Cochlear nerve injuries caused by cerebellopontine angle manipulations

An electrophysiological and morphological study in dogs

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Changes in the response from the cochlear nerve in dogs resulting from cerebellopontine angle (CPA) manipulations were correlated with histological changes in the nerve. The aim of this study was to determine the mechanisms underlying hearing deficits incurred as a result of manipulations in the CPA. Compound action potentials (CAP) were recorded from the cochlear nerve in response to click stimulation before, during, and after cerebellar and eighth nerve retractions were performed under anesthesia. The retractions were carried out to elicit different degrees of change in the latency and waveform of the CAP. About 30 minutes after completion of the manipulations, the dogs were perfused with a fixative and their cochlear nerves and brain stems were prepared for histological studies. The results showed that retraction of the eighth nerve caused a disintegration of the myelin sheath, and there were multiple and extensive foci of petechial hemorrhage and thromboses of the vasa nervorum of the cochlear nerve.

In two dogs in which retraction was carried to a point at which the N2 peak of the CAP was abruptly obliterated, there was a separation of the central and peripheral myelin junction (Obersteiner-Redlich (OR) zone) and bleeding from the vasa nervorum at the OR zone. In the dogs in which the changes in the CAP had almost recovered before fixative perfusion, there were petechial hemorrhages within the cochlear nerve trunk, thus showing that improvement of electrophysiological responses may not always correlate with the absence of morphological changes.

**KEY WORDS** • Obersteiner-Redlich zone • cochlear nerve • compound action potentials • cerebellopontine angle • nerve injury • dog

RESERVATION of hearing is an important consideration in neurosurgical operations such as microvascular decompression of the cranial nerves and resection of acoustic neuromas. It has been known for a long time that the cochlear nerve is vulnerable, and that even delicate operative manipulations can injure the cochlear nerve sufficiently to cause permanent hearing loss. As these operative procedures are being performed more frequently, the need to find ways to decrease hearing damage has become greater. However, the precise mechanisms leading to hearing deficits from surgical manipulation of the cochlear nerve are unknown.

In the present study in dogs, we recorded the compound action potentials (CAP) from the auditory nerve and examined the cochlear nerve by light and electron microscopy after surgical manipulations similar to those that commonly occur during neurosurgical operations in the cerebellopontine angle (CPA). It has been shown that CAP recorded from the cochlear nerve are of value in intraoperative monitoring of patients undergoing operations involving manipulation of the eighth cranial nerve; recording CAP is especially useful because they do not require time-consuming averaging as do brain-stem auditory evoked potentials (BAEP). This method is now increasing in use for monitoring the auditory system in such operations. The results of recording CAP from the cochlear nerve during manipulations were correlated with the histopathological findings of the cochlear nerve and brain stem.

**Materials and Methods**

This study included 10 adult mongrel dogs, each weighing 10 to 12 kg. The dogs were anesthetized with sodium pentobarbital (Nembutal, 25 mg/kg) administered intravenously. The electrocardiogram was moni-
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FIG. 1. Photomicrographs showing the normal Obersteiner-Redlich (OR) zone of the eighth cranial nerve of a dog. Left: The OR zone is outlined by open arrows. Note the convex shape and numerous blood vessels (small arrows) within the nerve, which are free of red blood cells. C = central portion of the nerve; P = peripheral portion of the nerve. Toluidine blue, × 100. Right: Higher magnification of the OR zone. Large arrows indicate the transitional zone. Blood vessels (small arrows) are visible on the central (C) side of the zone. P = peripheral portion. Toluidine blue, × 450.

tored, and the rectal temperature was maintained between 36° and 38°C with the aid of a heating pad. Respirations were controlled with an animal respirator, and Innovar-Vet* was administered intermittently to maintain anesthesia. Each animal was positioned in the prone position with the head fixed, and a right retro-mastoid craniectomy was performed under a surgical microscope. The lateral edge of the right cerebellar hemisphere was retracted medially to expose the root entry zone of the eighth nerve, and the eighth nerve was gently retracted caudally to rostrally with a blunt nerve hook.†

In some dogs the cerebrospinal fluid was released through a small incision in the arachnoid membrane over the eighth nerve, then the cerebellar hemisphere and eighth nerve were manipulated from outside the arachnoid. Following this, a larger circumferential incision was made in the arachnoid membrane around the seventh and eighth cranial nerves, and the nerves were manipulated subarachnoidally.

