ORIGINAL ARTICLE

Effect of Hypothermia on Distortion Product Otoacoustic Emission Findings in Children Undergoing Congenital Open Heart Surgery

Erdinc Aydin, Guzin Akkuzu, Babur Akkuzu, Asli Donmez, Sukru Mercan, Ersin Ogus

Baskent University Faculty of Medicine Department of Otorhinolaryngology, Ankara, Turkey (EA, GA, BA)
Baskent University Faculty of Medicine Department of Anaesthesiology (AD)
Baskent University Faculty of Medicine Department of Cardiovascular Surgery (SM)
Baskent University Faculty of Medicine Department of Biostatistics (EO)

Objective; The aim of this study is to investigate the influence of extreme hypothermia on distortion product otoacoustic emissions (DPOAE) generated from the OHC of the organ of Corti. Temperature is controlled (within certain rigid limits) in warm-blooded animals including human beings. To investigate extreme hypothermia in our study we selected patients undergoing congenital open heart surgery where body temperature can be lowered over a large temperature interval. To monitor inner ear functions, we measured distortion product otoacoustic emissions that can be applied repeatedly in a cardiovascular operating room that is electrically and acoustically noisy.

Study Design; Prospective clinical trial.

Materials & Methods; Twenty-four pediatric patients (median age, 24 months) with congenital heart disease undergoing cardiopulmonary bypass (CPB) were involved in the study. The same anesthetic, surgical, and CPB protocols were used in all patients. Distortion product otoacoustic emission measurements were performed preoperatively, several times intraoperatively, and postoperatively.

Results; Inner ear functions diminished with the degree of hypothermia and returned to normal with warming (P<05). Other parameters such as presence of cyanotic disease, cross-clamping, and duration of CPB did not significantly affect distortion product otoacoustic emission measurements..

Conclusion; Congenital open heart surgery has no permanent effect on inner ear function. Hypothermia can cause transient loss of inner ear functions. To the best of our knowledge, this is the first study in the medical literature on human beings to show the effect of hypothermia on distortion product otoacoustic emission measurements.

Submitted : 13 November 2008   *Revised : 07 January 2009*   *Accepted   : 07 January 2009*

The mechanoacoustic auditory message is converted into nerve signals in the hair cells of the organ of Corti and is transmitted to the brainstem by the auditory nerve afferent neurons. Conversion and transmission involve ionic mechanisms that might react to body temperature. Otoacoustic emissions (OAE), noninvasively recorded from the external auditory canal, have enabled studies on the effects of body temperature on cochlear transduction mechanisms [1,2]. In both animals and human beings, active outer hair cell (OHC) micromechanical activity has been shown to generate mechanical vibrations underlying the OAE recorded from the external auditory canal [3]. These mechanical vibrations involve metabolic processes that are biochemical reactions that should be temperature dependent. Logically then, variations in body temperature should affect OAE. Temperature is controlled (within certain rigid limits) in warm-blooded animals including human beings. The aim of our study was to investigate the influence of extreme hypothermia on distortion product otoacoustic emissions (DPOAE) generated from the OHC of the organ of Corti. To date no study has investigated the influence of hypothermia on DPOAE in human beings.

Corresponding address:
Erdinc Aydin, MD, Associate Professor
Baskent University Faculty of Medicine Department of Otorhinolaryngology & Head and Neck Surgery
6. Cadde No:72/2 06490 Bahcelievler-Ankara/Turkey
Phone: +90 312 223 85 34; Fax: +90 312 215 75 97; e-mail: erdinca@baskent-ank.edu.tr

Materials & Methods

This study was approved by the Institutional Ethics Committee. The parents of all of the patients provided written informed consent. Twenty-eight pediatric patients with congenital heart disease scheduled for open heart surgery were included in the study. The day before surgery, an otologic examination was performed by an ear, nose, and throat specialist to verify the absence of chronic or acute otitis media and middle ear effusion. Also, cerumen was removed from occluded ear canals. Three patients had middle ear effusions, and 1 patient had hemorrhage from the ear canal while cleaning cerumen that precluded performing DPOAE measurements. These 4 patients were excluded from the study. The remaining 24 pediatric patients were included.

The same anesthetic, surgical, and CPB protocols were used in all of the patients. CPB was performed using a membrane oxygenator with prime volumes of 35 mL/kg. The pump flow and hematocrit were maintained at 2.5 to 3.0 L/minute/m_ and 28% to 30% respectively. Systemic hypothermia with a target core temperature of 24ºC to 26ºC, and a cold hyperkalemic cardioplegia solution was used. Appropriate cardiac corrective surgery was performed by the cardiovascular team according to the congenital cardiac anomaly.

