CONSUMPTION OF OMEGA-3 FATTY ACIDS AND FISH AND RISK OF AGE-RELATED HEARING LOSS1-3

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ABSTRACT

Background: Identification of modifiable risk factors that could prevent or slow the development of age-related hearing loss (presbycusis) would be valuable. Dietary polyunsaturated fatty acid (PUFA) intake may be related to age-related hearing loss.

Objective: We aimed to determine the association between dietary intakes of omega-3 (n-3) PUFAs and fish and the risk of presbycusis.

Design: The Blue Mountains Hearing Study is a population-based survey of age-related hearing loss (1997–1999 to 2002–2004). We collected dietary data by using a semiquantitative food-frequency questionnaire and calculated PUFA and fish intakes. In 2956 participants (aged ≥50 y), we measured presbycusis, which we defined as the pure-tone average of frequencies 0.5, 1.0, 2.0, and 4.0 kHz >25 decibels of hearing loss.

Results: There was an inverse association between total n-3 PUFA intake and prevalent hearing loss [odds ratio (OR) per SD increase in energy-adjusted n-3 PUFAs: 0.89; 95% CI: 0.81, 0.99]. There was an inverse association between long-chain n-3 PUFAs and incident hearing loss (OR per SD increase in long-chain n-3 PUFAs: 0.76; 95% CI: 0.60, 0.97). Participants who had ≥2 servings of fish/wk compared with participants who had <1 serving of fish/wk had a significantly reduced risk (42%) of developing presbycusis at follow-up (multivariate-adjusted OR: 0.58; 95% CI: 0.35, 0.95). There was an association between consumption of ≥1 to <2 servings/wk of fish and a reduced risk of a progression of hearing loss (OR: 0.53; 95% CI: 0.32, 0.88).

Conclusions: There was an inverse association between higher intakes of long-chain n-3 PUFAs and regular weekly consumption of fish and hearing loss. Dietary intervention with n-3 PUFAs could prevent or delay the development of age-related hearing loss. Am J Clin Nutr 2010;92:416–21.

INTRODUCTION

Age-related hearing loss (HL) (presbycusis) is a common and underrecognized health problem in the older subpopulation (1). In older adults it is second only to arthritis as a handicapping condition (2), which implies a significant burden for sufferers and for those who communicate with them (3). The medical and socioeconomic costs are immense, and given the increase in the world’s population and that the number of older adults is expected to more than double by 2030, this burden is escalating (3). Hence, the identification of risk factors and the development of preventive strategies are essential to reduce the effect and burden of age-related HL on the global aging population.
between dietary intakes of PUFAs and presbycusis, and 2) to determine whether consumption of a diet high in fish protects against the development of HL.

SUBJECTS AND METHODS

Study population

The Blue Mountains Hearing Study (BMHS) is a population-based survey of age-related HL conducted during the years 1997–2004 in participants of the Blue Mountains Eye Study (BMES) cohort (13). During 1992–1994, 3654 participants based survey of age-related HL conducted during the years BMES-1. Surviving baseline participants were invited to attend 5-y follow-up examinations (1997–1999; BMES-2) at which 2334 (75.1% of survivors) and an additional 1174 newly eligible residents (ie, those who had moved into the study area or study age group) were examined. At the 10-y follow-up (2002–2004; BMES-3), 1952 participants (75.6% of survivors) were re-examined. Hearing was measured at BMES-2 and BMES-3 (ie, in BMES-2, 2956 participants aged ≥50 y had audiometric testing done).

Dietary data

Dietary data were collected by using a 145-item self-administered food-frequency questionnaire (FFQ) that was modified for the Australian diet and vernacular from an early Willett FFQ (14) and included reference portion sizes. Participants used a 9-category frequency scale to indicate the usual frequency of consuming individual food items during the past year. The FFQ included details about frequency estimates and details about fatty acid supplements and was used to permit a more detailed analysis of fatty acids.

