International Congress Series 1254 (2003) 81–88

Effects of otitis media with effusion on central auditory function

David R. Moore*, Douglas E.H. Hartley, Sarah C.M. Hogan[1]

University Laboratory of Physiology, University of Oxford, Parks Road, Oxford, OX1 3PT, UK

Abstract

Conductive hearing loss attenuates and delays sound passing through the middle ear. This impairs binaural hearing and other central auditory functions dependent on high fidelity sound transmission. Persistent conductive loss leads to central impairments that persist after the peripheral loss has resolved. For example, children who have had multiple episodes of otitis media with effusion (OME) in the first few years of life may have poor detection of sounds in noisy environments, evidenced by reduced binaural unmasking (BU). Recent research shows that a 'threshold' level of OME is required to produce impaired BU. Children who had OME in one or both ears for more than about 50% of the first 5 years had reduced BU. Animal research, using long-term ear plugging, suggests that total OME duration, rather than age at the time of having the disease, determines its effect on BU. Animals reared with bilateral (but not unilateral) ear plugs also have poor auditory temporal resolution, and reduced sensitivity to short tones in the presence of background noise, after plug removal. However, given time (6–24 months) and training, all animals regained normal temporal resolution.

Keywords: Conductive hearing loss; Binaural hearing; Earplug; Auditory training; Auditory plasticity; Auditory processing disorder; Temporal resolution

1. Introduction

Protracted otitis media with effusion (OME) has been associated with a number of sensory, cognitive and social difficulties that are suggestive of impaired brain function [1].

* Corresponding author. MRC Institute of Hearing Research, University Park, Nottingham NG7 2RD, UK. Tel.: +44-1159-223431; fax: +44-1159-518503.

E-mail address: davem@ihr.mrc.ac.uk (D.R. Moore).

[1] Present address: The Burwood Centre for Childhood Deafness, Pigeons Farm Road, Thatcham, Berkshire RG19 8XA, UK.

0531-5131/
doi:10.1016/S0531-5131(03)01089-6

However, the extent to which these difficulties are caused by OME or, whether they even exist at all, remains controversial. Laboratory-based studies of the effect of OME, and of conductive hearing loss in general, provide objective information for the assessment of this controversy. In this paper, we review the evidence for changes in the central auditory system that are produced by conductive hearing loss. The evidence is drawn both from psychoacoustic evaluation of children with a known history of OME and from animal studies, mainly involving long-term ear plugging. These results support the belief that OME does affect brain function and that the neural consequences of the OME outlive the peripheral hearing loss. The extent to which these consequences affect an individual's behavioural development seems to be dependent on other, non-auditory factors. One important and positive finding is that at least the sensory impairments produced by OME are reversible. The rate at which this occurs may be accelerated by active auditory training.

2. Prevalence of OME

To study the effect of OME on hearing and the brain, we have closely monitored the prevalence of middle ear effusions in a small ($n = 80$) sample of children during the first 6–7 years of life [2–4]. The children were quasi-randomly selected from the general population and were examined monthly during domiciliary visits using tympanometry, audiometry and otoscopy. Selected sub-groups attended the laboratory for further tests (below). Using a primary criterion of a flat (B-type) tympanogram in either ear, almost all the children had OME at least once during the study period, the peak prevalence occurring during the second year. Prevalence diminished gradually, and monotonically during subsequent years. However, the prevalence of unilateral effusion remained quite high throughout the study period. While a typical child had one or two positive diagnoses of OME each year, on average, a significant minority of children had profound, recurrent OME, which, in the most extreme 10% of cases, exceeded a 50% lifetime prevalence for the first five years of life. These children thus had OME more commonly than not.

3. Acoustics of OME

The presence of a flat tympanogram does not imply a hearing loss and, in fact, we sometimes found audiometrically normal thresholds in children who had OME, as reported by others [5]. More commonly, however, we found that active OME produced a hearing loss (up to 30 dB), often with the lower frequencies more adversely affected. This confirmed reports [5] of mild to moderately impaired hearing levels in OME.

In the laboratory, we have modelled the acoustic effects of OME by injecting the middle ear of anaesthetised gerbils with silicon oil while recording the cochlear microphonic response from the round window of the cochlea [6]. The results paralleled those found in children with OME. Some injections produced little hearing loss (attenuation), while others showed the same level (30–40 dB) of attenuation found in severe cases of OME. They also suggested, more surprisingly, that OME *delays* low

frequency sounds entering the inner ear by up to 150 μs. In cases of unilateral OME, both the attenuation and the delay produced by the effusion could produce major distortions of acoustic cues (interaural level and time differences) used for sound localization and other aspects of binaural hearing.