The patient group was composed of 14 females and 10 males (median age, 24 months; range, 4-108 months). Fifteen were acyanotic and 9 were cyanotic. Preoperatively, all these patients had DPOAE indicating normal cochlear integrity and hearing. DPOAE were obtained using ILO292 OAE, DP Echoport Plus device (Otodynamics Ltd., Hartfield, UK) and appropriate software (Otodynamics Ltd, 1999, v5.60y). Distortion product otoacoustic emission signals were evaluated as a function of stimulus intensity (input-output (I/O) function). Two primary pure tones at frequencies f1 and f2 were used in the test procedure. The level and the frequency ratio of the primaries were kept constant (L1= L2, f2/f1=1.22). The levels were increased in 5-dB steps from 35 to 70 dB sound pressure level (SPL). The I/O function was evaluated at f2 ranging from 1000 to 6000 Hz at 9 frequency bands. Preoperative and postoperative measurements were taken from both ears but intraoperatively, a single ear was chosen randomly as this was deemed to be more practical. Distortion product otoacoustic emission measurements were performed preoperatively the day before surgery and postoperatively the day after surgery. Intraoperative measurements were obtained just after induction of anesthesia, at the beginning of surgery, before initiation of CPB, at maximum hypothermia level, after cessation of CPB, and just before awakening. Rectal temperature measurements were followed throughout the operation. In patients with deep hypothermia, DPOAE measurements were taken at 2°C increments and decrements in rectal temperature.

Statistical analyses were conducted with SPSS software (Statistical Package for the Social Sciences, version 11.0, SPSS Inc, Chicago, IL, USA). A P value less than .05 was accepted as statistically significant.

Results

Intraoperative DPOAE measurements were obtained from the right ear in 14 and the left ear in 10 patients. Among 24 patients included in the study, 9 had cyanotic and 15 had acyanotic cardiac pathologies. The cardiac pathologies consisted of atrial septal defects, ventricular septal defects, tetralogy of Fallot, aortic coarctation, pulmonary artery stenosis, and combinations of these pathologies.

Three patients had total circulatory arrest with deep hypothermia (17°C -19°C), the remaining patients had CPB with varying degrees of hypothermia (22°C - 32°C). Eight patients had cardioplegic solution instilled to the heart. The duration of CPB varied between 18 and 114 minutes (median, 59 minutes). Parameters such as presence of cyanotic disease, cross-clamping, duration of CPB, and cardioplegic solution application did not significantly affect OAE measurements ($p > .05$).

There were no significant differences between preoperative and after the induction of anesthesia DPOAE measurements for each frequency band (P > .05).

There were no significant differences between preoperative and postoperative DPOAE measurements for each frequency band (P > .05).

Without exception, DPOAEs were affected during decreases in core temperature (p<0.05). An example of the DPOAE changes in the temperature domain from a representative subject is presented in Figure 1. DPOAE amplitude decreased with cooling and completely disappeared during deep hypothermia
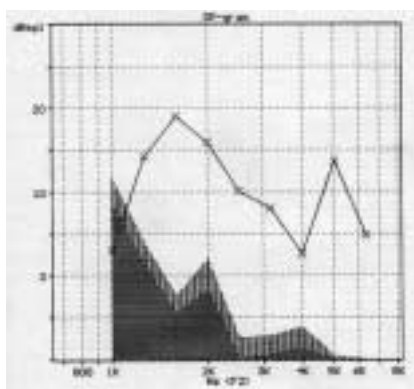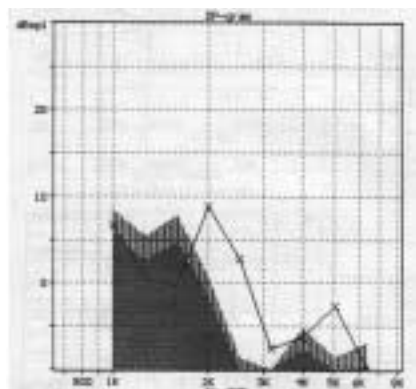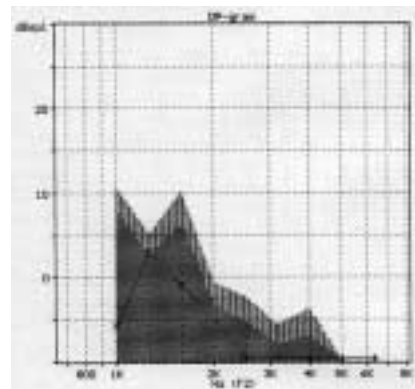