We extracted separate data on the frequency of consuming fish (any species plus the method of preparation) and oily fish (specifically salmon, tuna, and sardines). The FFQ was validated in 79 participants on 3 occasions during 1 y by using 4-d weighed-food records (15). The FFQ showed moderate to good agreement for ranking individuals according to their fat intakes (r for total fat = 0.68; r for saturated fatty acids = 0.67; r for monounsaturated fatty acids = 0.54; r for PUFA = 0.44) and correctly classified >70% of people within one quintile for all types of fat (15, 16).

Dietary intakes were estimated by using the Australian Food Composition Tables (NUTTAB95) (16) and its fatty acid supplement. Additional fatty acid food–composition data were added from the Royal Melbourne Institute of Technology database (17) (available on FoodWorks, version 3; Xyris Software Pty Ltd, Brisbane, Australia). Long chain n-3 PUFA were calculated from the sum of EPA (20:5n-3), docosapentaenoic acid (DPA; 22:5n-3), and DHA (22:6n-3). Total n-3 PUFA consumption was calculated by adding the intakes of long-chain n-3 PUFA and α-linolenic acid. The total n-6 PUFA consumption was calculated by adding the intakes of linoleic and arachidonic acids.

Audiologic examination

Pure-tone audiometry at both visits was performed by audiologists in sound-treated booths with standard TDH-39 earphones and Madsen OB822 audiometers (Madsen Electronics, Copenhagen, Denmark) that were calibrated regularly to Australian standards. Audiometric thresholds for air-conduction stimuli in both ears were established for frequencies at 250, 500, 1000, 2000, 4000, 6000, and 8000 Hz. We determined hearing impairment as the pure-tone average of audiometric hearing thresholds at 500,1000, 2000, and 4000 Hz (PTA0.5–4KHz) and defined any level of HL as PTA0.5–4KHz >25 decibels (dB) HL in the better of the 2 ears. This defined HL as bilateral.

A person was considered at risk of incident bilateral HL during the 5-y period if the PTA0.5–4KHz in the better ear was ≤25 dB HL at baseline. Incident bilateral HL was defined as a PTA0.5–4KHz >25 dB HL in the better ear at the 5-y follow-up examination in participants without HL at baseline. Participants with HL at baseline were considered at risk of progression of hearing impairment if the PTA0.5–4KHz in the better ear was >25 dB HL. A progression of hearing impairment was defined as a PTA0.5–4KHz at follow-up that was >5 dB HL higher than at baseline.

Statistical analyses

SAS statistical software (version 9.1; SAS Institute, Cary, NC) was used for analyses including t and chi-square tests and logistic regression. The association between dietary intakes of PUFAs, fish, and presbycusis were examined in logistic regression models with adjustment for age and sex and with further adjustment for confounders that were shown to be significantly associated with the prevalence (ie, education, smoking, previous history of diagnosed stroke and diabetes, family history of HL, and exposure to noise at work), and incidence (ie, family history of HL and exposure to noise at work) of HL in the older cohort. Dietary fatty acid intakes were energy-adjusted by using the residual method described by Willett and Stampfer (18). Results of logistic regression analysis are expressed as adjusted odds ratios (ORs) with 95% CIs. We assessed dietary intakes of PUFA both as categorized (quartiles; with the lowest quartile as the reference group) and as continuous (per SD) variables. Fish intake was analyzed by categorizing participants according to the frequency of consumption of standard serving sizes (145 g). The servings for each category were <1, ≥1 but <2, and ≥2/wk. Statistical significance was defined as P < 0.05.

