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The Time-Course of the Effects of Contralateral Sound on the Level of Distortion Product Otoacoustic Emissions

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SASAKI, N., KAWASE, T., OGURA, M. and TAKASAKA, T. *The Time-Course of the Effects of Contralateral Sound on the Level of Distortion Product Otoacoustic Emissions*. Tohoku J. Exp. Med., 2000, **191** (2), 71-78 —— The effects of the addition of contralateral noise on the level of distortion product otoacoustic emissions (DPOAEs) were examined. In the present study, the DPOAEs were recorded for a relatively long period (2 minutes), and the time-course of the effects of contralateral sound on the level of DPOAEs were considered. In general, the addition of the contralateral noise resulted in suppression of the level of DPOAEs. The time-course of this suppression appeared to depend on the level of the contralateral noise. When the level of the contralateral noise was low, the suppression of the level of DPOAEs seemed to be largely unchanged for at least 2 minutes. In contrast, when a relatively high level of contralateral noise was used, the suppression of the level of DPOAEs decreased with time. ——— contralateral sound; efferent; DPOAE; adaptation; human

The cochlea receives efferent innervation, by way of the olivocochlear bundle (OCB), from the superior olivary complex. These fibers consist of two major systems: unmyelinated fibers which originate in the lateral part of the superior olivary complex (LOC) and myelinated fibers which originate in the more medial part of the superior olivary complex (MOC) (Warr and Guinan 1979). LOC and MOC neurons primarily project to the inner hair cell and outer hair cell areas in the organ of Corti, respectively (Warr and Guinan 1979; Guinan et al. 1983).

As for the effective activation of this olivocochlear (OC) system, it is known that OC neurons can be activated by sound presented ipsilaterally or contralaterally (Fex 1962; Buno 1978; Cody and Johnstone 1982; Liberman 1988; Brown

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1989). Current evidence suggests that the MOC neurons projecting from the contralateral olivary complex to one cochlea, which constitute roughly two-thirds of the MOC neurons, respond best to sound presented ipsilaterally, and that those projecting from the ipsilateral olivary complex, which constitute one-third of the MOC neurons, respond best to contralateral sound (Liberman and Brown 1986; Liberman 1988). Therefore, in terms of the magnitude of the OC effects, the addition of contralateral sound might result in activation of only one-third of the total MOC neurons (Liberman 1988; Warren and Liberman 1989); however, the addition of contralateral sound is a convenient and non-invasive method for the observation of OC effects, which can be easily applied to investigations in humans.

As a possible method to assess the activity of the human efferent system, it is known that the sound-evoked OC effects can be assayed through the measurement of the otoacoustic emissions (OAEs), which are thought to reflect the function of the outer hair cells (OHCs) (Collet et al. 1990; Veuillet et al. 1991; Moulin et al. 1993; Liberman et al. 1996). By activating the OC-system, such as by applying contralateral sound stimulation, the level of OAEs can be suppressed. As to the effectiveness of contralateral sound, the magnitude of the level of suppression of the evoked OAEs (EOAEs) or distortion product OAEs (DPOAEs) has usually been focused on. The time course of the effects of OC activation, however, has not been fully investigated.

Recently, it has been reported that suppression of EOAEs caused by the addition of contralateral noise is unchanged after several minutes of contralateral acoustic stimulation (Giraud et al. 1997). In the present study, the time-course of the OC-mediated suppression of the level of DPOAEs during contralateral sound stimulation was investigated.

MATERIALS AND METHODS

Subjects

Nine ears of seven healthy subjects (5 males and 2 females, with a mean age of 26.9 years) were observed. No pathologic findings of the tympanic membrane and middle ear were observed by inspection. Standard tonal audiometry carried out in a soundproof room showed no elevation of pure-tone thresholds at the standard test frequencies of 0.25, 0.5, 1, 2, 4, and 8 kHz (within 20 dB HL at all tested frequencies) in any of the subjects.

