ORIGINAL ARTICLE

The Clinical Characteristics of Tinnitus in Patients with Vestibular Schwannoma

David M. Baguley, Ph.D., M.B.A.,[1] Rachel L. Humphriss, M.Sc.,[1] Patrick R. Axon, M.D., F.R.C.S.,[2] and David A. Moffat, B.Sc., F.R.C.S.[2]

ABSTRACT

Objectives: To review the symptoms, signs, and clinical findings in a large series of patients diagnosed with unilateral sporadic vestibular schwannoma (VS) to describe the clinical characteristics of tinnitus in this population. Further, to ascertain which of the proposed mechanisms of tinnitus generation in VS was supported. Design: Retrospective case note and database review. Setting: Tertiary university teaching hospital departments of audiology and neuro-otology. Participants: Nine hundred forty-one patients with unilateral sporadic VS, diagnosed during the period 1986 to 2002. Twenty-three additional patients were excluded due to missing clinical data. Main outcome measures: The presence or absence of tinnitus, and its rated subjective severity were analyzed in conjunction with data regarding patient demographics, symptoms, signs, and diagnostic audiovestibular test findings. Results: No statistical association at the 5% level was found between tinnitus presence/absence and patient age, gender, 2- to 4-kHz audiometric thresholds, ipsilateral auditory brainstem response abnormality, length of history, tumor side, nor caloric test abnormality. Statistically significant associations were found between tinnitus presence/absence and tumor size ($p = 0.012$) and type of hearing loss (progressive, sudden, fluctuant, nil) with a tendency for patients without hearing loss to be less likely to experience tinnitus. Statistically significant associations were identified between classification of tinnitus severity and age at diagnosis ($p < 0.001$) (greater age being associated with greater tinnitus severity), abnormal findings on caloric testing ($p = 0.01$) (abnormal calorics being associated with greater tinnitus severity), and tinnitus as a principal presenting symptom ($p < 0.001$) (this being associated with greater tinnitus severity). Conclusions: The analysis does not identify any single one of the proposed mechanisms for tinnitus as being the obvious culprit. In fact, even in a homogeneous group of patients such as

Departments of [1]Audiology and [2]Otolaryngology, Addenbrooke's Hospital, Cambridge, United Kingdom.

Address for correspondence and reprint requests: David M. Baguley, Audiology (94), Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, UK. E-mail: dmb29@cam.ac.uk.

Skull Base 2006;16:49–58.

Received: July 1, 2005. Accepted after revision: July 14, 2005.
Published online: February 13, 2006.
DOI 10.1055/s-2005-926216. ISSN 1531-5010.

this, there is evidence of multiple mechanisms that are not mutually exclusive. The association between increased tinnitus severity in older patients, patients with canal pareses on caloric testing, and with tinnitus as a principal presenting symptom should be borne in mind by the clinician.

KEYWORDS: Vestibular schwannoma, tinnitus, mechanisms

The objective of this study was to determine the evidence for physiological mechanisms for tinnitus in unilateral sporadic vestibular schwannoma (VS) by analyzing the presence or absence of tinnitus in conjunction with symptoms, signs, and tumor characteristics in a large patient cohort.

It has been reported that 73% of patients with VS experience tinnitus, and in at least one in ten patients tinnitus is the principal presenting symptom.[1] The utility of considering tinnitus in this patient group is that patients with VS are relatively homogeneous in pathophysiology, symptoms, and signs, which is in contrast to the wider population of individuals with tinnitus, who are very markedly heterogenous.[2]

POTENTIAL MECHANISMS OF TINNITUS GENERATION

Several potential mechanisms of tinnitus generation in VS have been suggested in the literature:

- Ephaptic coupling of cochlear nerve fibers by compression[3–5]
- Cochlear dysfunction by ischemia or by biochemical degradation[6–8]
- Efferent system dysfunction following compression of the efferent fibers in the inferior vestibular nerve[9]
- Cortical reorganization following hearing loss[10]

These mechanisms by which tinnitus may be generated in a patient with VS are described in detail below—however, these are not mutually exclusive.