RESULTS

Cross-sectional HL data were obtained from 2956 BMHS participants. This sample comprised 2015 participants from the original BMES-1 study and 941 participants from the extension study. Of the 2956 participants examined in the BMHS, 2535 had complete dietary data, which left 2442 participants (1690 participants from the original BMES-1 study and 941 participants from the extension study). Of these, 55 subjects were included as they reported HL from birth or gave a history of osteosclerosis and/or had audiometric evidence of conductive HL, and a further 24 subjects were excluded as they did not have complete audiologic data, which left 2442 participants (1690 participants from the original BMES-1 and 752 participants from the extension study). In these participants, 782 (32.0%) subjects had any level of HL (>25 dB HL) (or prevalent HL ascertained at the first audiogram) and 1660 (68.0%) subjects had normal hearing. Compared with participants without HL, participants with any HL were older, more likely to be men, not tertiary qualified, and
exposed to workplace noise and have a doctor-diagnosed history of stroke or type 2 diabetes (Table 1).

A significant inverse association between total n–3 PUFAs intake (assessed as a continuous variable) and age-related HL is shown in Table 2; the per SD increase in energy-adjusted n–3 PUFAs intake was associated with a 11% decrease in the prevalence of any HL (>25 dB HL) (multivariate-adjusted OR: 0.89; 95% CI 0.81, 0.99). There were no significant associations observed between dietary intakes of a-linolenic acid, total n–6 PUFAs, and the prevalence of HL (data not shown). Significant associations were also not observed between the dietary intakes of long-chain n–3 PUFAs or fish and the prevalence of HL (Table 2).

There were 1184 survivors out of the 1690 original participants in the BMHS-1 cohort (70.1% participation rate) with complete dietary data who were reexamined at the 5-y follow-up. Incidence analyses involved 798 (67.4%) participants who had normal hearing at the baseline hearing study and participated in the 5-y follow-up study. Of these participants, 141 (17.7%) participants had incident HL and 657 (82.3%) participants had normal hearing function. We analyzed the different components of dietary PUFAs as quartiles and observed that an increasing intake of total n–3 PUFAs was associated with a nonsignificant trend for incident HL (P = 0.07). The associations between dietary intakes of PUFAs (assessed as a continuous variable) at baseline and the risk of developing incident HL at the 5-y follow-up are summarized in Table 3. A significant longitudinal association between the total n–3 PUFAs intake and HL was not observed; however, the per SD increase in energy-adjusted long-chain n–3 PUFAs intake was associated with a 24% decrease in the 5-y incidence of HL (Table 3). Further adjustment for additional dietary factors such as folate and alcohol consumption and other covariates (eg, hypertension and diabetes) did not greatly change the resulting ORs and 95% CIs (data not shown). To confirm a linear increase in risk as presented in Table 3, we used the locally weighted scatter-plot smoothing method to plot the log

### Table 1
Baseline epidemiologic and clinical characteristics of study subjects aged ≥50 y

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No hearing loss (n = 1660; 68.0%)</th>
<th>Any hearing loss (n = 782; 32.0%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men [n (%)]</td>
<td>656 (39.5)</td>
<td>397 (50.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age (y)</td>
<td>63.5 ± 7.8</td>
<td>72.7 ± 8.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No tertiary qualifications [n (%)]</td>
<td>483 (31.0)</td>
<td>312 (42.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Exposure to workplace noise [n (%)]</td>
<td>565 (34.2)</td>
<td>331 (42.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoker [n (%)]</td>
<td>163 (9.8)</td>
<td>63 (8.1)</td>
<td>0.17</td>
</tr>
<tr>
<td>Family history of hearing loss [n (%)]</td>
<td>722 (43.5)</td>
<td>356 (45.5)</td>
<td>0.35</td>
</tr>
<tr>
<td>History of stroke [n (%)]</td>
<td>46 (2.8)</td>
<td>52 (6.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>History of type 2 diabetes [n (%)]</td>
<td>131 (7.9)</td>
<td>98 (12.5)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Fish servings/wk [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>531 (32.0)</td>
<td>254 (32.5)</td>
<td></td>
</tr>
<tr>
<td>≥1 to &lt;2</td>
<td>554 (33.4)</td>
<td>270 (34.5)</td>
<td>0.71</td>
</tr>
<tr>
<td>≥2</td>
<td>575 (34.6)</td>
<td>258 (33.0)</td>
<td></td>
</tr>
<tr>
<td>Total n–3 PUFAs</td>
<td>1.21 ± 0.49</td>
<td>1.17 ± 0.46</td>
<td>0.08</td>
</tr>
<tr>
<td>Long-chain n–3 PUFAs</td>
<td>0.27 ± 0.30</td>
<td>0.25 ± 0.30</td>
<td>0.39</td>
</tr>
</tbody>
</table>