Measurement of DPOAEs

The level of DPOAEs at $2f_1$-f_2 was measured using a system from Etymotic Research (earphone: ER-2; microphone: ER-10B; IBM PC-based DSP board: Ariel DSP 16+; software: CUBDIS, version 2.4, Mountainside, NJ, USA). Equilevel primaries ($L_1 = L_2$) at a frequency ratio of $f_2/f_1 = 1.2$ were used. DPOAEs measurements were carried out at 4000, 2000, and 1500 Hz of f_2. Initially, primaries at the level of 45 dB SPL were used for the measurement of

DPOAEs. However, when no significant level of DPOAE was recorded, the levels of the primaries were elevated by 5-dB steps up to the level at which a significant level of DPOAEs (5 dB above the level of noise floor) could be observed. Using this minimal sound pressure levels of the primaries to produce significant levels of DPOAEs, the effects of contralateral noise were examined for each test condition. Continuous broadband (white) noise generated by a random noise generator (NF Model WG-721A, Yokohama) was used for the sound presented to the contralateral ear. In most subjects, the level of contralateral noise was 60 dB SPL; on the other hand, in some subjects, the level of noise was changed by 10-dB steps. The levels of DPOAEs were measured repeatedly every 5 seconds.

Measurements of acoustic reflex of the middle ear muscles

Contralateral sound stimulation can cause the acoustic reflex of the middle ear muscles (MEMs), which might affect the level of DPOAEs. In the present study, in order to know the possible participation of the acoustic reflex in the obtained results, the acoustic reflex threshold (ART) of the MEMs was measured by means of an impedance audiometer (model TA-2C; Teledyne Avionics, Charlottesville, VA, USA) with a probe tone of 226 Hz in all the participants. In this device, impedance changes are represented by a compliance value which is shown by an equivalent volume of air in cubic centimeters (cc). Impedance changes induced by MEM contraction were recorded on an X-Y plotter in the device. Broadband noise, which was used for the sound presented to the contralateral ear to evoke the OC-activity, was also used for the activator to elicit the acoustic reflex. The level of the elicitor was changed by 5-dB steps. In the present study, the ART was defined as the sound level which resulted in a compliance change of 0.02 cc, which is the recommended criterion of this device.

All parts of the present study were performed in accordance with the guidelines of the Declaration of Helsinki.

RESULTS

The effects of contralateral noise on the level of DPOAEs were examined in 9 ears of 7 subjects. DPOAEs were measured every 5 seconds for 6 minutes. After recording the DPOAEs for 2 minutes without contralateral noise, the effects of the addition of the contralateral noise at 60 dB SPL on the level of DPOAEs were monitored for 2 minutes. The DPOAEs were then measured again for 2 minutes without contralateral noise. In Fig. 1, average changes of the DP level during the presentation of contralateral sound (the difference of the DP levels with and without contralateral noise) are shown for all the conditions tested. Relatively large changes were observed when the DPOAEs were examined at f_2 frequencies of 1500 and 2000. To further observe the time-course of the DP suppression during the addition of contralateral noise, the levels of DPOAEs are plotted as a function of time in subjects who showed a relatively large suppression