Ephaptic Coupling

It has been suggested that as a VS grows and takes up space within the internal auditory canal, it compresses auditory nerve fibers causing them to "cross talk" by ephaptic coupling.[3–5] Sunderland[11] noted that the formation of such "artificial synapses" was characteristic of "any injury . . . that leads to failure of the insulating properties of the nerve sheath, whether it be nerve section, crushing by ligature, or even moderate compression, introduces . . . an artificial synapse created where denuded axons are in contact." This phenomenon would mean that the random firing of one or more nerve fibers would generate a pattern across many fibers of the auditory nerve, this being perceived as a tinnitus sound.

Cochlear Dysfunction

The finding that a proportion of patients with VS have an associated cochlear hearing loss[12–14] may suggest cochlear involvement in tinnitus generation. Moffat et al[15] noted audiological findings that were indicative of a cochlear or mixed cochlear/retrocochlear lesion in 36 of a series of 49 patients with sporadic unilateral VS (73%). Prasher et al[12] reported absent transient evoked otoacoustic emissions (TEOAE) in 19 of 26 patients with VS (73%): in all patients in whom TEOAE was absent, a hearing loss of 40 dB HL (hearing loss) or greater was present, and this was assumed to be cochlear in origin. Telischi et al[16] undertook distortion product otoacoustic emission (DPOAE) measurements in 44 patients with unilateral VS. On the basis of the presence or absence of the DPAOE, 26 tumor ears (59%) were classified as having a cochlear loss: 13

(30%) classified as retrocochlear (DPOAE recorded in the presence of a hearing loss >40 dB), and 5 (11%) as mixed. Ferber-Viart and associates[17] attempted TEOAE recordings in 168 ears with VS, and in 79% were not able to demonstrate good cochlear function, thus indicating a cochlear dysfunction in addition to the tumor. Ferguson and associates[14] were unable to evoke TEOAE in 78 patients of a series of 100 with unilateral VS. Thus an initially controversial speculation by Bonfils and Uziel[18] that "acoustic tumors usually produce a cochlear hearing loss" is supported by the subsequent literature.

There has been little specific consideration in the literature of the pathophysiological mechanisms of cochlear hearing loss in VS. Schucknecht[7] proposed the mechanisms of ischemia causing atrophy of the cochlea and the vestibular labyrinth by compromising blood flow in the internal labyrinthine artery which runs through the internal auditory canal (IAC) and/or biochemical degradation of the cochlea and the vestibular labyrinth. Evidence for ischemic and biochemical vestibular labyrinth injury in VS has been reported by Jahnke and Neuman[8] who studied specimens taken from nine patients during translabyrinthine surgery. Examination with electronmicroscopy demonstrated significant degenerative changes that were thought to be the result of prolonged protein intoxication of the labyrinth (via increased perilymph protein concentrations) and by compression of labyrinthine blood vessels by the tumor. Similar mechanisms were suggested for cochlear dysfunction in such cases. O'Connor and colleagues[6] had earlier identified high protein levels in the perilymph of patients with VS, though not in a patient group with meningioma in the IAC, and suggested that this may be a mechanism specific to VS.

