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Methodological paper

Otoacoustic detection of risk of early hearing loss in ears with normal audiograms: A 3-year follow-up study

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ABSTRACT

Introduction: Distortion product otoacoustic emissions (DPOAEs) are known to represent the contractile amplifier function of cochlear outer hair cells. It is known that low or absent DPOAEs are associated with hearing loss on audiograms. However, low DPOAEs can also be found associated with normal audiograms. It is unknown whether low DPOAEs in normal hearing ears are risk markers for subsequent early hearing loss when subjects are exposed to noise.
Materials and methods: A 3-year follow-up study was carried out on a population of pilots aged 20–40 years ($n = 521$). Data collection consisted of tonal audiograms, DPOAEs measurements with a calculation of an index of abnormality (the IaDPOAE). Of the 521 pilots enrolled, 350 (67%) had follow-up data 3 years later. In pilots with normal audiograms ($n = 219$, all frequencies = 10 dB HL), we observed the occurrence of hearing threshold shifts after 3 years depending on whether the IaDPOAE was initially high (group 1) or low (group 2). We used this index to test the hypothesis that reduced DPOAEs levels are potential ear vulnerability biomarkers in apparent normal hearing ears.
Results: After a 3-year follow-up, the initial IaDPOAE in normal hearing subjects was correlated with final noise-induced hearing threshold shifts at high frequencies ($p < 0.01$). The occurrence of abnormal audiograms was significantly higher in group 1 compared to group 2 ($p = 0.003$). In group 1, 13% of audiograms were found with at least one frequency $\geqslant$25 dB HL compared to 3% of audiograms in group 2. In both groups, impairments occurred at high frequencies and hearing in the 4 kHz frequency range was significantly more impaired in group 1 ($p = 0.035$).
Group 1 was associated with a relative risk of 2.29 (95% CI 1.26–4.16, $p = 0.005$) of sustaining early hearing loss. There was no significant differences between groups for age and noise exposure.
Discussion: In adults with a normal audiogram, ear vulnerability to noise could be elicited by the use of objective DPOAE measurements. A high IaDPOAE that corresponded to reduced DPOAE levels constitutes a risk for early hearing loss. This study emphasised the interest of DPOAE measurements in public health and occupational noise prevention policies. The IaDPOAE calculation may also be interesting for clinicians because no DPOAE index of abnormality is currently available.
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1. Introduction

For many years now occupational physicians and military physicians have been interested in using an objective index that could help them to decide if an individual is more at risk of early hearing loss, especially if exposed to noise.

Studies carried out by Kemp (Kemp et al., 1990), Gorga and colleagues (Dorn et al., 1999; Dorn et al., 2001; Gorga et al., 1997; Gorga et al., 1999; Gorga et al., 2000; Gorga et al., 2002; Gorga et al., 2003; Neely et al., 2003), on the development of research on distortion product otoacoustic emissions (DPOAEs) stimulated the hope of finding such an index, but there are almost no longitudinal studies in normal hearing adults. DPOAEs rely on the contractile properties of the outer hair cells. In response to tonal sound stimuli, these cells can generate retrograde wave sounds, the intensity of which can be captured and recorded by a very sensitive probe microphone in the external auditory canal. DPOAEs are essentially used to study cochlear oxidative stress with regard to deleterious agents in numerous studies on animals because they can provide an objective measurement of outer hair cell selective impairments at various corresponding frequency range of the cochlea (Avan et al., 1990; Lataye et al., 2003; Lukashkin et al., 2002; Mom et al., 1999; van Dijk et al., 2003; Whitehead et al., 1992). In neonates, absence of DPOAEs is a sign of severe deafness (Janssen et al., 2006; Swanepoel de et al., 2006; Tsui et al., 2008;

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Wagner et al., 2008; Xu and Li, 2005). In adults, the presence of hearing loss on audiograms is usually associated with low or absent DPOAEs (Cianfrone et al., 2000; Gorga et al., 1999; Harris, 1990; Johnson et al., 2007; Nagy et al., 2002; Sisto et al., 2007; Stover et al., 1996; Wagner et al., 2005). In some studies, normal hearing subjects have been demonstrated to have reduced DPOAEs (Job and Nottet, 2002; Lutman and Deeks, 1999; Shiomi et al., 1997) compared to others, and the physician did not have an appropriate scientific method of deciding if their DPOAE results could reveal a vulnerability that could lead to a more rapid decrease of hearing capabilities. Some factors had been reported in cross-sectional studies in normal hearing subjects to cause DPOAEs reductions. Age in normal hearing subjects has been shown to reduce DPOAEs (Uchida et al., 2008). Also, reduced levels of DPOAEs were shown by Shiomi (Shiomi et al., 1997) and Job (Job et al., 2007) to be associated with susceptibility to tinnitus. Because of the lack of longitudinal studies, the use of DPOAEs is still limited to the use of deafness detection in neonates and to the use of objective confirmations of hearing damage when audiograms are abnormal in adults.

In this study, we use a longitudinal study to demonstrate that DPOAEs could be useful to elicit a vulnerability at noise exposure. This vulnerability led to a more rapid impairment of hearing.

