Review article

Diagnostic challenges and safety considerations in cochlear implantation under the age of 12 months

Petros V. Vlastarakos [a,*], Dimitrios Candiloros [b], George Papacharalampous [c], Evangelia Tavoulari [d], George Kampessis [b], George Mochloulis [a], Thomas P. Nikolopoulos [d]

[a] ENT Dept., Lister Hospital, Coreys Mill Lane, SG1 4AB Stevenage, Hertfordshire, United Kingdom
[b] ENT Dept., Hippokrateion General Hospital of Athens, Greece
[c] ENT Dept., Elpis Municipal Hospital of Athens, Greece
[d] ENT Dept., Atticon University Hospital of Athens, Greece

ABSTRACT

Aim: To review the current knowledge on cochlear implantation in infancy, regarding diagnostic, surgical and anesthetic challenges.
Study-design: Meta-analysis. EBM level: II.
Materials/methods: Literature-review from Medline and database sources. Related books were also included.
Study selection: Meta-analyses, prospective controlled studies, prospective/retrospective cohort studies, guidelines, review articles.
Data synthesis: The diagnosis of profound hearing loss in infancy, although challenging, can be confirmed with acceptable certainty when objective measures (ABR, ASSR, OAEs) and behavioural assessments are combined in experienced centres. Reliable assessment of the prelexical domains of infant development is also important and feasible using appropriate evaluation techniques. Overall, 125 implanted infants were identified in the present meta-analysis; no major anesthetic complication was reported. The rate of surgical complications was found to be 8.8% (3.2% major complications) quite similar to the respective percentages in older implanted children (major complications ranging from 2.3% to 4.1%).
Conclusion: Assessment of hearing in infancy is feasible with adequate reliability. If parental expectations are realistic and hearing aid trial unsuccessful, cochlear implantation can be performed in otherwise healthy infants, provided that the attending pediatric anesthesiologist is considerably experienced and appropriate facilities of pediatric perioperative care are readily available. A number of concerns, with regard to anatomic constraints, existing co-morbidities or additional disorders, tuning difficulties, and special phases of the developing child should be also taken into account. The present meta-analysis did not find an increased rate of anesthetic or surgical complications in infant implantees, although long-term follow-up and large numbers are lacking.

© 2009 Elsevier Ireland Ltd. All rights reserved.

Contents

* Corresponding author. Personal address: 64 Morecambe Close, Stevenage Hertfordshire, SG1 2BF, UK. Tel.: +44 7774567429/+441438743065; fax: +30 2109714870.
E-mail addresses: pevlast@hotmail.com, pevlast@yahoo.gr (P.V. Vlastarakos).

1. Introduction

The introduction of universal neonatal hearing screening in some countries and the establishment of screening programs for high-risk infants in several others has facilitated early identification, referral, and diagnosis of children with hearing loss [1]. This in turn has led to early clinical interventions and a steadily decreasing age of cochlear implantation in profoundly deaf children [2].

Cochlear implantation in a young age ensures that the hearing impaired child will receive the maximum amount of auditory information during the critical periods for spoken language development, thus reducing the effects of auditory deprivation [3]. The potential of achieving age-appropriate spoken language skills has additionally led to a strong trend towards performing cochlear implantation in infancy [4]. The primary implication of the latter is that a sooner acquired spoken language competence may also enable an earlier and more successful transition to the mainstream educational system.

However, the uncertain means of assessing the exact auditory and developmental status in very young infants, hidden additional disabilities in this age group, and the surgical and anesthesiologic risks, which may be associated with performing an elective procedure so early in a child's life, should be taken into account, when considering cochlear implantation in infancy.

The aim of the present paper is to review the current knowledge on pediatric cochlear implantation before the age of 12 months, with regard to the diagnostic, surgical and anesthetic challenges associated with cochlear implantation in this age group. Specific concerns regarding device and user-related parameters will also be explored.

2. Materials and methods

An extensive search of the literature was performed in Medline, Embase, Scopus, and Intute, from 1982 to December 2008, with two main objectives:

(a) Evaluation of the methods for assessing an infant's hearing and their respective reliability.
(b) Assessment of the surgical and anesthetic risks associated with an elective procedure (cochlear implantation) during the first year of life.

During the search, the keywords "cochlear implants", "age", "infants", "under 1", "ASSR", "ABR", "OAE", "risk", "surgery", and "anesthesia" were utilized. The keywords "cochlear implants", "infants", and "under 1" were considered primary and were either combined to each of the other keywords individually, or used in groups of 3.

3. Results

Three meta-analyses, 4 prospective controlled studies, 25 prospective studies, 21 retrospective studies, 1 guideline, 8 review articles and 4 books met the defined criteria and were included in study selection.