Efferent System Dysfunction

An alternative hypothesis considers the presence of medial and lateral efferent fibers within the inferior division of the vestibular nerve.[9] A VS arising from or impinging upon the inferior vestibular nerve might be expected to reduce the effectiveness of efferent influence upon the cochlea, and thus perhaps cause signals in the afferent peripheral auditory pathway to be perceived as more intense than would otherwise be the case. Thus a "tinnitus signal" might appear more intense as a result of the lesion in the internal auditory meatus. Maurer et al[19] recorded TEOAE in 6 of 20 patients with unilateral VS. The amplitudes of these emissions were significantly smaller than those in a normal control group. The application of contralateral white noise (40, 50, 60 dB HL) did not suppress the amplitude of the TEOAE in the tumor ears, but in the ear without tumor greater suppression effects were noted than in the control group. Maurer and coworkers[19] tentatively suggested that the VS had reduced efferent function on the affected side, and that some counterintuitive effect was present contralaterally. This study contained the suggestion that a VS compressing the vestibular divisions of the VIIIth nerve, specifically the inferior, affects the efficacy of the efferent function on that side. It should be noted however that this effect was demonstrable in only a minority of patients. No mention of the tinnitus experiences of these patients was made.

Baguley et al[20] reviewed the effect upon tinnitus of vestibular nerve section, which involves section of the auditory medial efferent fibers which run in the inferior vestibular nerve. While this procedure is almost exclusively applied to patients with Meniere's disease that has proved refractory to medical treatment, it does represent an opportunity to determine if ablation of the medial efferent system influences tinnitus. Reviewing 18 papers reporting surgical series involving a total of 1318 patients, the authors reported that there was no evidence of a consistent exacerbation of tinnitus following vestibular nerve section, causing them to question the influence of the efferent system upon tinnitus.

Cortical Reorganization

There is a good evidence of plastic change in the central auditory system following change in

peripheral function in both animals[21,22] and humans.[23,24] Further, there is a hypothesis that a consequence of such change may be overrepresentation of certain auditory frequencies[25] and of spontaneous bursting at boundary areas in the primary auditory cortex[10,26]; there is a growing body of evidence that these may be mechanisms of tinnitus.[27,28]

Given that a VS is associated with a hearing loss in the majority of cases, and that this is due to change in cochlear and/or cochlear nerve function,[7] some cortical plastic change should be expected as a consequence. In this event any associated tinnitus should be similar in generation to tinnitus in general that is associated with hearing loss. It would also follow that if the peripheral status were to change further, such as with destructive (translabyrinthine) surgery, then the tinnitus would change as a consequence.

The Present Study

The objective of the present study was to review the symptoms, signs, and clinical findings in a large series of patients diagnosed with unilateral sporadic VS to ascertain which of the proposed mechanisms of tinnitus in VS was supported.

METHODS

This study entailed a retrospective case note review of patients seen at Addenbrooke's Hospital, Cambridge, over the period 1986 to 2002, with a diagnosis of unilateral sporadic VS. Broadly speaking, in the period 1986 to 1992 that diagnosis was made with computed tomography scans, patients having first been screened using auditory brainstem responses (ABR). In the early 1990s, magnetic resonance imaging became available for clinical use and was utilized as the investigation of choice in cases of a suspected VS. The initial ABR screen was then set aside due to suboptimal sensitivity and specificity.[29]

Data regarding symptoms, signs, and diagnostic test results were recorded in case notes and in a computer database at the time of diagnosis by either a consultant neuro-otologist (DAM, PRA), consultant scientist (DB), or a neuro-otological clinical fellow. The following data were elicited from patient case notes and appropriate databases:

- Patient age at operation, gender
- Length of history (months)
- Tumor side
- Tumor size (maximum diameter on definitive radiology, coded ordinally)
- Date of operation
- Principal symptom
- Presence of
  - Hearing loss (progressive, sudden, fluctuant)
  - Imbalance
- Tinnitus
  - Presence or absence
  - Severity (see below)
- Audiometric thresholds (performed by British Society of Audiology standard techniques[30,31])
- Canal paresis on caloric test results (performed by British Society of Audiology standard techniques,[32] $\geq$25% paresis abnormal)
- ABR results (standard techniques,[33] abnormal $>$ 1 SD from normative data, or poor morphology)
  - Ipsilateral to tumor
  - Contralateral to tumor

The tinnitus severity data elicited from case notes had been recorded according to the Klockoff and Lindblom[34] classification with a slight modification.[35] Data are described in Table 1.

