Original Paper

Audiology & Neurotology

Audiol Neurotol 2008;13:281–292
DOI: 10.1159/000124276

Received: November 22, 2007
Accepted after revision: November 28, 2007
Published online: April 7, 2008

Testing the Diagnostic Value of Electrical Ear Canal Stimulation in Cochlear Implant Candidates by Functional Magnetic Resonance Imaging

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Key Words
Ear canal stimulation · Promontory test · Cochlear implant · Functional magnetic resonance imaging

Abstract
Prior to cochlear implant (CI) surgery in children, the integrity of the auditory pathway is sometimes assessed by electrical ear canal stimulation (ECS). However, the evaluation of reactions as auditory is subjective. To test the prognostic value of ECS, functional magnetic resonance imaging (fMRI) was performed during ECS vicariously in 18 adult CI candidates. Activation of the primary auditory cortex was detected in 9 of 16 cases when auditory sensations during ECS occurred, and tended to be more bilaterally distributed in CI candidates than in normal-hearing controls. ECS sensations only tended to correlate with fMRI activations. However, solely frequency discrimination during electrical stimulation predicted CI outcome, but neither other auditory sensations nor fMRI activations did so satisfactorily, which limits the diagnostic value of these measures. Instead, preoperative residual hearing (nonamplified and amplified) was a robust predictor for CI benefit.

K. Neumann and C. Preibisch contributed equally to this work.

Introduction

Electrical stimulation of the auditory nerve, such as the promontory test (PT), is frequently employed before cochlear implantation of profoundly deaf patients in order to ascertain the intactness of the auditory pathway [Schmidt et al., 2003]. Because patient compliance is obligatory, PT is unfeasible in young children and persons with intellectual or multiple disabilities. Therefore, noninvasive electrical ear canal stimulation (ECS) with an electrode placed in the outer ear canal is sometimes applied in these persons, in some European cochlear implant (CI) centers. In ECS the electrical current is assumed to stimulate the cochlear nerve as well as the (residual) functioning hair cells [Dillier and Spillmann, 1977].

Most US American centers which test children preoperatively measure electrical auditory brainstem response audiometry with a promontory needle electrode. However, this procedure requires general anesthesia, and CI children with no preoperative auditory brainstem response may perform as well as children with auditory brainstem response [Nikolopoulos et al., 2000]. ECS, on the other hand, is well tolerated by infant CI candidates and avoids repeated general anesthesia which bears risks particularly for children. The electrode is not very dis-

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turbing because it is pulled through the earmolds of the children's hearing aids and inserted with the mold into the ear canal. As the stimulation is done via infrared signals, the children can play during the test and are only occasionally distracted by the stimulus.

Indications for cochlear implantation have been extended considerably during the last decade [Gstoettner et al., 2005]. Increased experience and confidence in this therapy have been paralleled by a seemingly reduced importance of PT and ECS. Many CI surgeons now base their therapy indications mainly on the patient history, conventional audiometry, and auditory brainstem response audiometry, and perform the operation without PT or ECS, or do so even if these tests fail. Monitoring of electrically evoked auditory brainstem responses and electrically evoked compound action potentials of the auditory nerve via bidirectional telemetry can test the integrity of the auditory pathway and confirm the correct positioning of a cochlear or brainstem stimulator [Alegre et al., 1999; Otto et al., 2005], but this can only be done during surgery. Although recent studies cast doubt on the use of PT to predict CI utility [Albu and Babighian, 1997], in many CI centers PT and/or ECS are still considered useful preoperative tools. Because children have a shorter distance from the ear canal to the auditory nerve and a higher skin conductivity than adults, ECS in children might possibly yield better results than PT in adults. ECS is preferentially applied in prelingually deaf children without utilizable residual hearing who do not show detectable auditory brainstem responses and do not benefit from hearing aids. The presence of ECS responses may also contribute to a positive CI decision in cases of congenital malformations, cochlear nerve dysplasia, suspected aplasia, or narrow internal auditory canal [Nikolopoulos et al., 2000]. Furthermore, patients with an intellectual disability or with multiple handicaps are occasionally tested with ECS because conventional audiometric tests often do not deliver clear results, and the benefit from hearing aids remains uncertain as well. However, it is well known that children with intellectual disabilities may still benefit considerably from a CI, especially if implanted early in childhood [Waltzman and Roland, 2005]. With the extension of CI indications, more candidates who belong to the above groups receive a CI, and consequently need a preoperative test of the functional integrity of the auditory pathway. Thus, ECS may be decreasingly applied in standard CI cases but still carries importance in the special cases described above, where it is sometimes the only tool to estimate the electrical accessibility of the auditory cortex by a CI without general anesthesia.

Lesinski et al. [1997] reported that in adults PT and ECS evoked auditory sensations in 83 and 76% of investigated ears, respectively. Sensations which are not clearly auditory but have a vibrotactile component, which may be perceived as vibrations, humming, buzzing, and non-auditory sensations (electrification, pain), have been reported for ECS [Neumann et al., 2002; Schmidt et al., 2003] and PT as well. In studies comparing both methods these sensations occurred more often during ECS [Lesinski et al., 1997; Spies et al., 1993]. Young deaf children cannot deliver verbal reports about the quality of ESC sensations reliably, if at all. However, clinical experience from pediatric behavioral observation audiometry suggests that reactions of children to ECS are mostly auditory, but with only dubious validity. A possible way to reduce this uncertainty may be to investigate the neuronal correlates of ECS in the auditory cortex with functional neuroimaging methods, vicariously in adults because of infeasibility in infants due to technical and ethical reasons.

Functional magnetic resonance imaging (fMRI) detects circumscribed cortical activation upon external stimulation in an excellent spatial resolution by measuring the local increase in oxygen supply induced by a sensory, motor, or cognitive task [Ogawa et al., 1993]. Cortical activation after electrical stimulation of the auditory nerve in deaf adults has been observed predominantly in the contralateral and to a lesser degree also in the ipsilateral auditory cortex [Alwatban et al., 2002; Berthezene et al., 1997; Neumann et al., 2002; Schmidt et al., 2003].

fMRI activation of the primary auditory cortex has been demonstrated during electrical stimulation of the promontory [Alwatban et al., 2002; Berthezene et al., 1997; Schmidt et al., 2003] as well as during ECS [Hofmann et al., 1999; Knaus et al., 2000]. Promontory stimulation induced activation in the contralateral auditory cortex in 85% of deaf patients who reported auditory sensations, whereas only 25% of patients without auditory sensations showed comparable activations [Schmidt et al., 2003]. ECS yielded auditory cortex activation in 3 out of 5 patients [Hofmann et al., 1999]. Because of the very small sample size of the latter study, it is impossible to compare the value of both PT and ECS for CI indication fairly. Also, a validation with outcome data is desirable.