4. OME and the central auditory system

Sounds are transduced in the cochlea into neural impulses that are conveyed with great fidelity to the auditory brainstem, which is specially adapted to handling time sensitive activity [7,8]. This ensures that signals from the two ears normally arrive at the medial superior olivary nucleus (MSO) with their timing relation intact, enabling further integrative processing that forms the basis of interaural time difference detection. Similarly, interaural level differences are encoded with considerable precision by the firing rate of neurons in the lateral superior olive (LSO). Distortions of these binaural cues changes not only the immediate relation between the incoming impulse volleys from the two ears, but also can act post-synaptically, via neurotransmitter receptors and intracellular signalling pathways, to change the way that target neurons process sound related information in the future. Higher up in the auditory system, neurons are less sensitive to the precise temporal and spatial features of a stimulus, but may be more sensitive to changing input [9].

Against this background, it has been shown that long-term conductive hearing loss in animals can change the anatomy and physiology of the central auditory system [10]. For example, the relative size of neuron dendrites in the MSO that are innervated by axons deriving from each ear have been shown to change following a unilateral conductive loss [11]. The balance of inputs to higher levels of the brain can also be changed by unilateral earplugging, a form of conductive loss that quite closely models the acoustic effects of OME [12]. Physiologically, unilateral earplugs can change the spatial sensitivity of neurons in the auditory midbrain [13,14], a process that has been found to adapt with long-term insertion of the plugs. These and many other findings show that the auditory system and, indeed, the whole brain, responds dynamically to the level of neural input it receives from the ears.

5. OME and binaural hearing

Based on animal research, we reasoned that OME, particularly unilateral or asymmetric OME, may compromise binaural hearing in children, both during and after the effusion. In an initial study [15] we found that children who had visited an ENT clinic for recurrent OME did, in fact, perform more poorly on a test of binaural hearing than age-matched children with no known history of OME (Fig. 1). Very similar results were reported in an independent study by Pillsbury et al. [16]. The test of binaural hearing used was the masking level difference (MLD; Fig. 1A), a laboratory measure of the binaural contribution to the ‘cocktail party effect’. The MLD reflects the ability of the auditory system to distinguish sounds based only on their binaural qualities. It should be noted that, at the