1 BMHS, Blue Mountains Hearing Study; PUFAs, polyunsaturated fatty acids.
2 Mean ± SD (all such values).

### Table 2
Associations between baseline dietary intake of polyunsaturated fatty acids (PUFAs) and consumption of fish and the prevalence of hearing loss (HL)

<table>
<thead>
<tr>
<th>Energy-adjusted fatty acid intake</th>
<th>Values</th>
<th>Age- and sex-adjusted</th>
<th>Multivariate-adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total n–3 PUFAs</td>
<td>1.20 (0.05–4.85)</td>
<td>0.91 (0.82, 1.00)</td>
<td>0.89 (0.81, 0.99)</td>
</tr>
<tr>
<td>Long-chain n–3 PUFAs</td>
<td>0.26 (0.00–4.18)</td>
<td>0.97 (0.88, 1.08)</td>
<td>0.97 (0.88, 1.08)</td>
</tr>
<tr>
<td>Fish servings/wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>254/785</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>≥1 to &lt;2</td>
<td>270/824</td>
<td>0.95 (0.75, 1.21)</td>
<td>0.95 (0.74, 1.23)</td>
</tr>
<tr>
<td>≥2</td>
<td>258/833</td>
<td>0.91 (0.72, 1.16)</td>
<td>0.94 (0.73, 1.21)</td>
</tr>
<tr>
<td>P for trend</td>
<td>0.46</td>
<td>0.65</td>
<td></td>
</tr>
</tbody>
</table>

1 dB, decibels. For total n–3 PUFAs, 1 SD = 0.78, and for long-chain n–3 PUFAs, 1 SD = 0.30.
2 Logistic regression analysis adjusted for age, sex, education, exposure to noise at work, family history of HL, smoking, previous history of diagnosed stroke, and diabetes.
3 Mean; range in parentheses (all such values).
4 Odds ratio per 1 SD; 95% CI in parentheses (all such values).
5 No. of cases/no. at risk (all such values).
OR of HL incidence compared with dietary intake of long-chain n–3 PUFAs (data not shown). The shape of the locally weighted scatter-plot smoothing curve also suggested that there was a linear relation between long-chain n–3 PUFA intake and incident HL.

At the baseline hearing examination, participants who reported having ≥2 servings of fish/wk compared with those who consumed <1 serving of fish/wk had a significantly reduced (42%) risk of developing age-related HL at the 5-y follow-up (Table 4). This relation with HL was not observed in participants who reported consuming ≥1 but <2 servings of fish/wk. In addition, we determined whether the use of fish-oil supplements had a protective effect on the hearing function of older adults. At baseline, 88 participants reported taking fish-oil supplements and were followed at the 5-y hearing examination. These participants were no less likely to develop HL than those who did not take fish-oil supplements (reference group) (multivariate-adjusted OR: 1.28; 95% CI: 0.71, 2.31).

Finally, we examined whether fish consumption was associated with the progression of HL (ie, PTA0.5–4 KHz at follow-up) (Table 4). Of these participants, 182 (47.2%) showed a worsening or progression in HL at follow-up. In this group, participants who had ≥1 but <2 servings of fish/wk at baseline were less likely to experience a worsening in hearing function over the 5 y than participants who had <1 serving of fish/wk (age-/sex-adjusted OR: 0.54; 95% CI 0.33, 0.90).

