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Research paper

A model of real time monitoring of the cochlear function during an induced local ischemia

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Abstract

The aim of this study was to investigate the utility of distortion product otoacoustic emissions (DPOAEs) in intraoperative monitoring (IM) of cochlear ischemic episodes in animals during internal auditory artery (IAA) compression. The IAA was exposed using the posterior fossa approach and then compressed for 3 and 5 min intervals to effect ischemia. DPOAE amplitudes and phases were measured at 4, 8, and 12 kHz geometric mean frequency (GMF). In each monitored ear, laser-Doppler cochlear blood flow (CBF) was measured. All IAA compressions resulted in rapid decrease of DPOAE amplitude and CBF, with simultaneous DPOAE phase increase. DPOAE phase changes were found to increase consistently within several seconds of IAA compression, while corresponding DPOAE amplitudes changed more slowly, with up to 30–40 s delays. Following IAA release, DPOAEs at 12 kHz GMF were characterized by longer delays in returning to baseline than those measured at lower frequencies. In some cases, CBF did not return to baseline. In this animal model, DPOAEs were found to be sensitive measures of cochlear function during transient cochlear ischemic episodes, suggesting the utility of DPOAE monitoring of auditory function during surgery of cerebello-pontine angle tumors.

Keywords: Otoacoustic emissions; Cochlear blood flow; Cochlear ischemia; Cochlear reperfusion

1. Introduction

Intraoperative monitoring during surgery in the cerebello-pontine angle (CPA) minimizes the risk of damaging neural structures such as the facial, the vestibulocochlear and the trigeminal nerves (Moller, 1996; Colletti and Fiorino, 1998; Telischi et al., 1998; Battista et al., 2000). Electrophysiological measurements using auditory brainstem responses (ABR), electrocochleography (ECochG), cochlear nerve compound action potential (CAP) and responses recorded from cochlear nuclei provide direct information about the functional status of the auditory pathway during CPA tumor surgery. Some changes, however, such as those evoked by ischemia of the cochlea, are detectable only after some delay (Lenarz and Ernst, 1992; Colletti and Fiorino, 1998; Kuroki and Moller, 1995; Moller, 1996; Telischi et al., 1998; Battista et al., 2000). Thus, maximum shortening of this delay provides surgeons with timely information about cochlear blood flow (CBF) changes and the resulting reduction of auditory function may prevent permanent ischemic damage to the auditory endorgan during CPA tumor surgery. Intraoperative

Abbreviations: ABR, auditory brainstem responses; BL, baseline; CAP, compound action potential; CBF, cochlear blood flow; CPA, cerebello-pontine angle; DPOAEs, distortion product otoacoustic emissions; ECochG, electrocochleography; EP, endocochlear potential; GMF, geometric mean frequency; IAC, internal auditory canal; IAA, internal auditory artery; IHCs, inner hair cells; IM, intraoperative monitoring; LD, laser-Doppler; LD-CBF, laser-Doppler cochlear blood flow; OAEs, otoacoustic emissions; OHCs, outer hair cells; ROS, reactive oxygen species; SPL, sound pressure level; TEOAEs, transiently evoked otoacoustic emissions

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monitoring of hearing status also was found to be very useful during CPA region surgery due to hemifacial spasm or trigeminal neuralgias treated by microvascular decompression (Fischer, 1989; Hatayama and Moller, 1998; Linden et al., 1997; Moller, 1992).

Evoked otoacoustic emissions (OAEs), are measures of acoustic energy recorded from the ear canal and generated from the cochlea in response to acoustic stimulation (Kemp, 1978; Probst et al., 1991). It is thought that OAEs reflect the function of the cochlea that is associated with electromotility of the outer hair cells (OHCs) that are extremely sensitive to such harmful factors as excessive noise, ototoxic drugs, and hypoxic or anoxic conditions. Such insults can quickly alter OHC function, which results in either reduced or absent OAEs, depending on the severity of the damage (Lonsbury-Martin et al., 1987; Brownell, 1990; Probst et al., 1991; Whitehead et al., 1992b; Prasher et al., 1995; Namyslowski et al., 2001). In particular, the evoked emissions that are used most commonly for clinical applications are the transiently evoked (TEOAEs) and distortion-product (DPOAEs) OAEs (Probst et al., 1991).

The role of the internal auditory artery (IAA) and the anterior inferior cerebellar artery (AICA), if they escaped earlier damage by the invading tumor, in occurrence of hearing loss after removal of CPA tumors, may be underestimated. There is evidence that cochlear ischemia may be involved in sudden hearing losses, presbycusis, CPA tumors, and noise induced hearing loss (Prasher et al., 1995; Subramaniam et al., 1995; Seidman et al., 1999; Nelson and Hinojosa, 2003).