Data were collated in a Filemaker Pro database running on an Apple Macintosh G4 computer (system 10.1), and statistical analysis was undertaken with SPSS.

RESULTS

Retrospective case review identified 941 individuals identified with VS in whom the majority of relevant data was available: 23 further cases were excluded on

Table 1 Klockhoff and Lindblom[34] Classification of Tinnitus Severity

Nil	No tinnitus
Mild (Klockoff Grade I)	Tinnitus is audible only in quiet environments
Moderate (Klockoff Grade II)	Tinnitus is audible only in ordinary acoustic environments, but masked by loud environmental sounds; it can disturb going to sleep, but not sleep in general
Severe (Klockoff Grade III)	Tinnitus is audible in all acoustic environments, disturbs going to sleep, can disturb sleep in general, and is a dominating problem that affects quality of life

the basis of missing tinnitus data, so that the total series had numbered 963. Of the cases included in the analysis, 487 (52%) were male and 454 (48%) female. The mean age was 54.3 years (SD 13.3 years). Tinnitus was present in 717 individuals (76%) and absent in 224 (24%). Data regarding tumor side were available for analysis in 821 cases. The VS was on the right in 405 cases (49.6%) and the left in 412 (50.4%). Tumor size distribution is detailed in Table 2.

The presenting symptom (data available in $n = 939$) was progressive hearing loss in 575 (61%), sudden hearing loss in 77 (8%), tinnitus in 114 (12%), imbalance in 95 (11%), and other in 78 (8%). Caloric function in the tumor ear was reported as normal in 116 cases (16%), reduced ($\geq 25\%$) in 215 (30%), and absent in 375 (54%) (total $n = 706$). Patients had self-reported their hearing loss as progressive (800, 85.5%), sudden (91, 10%), nil (41, 4%) or fluctuating (3, 0.5%) (data available in $n = 935$). Ipsilateral ABR results were found for 476 patients: of these 70 (15%) were normal and 406 (85%) abnormal. Contralateral ABR results were found for 470 patients: of these 405 (87%) were normal and 65 (13%) abnormal.

Table 2 Tumor Sizes in the Study Group*

Tumor Size (maximum diameter in cm)	Number of Patients
< 1.5	169 (20%)
1.5–2.4	279 (34%)
2.5–3.4	186 (23%)
3.5–4.4	118 (15%)
> 4.4	63 (8%)

*Data available in $n = 815$.

Analysis indicated no significant difference ($p > 0.05$) between the tinnitus and nontinnitus groups on the following variables:

- Age ($n = 941$, $p = 0.141$, t-test)
- Gender ($n = 941$, $p = 0.319$, chi-square)
- Ipsilateral (to tumor) audiometric threshold at 4 kHz ($n = 745$, $p = 0.517$, t-test)
- Mean ipsilateral (to tumor) audiometric threshold at 2 kHz and 4 kHz ($n = 574$, $p = 0.847$, t-test)
- Ipsilateral (to tumor) ABR abnormality ($n = 476$, $p = 0.125$, chi-square)
- Length of history ($n = 710$, mean 40.6, SD 46.7 months, $p = 0.604$. Mann-Whitney U test)
- Tumor side ($n = 821$, $p = 0.453$, chi-square)
- Caloric test abnormality ($n = 706$, $p = 0.138$, chi-square)

A statistically significant association was identified between tumor size (maximum diameter on radiology, ordinal data) ($n = 815$, $p = 0.012$, chi-square) and the presence of tinnitus. This was not linear, so that a simple relationship cannot be ascertained (Table 3). An association between tumor size 2.5 to 4.4 cm and decreased prevalence was noted.

A further association was found between type of hearing loss (progressive, sudden, fluctuant, or nil) and presence of tinnitus ($n = 935$, $p = 0.006$, chi-square) (Table 4). This again is complex and potentially multifactorial, with a tendency for patients without hearing loss to be less likely to experience tinnitus. Detailed analysis did not indicate an increased prevalence of tinnitus in patients who had undergone a sudden hearing loss ($n = 91$, $p = 0.920$, Fisher's exact test).