ECS requires conductive material in the ear canal, which poses a safety problem during fMRI. High static magnetic fields exert strong forces on ferromagnetic objects leading to rotational motion, and translations occur along the magnetic gradient in inhomogeneous fields. These motions may cause serious injuries. Moreover,

electric currents in conducting loops give rise to forces and motion, and vice versa. A considerable risk also emanates from pulsed radio frequencies and the time-varying magnetic field gradient. Induced voltages may cause nerve stimulation and burns [Kanal, 1992]. It is therefore important to avoid potential hazardous interactions of conductive and ferromagnetic materials with the static, the time-varying magnetic, and the pulsed electromagnetic radio frequency fields. It has been demonstrated that safe electrical stimulation inside the MR scanner is possible with appropriate measures and precautions, such as the application of certain stimulation and scanning protocols, special stimulation electrodes, shielding of stimulation cables, disconnecting electrodes during scanning, and avoiding conductive loops [Hofmann et al., 1999; Lemieux et al., 1997; Teissl et al., 1999]. The present study was conducted under considerations of these safety precautions.

ECS in children yields a large proportion of results which are difficult to interpret. In order to shed light on the interpretation of ECS results, this study investigates ECS-related auditory cortex activations with fMRI, vicariously in adults. Consequently, the main purpose of this study was the evaluation of the predictive value of ECS for CI outcome under inclusion of fMRI data. Reactions to ECS were correlated with fMRI activation pattern, and the potential predictive value of ECS and of fMRI was estimated, each one in and by itself. Additionally, it was considered worthwhile to evaluate the predictive value of other diagnostic measures for CI benefit, such as aided and unaided preoperative hearing in comparison with (1) responses to electrical auditory pathway stimulation by ECS or PT, and (2) fMRI activations. Normal-hearing control subjects were included in the study. However, because they received both electrical stimulation and acoustic stimulation by the scanner noise, they were only included for (1) identification of the primary auditory cortex regions within whose borders ECS-induced activations in deaf subjects are to be expected as well, and (2) for comparing the lateralization of activations.

Methods

Subjects

Patients were 8 male and 10 female profoundly deaf CI candidates (mean age 55 years, range 30–75). Control subjects were 3 male and 2 female normal-hearing and healthy persons (mean age 27 years, range 24–31). The study was performed in accordance with the guidelines of the Declaration of Helsinki and was approved by the local ethics commission. All subjects gave written informed consent for participation.

Ear microscopy and tympanometry indicated in all patients normal outer and middle ear conditions. Otoacoustic emissions and stapedius reflexes were absent. Pure-tone audiometry (PTA) as averaged for 1, 2, and 3 kHz revealed a severe to profound hearing loss in 6 ears (80 dB HL $\leq$ PTA $\leq$ 90 dB HL), a profound hearing loss (PTA $\geq$90 dB HL) with residual hearing in 21 ears, and a profound hearing loss without residual hearing (noted as 'deaf' in table 1) in 9 ears. Speech audiometry in quiet with the German Freiburger speech test for monosyllables and numerals, both with hearing aids at 65 and 80 dB HL, defined the utilizable preoperative amplified hearing. Only data for 80 dB HL are presented because 65 dB HL frequently did not yield sufficient word recognition.

The hearing loss was caused by meningitis in 2 patients, by epidemic parotitis infection in another one, and occurred as familial or progressive hearing loss with unknown causes in the remaining 15 cases. Preoperative high-resolution CTs and MRIs did not detect relevant abnormalities of the cochlea and the auditory pathway in any subject. CTs and MRIs did not indicate abnormal brain regions, and patient history and physical examination did not reveal neurological or other severe diseases except in 3 cases: 1 patient had a diabetic neuropathy, with a global loss of brain volume, and 2 patients were deafened by meningitis. One of the latter 2 patients later suffered from Hodgkin's disease, with 2 relapses. He was treated among others with chemotherapy and showed signs of a previous infection in the cerebrospinal fluid.

Procedure

Before and during fMRI, ECS was performed in all patients in either one (13 patients) or both ears (5 patients), with a total of 23 ears. The decision between ECS in one or two ears depended upon participant compliance or temporal limitations due to multiple measurements with several frequencies or intensities in one ear. An additional PT was carried out in 13 patients (17 ears). Because ECS was also performed, 5 patients did not comply with an invasive PT. ECS was carried out in all control participants monaurally (5 ears). The participants were asked to describe their sensations upon stimulation. These sensations as well as those obtained during fMRI were classified into (1) 'clearly auditory', (2) 'uncertain auditory' (difficulties differentiating between auditory and vibrotactile sensations like humming, vibrating and buzzing), (3) 'nonauditory' when sensations were rather pricking or electrifying, and (4) 'no' sensations. Beyond sensations, threshold level, temporal difference limen (TDL), frequency differentiation (FD), and dynamic range between threshold and uncomfortable level were documented for PT.

Electrical Ear Canal Stimulation

The main part of the experimental setup and necessary safety precautions are described elsewhere [Hofmann et al., 1999]. Stimulation was performed with the EAM V02 FMRI, an fMRI-adapted version of the commercially available electro-audiometer EAM® (MED-EL Medical Electronics GmbH, Innsbruck, Austria). The setup included an electro-audiometer (EAM) control box which controlled both the stimulator and a trigger box via infrared signals. From the stimulator a stimulation electrode and a reference electrode led to the participant. The stimulation electrode was positioned in the external ear canal. The reference elec-

Table 1. CI candidates: variables for preoperative diagnostics, fMRI, and outcome after CI surgery