2. Materials and methods

2.1. Subjects

We chose a population of pilots because noise exposure was intense, regular, continuous and without acute acoustic trauma due to impulsive noise. Regular noise exposure may be calibrated by the number of hours of flight. Acoustic pressure ranges from 90 to 110 dB A (idling speed) and from 110 to 140 dB A (flat-out speed). Protection is provided by headsets.

In all, data from 521 French pilots aged 20–40 years were collected by an ear–nose–throat (ENT) specialist, between October 2003 and October 2004 at the aircrew medical centre, near Paris. Data were collected during pilots' annual medical check-up and far from periods of noise exposure (i.e., 24 h, at least). Written, informed consent was obtained from each subjects.

Between October 2006 and October 2007, pilots audiometric data were recollected with the same device, the same clinician and the same experimental protocol. Data from the two date points were compared.

2.2. Questionnaire

Pilots were interviewed by the ENT specialist with a standardized questionnaire. Age and gender were recorded. For aircraft noise exposure, hours of flight, years of flight, type of aircraft (i.e., fighter, transport and helicopter) flown and type of headsets were recorded.

Risk-factors or symptoms associated with noise that could affect hearing include: history of acute acoustic trauma, noisy leisure exposure, presence of chronic tinnitus, history of otitis media, otitis due to air pressure and head injury.

2.3. Audiological examinations

Prior to tonal audiograms, the pilots underwent an otoscopy to check that there were no obstructions in the ear canal.

2.4. Tonal audiograms

Tonal audiograms were collected in a sound proof simple-walled booth (Elstar, Paris) with an average noise attenuation of 35 dB SPL. Hearing levels (HL) were measured by trained clinician at seven pure tone frequencies (0.250, 0.500, 1, 2, 3, 4 and 8 kHz) in each ear. The sound level was systematically increased and decreased by steps of 5 dB to find the critical value (i.e. the threshold) that separated the audible from the inaudible range, using a clinical audiometer (Interacoustic; model AC40; Assens, Denmark). The audiometer was calibrated according to the standards of the International Organization for Standardization, ISO 389 and checked every year. During the test, if sounds intensity was audible at 10 dB HL lower intensities were not tested.

2.5. DP-grams

Following an ear examination and audiograms, DPOAEs were measured using commercial equipment (Grason–Stadler GSI 60 system). The stimuli consisted of two pures tones ($f1$ and $f2$; $f2/f1 = 1.2$) presented simultaneously, with the lower frequency stimulus at 65 dB SPL and the higher frequency primary tone at 55 dB SPL. Intensity levels in dB of the $2f1–f2$ DPOAEs and corresponding noise floor were registered and displayed as a function of f2. DP-grams at eight points/octave over a four-octave-frequency range, were recorded (a total of 32 measurements). The total duration of measurements per ear was 3 min. During measurements, noise floors were typically -10 ± 5 dB, over the 1- and 8-kHz regions and -20 ± 5 dB over the 2–4 kHz frequency ranges. DPOAE responses were valid when signal/noise ratio was at least $\geqslant 2$ dB.

2.6. The DPOAE index of abnormality, IaDPOAE

We used an index of abnormality to test our hypothesis that reduced DPOAEs in apparent normal hearing subjects might reveal a vulnerability to noise.

2.7. Study providing DPOAE reference curves

We extracted reference curve values from a previous study where the DP-gram protocol and the DPOAE system was the same as in the present study (Job and Nottet, 2002). The study took place in the medical department of the army recruitment centre. Subjects were aged 18–24 years. As a pre-selection criterion, only those having normal bilateral audiograms (i.e., $\leqslant 15$ dB HL on 0.5, 1, 2, 4 and 8 kHz, with a 5-dB step method) were examined and interviewed.

Otoscopies were carried out with an otomicroscope by an otolaryngologist and by other physicians trained by the specialist. Type A tympanograms were required (i.e., values comprised from 0.5 to 1.6 ml for middle ear mobility and ±50 daPa for the pressure peak). Impedance tympanometric measurements were conducted using standard clinical instrumentation, a 226 Hz probe tone (Grason-Stadler GSI 75). In addition, young subjects were administered a short questionnaire about their possible histories of otitis media (i.e., repeated episodes or myringotomy). This information was checked in the subjects' personal health records. Subjects with eardrum abnormalities of any kind, including dull, cicatricial, bulging, retracted or tympanosclerotic eardrum were not in the reference group. Lastly, we checked that they had no particular intense exposure to noise. Finally, DPOAEs data from 69 subjects (119 ears) were considered as a reference population for this particular DPgram protocol. No audiogram frequencies exceeded 10 dB HL in this ear group. In Fig. 1, DPOAEs means and standard deviations (-1 SD and -2 SD) for each DPOAE values could be implement in the software of the GSI system or any open system and could be displayed for each ear tested. Thus, it was possible for the clinician to calculate a statistical index of abnormal DPOAEs (the IaDPOAE) for each ear at the end of the test. Finally The IaDPOAE calculation was standardized using a computer program.

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