Table 3 Tumor Size and Tinnitus Presence

Tumor Size (maximum diameter in cm)	Number	Tinnitus Present	Tinnitus Absent
< 1.5 cm	169	138 (81.7%)	31 (18.3%)
1.5–2.4 cm	279	222 (79.6%)	57 (20.4%)
2.5–3.4 cm	186	135 (72.6%)	51 (27.4%)
3.5–4.4 cm	118	83 (70.3%)	35 (29.7%)
> 4.5 cm	63	49 (77.8%)	14 (22.2%)

Analysis of the relationship between contralateral (to tumor) ABR findings and the presence of tinnitus identified a statistically significant association ($p = 0.047$, chi-square) such that patients with abnormal ABR in the contralateral ear were more likely to experience tinnitus.

Tinnitus severity data, coded as none, mild, moderate, or severe by the modified Klockoff and Lindblom[34] criteria, were available on 885 patients. In 383 (43%), there was no tinnitus, in 273 (31%) tinnitus was mild, in 19 (2%) it was moderate, and in 210 (24%) it was severe. Analysis was undertaken to identify possible associations with tinnitus severity. No significant associations were identified with the following:

- Mean 2 kHz and 4 kHz audiometric thresholds ($n = 569$, $p = 0.080$, t-test)
- Type of symptomatic hearing loss (nil, progressive, sudden, fluctuant) ($n = 881$, $p = 0.111$, chi-square)
- Ipsilateral ABR findings (normal vs. abnormal) ($n = 576$, $p = 0.378$, chi-square)
- Contralateral ABR findings (normal vs abnormal) ($n = 480$, $p = 0.627$, chi-square) or
- Tumor side ($n = 791$, $p = 0.459$, chi-square).

Table 4 Type of Hearing Loss and Presence of Tinnitus

Type of Hearing Loss	Number (total = 935)	Tinnitus Present	Tinnitus Absent
Progressive SNHL	800	611 (76.4%)	189 (23.6%)
Sudden SNHL	91	76 (83.5%)	15 (16.5%)
Nil	41	22 (53.7%)	19 (46.3%)
Fluctuant	3	0 (0%)	3 (100%)

SNHL, sensorineural hearing loss.

A significant association between tinnitus severity was identified with age at diagnosis ($n = 885$, $p < 0.001$, t-test), greater severity being recorded with greater age. Abnormal findings on caloric testing were associated with greater tinnitus severity ($n = 706$, $p = 0.01$, chi-square). Those patients who reported tinnitus as their principal symptom ($n = 114$) reported more severe tinnitus than those who did not ($n = 778$) ($p < 0.001$, chi-square).

DISCUSSION

These results should be considered in the context of the potential models of tinnitus generation that have been listed above. The hypothesis that tinnitus generation is associated with cochlear hearing loss was not directly tested in a manner which determined the cochlear component of a hearing loss, as OAE data were not available for these patients. No association between high frequency hearing thresholds (4 kHz alone and 2 to 4 kHz mean) and tinnitus presence or absence was identified, however.

A potential role for ephaptic coupling in the cochlear nerve as a tinnitus mechanism[3–5] was addressed by this analysis, in that this situation might reasonably be associated with ABR abnormality, nerve compression being a mechanism for

ABR latency prolongation in this condition. No association between ipsilateral ABR results and tinnitus presence or severity was identified, however, and so a potential role for this mechanism remains unproven.

There was, however, a statistical association between the presence of tinnitus and contralateral ABR abnormality, such that an individual was more likely to report tinnitus if contralateral ABR were abnormal. The mechanism of contralateral ABR abnormality in patients with VS is thought to be brainstem compression,[15,36,37] and this may potentially have a role in tinnitus generation, though it is at odds with the association between tumor size 2.5 to 4.4 cm and decreased likelihood of tinnitus. These issues have not previously been reported.