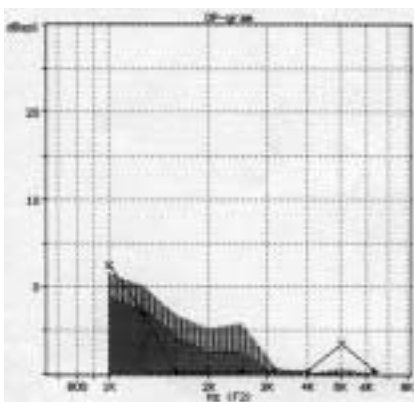**Figure 1a: 37ºC** **Figure 1b:** 31ºC **Figure 1c:** 25ºC
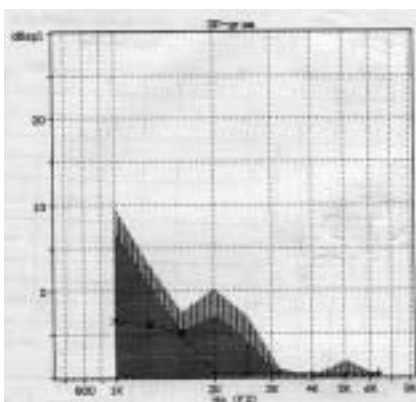
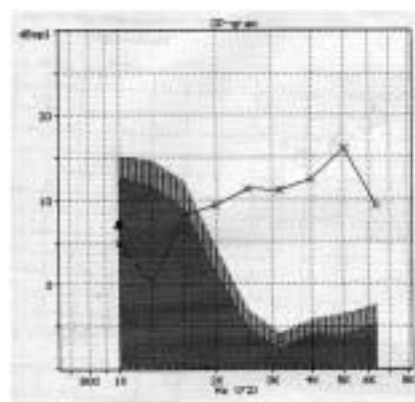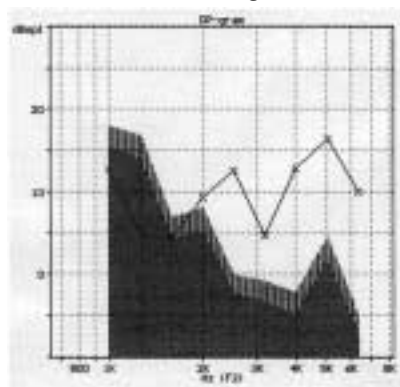**Figure 1d:** 19 ºC **Figure 1e:** 23 ºC **Figure 1f:** 33 ºC
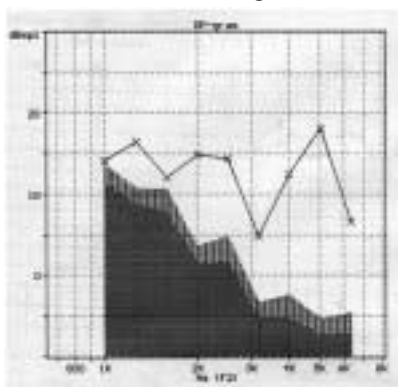
Figure 1g: 35 ºC **Figure 1h:** 37 ºC