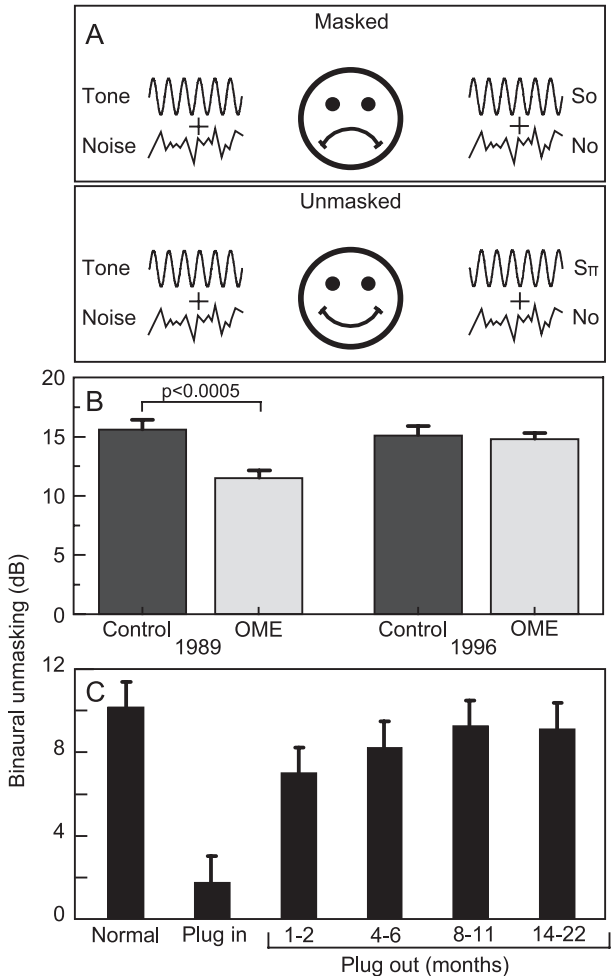

Fig. 1. Binaural hearing following OME. (A) The masking level difference (MLD). In the 'Masked' condition, a low frequency tone (So) and a masking noise (No) are presented identically to the two ears. The level of the tone is reduced until it is just masked by the noise. If the phase of the tone to one ear is flipped by 180° (Sπ), the tone is 'Unmasked'; it becomes audible and its level must be reduced further until it is again masked by the noise. The difference between the tone thresholds in the Masked and Unmasked conditions is the MLD. (B) The effect of previous OME on the MLD in children. In these studies [14,16], children in the OME group had a history of recurrent OME prior to the age of 5 years and had been referred to the local ENT clinic, where most of them had received tympanostomy tubes. Following recovery from the OME, confirmed by normal audiograms, the MLD was first measured at the age of 6–12 years, in 1989. Compared with children in the Control group (no known OME), those in the OME group had significantly ($p < 0.0005$) reduced MLDs. However, when re-tested 7 years later, in 1996, samples of both the original groups had normal MLDs, showing a recovery of binaural hearing. (C) Ferrets had the MLD [18] abolished by unilateral ear plugging ('Plug in'). Immediately after the plug was removed, the MLD in both infant and adult plugged animals remained significantly reduced. Following several months of unplugging, the MLD gradually returned to control levels.

time of MLD testing, the children were all OME free. Moreover, no relation was found between MLD and auditory thresholds. These results, plus the binaural nature of the MLD task, confirm that the hearing impairment was central in origin.

In subsequent research [17], we showed by re-examining the same group of children studied previously, that the binaural impairment produced by OME is reversible (Fig. 1B). Careful studies of the recovery of the MLD in children following middle ear surgery [18] have shown that it takes in the region of two years for binaural hearing to recover fully from severe OME. In our recent work, we have also shown that a minimum level of OME is required to impair binaural hearing [4]. In a sub-group of children from our OME prevalence study (above), we have shown a non-linear relationship between the lifetime history of OME and the level of the MLD. Only children who had the highest prevalence (>50%) of OME had impaired binaural hearing.

Further aspects of the effects of OME on binaural hearing have been pursued in animal experiments where it is possible to control factors such as the age at onset, the duration and the laterality of a conductive hearing loss. Some of this research closely paralleled our human studies by examining the MLD in ferrets who had received unilateral earplugs for many months (Fig. 1C) [19]. As in the children with OME, we found that ferrets ear plugged in infancy had reduced MLDs, both during plugging and after the plugs were removed, compared with control ferrets. Interestingly, we found that adult ferrets had identical responses to ear plugging, showing that, for this deprivation and type of task, there does not appear to be a developmental 'sensitive period'. A study of the MLD in adult humans who had long-term otosclerosis surgically corrected reached a similar conclusion [20].

Absolute sound localization uses a variety of cues, but accurate binaural hearing is required to perform the task well. Ferrets can perform sound localization to a high level of accuracy. Unilaterally ear plugged ferrets initially performed poorly but, with practice and time, were able to perform a localization task accurately [21]. As for the MLD task, adult plugged animals performed similarly to those reared with earplugs. In this task, however, 'recovery' (increased localization accuracy) occurred while the earplugs were in place. The importance of learning in the recovery process was demonstrated by the finding that ferrets recovered to the same degree following a given number of test sessions, irrespective of whether the test sessions were given daily or once every six days.

These studies of binaural hearing in humans and animals have shown how major, long-term changes in the balance of input from the two ears to the brain can change the way in which the brain processes sounds. OME and other forms of conductive hearing loss appear to 'instruct' brain circuits to make inappropriate connections. However, when the hearing loss is removed, the brain re-establishes appropriate connectivity, a process that is enhanced by active training.

6. OME and temporal hearing

Temporal hearing is the ability to separate (resolve) and integrate sounds perceptually over time. There has been much recent interest in the hypothesis that language based learning impairments in children are caused, in part or in whole, by a deficit in auditory

temporal resolution [22–24]. Because OME has also been associated with language impairments, we have investigated the impact of OME in children and of ear plugging in ferrets on a laboratory measure of temporal resolution, auditory backward masking (BM; Fig. 2). BM measures the degree to which detection of a sound is influenced by a following, but non-overlapping (in time), sound.