However, this association was not observed in participants who consumed ≥2 servings of fish/wk. The progression of HL was not associated with dietary intakes of n–3 PUFAs (data not shown).

**DISCUSSION**

To our knowledge, the potential influence of n–3 PUFAs and fish consumption on auditory function has not been investigated. Our cohort study indicated that dietary total n–3 PUFAs was significantly and inversely associated with the prevalence of HL. A higher dietary intake of long-chain n–3 PUFAs was associated with a 24% decreased risk of developing incident HL. This minor inconsistency between the prevalence and incidence findings could be related to statistical power issues. However, in general the direction of the association between n–3 PUFA intake and HL was the same cross-sectionally and longitudinally. We also observed that regular consumption of fish in the diet was negatively associated with the 5-y incidence and progression of HL in older adults. These data suggest that n–3 fatty acids and fish have a role in maintaining healthy auditory function in addition to their roles in the prevention and modulation of certain diseases (eg, ischemic heart disease, stroke, and autoimmune disorders) (12).

To explain our findings, we draw on results from animal models that demonstrated that maintaining adequate blood flow to the cochlea is critical to cochlear function (19). As such, a decrease in blood supply to the cochlea because of some degree

**TABLE 4**

<table>
<thead>
<tr>
<th>Incident HL (≥25 dB HL) (n = 141; 17.7%)</th>
<th>Progression of HL (≥5 dB HL) (n = 182; 47.2%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases/no. at risk</td>
<td>Age- and sex-adjusted</td>
</tr>
<tr>
<td>Fish servings/wk</td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>46/261</td>
</tr>
<tr>
<td>≥1 to &lt;2</td>
<td>61/264</td>
</tr>
<tr>
<td>≥2</td>
<td>34/239</td>
</tr>
<tr>
<td>P for trend</td>
<td>0.03</td>
</tr>
</tbody>
</table>

1 dB, decibels.

2 Logistic regression analysis adjusted for age, sex, exposure to noise at work, and family history of HL.

3 Odds ratio; 95% CI in parentheses (all such values).

4 Mean; range in parentheses (all such values).

5 Odds ratio per 1 SD; 95% CI in parentheses (all such values).

6 Odds ratio; 95% CI in parentheses (all such values).
of cardiovascular disease may cause cochlear degeneration with a possible decrease in cochlear function and lead to HL (19). Given that dietary long-chain n-3 PUFAs and fish have been shown to prevent heart disease through a variety of actions including hypolipidemic properties, triglyceride lowering, and antiinflammatory and antiatherothrombotic properties (12), these properties of fatty acids may also be beneficial in maintaining adequate vascular supply to the cochlear and, hence, in preventing age-related HL.

There is little doubt that long-chain n-3 PUFAs in fish are the key nutrients in fish that are responsible for the health benefits and cardiovascular disease prevention (10–12). Given the importance of inflammation at all stages of coronary artery and systemic atherogenesis (20), it has also been suggested that regular consumption of fish attenuates inflammatory processes by antagonizing proinflammatory cytokines that increase the risk of cardiovascular disease (21). A lowering of blood pressure and improvements in vascular reactivity or endothelial function could also be mechanisms that operate in observational studies of fish and vascular disease (22). These data on fish from previous studies may help explain the significant inverse association between regular fish consumption and the 5-y incidence of age-related HL observed in the older cohort in our study. This is relevant because vascular risk factors such as high blood pressure and serum lipids were shown to be associated with HL in large population-based studies such as the Framingham Heart Study (n = 1662) (8) and the Baltimore Longitudinal Study of Aging (n = 531) (23).