Figure 1. DPOAE changes in the temperature domain from a representative subject undergoing congenital open heart surgery. Recordings represent the cooling down period (Figure 1a:37ºC; 1b:31ºC; 1c:25ºC; 1d:19 ºC) and warming up period (Figure 1e:23 ºC; 1f:33 ºC; 1g: 35 ºC; 1h: 37 ºC), respectively.
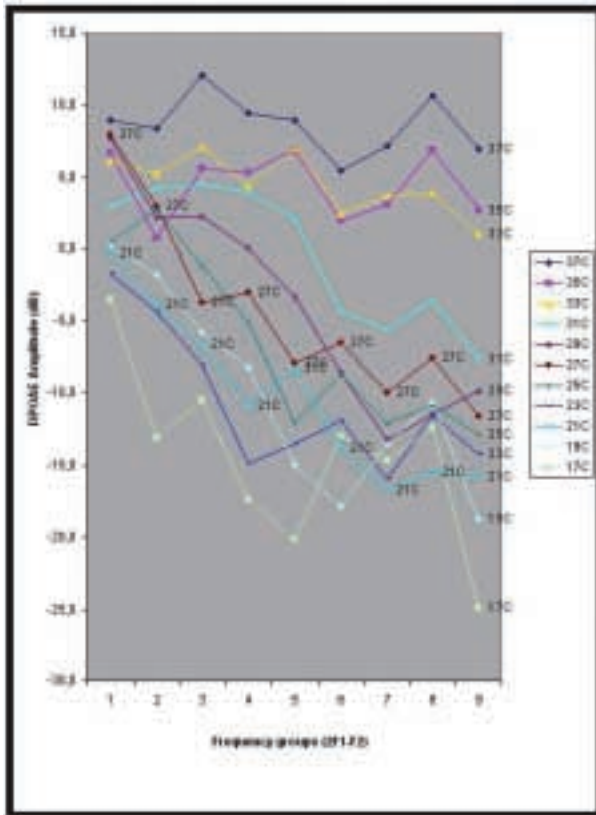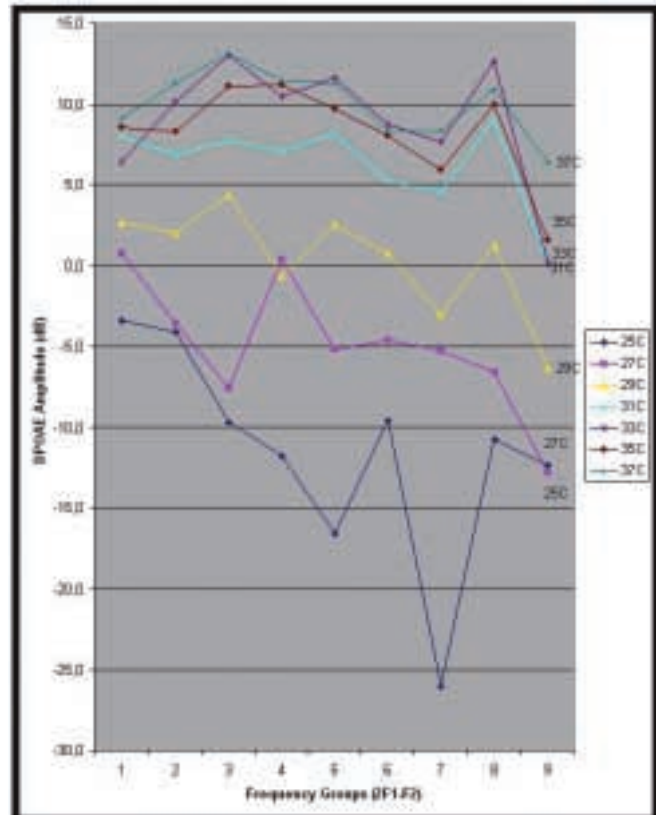
Figure 2a

Figure 2b

Figure 2. The average DPOAE changes during cooling and warming are demonstrated in Figures 2 a and b, respectively. Each line is designated by the corresponding temperature.

(<30°C). DPOAEs then returned back to normal with rewarming. It was not possible to find a frequency band that systematically disappeared or reappeared first or last in all subjects. The average DPOAE changes during cooling and warming are demonstrated in Figures 2 a and b, respectively.

Discussion

The mechanoacoustic auditory message is converted into nerve signals in the hair cells of the organ of Corti and transmitted to the brainstem by the auditory nerve afferent neurons. Conversion and transmission involve ionic mechanisms that might react to body temperature. There are many ways that temperature might affect OHC activity, through direct temperature dependence of channel gating kinetics, through direct temperature dependence of contractile mechanisms, through temperature dependence of metabolic pathways and metabolite logistical pathways such as oxygen transport.

The literature concerning the influence of temperature on OAE amplitude and frequency in amphibians and reptiles is abundant, most likely because they are cold blooded animals and can easily change their body temperature over a large temperature range [4,5]. For these species, a clear and reversible effect is observed. Reducing the body temperature in frogs reduced the frequency of spontaneous otoacoustic emissions (SOAE) [4]. However, the hearing organ in frogs is different from the organ of Corti in human beings. The hair cells of frogs are embedded in a relatively solid structure and no basilar membrane exists. Therefore, these findings cannot be extrapolated to humans [2]. Spontaneous otoacoustic emissions in the ear canal of the Australian bobtail lizard are temperature sensitive and shift their frequency up with increases in temperature-an effect that is fully reversible [5].