The potential role of efferent system dysfunction was indirectly investigated with the use of caloric results. Caloric stimulation of the horizontal semicircular canal is innervated by the superior vestibular nerve, and hence in a VS patient with normal caloric function the tumor effects may be confined to the inferior vestibular nerve with no or minimal impact upon superior vestibular nerve function. One might thus consider the presence of medial and lateral efferent fibers within the inferior division of the vestibular nerve.[9] A VS arising from or impinging upon the inferior vestibular nerve might be expected to reduce the effectiveness of efferent influence upon the cochlea, and thus perhaps cause signals in the afferent peripheral auditory pathway to be perceived as more intense than would otherwise be the case. A hypothesis can be derived from this in that tinnitus, if influenced by auditory efferent dysfunction, might be more prevalent in patients with normal caloric function. This association was not demonstrated, though the finding was made that there is an association between increased tinnitus severity and caloric test abnormality. The inference is that efferent dysfunction may not directly cause tinnitus, but may play a role in exacerbation, though this is at odds with other work indicating that efferent dysfunction following section of the auditory efferents in the human vestibular nerve does not lead to troublesome tinnitus.[20]

The final mechanism considered is that of cortical reorganization following change in the status of the auditory periphery, which in the case of sudden change (hearing loss) can lead to border areas that are spontaneously active.[10] No association between sudden hearing loss and tinnitus presence or severity was identified, however.

There is an apparent disparity between two aspects of the recording of tinnitus status. It was found that in the 941 patients in whom data were available, tinnitus was present in 717 patients (76%) and absent in 224 (24%). However, in the 885 patients in whom severity coding was available, the tinnitus severity data (Table 1) indicated no tinnitus in 383 (43%), mild tinnitus in 273 (31%), moderate in 19 (2%), and in 210 (24%) severe. Thus there is disparity between the numbers of patients without tinnitus. One interpretation is that in some clinicians' mind the severity classification "none" (Table 1) meant no handicap rather than no tinnitus. Tinnitus intensity and handicap have recently been demonstrated to be independent[38] and this appears to be a shortcoming of the Klockhoff and Lindblom[34] classification.

The association between tinnitus severity and patient age has not been previously reported in patients with VS and is also of interest. The mechanisms that underlie this may be complex. Patients may have greater age-related hearing loss, and more likelihood of tinnitus coincidental to their VS, when of greater age, and it is possible that there is an additive or synergistic effect regarding tinnitus between this and the VS. Other factors involved may include the reduced neural plasticity in the auditory system reported with age[39] and reports that elderly patients in general find tinnitus to be harder to bear.[40,41]

The finding that patients who have tinnitus as their principal presenting symptom have tinnitus that is more severe than other patients with VS is congruent with the view that it is this distressingly severe tinnitus that led them to seek medical attention. This indicates to the clinician that these patients warrant careful explanation of their tinnitus and appropriate tinnitus therapy as they wait for

surgery or radiosurgery or are enrolled in a "watch, wait, rescan" program.

There are other important clinical implications of this study. The first is that the clinician should be aware of the association identified between increased age, tinnitus as the presenting symptom, and tumor size, with tinnitus presence and severity. These findings should be borne in mind when seeing patients with this condition and when deciding whom to refer for tinnitus therapy.

An important caveat about this study should be considered. While every effort was made to obtain a comprehensive dataset, the retrospective nature of this study meant that a proportion of data was unavailable due to missing case notes and missing data within case notes. This is a potential source of bias and should be borne in mind when considering the findings. The number of patients studied is large, however, for this rare condition, so any bias deriving from missing data may be small.

From the present study it seems that even when a relatively homogeneous patient population with tinnitus is considered, such as those diagnosed with a VS, there appear to be multiple mechanisms that underlie the tinnitus perception. This complex phenomenon remains an important focus for future research.