4. Discussion

4.1. Hearing assessment in infants—evaluation of additional disorders

The widespread application of neonatal hearing screening programs in some countries has resulted in the assessment of the hearing acuity of approximately 85–99% of newborns within the first few days of their life [5]. As a consequence, very early referral, diagnosis and management of infants with hearing loss are now feasible in the developed world. Thus, it is of great importance that the related methods accurately reflect the behavioural audiogram [6].

However, visual reinforcement audiometry (VRA) which may be used for behavioural testing in late infancy, is not applicable in young infants [7], due to their inability to make reliable direct head-turn responses towards sound sources [8]. In addition, children with additional disorders as well as prematurity may also not be able to complete VRA testing [9]. Objective audiometric tests (OAE, ABR, and ASSR) may be the only method of assessing candidacy for early cochlear implantation, not only in terms of identifying potential pediatric implantees, but also in order to exclude possibly inappropriate recipients (i.e. children lacking bilateral profound hearing loss).

Apart from scientific dilemmas, reliable diagnosis is very important to parents and family. Parents may indeed experience significant emotional stress during and following hearing assessment. Hence, both the diagnostic process and the certainty of the diagnosis are considered central for them to accept the problem and participate in future management [10]. In addition, parental and family bonding and behaviour towards the infant, along with their trust to physicians may be disturbed when the diagnosis is inaccurate or doubtful.

Even though clinical audiology has made significant progress during the last decades, none of the three objective tests typically performed in most specialist centres (otoacoustic emissions—OAEs, auditory brainstem responses—ABRs and auditory steady state responses—ASSRs) are perfect [9]. ABRs have been widely used for a long period of time, providing us with extensive data regarding their strengths and weaknesses. As they do not require any voluntary response from the examined infant, they are considered an objective technique for the assessment of hearing thresholds. However, the determination of the obtained waveforms and the estimated level of hearing can be subjective processes, which may, in large part, rely on the examiner's experience [11–13]. Even after applying the strictest diagnostic criteria and obtaining more than one waveforms in each stimulus, challenges with regard to the accuracy of the investigation, especially in difficult cases, may be encountered [14]. Moreover, ABRs assess a narrow frequency range; therefore cases with useful residual hearing (i.e. normal or near normal hearing in the lower frequencies) are usually missed, thus resulting to inappropriate amplification.

ASSRs are a relatively recent method which shows better specificity in various frequencies compared to ABRs [15]. They are also more objective, as they relate the prediction of an auditory response to statistical criteria, which are incorporated in their software, and not to the examiner's level of expertise. ASSR thresholds determined in infancy have been found to highly correlate to behavioural hearing levels obtained later in childhood, both for children with normal hearing and for sufferers of varying degrees of sensorineural hearing loss [16]. They seem, however, at least partially affected by the maturational development during the first weeks of life, thus demonstrating variable results across subjects during this period [17,18]. Hence, postponement of the examination, until after the immediate neonatal period may be required [19]. In addition, even though the detection of a positive response is objective, the measurement protocol has to be well considered and a critical approach is required during response interpretation. Indeed, when a variable recording length is allowed, the acceptance criterion of the statistical test needs adjustments in order to ensure a tolerable error rate [20]. Although more widespread use of this method is necessary to determine its full potentials and related weaknesses, ASSRs seem a very promising assessment method in identifying our target population for pediatric cochlear implant surgery [21].

OAEs, on the other hand, display overlapping results in impaired and normal-hearing populations. Although their sensitivity and specificity can be improved with different analysis tools, they remain useful only in the hearing screening stage and in identifying children with auditory neuropathy [22]. OAEs are totally inadequate, however, in the diagnosis of profound deafness, as they are not able to discriminate an infant with moderate, severe, or profound deafness [21].

In addition to auditory assessment, a reliable evaluation of the prelexical domains of infant development is very important, as it may provide clinicians with information, with regard to the preverbal skills of infant cochlear implant candidates at specific developmental stages. Indeed, the examination of complex prelinguistic vocalization types by measures of vocal development is necessary to document the progress of children who are expected to acquire speech at later-than-typical ages (such as infant implantees) [23], even though the nature of prelinguistic vocalizations itself has long been a subject of speculation and model building [24]. Such assessments, however, can only be considered as adjunctive to formal audiologic evaluation, and provide only indirect information with regard to implant candidacy.