Compound action potentials were recorded from the cochlear nerve near the brain stem with the reference electrode placed in the dorsal aspect of the neck. The ground electrode was placed on the nose. A Teflon-insulated silver wire with the tip bared was placed for intracranial recording, and needle electrodes were used for reference and ground.‡ Click stimuli (30-V, 20-μsec rectangular pulses generated by a stimulator) were presented through an earphone to the animal's right ear at a rate of 10 pulses/sec.§ The responses were amplified with bandpass filters set between 3 Hz and 10 kHz.¶ Responses were averaged and stored by a computer, and hard copies were made later. The CAP were displayed on an oscilloscope without averaging. All potentials are shown with negativity upward. Recordings of


† Insulated silver wire, Type AGE 10T, manufactured by Medwire Corp., Mount Vernon, New York; subdermal electrodes, Type E2, manufactured by Grass Instrument Co., Quincy, Massachusetts.

‡ Stimulator, Model SD9, manufactured by Grass Instrument Co., Quincy, Massachusetts; Realistic micro-stereo earphone obtained from Radio Shack, a division of Tandy Corp., Fort Worth, Texas.

§ Amplifier, Model P511K, manufactured by Grass Instrument Co., Quincy, Massachusetts.
the BAEP were made differentially from the vertex and mastoid before the operation and before manipulation of the eighth nerve so as to monitor the integrity of the auditory system during the operation.

About 30 minutes after completion of the manipulations, while still anesthetized, each animal was perfused via the aorta with 4% paraformaldehyde, 0.5% glutaraldehyde, and 0.54% dextrose in 0.1 M phosphate buffer (pH 7.2 to 7.4). Simultaneously, the CPA on the operative side was irrigated with the same fixatives. Two hours later, both of the temporal bones and the brain stem were taken out en bloc and immersed in the same solution overnight at 4°C. The next day, the cochlear nerve was removed from its modiolar portion to the brain stem and was sectioned longitudinally under a surgical microscope. The nerve was then cut into small blocks. After rinsing with 0.1 M phosphate buffer, the blocks were postfixed with 2% OsO4 in 0.1 M phosphate buffer for 2 hours. Following dehydration in ascending concentrations of ethanol, the specimens were embedded in Epon-Araldite. Thick sections were cut, stained with toluidine blue solution, and examined with a light microscope. Ultrathin sections were also cut, stained with uranyl acetate and lead citrate, and examined in a Philips $300 or JEOL 100CX transmission electron microscope. The nonoperated side of each brain served as the control. When the control side contained unacceptable artifacts, the animal was excluded from the study.

Results

In dogs, the transitional zone from the peripheral myelin to the central myelin (the Obersteiner-Redlich (OR) zone)\(^4\) of the cochlear nerve is situated within the internal auditory canal. This transitional zone appears dome-shaped, with the convex side toward the periphery in man\(^1,10,19\) and in the rat.\(^16\)

As a result of our perfusion methods, the blood vessels in the nerves on the control side were free from red blood cells. The number of blood vessels supplying the cochlear nerve (vasa nervorum) was significantly greater in the peripheral portion than in the central portion (Fig. 1 left). A group of vasa nervorum was often seen just central to the transitional zone (Fig. 1 right).

The auditory evoked potentials (the CAP) recorded from the proximal part of the cochlear nerve consisted of two negative peaks, N\(_1\) and N\(_2\) (Fig. 2). The N\(_2\) potentials in small animals are considered to be generated mainly by the cochlear nucleus\(^8\) (Fig. 3). In six dogs the manipulations were carried to a point at which the N\(_1\) and N\(_2\) latencies were prolonged and the N\(_1\) and N\(_2\) amplitudes decreased as the initial positivity deepened; however, retraction was terminated before the N\(_2\) peak was lost (Fig. 2). In these animals most of the preinsult waveforms reappeared after release of the retractor, but the histological changes in the cochlear nerves of some of these dogs were significant; petechial hemorrhages were detected at the portion of the nerve that had been compressed (Fig. 4), although the OR zones and the cells of the cochlear nucleus appeared to be normal.
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In two dogs manipulations were carried to the point where the N2 components of the CAP were no longer identifiable. There was only slight recovery of the N2 peak after retraction was released in these dogs (Fig. 3). Histological examination of these cases showed an extensive hemorrhage in the cochlear nerve, occupying almost the entire compressed portion of the cochlear nerve trunk, and intravascular clots were observed (Fig. 5 left). There were also petechial hemorrhages in the OR zone, although the nerve was manipulated at some distance from the OR zone. The junctional zone was not separated, however (Fig. 5 upper right). Most of the cochlear nucleus cells stained normally; only a few cochlear nucleus cells that were located toward the eighth nerve side appeared dark (Fig. 5 lower right), showing that the effects of CPA manipulations did not extend to the brain stem.