CBF and cochlear ischemia have been studied for many years. The first study by Perlman et al. (1959), in which CBF was measured microscopically estimating stria vascularis vessels, showed that during cochlear ischemia OHCs and spiral ganglion cells were the first structures to be damaged irreversibly. Miller et al. (1983) were among the first to apply laser-Doppler (LD) flowmetry techniques to measure CBF and to evaluate cochlear ischemia in guinea pigs. Other animal models of cochlear ischemia/reperfusion CBF monitoring in the literature include rats (Scheibe et al., 1990), gerbils (Ren et al., 1995), and rabbits (Mom et al., 1999). To date, only a few experimental studies measuring CBF in humans have been published. In the first papers, researchers measured CBF by placing the laser probe on promontory and showed that relatively thick cochlear bone attenuated the laser energy, significantly limiting its use in humans (Scheibe et al., 1990; Miller et al., 1991). Recently, LD flowmetry was used to evaluate CBF in patients during cochlear implantation by placing the probe tip into the cochleostomy site. Significant reduction in CBF was seen in patients more than 40 years old with idiopathic sensorineural hearing loss and in patients with cochlear calcification following meningitis (Nakashima et al., 2004). Albera et al. (2003) measured LD CBF from the cochlear promontory of patients during general anesthesia who were being operated during controlled systemic hypotension. They showed a decrease in CBF in patients during administration of the intravenous anesthetic propofol. Other studies have shown changes in CBF in patients with Meniere's disease, sudden hearing loss (Selmani et al., 2001), and perilymphatic fistula (Nakashima and Yanagita, 1995). Alteration of the cochlear microcirculation via round window drug application has also been studied (Haapaniemi et al., 2001; Miller et al., 1994).

To study the role of surgically induced vascular trauma during the course of CPA surgery, an animal model of intraoperative monitoring of CBF and cochlear function was developed. OAEs, especially DPOAEs, were chosen based on the following qualities: simple, non-invasive, objective, efficient (Rebillard and Lavigne-Rebillard, 1992; Widick et al., 1994; Telischi et al., 1999; Mom et al., 1997, 1999). DPOAEs evoked by low-level primary tones have been shown to be quite sensitive to changes in and, in fact, be a good proxy for CBF (Lonsbury-Martin et al., 1987; Whitehead et al., 1992b; Mom et al., 1999). The combination of LD CBF and DPOAE identified different events causing reversible and irreversible cochlear function changes, including IAA vasospasm and reversible cochlear ischemia, during surgical manipulations Telischi et al., 1999; Mom et al., 2000; Morawski et al., 2003a,b, 2004.

The authors of the present study investigated the utility of DPOAEs in intraoperative monitoring of cochlear ischemic episodes in animals during the inner ear artery (IAA) compression. The purpose of this study was to elaborate DPOAE intraoperative monitoring data collected during animal experiments and analyze the patterns of DPOAE amplitude and phase changes observed during cochlear ischemia-reperfusion episodes. Developed DPOAE models may be applied to interpret of DPOAEs recorded during CPA surgery in humans.

2. Methods

2.1. Animal model

Ten young (2.5-6-mo old) albino rabbits weighing between 2.5 and 4.0 kg were used for this study. The protocol for the care and use of rabbits was approved by the Institutional Animal Care and Use Committee. Several days prior to experimentation, DPOAEs at 2f1-f2 were obtained from each ear to assess adequate cochlear function using standard techniques. Briefly, two equilevel ($L1 = L2$) primary tones at an optimal f2/f1 ratio of 1.25 were acoustically mixed and presented to the ear via a custom-designed probe sealed tightly into the external auditory canal. DPOAE levels as a function of frequency, i.e., DP-grams, were plotted from 1–12 kHz for equilevel primary tones from 45 to 75 dB sound pressure level (SPL) at 5-dB intervals. During the actual experimental manipulations of CBF, DP-tracking functions at 4, 8, and 12 kHz were obtained by monitoring DPOAE levels in response to $L1 = L2 = 60$ dB SPL primary tones. For both DP-grams and the DP-tracking functions, DPOAE frequencies were converted to the geometric mean frequency (GMF) to adequately describe the generator site in rabbits for 2f1-f2 DPOAEs at the stimulus levels used here. These steps were repeated just prior to surgery and also following the opening of the middle ear cavity to ensure continued normal cochlear function. The stimulus generation and DPOAE-measurement equipment have been described in detail in previous reports (Lonsbury-Martin et al., 1987; Whitehead et al., 1992a,b).