Moreover, the fact that a number of under 1-year-old implant candidates may have additional disabilities (i.e. autism) [25], some of which may not be able to be detected at this young age needs to be also stressed. Having other disabilities would not usually preclude implantation, but would certainly alter the level of expectation, raise the possibility of considering additional therapeutic measures, and even necessitate postponement of the operation until the child is slightly older, in order for more informed prognosis to be obtained [5,26]. Diagnostic problems in this case are caused by the fact that a fundamental problem in cognition, language, or behaviour may have secondary effects on other areas, thus producing difficulties in separating cause from effect [27]. Language and problem-solving milestones seem to provide the best insights into the infant's intellectual potential in doubtful situations [28].

4.2. Anesthetic risk in children under the age of 1 year

In addition to the diagnostic challenges regarding the assessment of hearing loss in infancy, potential anesthetic risks that may be associated with this population may also influence the decision for a surgical intervention. Indeed, even though improvements in complication rates have been consistently observed during the last 50 years [29], anesthesia-related adverse events may still concern up to 35% of pediatric cases, whereas the respective percentage in adults is approximately half as much (17%) [30]. The severity of such events may vary considerably and include intraoperative incidents, events in the recovery room, or postoperative anesthetic complications. Moreover, both major and minor adverse events are included in these numbers. However, the overall risk of anesthetic complications appears to be affected by the age of the child, being significantly higher in children younger than 1-year old compared with older age groups [31,32]. Thus, it has been estimated that critical incidents occur 4 times more frequently in infants, with cardiovascular and respiratory incidents posing as the main areas of concern [31]. Among the latter, laryngospasm seems to be the most frequent adverse event [31,33], resulting in a compromised airway, which can quickly lead to hypoxemia and bradycardia [34,35]. Cardiovascular incidents, on the other hand, either related to anesthetic medications, or associated with blood loss represent an additional risk for the infant equilibrium [33]. Anesthesia-related stress represents another critical issue, because infants are born with normal vagal responses, whereas

their sympathetic nervous system is still immature [34]. As a result, blood pressure instability and a decrease in their heart rate may also cause serious concerns during surgery. Intraoperative temperature monitoring is also essential in very young patients, not only because the large body surface in comparison to their body weight, and the thin infantile skin may easily result in severe hypothermia, but also because, due to the relatively narrow surgical field, prolonged cochlear implantation may in fact increase the overall body temperature with the same ease [36].

Despite the above-mentioned challenges of surgical interventions in infancy, a number of studies have reported that young age alone is not the only determinant of pediatric anesthetic risk. The physical status as defined by the American Society of Anesthesiology (ASA), the presence of a pediatric anesthetist, and the emergency status of the operation also seem to influence the rate and severity of anesthetic complications [35]. Thus, an ASA physical status of 1 or 2, which is reasonably common in pediatric implant candidates, is associated with a lower incidence of anesthesia-related cardiac arrests in infants, compared to ASA grades between 3 and 5 [35,37,38]. In addition, Keenan at al. demonstrated that the presence of a pediatric anesthetist has a significant effect on patient outcomes in children younger than 1-year old, minimizing the likelihood of intraoperative bradycardia and cardiac arrest in this age group [39]. Efficient airway management should always be taken into account and represents an essential requirement when administering anesthesia to infants, as even brief periods of suboptimal ventilation may easily promote lung atelectasis [36]. Furthermore, increased surveillance is also necessary in certain infant subpopulations postoperatively (i.e. preterm infants) [40,41] and even seemingly minor problems, such as obtaining intravenal access, may require considerable experience [34]. In addition, capillary sampling may be required if surgery is prolonged, in order to monitor the biochemical parameters and adjust the administered fluids [36]. Finally, emergency operations seem to be associated with an increased anesthetic risk for a fatal outcome [32,37,38], even though the potential absence of a pediatric anesthesiologist during these procedures may act as a confounding factor in this association [42]. Cochlear implantation, however, is not expected to have a high procedure-associated anesthetic risk, as it is typically performed on a scheduled basis.

Hence, not only does a number of factors beyond patient age seem to influence the risk of pediatric anesthesia, but even the impact of age may have been overestimated. Cohen et al. suggested that the highest rate of intraoperative anesthesia-related adverse events among infants occur during the first month of life, whereas older infants may demonstrate the same rate of complications as children 1–5 years of age [30]. These findings seem to support infant cochlear implantation, as the operation in most cases is not performed earlier than the sixth month of life.

The present meta-analysis of published interventional studies regarding cochlear implantation before the age of 12 months has identified 125 infant implantations. No major anesthetic complication with regard to this cohort of pediatric implantees has been reported in any of the published papers, which is considered very encouraging as a finding.