In contrast, relatively few studies have investigated the effect of temperature on OAE in mammals. Most

studies in mammals to investigate temperature effects on OAE have been performed by raising body temperature. A study in human beings conducted under hyperthermic conditions obtained in a climatic chamber revealed a significant amplitude decrease in transient evoked otoacoustic emissions (TEOAE) [2].

There are clues that hypothermia may reduce ischemic damage in animals. In Mongolian gerbils that lack posterior cerebral communicating arteries and have labyrinthine arteries nourished solely by the vertebral arteries, Watanabe and associates have shown that occluding both vertebral arteries for 15 minutes causes profound deafness and substantial loss of hair cells. Decreasing the whole body temperature by 5°C prevented hearing loss and progressive hair cell loss in the cochlea after transient ischemia [6].

Experimental studies have shown that ischemia-induced damage progresses after reperfusion in many organs such as the brain, heart, and liver [7,8]. Hypothermia is an effective way to protect against this injury especially in the brain [9]. Glutamate is closely related to ischemia reperfusion injury of the inner ear [10]. The effects of mild hypothermia are thought to be due to a reduction in glutamate toxicity, suppression of calcium influx into neurons, or prevention of nitric oxide production thus reducing free radical toxicity.[11-14]

Hypothermia also increases the survival time of isolated spinal neurons [15]. Experiments in mice have shown that hypothermia increases thresholds to the cochlear nerve envelope response and reduce the damaging effects of noise, whereas hyperthermia exacerbates the detrimental action [11].

In human beings, temperatures below body core temperatures are imposed for open heart bypass surgeries during which the body temperature can be lowered over a large temperature interval. A study of 30 patients undergoing open heart surgery under induced hypothermia in which TEOAE were recorded showed a clear influence of body temperature on the amplitudes and reproducibilities of the TEOAE [16].

Another study of 5 children during open heart bypass surgery, investigating the effect of hypothermia on TEOAE showed that TEOAE were totally abolished at tympanic temperatures of approximately 30°C, and that during rewarming, changes reversed and TEOAE returned to their initial prehypothermia status [1]. In this study the patients were under general anesthesia. This study does not mention the preanesthesia levels of TEOAE measurements. In both of these studies, TEOAE were measured. The total suppression of TEOAE was attributed to a temperature-dependant energy source. It is assumed that the frequency of otoacoustic emissions depends on electrical tuning of hair cells, the temperature dependence of emission frequency may result from the temperature dependence of calcium channel kinetics [4]. In our study we measured the DPOAE the day before the surgery and after the induction of anesthesia but there was no significant difference between these measures.

Previous animal studies have shown that the measured cochlear temperature was about the same as the rectal temperature, and also, changes in rectal temperature were parallel to the cochlear temperature [6,17,18]. Thus, in our study, instead of using an ear canal probe, we used rectal measurements, which is a routine application of the cardiovascular surgery team.

The 2 major techniques used to protect vital organs during cardiac repair are deep hypothermia with either TCA or CPB. With cardiac arrest, risks are primarily related to cerebral hypoxic-ischemic/reperfusion injury, and with CPB, these risks are related to embolic complications associated with the increased time of extracorporeal circulation [19]. In both of these situations in our study, these extreme conditions had no persistent detrimental effect with respect to OAE levels. There were no significant differences in preoperative and postoperative DPOAE measurements.

Sudden-onset hearing loss, which often results from disruption of cochlear function, is thought to be caused by an acute interruption of blood supply to the inner ear [6]. Reducing the cochlear temperature immediately after onset of sudden deafness may prevent progressive hearing loss. Also, it has been postulated that interruption of cochlear blood flow during acoustic

neuroma surgery causes postoperative sensorineural hearing loss [20,21]. There is an increasing trend to implant patients with residual hearing. . Thus, it is important during surgical drilling and implanting of the electrode to keep cochlear sensory cell damage to the lowest possible level. Hypothermic techniques during ear surgery could be beneficial in preserving serviceable hearing after internal acoustic canal surgery and cochlear implants [22]. Hypothermia by total body cooling is not so practical for ear operations. Studies to investigate the local cochlear cooling techniques in otolaryngology should be encouraged [23].

Conclusion

Hypothermia causes a transient loss of inner ear functions. To our knowledge, ours is the first study in the medical literature, on human beings, showing the effect of hypothermia on distortion product otoacoustic emission measurements.

References

1. Veuillet E, Gartner M, Champsaur G, Neidecker J, Collet L. Effects of hypothermia on cochlear micromechanical properties in humans. J Neurol Sci 1997; 145:69-76.