Patient	Age	Sex	Preop. hearing loss without HA	Preop. word recog. with HA 80 dB, %	Stim. ear (ECS)	Sensation during ECS	Sensation during PT	ECS freq. Hz	Intens. μA	Quality of fMRI activation; r_{max}; f	Outcome with CI			
											CI side; type	HSM %	HSM in noise, %	word recognition, %
1	75	f	r[1] profnd	no HA	right	auditory	nonaudit.	63	1613	uncertain; 0.50				
			l profnd	M 0; N 20	left	auditory	auditory	63	904	motion artifacts	left; Combi-40+	65	47	M 55; N 100
2	67	f	r profnd	M 0; N 0										
			l profnd	M 0; N 0	left	auditory	n.d.	63	1613	acceptable; 0.38	left; Combi-40+	40	10	M 20; N 100
3	64	m	r profnd	M 0; N 35	right	auditory	auditory	63	253	uncertain; 0.46	right; Combi-40+	75	18	M 45
			l profnd	M 0; N 80	left	auditory	auditory	63	1436	acceptable; 0.54; 88				
4	31	f	r deaf	M 0; N 0	right	auditory	auditory	63	183	technical problems	right; Combi-40+	n.d.	n.d.	M 20; N 20
			l deaf	M 0; N 60			auditory	63	158					
5	32	f	r profnd	M 5; N 80	right	auditory	auditory	63	1613	perfect; 0.50; 83.6	right; Nucleus 24R (ST)	78	13	M 30; N 100
			l profnd	M 5; N 70				63	1284	perfect; 0.40; 53.2				
6	72	m	r profnd	no HA	right	uncertain	uncertain	63	645	motion artifacts	no CI			
			l profnd	M 0; N 50				125	1613	motion artifacts				
7	30	m	r profnd	M 10; N 70				63	721	perfect; 0.56; 96.5	left; Combi-40+	94	29	M 65
			l profnd	M 10; N 80	left	auditory	auditory	63	659	perfect; 0.60; 95.3				
8	64	m	r sev/profnd	M 70; N 70	right	uncertain	not tolerated	63	1613	acceptable; 0.60; 9.3				
			l profnd	no HA			uncertain				left; Combi-40+	98	65	M 80; N 100
9	68	m	r sev/profnd	M 20; N 100										
			l deaf	no HA	left	auditory	auditory	63	323	no activation	left; Combi-40+	21	2	M 60; N 90
10	44	f	r sev/profnd	M 10; N 50	right	uncertain	auditory	125	1245	uncertain; 0.48	right; Combi-40+	97	44	M 85
			l sev/profnd	M 40; N 65				1000	1613	motion artifacts				
11	53	f	r deaf	no HA			uncertain	63	365	poor compliance	no CI			
			l deaf	no HA	left	uncertain	uncertain	250	810	poor compliance				
12	38	f	r profnd	M 60; N 60	right	auditory	no test	63	645	perfect; 0.74; 65.0	right; Nucleus 24R (ST)	75	70	M 65; N 75
			l profnd	M 0; N 50				63	512	perfect; 0.62; 67.5				
13	56	f	r profnd	M 5; N 60	right	auditory	nonaudit.	63	512	technical problems	right; Combi-40	91	72	M 75; N 100
			l profnd	M 20; N 70	left	auditory	n.d.	63	512	technical problems				
14	41	m	r deaf	M 0; N 0				63	361	no activation	right; Combi-40	0	0	M 0; N 15
			l sev/profnd	M 55; N 60	left	non-audit.	no sensat.	63	323	no activation				
15	57	f	r profnd	M 0; N 0	right	auditory	uncertain	63	1018	perfect; 0.75; 88.2				
			l profnd	M 0; N 0	left	auditory	auditory	63	725	perfect; 0.63; 89.7	left; Combi-40	37	0	M 30; N 90
16	71	f	r profnd	M 0; N 90	right	uncertain	no test	63	323	acceptable; 0.48; 9.9				
			l profnd	no HA							left; Combi-40	43	n.d.	M 15; N 50
17	59	m	r deaf	no HA	right	auditory	auditory	63	810	acceptable; 0.40; 33.5			n.d.	M 40; N 100
			l sev/profnd	M 15; N 90	left	auditory	auditory	63	904	acceptable; 0.42; 43.4	left; Combi-40	n.d.		
18	75	m	r deaf	M 0; N 0				63	183	uncertain; 0.38				
			l deaf	M 0; N 0	left	uncertain	uncertain	125	158	uncertain; 0.42	left; Nucleus 24M	32	n.d.	M 10; N 40
								500	361	no activation				

HA = Hearing aids; M = percent understood monosyllabic words; N = percent understood two-digit numerals, both in the Freiburger speech audiometry tests; freq. = frequency; intens. = intensity; f = percentage of activated pixels inside the auditory cortex; HSM in noise = signal-to-noise ratio 10 dB; profnd = profound; sev = severe; n.d. = no data.

[1] First row for each patient always right ear, second row left ear.

trode was placed on the mastoid. For safety reasons, the electrode leads were disconnected by two photo resistors during measurements. The light for switching the photo resistors was provided by the trigger box which also controlled the timing of the measurements by triggering the MR scanner appropriately. This setup ensured that electrical stimulation was only applied between measurements and that no heating of the electrodes could occur. Stimuli were rectangular bursts (5 Hz). Their frequencies and currents were selected with the control box. Data were acquired in short intervals of 0.7 s. The stimulation paradigm consisted of 8 or 12 periods of stimulation alternating with rest. The duration of a single stimulation or rest period was about 20 s and the duty cycle of electrical stimulation was 72.3% (3 s of stimulation in each repetition time period of 4.15 s).

Participants were stimulated monaurally during one session using a silver electrode with a ball-shaped tip positioned close to the tympanic membrane. The external auditory meatus was completely filled with 0.9% saline and sealed with an earplug. Best stimulation conditions were achieved when the electrode was placed as close as possible to the tympanic membrane. The electrode was covered by a layer of cotton, about 1 mm thick, to avoid direct contact with the ear canal skin. An optimum thickness of the cotton wrapping had to prevent both undue isolation effects and electric-like sensations already with low stimulation currents. If only nonauditory sensations were evoked, the electrode was repositioned several times. A waiting period between electrode insertion and stimulation of about 15 min improved electrical conductivity.

Stimulation frequencies ranged from 63 to 1000 Hz, but a frequency of 63 Hz was used in most cases, as most patients sensed best hearing at these low frequencies. Three patients were stimulated with two frequencies at the same ear, and 1 patient with three frequencies. Stimulation currents reached up to 1.6 mA and remained in each individual case well below the discomfort level. Five CI candidates and 1 control participant were stimulated with two different stimulation intensities for the same ear and frequency, with one intensity just below the discomfort level and the other noticeably below the discomfort level, but still high enough to evoke an auditory sensation. The remaining participants were stimulated with only one intensity. For each participant, the optimal stimulation frequency and current to evoke auditory sensations were determined with the EAM V02 FMRI immediately before fMRI. Thereafter, participants were moved into the scanner without changing head position and electrode placement. Two normal-hearing control participants were tested on 2 separate days in order to determine retest reliability.

Data Acquisition

fMRI was performed with a 1.5-tesla scanner (Siemens Magnetom Vision, Siemens Medical Systems, Erlangen, Germany) using the standard circular polarized head coil and gradient-echo echo planar imaging sequences. Echo time and repetition time were 66 ms and 4.15 s, respectively. Four oblique slices in an axial plane running parallel to the sylvian fissure were acquired. Slice thickness was 4 mm, and a matrix size of 64 × 64 or 128 × 128 was used. A total of 88 or 128 measurements were taken while periods of stimulation alternated with periods of rest. At the end of the session, anatomical images were obtained in identical slices, using a T_1-weighted gradient-echo scan.