Taken together these data, do not preclude cochlear implantation in children less than 1-year old due to the anesthetic risk alone, provided that the infant candidates are relatively healthy, the attending anesthetist is considerably experienced in handling patients of this age group, and appropriate facilities of pediatric perioperative care are readily available [21,36]. However, the potential impact of anesthetic agents in the developing brain continues to represent a controversial issue [43,44] and is still a subject of ongoing investigation [36].

4.3. Surgical and technical considerations in infancy

A number of surgical issues should also be taken into account when implanting an infant. Anatomical constraints, existing co-morbidities, limitations with regard to blood loss and aesthetic concerns may have considerable bearing on the expected complication rates. Additional challenges also include device parameters and tuning, in an age that co-operation on behalf of the child is very difficult or impossible.

Small incision cochlear implant surgery seems ideal for infants, as it may improve the aesthetic outcome and reduce the postoperative morbidity of implanted infants [45]. The technique involves performing a very short, oblique, straight post-auricular incision halfway between the hairline and the apex of the pinna, thus avoiding either an extended incision, or shaving the child's hair. This can significantly reduce the psychologic trauma of the intervention for the child's parents, thus improving the accept-ability of the procedure. Risks of flap-related postoperative complications are also minimized [46].

The placement of the receiver-stimulator also requires special consideration in children younger than 1-year old [25,47]. Because of the usually thin skull [48], exposure of the dura is often necessary in order to achieve sufficient depression and lower the profile of the receiver-stimulator [45,48–53]. The latter may be useful for the stabilisation of the device and prevention of skin necrosis, or traumatic dislodgement of the receiver–stimulator from the frequent falls when these children are starting to walk [5,48]. The present meta-analysis did not find enough evidence to suggest that additional or special measures to secure the device in the 'bed' should be employed such as ligature fixation, the use of polypropylene mesh, or titanium screws, especially if the periosteum flap and the special pocket under it keep the device in place.

In addition, the significant post-natal growth of the mastoid and the external auditory canal should also be taken into account, and the array fixation should allow up to 25 mm leadwire lengthening [54,55], otherwise wire breakdowns are likely to occur [25]. Positioning of the coil above the apex of the pinna and slightly angled towards the inferior margin of the incision may also ensure that the coil will not become dislodged when the child is resting at his/her seat [48].

The incompletely developed mastoid tip in children under 1-year old and the limited pneumatisation that may be encountered in this age requires careful drilling during cortical mastoidectomy, not only because the facial nerve is positioned more superficially, but also due to the remaining marrow content in the mastoid [5,48]. However, adequate pneumatisation of the mastoid antrum can be expected in the majority of cases, thus facilitating safe identification of the surgical landmarks. The presence of marrow content may be more troublesome, as persistent bleeding may complicate attempts to reach the area of the facial recess [48]. The prevention of the latter in particular, is of paramount importance in order to avoid hypovolemic effects, which may lead to cardiovascular compromise in the very young patient. The margin of safety for an infant aged 6 to 12 months, with an average body weight between 8 and 10 kg, is actually quite limited, taking into account that his/her total blood volume is approximately 80 ml/kg. Given the fact that it is not considered safe for any acute blood loss to exceed 10% of the circulating blood volume, the maximum quantity of blood loss permitted may range between 64 and 80 ml [56,57].

Another area of surgical concern is the actual dimensions of the facial recess in infants. The middle and inner ear are adult size at birth and the facial recess is also fully developed in neonates [54]. However, the absence of facial recess growth after birth may result in a narrow facial recess in cases of prematurity [54,58], thus

impeding the safe angulation of the drill away from the facial nerve and the placement of the insertion tool through the opening [47]. A laterally and inferiorly located stapedial tendon, which is not infrequently observed at this age group, may also result in inadequate view through the facial recess and impede satisfying access to area of the cochleostomy [47], thus increasing the risk for complications.

The duration of surgery has long been considered as an important factor for infants who are scheduled to undergo an elective operation. Nevertheless, even prolonged surgery may not be independently considered as a risk factor for infant cochlear implantation, if good anesthetic practise has been ensured [36]. Operating times of up to 4.5 h without adverse effects have been reported in infants not older than 7 months [25]. Hence, under appropriate pediatric anesthetic care, even prolonged surgical procedures can be safely performed, if the blood loss remains minimal [36].

Surgical complications represent a major issue not only for surgeons but also for parents, and should be thoroughly analysed before obtaining the informed consent. The present meta-analysis identified only 11 complications in 125 infant implantees (8.8%), which involved incidents of both minor and major degrees of severity as defined by the Nottingham team [59] (Table 1). Compared to older implanted children, the risk of developing a major complication in infant implantees does not actually seem to be significantly different. Indeed, the risk of a major complication in older children varies from 2.3% to 4.1% in different patient series [59,60], whilst the respective percentage in infant implantees, as estimated from the present meta-analysis, is 3.2%. Moreover, no case of cholesteatoma has ever been reported following implanta-tion in infants, compared to an incidence of approximately 2.4% in older implanted children [60]. However, caution should be exercised in interpreting these comparisons, as long-term out-comes are still lacking in infant implantees and the potential appearance of cholesteatomas or other complications may need several years to be encountered.