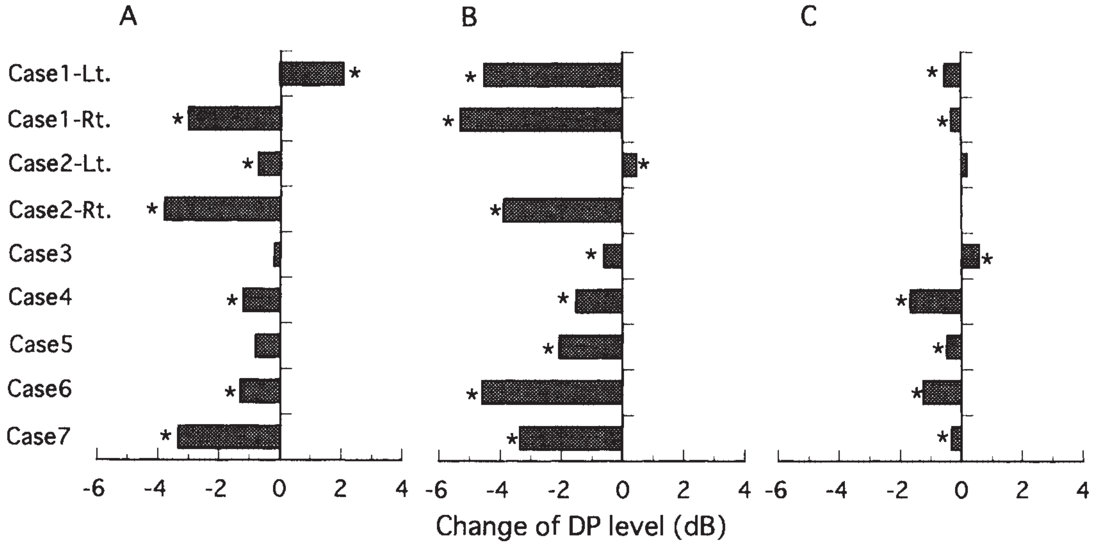

Fig. 1. Average change of the level of DPOAEs during the presentation of contralateral noise (60 dB SPL). The difference between the average DP level during the presentation of contralateral noise (average of 24 data of DP-level which were measured during the addition of contralateral noise) and that without contralateral noise (average of 24 data of DP-level which were measured before the addition of contralateral noise) were analyzed for all the subjects. The effects of contralateral noise, which were observed for the DPOAEs measured at 1500, 2000 and 4000 Hz of f_2, are represented in Figs. 1A, B and C, respectively. Asterisks indicate the points at which significant changes were observed in the level of DPOAEs when contralateral noise was presented ($p < 0.05$, t-test). Lt, left; Rt, right.

of the level of DPOAEs by the addition of contralateral noise (case 1-right, 2 kHz; case 1-left, 1.5 kHz, 2 kHz; case 2-right, 1.5 kHz, 2 kHz; case 6, 2 kHz; case 7, 1.5 kHz, 2 kHz) in Fig. 2. The effects of contralateral noise reflected by the suppression of the level of DPOAEs appeared to decrease with time. The average DP-levels during the 30 seconds immediately after the onset of the contralateral noise were significantly suppressed as compared with those of the last 30 seconds just before the termination of the contralateral noise.

In a particular subject who showed a relatively large suppression of the level of DPOAEs by the presentation of contralateral acoustic stimulation (case 2-right, 2 kHz), the effects of changing the level of the contralateral noise on the time-course of suppression in DPOAEs were observed (Fig. 3). In this subject, a contralaterally induced acoustic reflex of the middle ear muscles was not observed up to a level of 70 dB SPL of broadband noise. A significant suppression was observed from a level much lower than the ART. Moreover, the suppression of the the level of DPOAEs during the presentation of contralateral noise tended to decrease when a relatively higher level of contralateral noise was used. On the other hand, the suppression of the the level of DPOAEs did not show any remarkable adaptation when the lower level contralateral noise was used.