Data Analysis

Statistical analysis of the fMRI data was performed with BrainVoyager2000® (Brain Innovation B.V., Maastricht, The Netherlands). Data preprocessing comprised 2-dimensional motion correction and temporal smoothing with linear trend removal and a high-pass filter with a cutoff frequency of 3 cycles. Statistical analysis was based on a correlation analysis with a boxcar time course convolved with a hemodynamic response function. To assess the reliability of the detected activation, the maximum correlation coefficient r_{max} was determined within the primary auditory cortex for each fMRI experiment separately. Subsequently, the correlation coefficient r was set to 66% of the individual maximum value in order to obtain a comparable amount of activation in each experiment [Moser et al., 1996]. Depending on the size of the activated area within the primary auditory cortex and the extent and distribution of artifactual false-positive activation elsewhere, the activation was rated as 'perfect', 'acceptable', 'questionable', or 'no activation' for which typical examples are shown in figure 1. In order to be rated as 'perfect' activation clusters had to be reasonably sized and absolutely confined to the primary auditory cortex. Activation was rated 'acceptable' when either small activation foci were detected isolated within the auditory cortex or robust activation clusters were accompanied by only minor artifactual activation outside the auditory cortex. 'Questionable' activation featured quite small activation foci within the primary auditory cortex together with a sizeable amount of artifactual activation. The category 'no activation' referred to either no significantly correlated clusters within the auditory cortex at all, or to uniformly distributed artifactual activation. Of course, the value of the maximum correlation coefficient played an important role. Perfect activation was always accompanied by high maximum correlation coefficients, whereas acceptable and questionable activation showed an overlap at medium values. In experiments classified as 'no activation', no significant activation in the primary auditory cortex occurred either at a very low threshold or only after more or less equally distributed 'activation' all over the brain appeared. For experiments with clearly recognizable activation the percentage of activated voxels within the auditory cortex was calculated. The primary auditory cortex was identified by landmarks within Heschl's gyrus as described by Brechmann et al. [2002] who parcellated the auditory cortex using a combination of anatomical landmarks and spatial fMRI activation patterns. For display, significantly activated pixels were color coded and overlaid onto T_1-weighted images of the same slices.

In previous studies, monaural acoustic stimulation under fMRI or PET had revealed a stronger lateralization of the cortical response towards the contralateral hemisphere and a more restricted activation in normal-hearing subjects compared with monaurally or binaurally deaf subjects, who were stimulated either acoustically or via CI [Bilecen et al., 2000; Ito et al., 2004; Scheffler et al., 1998]. Therefore, laterality indices (LI) were calculated for all participants with 'perfect' or 'acceptable' activation as $LI = (V_{contr} - V_{ipsi})/(V_{contr} + V_{ipsi})$, where V_{contr} and V_{ipsi} denote the number of the activated voxels in the contralateral and ipsilateral cortices, respectively.

Sixteen of the 18 CI candidates received a CI and thus provided outcome data. Speech recognition was tested in quiet with the open-set German Freiburger speech test for monosyllabic words and numerals at 70 dB HL. Sentence intelligibility in quiet

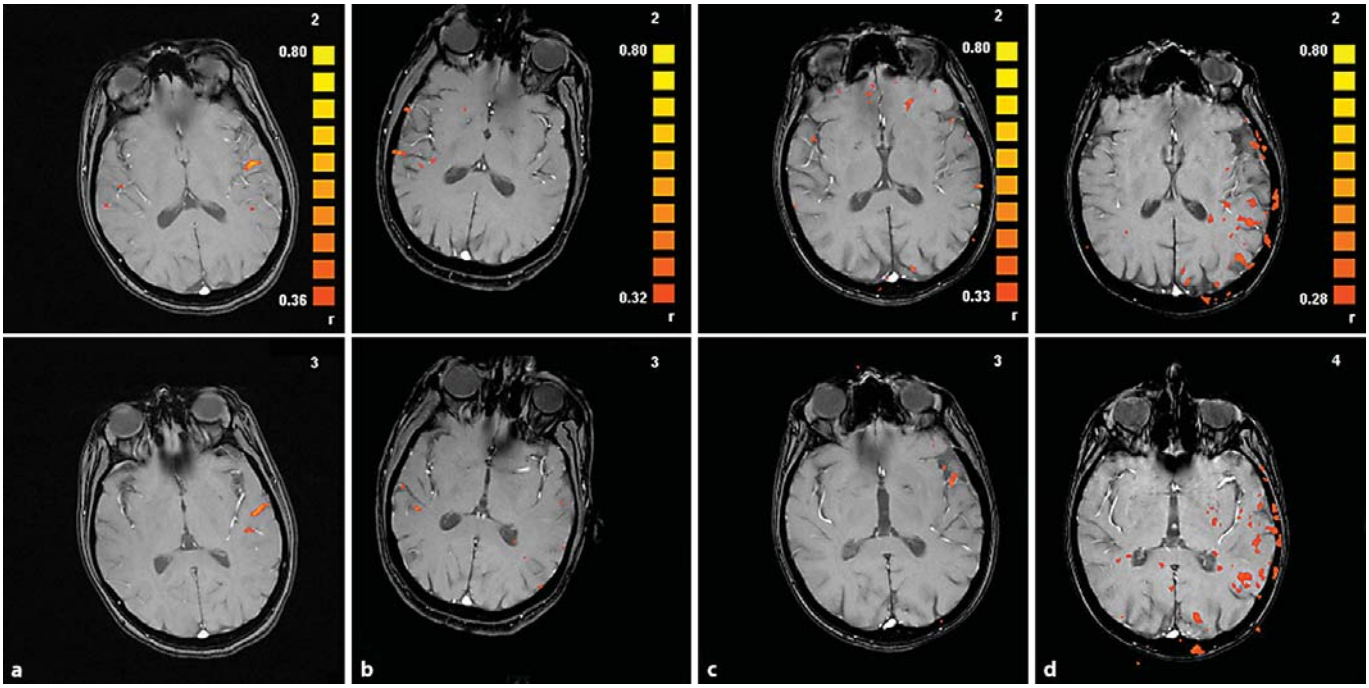

Fig. 1. Typical examples of fMRI activations in the primary auditory cortex rated as 'perfect' (**a**), 'acceptable' (**b**), 'questionable' (**c**), and 'no activation' (**d**).

and noise (signal-to-noise ratio 10 dB) was assessed with the German HSM sentence test [Hochmair-Desoyer et al., 1997]. Speech audiometry was performed within 6 weeks prior to CI surgery (see above) and 6 months after surgery. The overall mean outcome was calculated as the mean of the 4 ranked outcome variables. Spearman rank correlations were calculated to quantify the relations between preoperative residual hearing scores, sensations during ECS and PT, PT subtests, fMRI activations, and CI outcome.

Whenever it was appropriate to consider ears separately and independently, the analysis was performed on ears instead of subjects. Results are thus given either for ears or for subjects.

Results

Preoperative audiometric data, PT and ECS responses, ECS parameters for fMRI, cerebral activation patterns, and CI outcome data for each patient are summarized in table 1. Relevant ECS and fMRI measures of the control participants are shown in table 2.