In two other dogs there was an abrupt decrease in the amplitude of the N2 component during the manipulation, while the N1 component remained nearly unchanged. In these animals there was little or no recovery of the N2 component after the manipulations (Fig. 6). Histological studies of these animals showed multiple hemorrhages at the OR zone, and the central and peripheral portions of the nerve were almost separated (Fig. 7 left). Electron microscopy showed that the axons were most probably disrupted at the node of Ranvier of the OR zone (borderline node of Ranvier). The blood vessels were often seen in the “cleft” between the central and peripheral myelins, suggesting that these blood vessels might have been the source of bleeding (Fig. 7 right).

Discussion

The results of the present study show that even manipulations of the cochlear nerve that result in moderate changes in the CAP result in detectable morphological changes in the cochlear nerve. When the change in the recorded CAP was restricted to a shift in latency,
the histological changes were relatively small. However, when more extensive changes in the CAP occurred, such as a noticeable decrease in the amplitude of the N2 component, the histological alterations in the cochlear nerve were much more extensive.

The central myelin at the OR zone is embedded in fragile astrocytic glial processes (glial fringe), whereas the peripheral portion of the nerve is reinforced by the collagen in the endoneurium.13,16 The vascular system is also different between the peripheral and central portions of the cochlear nerve; the arterial system is much more sparse and irregular in the central than in the peripheral portion.5,13 Our histological data indicated that cochlear nerve injury occurred at the site of the compressed portion of the cochlear nerve and/or at the OR zone. Loss of the N2 component of the CAP may reflect nerve conduction impairment at these locations because the N2 component in small animals is generated in the cochlear nucleus --- a location more proximal to the site of compression as well as the OR zone.

It is well known that lateral-to-medial retraction of the cerebellum in posterior fossa surgery is more dangerous to hearing than retraction in a caudal-to-rostral direction.4 The present study confirms this and indicates that the reason that such retraction causes a loss of hearing may be axon separation at the OR zone.

Investigators have discussed what degree of change in the electrophysiological recordings (either CAP or BAEP) can be permitted during operations without permanent auditory deficits being caused.2,12 Some have claimed that quite extensive changes in the BAEP can be allowed without permanent hearing loss resulting.2 However, our results seem to indicate that, even in cases in which manipulation causes only small changes in the CAP and even if the CAP improve after termination of the manipulation, microhemorrhages in the cochlear nerve may remain. Thus, it seems that any noticeable change in the CAP indicates a potential for histologically recognizable injury to the cochlear nerve.

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The present study also suggests that an abrupt decrease in the amplitude of the N2 components is an indication of avulsion of the OR zone of the cochlear nerve, and this may be evidence of a more serious injury than gradual deterioration.

The findings of the present study also show that epiarachnoid retraction of the eighth nerve led to much less striking change in the CAP than did subarachnoid retraction. This means that the arachnoid membrane may help to prevent injury to the eighth nerve during manipulation. The reason for this may be found in the fact that the arachnoid membrane adheres to the meningeal layer of the dura mater inside the internal auditory canal. Since the arachnoid membrane cannot be pulled out from the internal auditory canal, the cochlear nerve is protected from being stretched when it is pulled epiarachnoidally. After the arachnoid membrane is incised, each CPA manipulation easily transmits force to the OR zone of the cochlear nerve.

It has been noted clinically that residual postoperative hearing may disappear within several days after an operation. Our study indicates that there may be blood flow disturbances in vessels of small diameter in the compressed region of the nerve. This may be the aggravating factor in postoperative nerve edema. Microvascular obstruction 3 hours after a cerebral contusion is reported to be more extensive than within 1 hour after an insult, suggesting that microvascular changes after insult progress over time. These facts emphasize the difficulty of using intraoperative changes in CAP to predict what degree of deterioration in hearing might persist postoperatively.

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