As the implant population becomes younger, a number of existing co-morbidities should also be taken into account. Hence, otitis media with effusion may reach a prevalence of 36% at the age of 8 months [61] and a significant number of infants may also present with pre-implantation history of ear infections that require cautious management [1]. Many surgeons perform cochlear implantation as a second operation in patients whose ears have been drained after tympanostomy tube insertion [62], whilst tympanostomy tubes are also recommended for otitis-prone pediatric implantees [63]. Removing the tympanostomy tube at the time of implantation and placing a temporalis fascia graft underneath the eardrum is a common practice. However, tympanostomy tubes have also been placed at the time of cochlear implantation with no reported post-operative

Table 1
Surgery-related complications regarding cochlear implantation in infancy.

Severity of complications		No. of cases	Type of management
Minor	AOM	1	Conservative
	Seroma	2	Conservative
	Suture extrusion	1	Conservative
	CSF leak	1	Surgical
	Blood volume loss[a]	1	Conservative
	Mastoiditis	1	Conservative
Major	Flap breakdown	2	Surgical n/r
	Device breakdown	1	Surgical
	Device infection	1	Surgical

AOM: acute otitis media; CSF: cerebrospinal fluid; n/r: not reported.
[a] Only excessive due to young age.

complications [47], although the communication of the external ear canal with the middle ear through the tube, and with the inner ear through the cochleostomy, theoretically increases the risk of serious infections. Finally, the incidence of otitis media following cochlear implantation in older children was reported as lower [64], either because of the improved middle ear aeration which can follow the mastoidectomy, and/or due to the natural history of the disease.

The aforementioned co-morbidity issues in infant implantees often put otologists in difficult situations regarding the most appropriate time for implantation. Situations such as post-meningitic cochlear obliteration on the other hand, may push otologists to intervene earlier. This condition may be detected on MRI scans as early as 2 months after the infection, and can make cochlear implantation an urgent procedure in order to avoid the ossification, which makes full electrode insertion difficult or impossible [48,65,66].

Finally, with regard to the additional challenges that may be encountered after cochlear implantation in infancy, device parameters such as postoperative fitting may prove troublesome in an infant who does not co-operate, and VRA may also not be easily applicable (as was analysed in detail previously). Although device tuning is always adjusted over time and is not expected to be definitive from the first fitting sessions, a close approximation is desired in order to ensure adequate listening conditions for the implanted infant, otherwise the whole issue of early implantation may be jeopardised. Nevertheless, stapedial reflexes and the advances in neural response telemetry in conjunction with behavioural audiometric techniques have proven quite helpful in addressing this issue, especially in experienced centres [1,5,25,26].

5. Conclusion

The diagnosis of profound hearing loss in infancy, although challenging, can be confirmed with acceptable certainty when objective measures (ABR, ASSR, OAEs) and behavioural assessments are combined in experienced centres. Reliable assessment of the prelexical domains of infant development is also important and feasible using appropriate evaluation techniques. If parental expectations are realistic and hearing aid trial unsuccessful, cochlear implantation can be performed in otherwise healthy infants, provided that the attending pediatric anesthesiologist is considerably experienced and appropriate facilities of pediatric perioperative care are readily available. A number of concerns, with regard to anatomic constraints, existing co-morbidities or additional disorders, tuning difficulties, and special phases of the developing child should be also taken into account. The present meta-analysis did not find an increased rate of anesthetic or surgical complications in infant implantees, although long-term follow-up and large numbers are lacking.