ECS and fMRI Activations

CI Candidates

Auditory sensations could not be evoked with ECS in all cases, even after several electrode replacements. Only 11 of 18 patients (16 of 23 ears) described 'clearly auditory' sensations (labeled as 'auditory' in table 1). Six patients (6 ears) reported 'uncertain auditory' sensations ('uncertain' in table 1). Patient 14, who suffered from Hodgkin's disease (1 ear), felt only electrifying and pricking sensations ('non-auditory' in table 1).

The data of only 17 of the examined 23 ears could be included in the analysis of fMRI activations. Technical problems, motion artifacts, or insufficient compliance prevented the inclusion of the remaining ears. In 11 ears, ECS led to a 'perfect' (5 ears) or 'acceptable' (6 ears) activation of the primary auditory cortex, in 4 ears to 'questionable' activations, and in 2 ears to 'no activation'. 'Clear auditory' sensations were evoked with ECS in all 5 'perfect' cases and in 4 of the 6 'acceptable' cases.

From the 16 ears in which ECS evoked a 'clear auditory' sensation, a primary auditory cortex activation rated at least 'acceptable' was detected in 9 cases. In 2 ears, activation was 'questionable', and in 1 ear, it was not detectable. In the remaining 4 ears, data had to be discarded because of motion artifacts or technical problems. Activation was thus detected in 9 of 12 ears in which a 'clear auditory' impression could be evoked and the examinations of which were technically unobjectionable. From the 6 ears

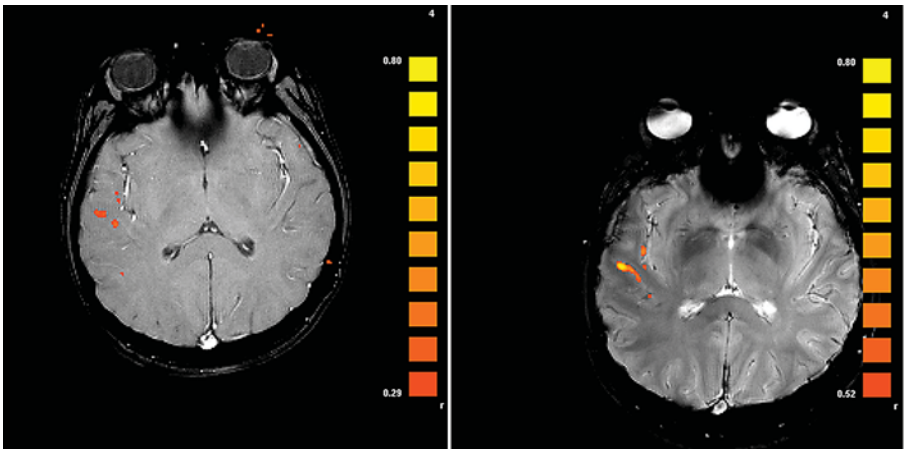

Fig. 2. fMRI activation maps of a normal-hearing subject: 'perfect' activation in the primary auditory cortex during consecutive imaging sessions on 2 different days.

Table 2. Control participants: variables for ECS and fMRI

Patient	Age	Sex	Stimulated ear	Sensations during ECS	Day	ECS frequency, Hz	Intensity μA	Quality of fMRI activation; r_{max}; f
1	31	m	left	no sensation		125	1436	no
2	27	m	right	auditory	1	1000	1613	perfect; 0.62; 74.5
					2	1000	1284	perfect; 0.56; 98.7
					2	1000	1284	perfect; 0.64; 97.9
3	28	m	right	auditory		1000	512	uncertain; 0.36
4	27	f	left	auditory	1	1000	1613	perfect; 0.78; 100
					2	1000	904	acceptable; 0.44; 40.7
					2	1000	904	acceptable; 0.35; 100
5	24	f	right	auditory		1000	810	no

f = Percentage of activated pixels inside the auditory cortex.

with the 'uncertain auditory' impression, 'perfect' or 'acceptable' activation could be detected in only 2 ears. The sole patient with 'no auditory' sensations (patient 14) did not show any activation of the auditory cortex.

Normal-Hearing Control Participants

Four of 5 control participants (4 of 5 ears) reported 'clear auditory' sensations under ECS. The lowest stimulation intensity for eliciting sensation was needed at 1000 Hz, the highest of the used stimulation frequencies, which is close to the frequency of best hearing in normal-hearing subjects. From these 4 participants, 2 showed 'perfect' or 'acceptable' activation even during consecutive imaging sessions on 2 different days (fig. 2) and with several stimulation intensities. The other 2 subjects showed 'questionable' or no activation. The fifth participant did not report any auditory sensation during ECS up to the upper limit of stimulation current, and did not show any activation.

Correlations between Diagnostic and CI Outcome Measures

Spearman rank correlations between diagnostic variables for the implanted ears, fMRI activation, and CI outcome are shown in table 3. There were significant correlations between preoperative residual hearing without

Table 3. Spearman rank correlations between diagnostic and CI outcome variables

Variable	Diagnostic variable			Postoperative speech recognition				
	PT sensation	ECS sensation	fMRI activation	MS	Num	HSM (S)	HSM (N)	mean outcome
Residual hearing, no HA	n.s.	n.s.	n.s.	0.52* (16)	0.73** (13)	0.76** (14)	0.50 (12)	0.69** (16)
Speech recognition, HA, MS 80 dB HL	n.s.	n.s.	n.s.	0.70** (13)	n.s.	0.74** (11)	0.61 (10)	0.78** (13)
Speech recognition, HA, Num 80 dB HL	n.s.	n.s.	n.s.	0.64* (13)	0.62 (10)	0.84** (11)	0.57 (10)	0.74** (13)
PT: Sensation		0.53* (18)	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
PT: FD	n.s.	n.s.	n.s.	0.81* (7)	0.89* (5)	0.93** (6)	0.86 (5)	0.76* (7)
ECS sensation			0.46 (17)	n.s.	0.64* (11)	n.s.	n.s.	n.s.
fMRI activation				n.s.	n.s.	n.s.	n.s.	n.s.

In parentheses are the number of subjects for each coefficient; * $p < 0.05$; ** $p < 0.01$; coefficients without asterisk: $p < 0.10$.
HA = Hearing aid; MS = monosyllables; Num = numerals; HSM (S) = Hochmair-Schulz-Moser Sentence Test (Sentences); HSM (N) = Hochmair-Schulz-Moser Sentence Test (Numerals); n.s. = not significant.

hearing aids and postoperative speech recognition ($\rho = 0.69$, $p < 0.01$, $n = 16$), between preoperative speech recognition with hearing aids and postoperative speech recognition with CI ($\rho = 0.78$, $p < 0.01$, $n = 13$ for preoperative monosyllables; $\rho = 0.74$, $p < 0.01$, $n = 13$ for preoperative numerals), and between sensations during PT and ECS ($\rho = 0.53$, $p < 0.05$, $n = 18$). Correlations were also calculated between threshold level, TDL, FD, and dynamic range during PT on the one hand, and all diagnostic and outcome variables on the other. Only FD of the later implanted ears correlated significantly with the assessed outcome variables, but not with sensations during PT. No other correlation was significant for this small sample, except for the correlation between sensations during ECS and the postoperative numerals in the Freiburger test ($\rho = 0.64$, $p < 0.05$, $n = 11$). That is, neither sensations during ECS and PT nor fMRI activations correlated with mean CI outcome.