ACKNOWLEDGMENT

This study is an element of a doctoral thesis by David Baguley at the University of Cambridge, supervised by Dr. Ian Winter, Department of Physiology. A TWJ (Thomas Wickham Jones Foundation) thesis writing grant was invaluable in the completion of this work. (www.twjfoundation.org)

REFERENCES

1. Moffat DA, Baguley DM, Beynon GJ, Da Cruz M. Clinical acumen and vestibular schwannoma. Am J Otol 1998;19:82–87
2. Moller AR. Similarities between chronic pain and tinnitus. Am J Otol 1997;18:577–585
3. Moller AR. Pathophysiology of tinnitus. Ann Otol Rhinol Laryngol 1984;93:39–44
4. Eggermont JJ. On the pathophysiology of tinnitus: a review and peripheral model. Hear Res 1990;48:111–124
5. Levine RA, Kiang NYS. A conversation about tinnitus. In: Vernon JA, Moller AR, eds. Mechanisms of Tinnitus. London, UK: Allyn and Bacon; 1995:149–160
6. O'Connor AF, France MW, Morrison AW. Perilymph total protein levels associated with cerebellopontine angle lesion. Am J Otol 1981;2:193–195
7. Schuknecht HF. Pathology of the Ear. 2nd ed. Philadelphia, PA: Lea and Febiger; 1993
8. Jahnke K, Neuman TA. The fine structure of vestibular end organs in acoustic neuroma patients. In: Tos M, Thomsen J, eds. Acoustic Neuroma. Amsterdam, The Netherlands: Kugler; 1992:203–207
9. Sahley TL, Nodar RH, Musiek FE. Efferent Auditory System: Structure and Function. San Diego, CA: Singular; 1997
10. Salvi RJ, Lockwood AH, Burkard R. Neural plasticity and tinnitus. In: Tyler RS, ed. Tinnitus Handbook. San Diego, CA: Singular; 2000:123–148
11. Sunderland S. Nerve Injuries and Their Repair: A Critical Appraisal. Edinburgh, UK: Churchill Livingstone; 1991
12. Prasher DK, Tun T, Brookes GB, Luxon LM. Mechanisms of hearing loss in acoustic neuroma: an otoacoustic emission study. Acta Otolaryngol 1995;115: 375–381
13. Quaranta A, Salluststio V, Scaringi L. Cochlear function in ears with vestibular schwannomas. In: Sanna M, Taibah A, Russo A, Mancini F, eds. Acoustic Neurinoma and Other CPA Tumors. Bologna, Italy: Monduzzi; 1999:43–50
14. Ferguson MA, O'Donoghue GM, Owen V. Contralateral suppression of transient evoked otoacoustic emissions in patients with cerebello-pontine angle tumor. Ear Hear 2001;22:173–181
15. Moffat DA, Hardy DG, Baguley DM. Strategy and benefits of acoustic neuroma searching. J Laryngol Otol 1989;103:51–59
16. Telischi FF, Roth J, Stagner BB, Lonsbury-Martin BL, Balkany TJ. Patterns of evoked otoacoustic emissions associated with acoustic neuromas. Laryngoscope 1995; 105:675–682
17. Ferber-Viart C, Colleaux B, Laoust L, Dubreuil C, Duclaux R. Is the presence of transient evoked otoacoustic emissions in ears with acoustic neuroma significant?. Laryngoscope 1998;108:605–609
18. Bonfils P, Uziel A. Evoked otoacoustic emissions in patients with acoustic neuromas. Am J Otol 1988;9:412–417
19. Maurer J, Hinni M, Beck A, Mann W. Effects of contralateral white noise stimulation on transitory evoked otoacoustic emissions in patients with acoustic neuroma. Otolaryngol Head Neck Surg 1995;112:369–374
20. Baguley DM, Axon P, Moffat DA, Winter IM. The effect of vestibular nerve section upon tinnitus. Clin Otolaryngol 2002;27:219–226