In children with a known lifetime prevalence of OME, we found no difference in BM threshold between children who had a 'high' or a 'low' prevalence of OME, suggesting that, among these children, OME does not impair temporal hearing after the peripheral hearing loss has resolved [25]. However, in ferrets, we found that 5–8 months of continuous, bilateral ear plugging from before the time at which hearing normally begins in this species (about the end of the first month post-partum) resulted in a substantial elevation of BM thresholds, indicating an impairment in temporal resolution (Fig. 2). Following 4–24 months of further training and testing, without ear plugging, the BM thresholds of the ferrets regained normal levels [26]. Long term, bilateral conductive hearing loss therefore reversibly impaired temporal hearing, suggesting the possibility that children with more severe examples of chronic OME than those examined in our prospective study could, in fact, acquire a temporal hearing deficit. This result also supports our latest findings on binaural hearing [4], that a 'threshold' level of OME may be necessary to observe central auditory processing disorders in children.

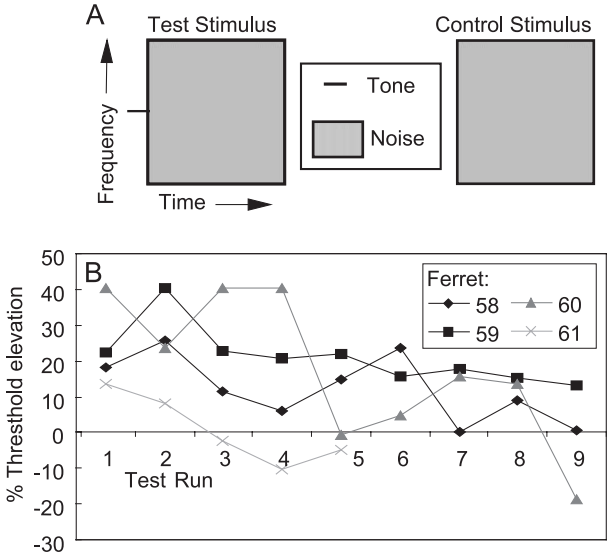

Fig. 2. Temporal hearing following bilateral ear plugging. (A) Auditory backward masking (BM) was measured in ferrets by training them to distinguish a tone followed by a noise ('Test stim.') from a noise alone ('Control stim.') stimulus (see Ref. [23] for further details of the BM stimulus). The level of the tone was reduced until it was just masked by the noise, and the Test and Control stimuli became indistinguishable. (B) Ferrets were reared from before the time of normal onset of hearing (about 28 days post-natal) until 6–9 months of age with binaural earplugs. The plugs were then removed. When tested for BU threshold and compared with ferrets that had never been ear-plugged, varying degrees and durations of threshold elevation were observed. All of the ferrets eventually regained normal BM thresholds but, for some of them, this process took nearly 2 years.

7. Conclusions

OME produces an intermittent, mild to moderate hearing loss that impairs central auditory function. In severe cases, it can have a long-term effect on binaural hearing and, if particularly severe, on temporal hearing. Fortunately, these central auditory processing disorders, while important and long lasting, are reversible. Nevertheless, the central auditory problems induced by OME seem likely to contribute to learning and social difficulties experienced by some children with chronic OME. Early intervention to eliminate the hearing loss produced by OME is desirable, if effective therapies can be implemented. Auditory training to improve listening performance may accelerate recovery following chronic OME.

Acknowledgements

The research reported here summarises much of the work of our laboratory in Oxford over the last 10 years. We are indebted to the following members of the lab: Mervyn Hardiman, Lesley Hulvershorn, Ollie Kacelnik, Andy King and Carl Parsons for their contributions to this work. The research was generously supported by the Medical Research Council, The Wellcome Trust, Defeating Deafness, the Oxford and Anglia Regional Health Authority and the John Ellerman Foundation.