Acknowledgement

References

[1] S.J. Dettman, D. Pinder, R.J. Briggs, R.C. Dowell, J.R. Leigh, Communication development in children who receive the cochlear implant younger than 12 months: risks versus benefits, Ear Hear. 28 (April(2 Suppl.)) (2007) 11S–18S.
[2] K. Schauwers, S. Gillis, K. Daemers, C. De Beukelaer, P.J. Govaerts, Cochlear implantation between 5 and 20 months of age: the onset of babbling and the audiologic outcome, Otol. Neurotol. 25 (May(3)) (2004) 263–270.
[3] V. Colletti, M. Carner, V. Miorelli, M. Guida, L. Colletti, F.G. Fiorino, Cochlear implantation at under 12 months: report on 10 patients, Laryngoscope. 115 (March(3)) (2005) 445–449.
[4] P.V. Vlastarakos, K. Proikas, G. Papacharalambous, I. Exadaktylou, G. Mochloulis, T.P. Nikolopoulos, Cochlear implantation under the first year of age—the outcomes. A critical systematic review and meta-analysis, Int. J. Pediatr. Otolaryngol. 2009 Nov 4 [Epub ahead of print].
[5] S.B. Waltzman, J.T. Roland Jr., Cochlear implantation in children younger than 12 months, Pediatrics 116 (October(4)) (2005) e487–e493.
[6] G. Rance, R. Roper, L. Symons, L.J. Moody, C. Poulis, M. Dourlay, T. Kelly, Hearing threshold estimation in infants using auditory steady-state responses, J. Am. Acad. Audiol. 16 (May(5)) (2005) 291–300.
[7] J.M. Moore, W.R. Wilson, G. Thompson, Visual reinforcement of head-turn responses in infants under 12 months of age, J. Speech Hear. Disord. 42 (August(3)) (1977) 328–334.
[8] R.K. Clifton, B.A. Morrongiello, J.W. Kulig, et al., Developmental changes in auditory localization in infancy, in: R. Aslin, J. Alberts, R. Petersen (Eds.), Development of Perception, Academic Press, New York, 1981, pp. 141–160 (quoted in Ref. [21]).
[9] S.J. Norton, M.P. Gorga, J.E. Widen, et al., Identification of neonatal hearing impairment: evaluation of transient evoked otoacoustic emission, distortion product otoacoustic emission, and auditory brain stem response test performance, Ear Hear. 21 (October(5)) (2000) 508–528.
[10] A.H. Graungaard, L. Skov, Why do we need a diagnosis? A qualitative study of parents' experiences, coping and needs, when the newborn child is severely disabled, Child Care Health Dev. 33 (May(3)) (2007) 296–307.
[11] Y.S. Sininger, Auditory brain stem response for objective measures of hearing, Ear Hear. 14 (February(1)) (1993) 23–30.
[12] S.A. Arnold, Objective versus visual detection of the auditory brain stem response, Ear Hear. 6 (May–June(3)) (1985) 144–150.
[13] S.M. Mason, On-line computer scoring of the auditory brainstem response for estimation of hearing threshold, Audiology 23 (3) (1984) 277–296.
[14] D. Gans, D. Del Zotto, K.D. Gans, Bias in scoring auditory brainstem responses, Br. J. Audiol. 26 (December(6)) (1992) 363–368.
[15] G. Rance, F. Rickards, Prediction of hearing threshold in infants using auditory steady-state evoked potentials, J. Am. Acad. Audiol. 13 (May(5)) (2002) 236–245.
[16] G. Rance, R.C. Dowell, F.W. Rickards, D.E. Beer, G.M. Clark, Steady-state evoked potential and behavioral hearing thresholds in a group of children with absent click-evoked auditory brain stem response, Ear Hear. 19 (February(1)) (1998) 48–61.
[17] G. Rance, D. Tomlin, F.W. Rickards, Comparison of auditory steady-state responses and tone-burst auditory brainstem responses in normal babies, Ear Hear. 27 (December(6)) (2006) 751–762.
[18] G. Rance, D. Tomlin, Maturation of auditory steady-state responses in normal babies, Ear Hear. 27 (February(1)) (2006) 20–29.
[19] M.S. John, D.K. Brown, P.J. Muir, T.W. Picton, Recording auditory steady-state responses in young infants, Ear Hear. 25 (December(6)) (2004) 539–553.
[20] H. Luts, B. Van Dun, J. Alaerts, J. Wouters, The influence of the detection paradigm in recording auditory steady-state responses, Ear Hear. 29 (August(4)) (2008) 638–650.
[21] R.F. Holt, M.A. Svirsky, An exploratory look at pediatric cochlear implantation: is earliest always best? Ear Hear. 29 (August(4)) (2008) 492–511.
[22] P.V. Vlastarakos, T.P. Nikolopoulos, E. Tavouari, G. Papacharalambous, S. Korres, Auditory neuropathy: endocochlear lesion or temporal processing impairment? Implications for diagnosis and management, Int. J. Pediatr. Otorhinolaryngol. (May) (2008) (Epub ahead of print).
[23] S. Nathani, D.J. Ertmer, R.E. Stark, Assessing vocal development in infants and toddlers, Clin. Ling. Phon. 20 (July(5)) (2006) 351–369.
[24] R. Jakobson, Child Language, Aphasia, and Phonological Universals, Mouton, The Hague, 1968 (quoted in Ref. [20]).
[25] D.M. Valencia, F.L. Rimell, B.J. Friedman, M.R. Oblander, J. Helmbrecht, Cochlear implantation in infants less than 12 months of age, Int. J. Pediatr. Otorhinolaryngol. 72 (June(6)) (2008) 767–773.
[26] A. Lesinski-Schiedat, A. Illg, R. Heermann, B. Bertram, T. Lenarz, Paediatric cochlear implantation in the first and in the second year of life: a comparative study, Cochlear Implants Int. 5 (December(4)) (2004) 146–159.
[27] K. Markiewicz, M. Pachalska, Diagnosis of severe developmental disorders in children under three years of age, Med. Sci. Monit. 13 (February(2)) (2007) CR89–CR99.
[28] P.A. Blasco, Pitfalls in developmental diagnosis, Pediatr. Clin. North Am. 38 (December(6)) (1991) 1425–1438.
[29] J.P. Morray, Anesthesia-related cardiac arrest in children. An update, Anesthesiol. Clin. North Am. 20 (March(1)) (2002) 1–28, v.
[30] M.M. Cohen, C.B. Cameron, P.G. Duncan, Pediatric anesthesia morbidity and mortality in the perioperative period, Anesth. Analg. 70 (February(2)) (1990) 160–167.
[31] C.L. Tay, G.M. Tan, S.B. Ng, Critical incidents in paediatric anaesthesia: an audit of 10 000 anaesthetics in Singapore, Paediatr. Anaesth. 11 (November(6)) (2001) 711–718.
[32] L. Tiret, Y. Nivoche, F. Hatton, J.M. Desmonts, G. Vourc'h, Complications related to anaesthesia in infants and children. A prospective survey of 40240 anaesthetics, Br. J. Anaesth. 61 (September(3)) (1988) 263–269.
[33] S.M. Bhananker, C. Ramamoorthy, J.M. Geiduschek, et al., Anesthesia-related cardiac arrest in children: update from the Pediatric Perioperative Cardiac Arrest Registry, Anesth. Analg. 105 (August(2)) (2007) 344–350.
[34] N.M. Young, Infant cochlear implantation and anesthetic risk, Ann. Otol. Rhinol. Laryngol. Suppl. 189 (May) (2002) 49–51.
[35] R.L. Keenan, J.H. Shapiro, F.R. Kane, P.M. Simpson, Bradycardia during anesthesia in infants. An epidemiologic study, Anesthesiology 80 (May(5)) (1994) 976–982.