21. Robertson D, Irvine DRF. Plasticity of frequency organization in auditory cortex of guinea pigs with partial unilateral deafness. J Comp Neurol 1989;282: 456–480
22. Rajan R, Irvine DRF, Wise LZ, Heil P. Effect of unilateral partial cochlear lesions in adult cats on the representation of lesioned and unlesioned cochleas in primary auditory cortex. J Comp Neurol 1993;338:17–49
23. Harrison RV, Nagasawa A, Smith DW, Stanton S, Mount RJ. Reorganisation of auditory cortex after neonatal high frequency cochlear hearing loss. Hear Res 1991;54:11–19
24. Dietrich V, Nieschalk M, Stoll W, Rajan R, Pantev C. Cortical reorganisation in patients with high frequency cochlear hearing loss. Hear Res 2001;158:95–101
25. Thai-Van H, Micheyl C, Moore BCJ, Collet L. Enhanced frequency discrimination near the hearing loss cut-off: a consequence of central auditory plasticity induced by cochlear damage?. Brain 2003;126:2235–2245
26. Salvi RJ, Wang J, Powers NL. Plasticity and reorganisation in the auditory brainstem: implications for tinnitus. In: Reich GE, Vernon JE, eds. Proceedings of the Fifth International Tinnitus Seminar 1995. Portland, OR: American Tinnitus Association; 1996: 457–466
27. Muhlnickel W, Elbert T, Taub E, Flor H. Reorganisation of auditory cortex in tinnitus. Proc Natl Acad Sci USA 1998;95:10340–10343
28. Norena A, Micheyl C, Chery-Croze S, Collet L. Psychoacoustic characterization of the tinnitus spectrum: implications for the underlying mechanisms of tinnitus. Audiol Neurootol 2002;7:358–369
29. Wilson DF, Talbot M, Mills L. A critical appraisal of the role of auditory brain stem response and magnetic resonance imaging in acoustic neuroma diagnosis. Am J Otol 1997;18:673–681
30. British Society of Audiology. Recommended procedure for pure-tone audiometry using a manually operated instrument. Br J Audiol 1981;15:213–216
31. British Society of Audiology. Recommended procedure for pure-tone bone-conduction audiometry without masking using a manually operated instrument. Br J Audiol 1985; 19:281–282
32. British Society of Audiology. Caloric test protocol. Br J Audiol 1999;33:179–184
33. Hall JW. Handbook of Auditory Evoked Responses. Boston, MA: Allyn and Bacon; 1992
34. Klockhoff I, Lindblom U. Meniere's disease and hydrochlorothiazide (Dichlotride)—a critical analysis of symptoms and therapeutic effects. Acta Otolaryngol 1967;63: 347–365
35. Baguley DM, Moffat DA, Hardy DG. What is the effect of translabyrinthine acoustic schwannoma removal upon tinnitus? J Laryngol Otol 1992;106:329–331
36. Nodar RH, Kinney SE. The contralateral effects of large tumours on brainstem auditory evoked potentials. Laryngoscope 1980;90:1762–1768
37. Musiek FE, Kibbe K. Auditory brainstem response wave IV–V abnormalities from the ear opposite large cerebellopontine angle lesions. Am J Otol 1986;7:253–257
38. Andersson G. Tinnitus loudness matchings in relation to annoyance and grading of severity. Auris Nasus Larynx 2003;30:129–133
39. Cacace AT. Expanding the biological basis of tinnitus: cross-modal origins and the role of neuroplasticity. Hear Res 2003;175:112–132
40. Erlandsson SI, Hallberg LRM, Axelsson A. Psychological and audiological correlates of perceived tinnitus severity. Audiology 1992;31:168–179
41. Davis AC, Rafaie EA. Epidemiology of tinnitus. In: Tyler RS, ed. Tinnitus Handbook. San Diego, CA: Singular; 2000:1–24