In Fig. 4, the degree of the suppression of the level of DPOAEs is plotted as

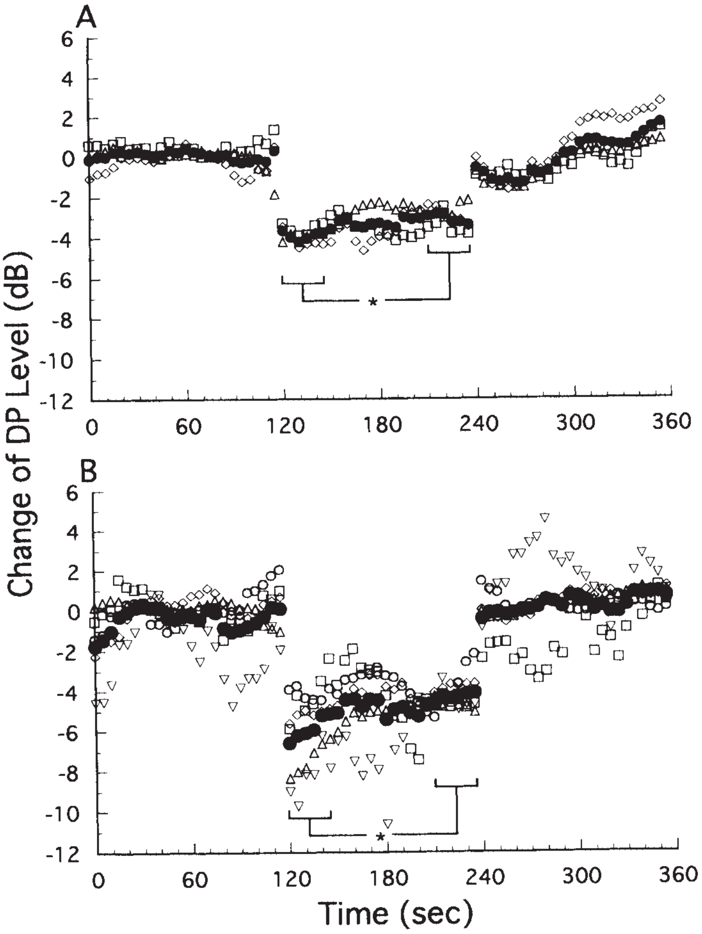

Fig. 2. Time course of the level of DPOAEs observed in subjects who showed significant DP change by the addition of contralateral noise. Average values ●, as well data from each subject (△, case 1-right [2 kHz]; ◇, case 1-left [1.5 kHz, 2 kHz]; □, case 2-right [1.5 kHz, 2 kHz]; ▽, case 6 [2 kHz]; ○, case 7 [1.5 kHz, 2 kHz]) are plotted. The average DP-level during the 30 seconds immediately after the onset of contralateral noise was significantly depressed as compared to that of the last 30 seconds just before the offset of contralateral noise (*$p<0.01$, *t*-test).

a function of ART for all the subjects. It appears that there was no correlation between the two parameters, although the largest suppression was observed in subjects with relatively low-level of ART.

DISCUSSION

As for the time course of the sound-evoked OC-effects, Giraud et al. (1997) recently reported that the suppression of otoacoustic emission was unchanged for several minutes during acoustic stimulation of the OCB. However, data in reports by several other authors (Wiederhold and Kiang 1970; Kujawa et al. 1993; Sridhar et al. 1995; Liberman et al. 1996) indicate that the OC-effects tended to decrease during the continuous stimulation of the OCB (electrically or acoustically). In the present study in which the time course of the suppression of DP was observed in subjects with considerable contralateral effects, the time course of the

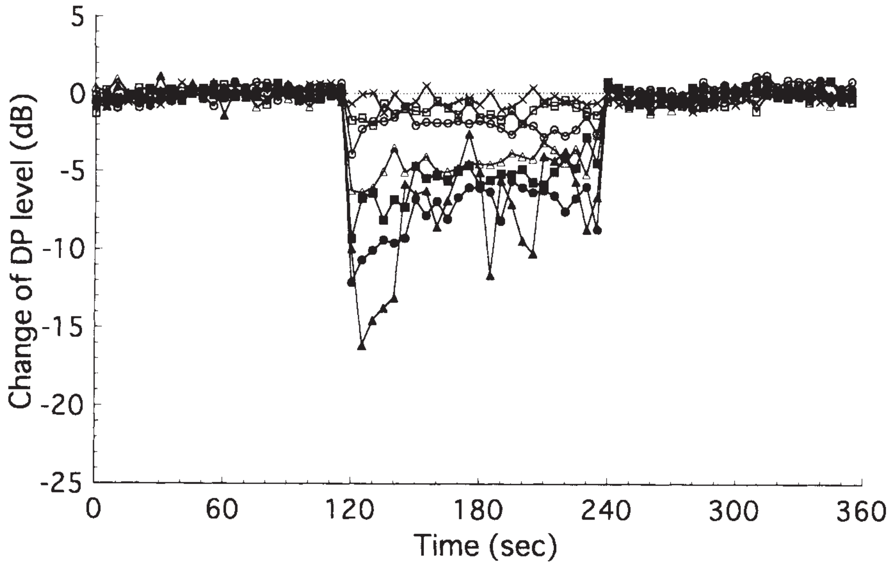

Fig. 3. Effects of changing the level of contralateral noise on the time course of depression in DPOAEs observed in a subject who showed relatively large depression as the result of the presentation of contralateral acoustic stimulation (case 2-right, DPOAEs for 2 kHz of f_2). The symbols in the figure indicate the data from different level of contralateral noise (×, 20 dB SPL; □, 30 dB SPL; ○, 40 dB SPL; △, 50 dB SPL; ■, 60 dB SPL; ●, 70 dB SPL; ▲, 80 dB SPL)