[36] M. Jöhr, A. Ho, C.S. Wagner, T. Linder, Ear surgery in infants under one year of age: its risks and implications for cochlear implant surgery, Otol. Neurotol. 29 (April(3)) (2008) 310–313.

[37] L. Gobbo Braz, J.R. Braz, N.S. Módolo, P. do Nascimento, B.A. Brushi, L. Raquel de Carvalho, Perioperative cardiac arrest and its mortality in children. A 9-year survey in a Brazilian tertiary teaching hospital, Paediatr. Anaesth. 16 (August(8)) (2006) 860–866.

[38] J.P. Morray, J.M. Geiduschek, C. Ramamoorthy, et al., Anesthesia-related cardiac arrest in children: initial findings of the Pediatric Perioperative Cardiac Arrest (POCA) Registry, Anesthesiology 93 (1) (2000 Jul) 6–14.

[39] R.L. Keenan, J.H. Shapiro, K. Dawson, Frequency of anesthetic cardiac arrests in infants: effect of pediatric anesthesiologists, J. Clin. Anesth. 3 (November–December(6)) (1991) 433–437.

[40] S. Malviya, J. Swartz, J. Lerman, Are all preterm infants younger than 60 weeks postconceptual age at risk for postanesthetic apnea? Anesthesiology 78 (June(6)) (1993) 1076–1081.

[41] C.D. Kurth, A.R. Spitzer, A.M. Broennle, J.J. Downes, Postoperative apnea in preterm infants, Anesthesiology 66 (April(4)) (1987) 483–488.

[42] R.L. Keenan, C.P. Boyan, Cardiac arrest due to anesthesia. A study of incidence and causes, J. Am. Med. Assoc. 253 (April(16)) (1985) 2373–2377.

[43] M. Jöhr, Does anesthesia damage children's brains? Anesthesist 55 (2006) 465–466 [article in German].

[44] A. Davidson, S. Soriano, Does anesthesia harm the developing brain-evidence or speculation? Paediatr. Anaesth. 14 (2004) 199–200.

[45] A.L. James, B.C. Papsin, Device fixation and small incision access for pediatric cochlear implants, Int. J. Pediatr. Otorhinolaryngol. 68 (August(8)) (2004) 1017–1022.

