by increasing the stimulus strength in the present experiment would be a manifestation of antidromic firing of motoneurons which send the small and high threshold fibers to the
muscles. Moreover, the complex potential followed by repeated stimulation of 100 pulses per second would also be attributed to the antidromic firing of motoneurons.

Besides the complex potential just mentioned, the author has recorded complex potential which may be distinguished by the following characteristics: (1) potential appearing coincidentally with the potential usually evoked by a weak stimulus (Fig. 1, B), (2) potential elicited only by repeated stimulation (Fig. 3, B), and (3) complex potential appearing incidentally by repeated stimulation (Fig. 3, C). Morphologically, it has been said that the oculomotor neurons have no axon collateral,1, 8 and that the oculomotor nerves are composed of 3 kinds of fibers, i.e., efferent, afferent, and sympathetic fibers. When one considers the morphological characteristics of the oculomotor nerve and nucleus, the above-mentioned behavior of the complex potential in the present experiment can be ascribed to a physiological phenomenon regarded as temporal inhibition or facilitation in the oculomotor neurons, of which firing states are determined by impulses conducted transsynaptically on the afferent fibers.

By the above statement, it can be easily understood that the complex potential could be divided into 2 categories: (1) one which is antidromic complex potential, the peaks of which are produced by the difference in conduction velocity of the oculomotor fibers, and (2) the other which is transsynaptic complex potential resulting from stimulation of the afferent fibers.

Concerning pathways of the afferent fibers in the oculomotor nerve, some authors believe that it courses in the oculomotor nerve itself,9-14 but others describe it as running to the midbrain with the trigeminal nerve, with which communication exists in the orbit or cavernous sinus.15-23 Since the transsynaptic complex potential was recorded after severance of the trigeminal nerve trunk in the present experiment, there is a possibility that the afferent fibers travel in the oculomotor nerve to the brain. Cooper and associates19 have reported that impulses conducted through low-threshold, proprioceptive afferent fibers were transmitted to the brainstem via the trigeminal nerve, while impulses through high-threshold fibers were conducted to the midbrain via the eye muscle nerve itself. Furthermore, Manni and associates22 have found that the soma of the afferent fiber of the eye muscle exists in the semilunar ganglion of trigeminal nerve. Consequently, in the present experiment it would be hard to exclude the possibility that a part of the afferent fibers which cause the transsynaptic complex potential would pass through the trigeminal nerve to the midbrain.

The fact that the transsynaptic complex potential was recorded in the oculomotor nucleus in the present experiment would indicate that the cell bodies of the afferent fiber exist in or near the nucleus, as previously reported.11, 14, 24, 25 However, since the transsynaptic complex potential could be recorded only in a localized area within the motoneuron pool, it might be assumed that there are a few synaptic connections which produce the complex potential in the nucleus. If this is true, the few synaptic connections would not be enough to execute a precise smooth movement of the eyes, and the existence of the afferent fibers as described by Cooper and associates,19 and Fillenz,20 which terminate in the mesencephalic nucleus of trigeminal nerve or its adjacent region of the midbrain, should be considered.

As previously reported,27 the implication that the oculomotor nucleus has received an inhibitory effect from the trigeminal nerve was confirmed by the evidence from the present experiment, in which the complex potential was more easily recorded after severance of the trigeminal nerve, especially of its first branch. An assumption that the inhibitory influence of the trigeminal nerve on the oculomotor nucleus would act through the internuncial neurons in the nucleus is postulated.
by the following facts. (1) As shown in Fig. 9, C, the complex potential was considered to be transsynaptically evoked because of its threshold for firing and response patterns to repeated stimulation of the inferior oblique nerve. The fact that repeated stimulation of the trigeminal first branch, at the same time, reduced the amplitude, and the reduction further increased after cessation of trigeminal stimulation, would support the above statement. (2) As seen in Fig. 8, the fact that complex potential has easily changed its pattern by stimulus strength and repeated stimulation of the inferior oblique nerve after severance of the trigeminal nerve, would support the claim.

In the oculomotor nucleus, it has not been found that the cells corresponded to the Renshaw's cell in the spinal motoneurons, which has a recurrent inhibitory effect on the motoneuron. Comparing the oculomotor motoneuron with the spinal one, it is interesting to note that the internuncial neurons in the oculomotor nucleus are inhibited continuously by the neurons which receive impulses from the trigeminal nerve, or an afferent pathway of the eye muscles.

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