References

[1] J.E. Roberts, et al., Otitis media and language learning sequelae: controversies and current research, Pediatrics (in press).
[2] S.C. Hogan, K.J. Stratford, D.R. Moore, Duration and recurrence of otitis media with effusion in children from birth to 3 years: prospective study using monthly otoscopy and tympanometry, Br. Med. J. 314 (1997) 350–353.
[3] S.C. Hogan, K.J. Stratford, D.R. Moore, Age and experience-related persistence of otitis media with effusion: a prospective study over five years, Assoc. Res. Otolaryngol. Abstr. 21 (1998) 124.
[4] S.C. Hogan, D.R. Moore, Impaired binaural hearing in children produced by a threshold level of middle ear disease, J. Assoc. Res. Otolaryngol. (2002) (in press).
[5] J.S. Gravel, I.F. Wallace, Effects of otitis media with effusion on hearing in the first 3 years of life, J. Speech Lang. Hear. Res. 43 (2000) 631–644.
[6] D.E.H. Hartley, D.R. Moore, Effects of conductive hearing loss on temporal aspects of sound transmission through the ear, Hear. Res. 177 (2003) 53–60.
[7] D. Oertel, The role of timing in the brain stem auditory nuclei of vertebrates, Ann. Rev. Physiol. 61 (1999) 497–519.
[8] L.O. Trussell, Modulation of transmitter release at giant synapses of the auditory system, Curr. Opin. Neurobiol. 12 (2002) 400–404.
[9] H.L. Read, J.A. Winer, C.E. Schreiner, Functional architecture of auditory cortex, Curr. Opin. Neurobiol. 12 (2002) 433–440.
[10] D.L. Tucci, N.B. Cant, D. Durham, Effects of conductive hearing loss on gerbil central auditory system activity in silence, Hear. Res. 155 (2001) 124–132.
[11] Z.D. Smith, L. Gray, E.W. Rubel, Afferent influences on brainstem auditory nuclei of the chicken: n. laminaris dendritic length following monaural conductive hearing loss, J. Comp. Neurol. 220 (1983) 199–205.

[12] D.R. Moore, M.E. Hutchings, A.J. King, N.E. Kowalchuk, Auditory brainstem of the ferret: some effects of rearing with a unilateral ear plug on the cochlea, cochlear nucleus and projections to the inferior colliculus, J. Neurosci. 9 (1989) 1213–1222.
[13] A.J. King, M.E. Hutchings, D.R. Moore, C. Blakemore, Developmental plasticity in the visual and auditory representations in the mammalian superior colliculus, Nature 332 (1988) 73–76.
[14] E.I. Knudsen, Instructed learning in the auditory localization pathway of the barn owl, Nature 417 (2002) 322–328.
[15] D.R. Moore, M.E. Hutchings, S.E. Meyer, Binaural masking level differences in children with a history of otitis media, Audiology 30 (1991) 91–101.
[16] H.C. Pillsbury, J.H. Grose, J.W. Hall, Otitis media with effusion in children. Binaural hearing before and after corrective surgery, Arch. Otolaryngol. Head Neck Surg. 117 (1991) 718–723.
[17] S.C. Hogan, S.E. Meyer, D.R. Moore, Binaural unmasking returns to normal in teenagers who had otitis media in infancy, Audiol. Neuro-Otol. 1 (1996) 104–111.
[18] J.W. Hall 3rd, J.H. Grose, H.C. Pillsbury, Long-term effects of chronic otitis media on binaural hearing in children, Arch. Otolaryngol. Head Neck Surg. 121 (1995) 847–852.
[19] D.R. Moore, J.E. Hine, Z.D. Jiang, H. Matsuda, C.H. Parsons, A.J. King, Conductive hearing loss produces a reversible binaural hearing impairment, J. Neurosci. 19 (1999) 8704–8711.
[20] J.W. Hall 3rd, J.H. Grose, Short-term and long-term effects on the masking level difference following middle ear surgery, J. Am. Acad. Audiol. 4 (1993) 307–312.
[21] A.J. King, C.H. Parsons, D.R. Moore, Plasticity in the neural coding of auditory space in the mammalian brain, Proc. Natl. Acad. Sci. U. S. A. 97 (2000) 11821–11828.
[22] P. Tallal, Children with language impairment can be accurately identified using temporal processing measures: a response to Zhang and Tomblin, Brain Lang. 65 (1998) 395–403. Brain Lang. 69 (1999) 222–229.
[23] P. Tallal, R.E. Stark, E.D. Mellits, Identification of language-impaired children on the basis of rapid perception and production skills, Brain Lang. 25 (1985) 314–322.
[24] B.A. Wright, L.J. Lombardino, W.M. King, C.S. Puranik, C.M. Leonard, M.M. Merzenich, Deficits in auditory temporal and spectral resolution in language-impaired children, Nature 387 (1997) 176–178.
[25] D.E.H. Hartley, C.V. Adams, S.C. Hogan, D.R. Moore, Temporal resolution and language abilities in children with a prospectively studied history of otitis media with effusion (OME), Abs. Assoc. Res. Otolaryngol. 24 (2001) 173.
[26] D.R. Moore, L.A. Hulvershorn, C.H. Parsons, O. Kacelnik, A.J. King, Auditory temporal resolution in ferrets following ear plugging, Soc. Neurosci. Abstr. 27 (2001) 823.13.