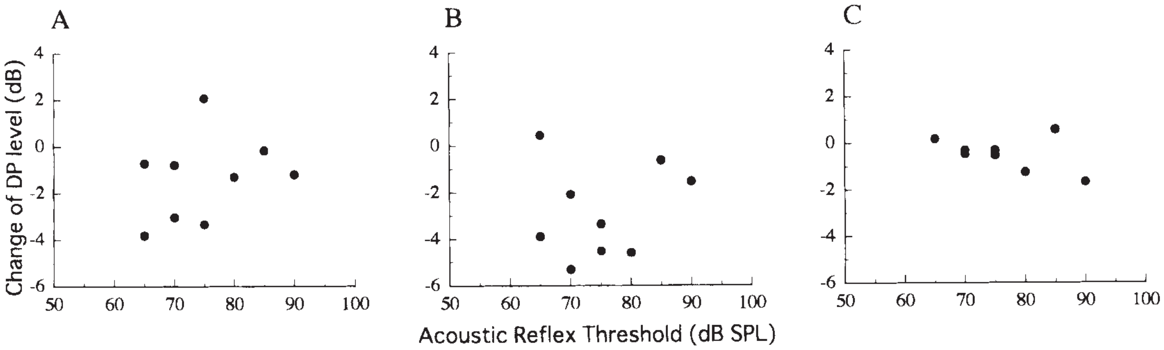

Fig. 4. Average changes of the level of DPOAEs during the presentation of contralateral noise (shown in Fig. 1) plotted as a function of ARTs for broadband noise.

DP suppression appeared to depend on the level of contralateral noise, as shown in Fig. 3. When the level of contralateral noise was low, the DP suppression seemed to remain unchanged for at least 2 minutes. On the contrary, when a relatively high level of contralateral noise was used, the suppression of DP decreased with time (Figs. 2 and 3). Evidence obtained in the present study suggests that a high level of acoustic stimulation may possibly cause adaptation, while a low level of stimulation may not. Actually, a relatively low level of contralateral noise (35 dB sensation level noise) was used in the study of Giraud et al. (1997). On the contrary, in the studies in which the adaptation phenomenon of OC-effects was indicated, electrical stimulation or a relatively high level of acoustic stimulation was used to evoke OC activation. Another factor possibly involved in the adaptive phenomenon observed with high-level acoustic stimuli is the acoustic reflex of the MEMs, which might enhance the adaptive phenomenon. However, in the present study, an adaptive phenomenon was observed at a level much lower than ART. Moreover, middle ear muscles were cut or de-innervated in the animal experiments in which an adaptive phenomenon was observed (Wiederhold and Kiang 1970; Kujawa et al. 1993; Sridhar et al. 1995; Liberman et al. 1996). Therefore, the acoustic reflex would not be essential for the adaptive phenomenon, although it is possibly enhanced by the contraction of MEMs, once the acoustic reflex was triggered in response to the higher level of contralateral noise. Actually, the adaptive phenomenon observed in the present study appeared to be much larger when a level of contralateral noise higher than ART was used (Fig. 3).

The sound-evoked OC effects assayed through the measurement of the OAEs has been widely used as an convenient clinical test to assess the activity of the human OC-efferent system. Usually the degree of the suppression of the OAEs has been used for the indication of the magnitude of the OC-reflex. The present results suggest that the timing of the data collection of OAEs during the addition of contralateral noise is critical for the degree of the suppression of the OAEs, especially when a higher level of contralateral noise is used. Therefore, depending on the protocol of the addition of contralateral noise, the suppression magnitude might be different. For example, in the case in which several series of OAEs are measured under conditions of the addition of contralateral noise, the contralateral suppression would be larger when the contralateral noise is always started just before the every measurement of OAEs. On the contrary, the suppression magnitude might be smaller, if the contralateral noise is applied continuously throughout the whole series of measurements of OAEs. Thus, it seems to be important to know the characteristics of the adaptive effects observed in the present study when the OC-activity was assessed as compared with the measurements of different protocols.