Laterality

Ten ears of 8 CI candidates and 2 ears of 2 normal-hearing participants, all with 'perfect' or 'acceptable' activation, were included in the laterality calculation. By visual inspection, a 'perfect' activation was found in all of the 6 included ears bilaterally, and an 'acceptable' activation in the remaining 6 cases predominantly contralaterally. Averaged over subjects, the laterality index LI was 0.72 in the control participants and 0.41 in the CI candidates. Hence, the 2 normal-hearing participants appeared to activate more contralaterally than the 8 deaf patients.

Stimulus Intensity

Six ears were stimulated with different currents for the same frequency. In 3 ears of the CI candidates and in 2 ears of the normal-hearing participants a 'perfect' or 'acceptable' activation could be evoked with both stimulus intensities. The different intensities did not lead to substantial differences in the activated regions of the auditory cortex.

Discussion

With respect to the question whether or not auditory activity has been elicited in people with ambiguous perceptions during ECS (or PT) the following findings were made. The sensations evoked by ECS in a small sample of profoundly deaf patients only tended to correlate with ECS-induced fMRI activations in the primary auditory cortex. From those cases with technically faultless fMRI recordings, the majority (9 of 12 ears, or 75%) with auditory sensations during ECS showed 'perfect' or 'acceptable' auditory cortex activations. This finding compares with direct stimulation of the promontory, where Schmidt et al. [2003] found activation in 22 of 26 (85%) patients who reported hearing sensations during scanning. In the study presented here, in 6 of 9 ears (66%) with auditory sensations in the PT, auditory cortex activations were evoked with fMRI. However, different from ECS here and from promontory stimulation in Schmidt et al. [2003], PT was not performed directly prior to scanning but during

further diagnostics. The remaining fMRI results are ambiguous. In 2 ears with auditory sensations, the activation was 'questionable', while not detectable in 1 ear. The stimulus intensity in these cases was possibly not high enough in order to evoke detectable auditory cortex activations [Berthezene et al., 1997]. Due to a small dynamic range between threshold and discomfort level or cutoff intensity for ECS, auditory sensations were mostly soft ones, but higher intensities were not justifiable. Because the auditory nerve is stimulated less directly by ECS than by a CI, uncomfortable electrifying or vibrotactile sensations during ECS may be obtained already at intensities which are just a bit higher than those which elicit soft hearing. Missing or insufficient activation patterns are common in fMRI. If there is an activation, it can be interpreted in the desired way. If there is no sufficient activation, this may have various causes and may not imply a nonfunctional neural pathway. From the 6 ears with 'uncertain auditory' impression, reliable activation could be detected in only 2 ears. The sole patient with 'no auditory' sensations did not show any auditory cortex activation. Thus, auditory sensations tend to elicit utilizable auditory cortex activations, while ambiguous sensations tend to cause more ambiguous activations and no sensations do not cause any activations. However, this is of secondary importance considering that the fMRI activations do not correlate with CI outcome.

Because deaf subjects do not hear any scanner noise, their auditory cortex activations might be interpreted as resulting solely from ECS. However, due to multisensory integration, auditory cortex activation might also be evoked by somatosensory stimulation, for example trigeminal stimulation [El-Kashlan and Shore, 2004; Schurmann et al., 2006]. In deaf subjects, auditory cortex activation may alternatively or additionally be evoked by stimulation of other sensory modalities due to a neural reorganization ('cross-modal' plasticity) [Finney et al., 2003; Shibata et al., 2001]. Therefore, the fMRI results presented here might be biased by activation in the auditory cortex which was not caused by auditory but by somatosensory stimulation. This argument constitutes a limitation of the present study, as it could be a reason why CI outcome did not correlate with ECS/fMRI responses. However, the following points counter this conclusion. (1) The insignificant correlation between these parameters was mainly due to those subjects with CI benefit despite lacking auditory cortex activation. (2) All patients with auditory cortex activation benefited from CI. (3) Contact of the electrode with the ear canal wall was avoided by the cotton wrapping of the electrode, thus minimizing vibrotactile stimulation. (4) The individual stimulation intensities remained below the pain thresholds. Thus, it appears that the auditory cortex activation in the CI candidates was induced mainly by the auditory system.

In all 6 ears with perfect or acceptable auditory cortex activation, the CI outcome was good. In the 3 ears in which ECS led to uncertain fMRI activations, the outcome ranged from rather poor to good. However, in the case of auditory ECS sensations but lacking fMRI activation (patient 9), the outcome was good. A CI therapy in such a case is therefore not contraindicated. ECS-induced fMRI activations may be absent or equivocal for various reasons, such as motion, technical, other artifacts, or even insufficient stimulus intensity. Hence, the following conclusions can be derived cautiously. If there are fMRI auditory cortex activations, a good outcome can be expected. If activations are uncertain, the outcome is uncertain as well; however, a certain CI benefit can be expected. If there is no fMRI activation, no outcome predictions can be made. Therefore, as also suggested for PET [Truy et al., 1995], fMRI does not seem to offer much advantage for screening CI candidates.

Because CI outcome could not be predicted by fMRI activations with sufficient reliability, predictors for CI benefit might be searched not in ECS-induced auditory cortex activations, but elsewhere, such as in preoperative residual hearing, preoperative speech recognition with amplification, and duration of deafness [Gomaa et al., 2003]. To search for good predictors we also calculated correlations of preoperative residual hearing (nonamplified and amplified) and ESC/PT sensations with CI outcome. Therefore, we also included those subjects who had no or only questionable fMRI activations in the analysis.

The described sensations evoked by ECS or PT did not predict CI outcome, as has also been reported by Hartmann et al. [1994], except for the correlation of ECS sensations with understood numerals. If ECS evoked an auditory or uncertain sensation – the latter happened in almost one third of the cases – the median of the mean outcome was at the 49th percentile and the worst mean outcome at the 20th percentile. There was only 1 case (1 ear) in which ECS revealed uncertain sensations, fMRI activations were obtained, and a CI was implanted in the same ear. The fMRI activations were uncertain and the CI outcome was only moderate. Patient 13, in whom PT evoked only vibrations in the ear to be supplied with a CI, benefited well, and a withheld CI therapy would have been unjustified. However, patient 14, who reported just

pricking and electrifying sensations and had neither fMRI activations nor intraoperative stapedius reflexes, did not benefit from his CI. Only a few case reports about CI benefit in patients who had not reacted to preoperative electrical stimulation but received a CI have come to our attention. Sensations might be absent due to a nonfunctioning auditory pathway or because the electrical field does not effectively reach relevant structures in the cochlea and the auditory nerve. Therefore, no final statement about CI indication in these cases can be made. However, because of uncertainty in outcome, caution is recommended.