2. Ferber-Viart C, Savourey G, Garcia C, Duclaux R, Bittel J, Collet L. Influence of hyperthermia on cochlear micromechanical properties in humans. Hear Res 1995; 91:202-7.

3. Kemp DT. Stimulated acoustic emissions from within the human auditory system. J Acoust Soc Am 1978; 64:1386-91.

4. Long GR, Van Dijk P, Wit HP. Temperature dependence of spontaneous otoacoustic emissions in the edible frog (Rana esculenta). Hear Res 1996; 98:22-8.

5. Manley GA, Koppl C. Spontaneous otoacoustic emissions in the bobtail lizard. III: Temperature effects. Hear Res 1994; 72:171-80.

6. Watanabe F, Koga K, Hakuba N, Gyo K. Hypothermia prevents hearing loss and progressive hair cell loss after transient cochlear ischemia in gerbils. Neuroscience 2001; 102:639-45.

7. McCord JM. Oxygen-derived free radicals in postischemic tissue injury. N Engl J Med 1985; 312:159-63.

8. Pulsinelli WA, Brierley JB, Plum F. Temporal profile of neuronal damage in a model of transient forebrain ischemia. Ann Neurol 1982; 11:491-8.

9. Dietrich WD, Busto R, Alonso O, Globus MY, Ginsberg MD. Intraischemic but not postischemic brain hypothermia protects chronically following global forebrain ischemia in rats. J Cereb Blood Flow Metab 1993; 13:541-9.

10. Puel JL, Pujol R, Tribillac F, Ladrech S, Eybalin M. Excitatory amino acid antagonists protect cochlear auditory neurons from excitotoxicity. J Comp Neurol 1994; 341:241-56.

11. Henry KR. Hyperthermia exacerbates and hypothermia protects from noise-induced threshold elevation of the cochlear nerve envelope response in the C57BL/6J mouse. Hear Res 2003; 179:88-96.

12. Hyodo J, Hakuba N, Koga K, et al. Hypothermia reduces glutamate efflux in perilymph following transient cochlear ischemia. Neuroreport 2001; 12:1983-7.

13. Mitani A, Kadoya F, Kataoka K. Temperature dependence of hypoxia-induced calcium accumulation in gerbil hippocampal slices. Brain Res 1991; 562:159-63.

14. Kader A, Frazzini VI, Baker CJ, Solomon RA, Trifiletti RR. Effect of mild hypothermia on nitric oxide synthesis during focal cerebral ischemia. Neurosurgery 1994; 35:272-7.

15. Lucas JH, Wang GF, Gross GW. Paradoxical effect of hypothermia on survival of lesioned and uninjured mammalian spinal neurons. Brain Res 1990; 517:354-7.

16. Seifert E, Lamprecht-Dinnesen A, Asfour B, Rotering H, Bone HG, Scheld HH. The influence of body temperature on transient evoked otoacoustic emissions. Br J Audiol 1998 ;32:387-98.

17. Henry KR, Chole RA. Hypothermia protects the cochlea from noise damage. Hear Res 1984; 16:225-30.

18. Eshraghi AA, Nehme O, Polak M, et al. Cochlear temperature correlates with both temporalis muscle and rectal temperatures. Application for testing the otoprotective effect of hypothermia. Acta Otolaryngol 2005; 125:922-8.

19. Bellinger DC, Wypij D, Kuban KC, et al. Developmental and neurological status of children at 4 years of age after heart surgery with hypothermic circulatory arrest or low-flow cardiopulmonary bypass. Circulation 1999; 100:526-32.

20. Levine RA, Ojemann RG, Montgomery WW, McGaffigan PM. Monitoring auditory evoked potentials during acoustic neuroma surgery. Insights into the mechanism of the hearing loss. Ann Otol Rhinol Laryngol 1984; 93:116-23.

21. Sekiya T, Iwabuchi T, Kamata S, Ishida T. Deterioration of auditory evoked potentials during cerebellopontine angle manipulations. An interpretation based on an experimental model in dogs. J Neurosurg 1985; 63:598-607.

22. Balkany TJ, Eshraghi AA, Jiao H, et al. Mild hypothermia protects auditory function during cochlear implant surgery. Laryngoscope 2005; 115:1543-7.

23. Smith LP, Eshraghi AA, Whitley DE, van de Water TR, Balkany TJ. Induction of localized cochlear hypothermia. Acta Otolaryngol 2007; 127:228-33.