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References

1) Brown, M.C. (1989) Morphology and response properties of single olivocochlear fibers in the guinea pig. *Hear. Res.*, **40**, 93–110.
2) Buno, W. (1978) Auditory nerve activity influenced by contralateral ear sound stimulation. *Exp. Neurol.*, **59**, 62–74.
3) Cody, A.R. & Johnstone, B.M. (1982) Acoustically evoked activity of single efferent neurons in the guinea pig cochlea. *J. Acoust. Soc. Am.*, **72**, 280–282.
4) Collet, L., Kemp, D.T., Veuillet, E., Duclaux, R., Moulin, A. & Morgon, A. (1990)

Effect of contralateral auditory stimuli on active cochlear micromechanical properties in human subjects. *Hear. Res.*, **43**, 251–262.

5) Fex, J. (1962) Auditory activity in centrifugal and centripetal cochlear fibers in cat. *Acta Physiol. Scand.*, **55**, *Suppl.*, **189**, 1–68.

6) Giraud, A.L., Collet, L. & Chery-Croze, S. (1997) Suppression of otoacoustic emission is unchanged after several minutes of contralateral acoustic stimulation. *Hear. Res.*, **109**, 78-82.

7) Guinan, J.J., Warr, W.B. & Norris, B.E. (1983) Differential olivocochlear projections from lateral vs. medial zones of the superior olivary complex. *J. Comp. Neurol.*, **221**, 358–370.

8) Kujawa, S.G., Glattke, T.J., Fallon, M. & Bobbin, R.P. (1993) Contralateral sound suppresses distortion product otoacoustic emissions through cholinergic mechanisms. *Hear. Res.*, **68**, 97-106.

9) Liberman, M.C. & Brown, M.C. (1986) Physiology and anatomy of single olivocochlear neurons in the cat. *Hear. Res.*, **24**, 17–36.

10) Liberman, M.C. (1988) Response properties of cochlear efferent neurons: Monaural vs. binaural stimulation and the effect of noise. *J. Neurophysiol.*, **60**, 1779-1798.

11) Liberman, M.C., Puria, M.C. & Guinan, J.J. (1996) The ipsilaterally evoked olivocochlear reflex causes rapid adaptation of the 2F1-F2 distortion product otoacoustic emission. *J. Acoust. Soc. Am.*, **99**, 3572–3584.

12) Moulin, A., Collet, L. & Duclaux, R. (1993) Contralateral auditory stimulation alters acoustic distortion products in humans. *Hear. Res.*, **65**, 193–210.

13) Sridhar, T.S., Liberman, M.C., Brown, M.C. & Sewell, W.F. (1995) A novel cholinergic "slow effect" of efferent stimulation on cochlear potentials in the Guinea pig. *J. Neurosci.*, **15**, 3667–3678.

14) Veuillet, E., Collet, L. & Duclaux, R. (1991) Effect of contralateral acoustic stimulation on active cochlear micromechanical properties in human subjects: dependence on stimulus variables. *J. Neurophysiol.*, **65**, 724–735.

15) Warren, E.H. & Liberman, M.C. (1989) Effects of contralateral sound on auditory-nerve responses. I. Contributions of cochlear efferents. *Hear. Res.*, **37**, 89–104.

16) Warr, W.B. & Guinan, J.J. (1979) Efferent innervation of the organ of Corti: Two separate systems. *Brain Res.*, **173**, 152–155.

17) Wiederhold, M.L. & Kiang, N.Y.S. (1970) Effects of electrical stimulation of the crossed olivocochlear bundle on single auditory nerve fibers in cat. *J. Acoust. Soc. Am.*, **48**, 950–965.