The absence of significant correlations between the described diagnostic and outcome variables might possibly also result from a type II error. Several correlations are considerable in magnitude, yet insignificant due to a small sample size.

ECS evoked auditory sensations numerically in more cases than did PT (70 vs. 57%), which is contrary to reports by others, but the difference was not significant. Schmidt et al. [2003] and Lesinski et al. [1997] reported 76% auditory sensations with ECS but 83% with PT in deaf patients, and Spies et al. [1993] 48 and 52%. The relatively high number of positive reactions to ECS may be due to particular care in test administration as described above. An invasive PT procedure may thus be reserved for special applications.

Sensations during PT correlated with those during ECS, but unlike ECS, PT sensations did not correlate with fMRI activations. Apart from chance in a relatively small sample, this discrepancy is to be expected because ECS sensations were obtained within the same setting as fMRI, and PT sensations were not. Among the PT subtests, which were not administered during ECS, only FD correlated with the outcome variables and may therefore be considered a predictor for CI benefit. The same predictive value can be expected for FD in ECS, which might be after all an argument for electrical stimulation prior to CI surgery, except for particular patients like children and persons with intellectual or multiple disabilities who are unable to provide adequate responses to frequency differences. TDL did not correlate with fMRI activation in the auditory cortex, which is different from the findings of Mortensen et al. [2005], who, in a PET experiment, found a positive correlation between TDL during promontory stimulation and activity in the right posterior middle temporal gyri. In other studies, PT did not predict CI outcome [Albu and Babighian, 1997].

Preoperative residual hearing and word recognition with hearing aids correlated with CI outcome. A predictability by preoperative hearing abilities has also been reported for prelingually deaf children [Kiefer et al., 2000]. Preoperative residual speech recognition has been reported to act as a 'trophic factor' that protects the spiral ganglion and the central auditory pathways from degeneration [Gomaa et al., 2003]. Therefore, preoperative hearing abilities predict CI outcome in postlingually deafened adult CI candidates if no neuronal degeneration has occurred due to a lengthy period of deafness.

Infant CI candidates often do not respond to conventional audiometry. As almost every child reacts to ECS, we sought to ascertain that those reactions were indeed auditory ones and therefore tested the neurofunctional correlates of the elicited sensations and the corresponding CI outcome vicariously in adults. However, patient history, conventional objective and behavioral observational audiometry, together with CT/MRI of the cochlea and the auditory nerve, seem to better predict CI benefit than ECS/PT and a corresponding fMRI. But in special cases, e.g. in auditory neuropathy with a normal or small nerve apparent in the MRI, they do not predict CI benefit with sufficient certainty [Buchman et al., 2006]. In such cases, a positive ECS response may contribute to a positive CI decision.

Laterality

Cortical activation upon unilateral electrical stimulation of the auditory nerve in bilaterally or unilaterally deaf subjects has been mainly observed bilaterally in PET and fMRI studies [Alwatban et al., 2002; Berthezene et al., 1997; Tschopp et al., 2000]. With normal-hearing subjects, however, unilateral acoustic stimulation evoked strong contralateralization of cortical fMRI response, and a binaural stimulation evoked a nearly balanced activation [Ito et al., 2004; Scheffler et al., 1998]. Bilecen et al. [2000] described a shift from contralateral activation during normal bilateral hearing to bilateral activation after a sudden unilateral hearing loss due to cochlear nerve resection. The findings of more bilateral activation in deaf than in normal-hearing subjects tended to be confirmed in the study presented here by a numerically lower mean LI in the 8 deaf subjects than in the 2 normal-hearing participants, indicating a compensatory reorganization with bilateral representation of unilateral stimulation.

Intensity

Brechmann et al. [2002] detected a more widespread auditory cortex activation with increasing stimulus in-

tensity, whereas we did not. The within-ear differences of stimulus intensities were possibly not large enough to create significant activation differences.

Conclusion

Absent correlations, with a sole exception, between sensations during PT or ECS and CI outcome make the predictive value of these indicators questionable. Even patients with no clear auditory sensations during PT or ECS may have good outcome from a CI therapy. If, however, any sensations other than pain are lacking during PT or ECS, a benefit from CI is uncertain. The sole exception was the significant correlation between sensations during ECS and recognition of numerals with CI. Although FD during PT predicts CI outcome, an invasive test seems unnecessary because testing FD is also possible with ECS. fMRI had no significant predictive value for CI outcome in this study with an admittedly small sample. Instead, robust predictors for CI outcome were residual hearing and aided speech recognition prior to CI therapy, and FD during PT. To predict CI outcome, these tests plus probably FD during ECS may be more useful, together with patient history, preoperative radiology, and nerve response telemetry, than functional imaging of electrical auditory pathway stimulation with ECS or PT. However, in special cases, the presence of an ECS response may contribute to a positive CI decision because it confirms proper functioning of auditory nerve fibers.

Acknowledgements

Christine Preibisch is funded by the Bundesministerium für Bildung und Forschung (Brain Imaging Center Frankfurt, DLR 01GO0203). We thank MED-EL Medical Electronics GmbH, Innsbruck, Austria, for providing the modified Electro Audiometer EAM V02 FMRI. We are especially grateful to Christian Teissl (formerly MED-EL Medical Electronics) who developed and checked the safety precautions of the stimulation device EAM V02 FMRI. Furthermore, we are grateful to Martin Voellinger, Ulrich Pilatus, and Carsten Thierfelder for their technical support, and to Julia Dee Campbell for language help in the preparation of the manuscript.

References

Albu S, Babighian G: Predictive factors in cochlear implants. Acta Otorhinolaryngol Belg 1997;51:11–16.

Alegre M, Iriarte J, Manrique M, Huarte A, Vanaclocha V, Artieda J: Auditory brain stem potentials evoked by electrical stimulation of cochlear nuclei during central auditive implant setting. Rev Neurol 1999:29: 198–200.

Alwatban AZ, Ludman CN, Mason SM, O'Donoghue GM, Peters AM, Morris PG: A method for the direct electrical stimulation of the auditory system in deaf subjects: a functional magnetic resonance imaging study. J Magn Reson Imaging 2002;16:6–12.

Berthezene Y, Truy E, Morgon A, Giard MH, Hermier M, Franconi JM, Froment JC: Auditory cortex activation in deaf subjects during cochlear electrical stimulation. Evaluation by functional magnetic resonance imaging. Invest Radiol 1997;32:297–301.

Bilecen D, Seifritz E, Radu EW, Schmid N, Wetzel S, Probst R, Scheffler K: Cortical reorganization after acute unilateral hearing loss traced by fMRI. Neurology 2000;54:765–767.