[46] G.M. O'Donoghue, T.P. Nikolopoulos, Minimal access surgery for pediatric cochlear implantation, Otol. Neurotol. 23 (November(6)) (2002) 891–894.

[47] J.B. Roberson, L.D. Kunda, K.R. Stidham, M.M. Inserra, W. Choe, L. Tonokawa, Modifications of standard cochlear implantation techniques for children under 18 months of age, Cochlear Implants Int. 7 (December(4)) (2006) 207–213.

[48] A.L. James, B.C. Papsin, Cochlear implant surgery at 12 months of age or younger, Laryngoscope 114 (December(12)) (2004) 2191–2195.

[49] R.T. Miyamoto, D.M. Houston, T. Bergeson, Cochlear implantation in deaf infants, Laryngoscope 115 (August(8)) (2005) 1376–1380.

[50] D.J. Lee, M. Driver, Cochlear implant fixation using titanium screws, Laryngoscope 115 (May(5)) (2005) 910–911.

[51] B.M. Davis, R.F. Labadie, S.O. McMenomey, D.S. Haynes, Cochlear implant fixation using polypropylene mesh and titanium screws, Laryngoscope 114 (December(12)) (2004) 2116–2118.

[52] H.R. Djalilian, T. King, R.A. Faust, S. Smith, S.C. Levine, Securing cochlear implants to the skull: two alternate methods, Ear Nose Throat J. 80 (March(3)) (2001) 171–173.

[53] R.A. Hoffman, N.L. Cohen, Surgical pitfalls in cochlear implantation, Laryngoscope 103 (7) (1993) 741–744.

[54] M.C. Dahm, R.K. Shepherd, G.M. Clark, The postnatal growth of the temporal bone and its implications for cochlear implantation in children, Acta Otolaryngol. Suppl. 505 (1993) 1–39.

[55] G.M. O'Donoghue, R.K. Jackler, W.M. Jenkins, R.A. Schindler, Cochlear implantation in children: the problem of head growth, Otolaryngol. Head Neck Surg. 94 (January(1)) (1986) 78–81.

[56] M. Jöhr, Kinderanästhesie, 6th ed., Elsevier/Urban and Fischer, München, Germany, 2004.

[57] E.F. Battersby, Paediatric anaesthesia, in: D.A. Adams, M.J. Cinnamond (Eds.), Scott-Brown's Otolaryngology, Butterworth-Heinemann, Oxford, UK, 1997, pp. 6–24.

[58] T.L. Eby, Development of the facial recess: implications for cochlear implantation, Laryngoscope 106 (May(5 Pt 2 Suppl. 80)) (1996) 1–7.

[59] K. Bhatia, K.P. Gibbin, T.P. Nikolopoulos, G.M. O'Donoghue, Surgical complications and their management in a series of 300 consecutive pediatric cochlear implantations, Otol. Neurotol. 25 (September(5)) (2004) 730–739.

[60] Y.S. Lin, F.P. Lee, S.C. Peng, Complications in children with long-term cochlear implants, ORL J. Otorhinolaryngol. Relat. Spec. 68 (4) (2006) 237–242 (Epub March 27, 2006).

[61] E.J. Midgley, C. Dewey, K. Pryce, A.R. Maw, The frequency of otitis media with effusion in British pre-school children: a guide for treatment. ALSPAC Study Team, Clin. Otolaryngol. Allied Sci. 25 (December(6)) (2000) 485–491.

[62] R.J. Kennedy, C. Shelton, Ventilation tubes and cochlear implants: what do we do? Otol. Neurotol. 26 (May(3)) (2005) 438–441.

[63] M. Luntz, C.B. Teszler, T. Shpak, Cochlear implantation in children with otitis media: second stage of a long-term prospective study, Int. J. Pediatr. Otorhinolaryngol. 68 (March(3)) (2004) 273–280.

[64] M. Luntz, J. Khalaila, A. Brodsky, T. Shpak, Cochlear implantation in children with otitis media: third stage of a long-term prospective study, Harefuah 146 (February(2)) (2007) 106–110, 166.

[65] S.S. Hehar, T.P. Nikolopoulos, K.P. Gibbin, G.M. O'Donoghue, Surgery and functional outcomes in deaf children receiving cochlear implants before age 2 years, Arch. Otolaryngol. Head Neck Surg. 128 (January) (2002) 11–14.

[66] M.A. Novak, R.C. Fifer, J.C. Barkmeier, J.B. Firszt, Labyrinthine ossification after meningitis: its implications for cochlear implantation, Otolaryngol. Head Neck Surg. 103 (September(3)) (1990) 351–356.