Brechmann A, Baumgart F, Scheich H: Sound-level-dependent representation of frequency modulations in human auditory cortex: a low-noise fMRI study. J Neurophysiol 2002; 87:423–433.

Buchman CA, Roush PA, Teagle HF, Brown CJ, Zdanski CJ, Grose JH: Auditory neuropathy characteristics in children with cochlear nerve deficiency. Ear Hear 2006;27:399–408.

Dillier N, Spillmann T: Ergebnisse der elektrischen Stimulation bei Normalhörenden, Schwerhörigen und Gehörlosen; in Kellerhals B, Fisch U, Mann J, Montandon P, de Reynier JP, Secrétan JP (eds): Aktuelle Probleme der Otorhinolaryngologie 1. Bern, Huber, 1977, pp 166–176.

El-Kashlan HK, Shore SE: Effects of trigeminal ganglion stimulation on the central auditory system. Hear Res 2004;189:25–30.

Finney EM, Clementz BA, Hickok G, Dobkins KR: Visual stimuli activate auditory cortex in deaf subjects: evidence from MEG. Neuroreport 2003;14:1425–1427.

Gomaa NA, Rubinstein JT, Lowder MW, Tyler RS, Gantz BJ: Residual speech perception and cochlear implant performance in postlingually deafened adults. Ear Hear 2003;24: 539–544.

Gstoettner W, Pok SM, Peters S, Kiefer J, Adunka O: Cochlear implantation with preservation of residual deep frequency hearing. HNO 2005;53:784–791.

Hartmann R, Pfennigdorff T, Klinke R: Evoked potentials from the auditory nerve following sinusoidal electrical stimulation of the cochlea: new possibilities for preoperative testing in cochlear-implant candidates? Acta Otolaryngol 1994;114:495–500.

Hochmair-Desoyer I, Schulz E, Moser L, Schmidt M: The HSM sentence test as a tool for evaluating the speech understanding in noise of cochlear implant users. Am J Otol 1997;18(6 suppl):S83.

Hofmann E, Preibisch C, Knaus C, Müller J, Kremser C, Teissl C: Noninvasive direct stimulation of the cochlear nerve for functional MR imaging of the auditory cortex. AJNR Am J Neuroradiol 1999;20:1970–1972.

Ito K, Momose T, Oku S, Ishimoto S, Yamasoba T, Sugasawa M, Kaga K: Cortical activation shortly after cochlear implantation. Audiol Neurootol 2004;9:282–293.

Kanal E: An overview of electromagnetic safety considerations associated with magnetic resonance imaging. Ann NY Acad Sci 1992;649: 204–224.

Kiefer J, von Ilberg C, Gall V, Diller G, Spelsberg A, Neumann K: Results from 88 prelingually deaf children with cochlear implants: an analysis of predictive factors. Adv Otorhinolaryngol 2000;57:202–208.

Knaus C, Hofmann E, Mueller J, Teissl C, Preibisch C: Functional magnetic resonance tomography of the auditory cortex during noninvasive stimulation of the cochlear nerve. Adv Otorhinolaryngol 2000;57:224–228.

Lemieux L, Allen PJ, Franconi F, Symms MR, Fish DR: Recording EEG during fMRI experiments: patient safety. Magn Reson Med 1997;38:943–952.

Lesinski A, Littmann X, Battmer RD, Lenarz T: Comparison of preoperative electrostimulation data using an ear-canal electrode and a promontory needle electrode. Am J Otol 1997;18(6 suppl):S88–S89.

Moser E, Teichtmeister C, Diemling M: Reproducibility and postprocessing of gradient-echo functional MRI to improve localization of brain activity in the human visual cortex. Magn Reson Imaging 1996;14:567–579.

Mortensen MV, Madsen S, Gjedde A: Use of time differences in normal hearing – Cortical processing of promontorial stimuli. Hear Res 2005;205:94–101.

Neumann K, Raab P, Preibisch C, Pilatus U, Hamm J, Lanfermann H, Kiefer J, Gall V: Auditory cortex activation during electrical ear canal stimulation in subjects with severe hearing loss – Preliminary results of a fMRI evaluation; in Kubo T, Takahashi Y, Iwaki T (eds): Cochlear Implants – An Update. The Hague, Kugler Publications, 2002, pp 41–46.

Nikolopoulos TP, Mason SM, Gibbin KP, O'Donoghue GM: The prognostic value of promontory electric auditory brain stem response in pediatric cochlear implantation. Ear Hear 2000;21:236–241.

Ogawa S, Menon RS, Tank DW, Kim SG, Merkle H, Ellermann JM, Ugurbil K: Functional brain mapping by blood oxygenation level-dependent contrast magnetic resonance imaging. A comparison of signal characteristics with a biophysical model. Biophys J 1993;64:803–812.

Otto SR, Waring MD, Kuchta J: Neural response telemetry and auditory/nonauditory sensations in 15 recipients of auditory brainstem implants. J Am Acad Audiol 2005;16:219–227.

Scheffler K, Bilecen D, Schmid N, Tschopp K, Seelig J: Auditory cortical responses in hearing subjects and unilateral deaf patients as detected by functional magnetic resonance imaging. Cereb Cortex 1998;8:156–163.

Schmidt AM, Weber BP, Vahid M, Zacharias R, Neuburger J, Witt M, Lenarz T, Becker H: Functional MR imaging of the auditory cortex with electrical stimulation of the promontory in 35 deaf patients before cochlea implantation. AJNR Am J Neuroradiol 2003;24:201–207.

Schurmann M, Caetano G, Hlushchuk Y, Jousmaki V, Hari R: Touch activates human auditory cortex. Neuroimage 2006;30:1325–1331.

Shibata DK, Kwok E, Zhong J, Shrier D, Numaguchi Y: Functional MR imaging of vision in the deaf. Acad Radiol 2001;8:598–604.

Spies TH, Snik AF, Mens LH, van den Broek P: Ear canal electrodes versus promontory electrodes in preoperative electrical stimulation for cochlear implant selection. Adv Otorhinolaryngol 1993;48:108–113.

Teissl C, Kremser C, Hochmair ES, Hochmair-Desoyer IJ: Magnetic resonance imaging and cochlear implants: compatibility and safety aspects. J Magn Reson Imaging 1999;9:26–38.

Truy E, Deiber MP, Cinotti L, Mauguiere F, Froment JC, Morgon A: Auditory cortex activity changes in long-term sensorineural deprivation during crude cochlear electrical stimulation: evaluation by positron emission tomography. Hear Res 1995;86:34–42.

Tschopp K, Schillinger C, Schmid N, Rausch M, Bilecen D, Scheffler K: Detection of central auditory compensation in unilateral deafness with functional magnetic resonance tomography. Laryngorhinootologie 2000;79:753–757.

Waltzman SB, Roland JT Jr: Cochlear implantation in children younger than 12 months. Pediatrics 2005;116:e487–e493.