In contrast, although vascular risk factors are believed to affect hearing through a diminished cochlear blood supply (8), the relative contributions of macrovascular disease and microvascular diseases to this process are unclear. Several lines of evidence suggest that microvascular disease that affects the cochlear striae vascularis may lead to HL, particularly low-frequency HL (8, 24). Indeed, using BMES participants, we previously showed a significant association of retinopathy and HL in women (25). This association was strongest for low-frequency HL. Given that cochlear microvascular disease may contribute to age-related HL and n-3 PUFA supplements may be of benefit in preventing diabetic retinopathy (an example of a microvascular disease) (26), we hypothesize that dietary intakes of long-chain n-3 PUFAs and fish may also have direct beneficial effects on hearing function by preserving the cochlear microcirculatory flow or by other mechanisms not yet defined (25).

Older persons with existing hearing impairment have a higher likelihood of experiencing a further decline in hearing acuity (27). This poor prognosis emphasizes the need for well-designed intervention strategies. Our results may have important public health implications, given that regular consumption (≥1 but <2 servings/wk) of fish in the diet was shown to slow the progression of an existing HL and, thus, could provide a rare opportunity to preserve residual hearing function. However, it needs to be highlighted that fish consumption >2 servings/wk did not protect against the progression of HL. This could indicate a threshold effect at 1–2 servings of fish/wk, with no increased protection at increased amounts of intake. Alternatively, our findings may be due to small numbers or chance, thus replication of these findings in other studies is important.

Dietary supplementation with fish oil n-3 fatty acids for ≥1 y was shown to significantly reduce the risk of cardiovascular deaths, sudden cardiac death, global mortality, and nonfatal cardiovascular events (28). We had relatively small numbers of participants who took fish-oil supplements at baseline (n = 88); as such, we did not have adequate statistical power to determine the association with HL. Second, we do not have data on the exact dosage of the supplementation, which makes it difficult to interpret the data.

Our study was not able to establish a significant association between dietary intake of α-linolenic acid (18:3n-3) and the incidence of HL. This is not surprising because α-linolenic acid is a plant n-3 fatty acid that is poorly converted (<5%) to EPA and DHA (29) and, therefore, is unlikely to have the same effects on vascular function in the cochlear as long-chain n-3 fatty acids.

While the population of adults with age-related HL continues to grow, identification and development of potential protective or therapeutic treatments becomes more and more potentially clinically significant (2). Our findings suggest a possible strategy to diminish the public burden of age-related HL by encouraging changes in the nutritional status of older adults. Ideally, the diet best designed to produce the optimal action to prevent HL would be similar to what has also been proposed for cardiovascular disease, ie, a diet low in saturated fatty acids and high in long-chain n-3 PUFAs from fish and fish oils (12).

Key strengths of our study include its representative population-based sample with relatively high participation, which minimized selection bias. Further, we used standardized, audiometric testing to measure hearing sensitivity. In addition, study participants were unaware of the study question, and our dietary data were collected before detection of the 5-y incidence of HL, which reduced the indication bias from behavioral changes after the HL was diagnosed. However, there are some study limitations to consider. First, our study was a longitudinal study with only 2 repeated observations, which resulted in a potential bias because of learning effects that could occur during audiometric testing. Second, dietary assessment by FFQ in which respondents have to estimate typical intake frequencies of food items and their portion sizes can potentially introduce measurement error and bias. We cannot rule this possibility out, but, overall, the validity of fatty acid categories compared with weighted food records was moderately good (15, 16). Third, findings from our study should be interpreted with caution as higher consumption of fish and n-3 fatty acid may be a surrogate marker for other underlying healthy lifestyle risk factors that could also protect against HL (eg, social and dietary factors). However, we investigated several potential confounders including cardiovascular risk factors (eg, diabetes and high blood pressure), socioeconomic status, and other dietary constituents (eg, folate, vitamin B-12, fruit, and vegetable intakes). These covariates were not significantly associated with the incidence of HL and, therefore, were excluded from the final most parsimonious model.

In conclusion, with the aging population in most westernized countries, it is expected that an increasing number of older adults will experience HL in their later years. Our findings suggest that a relatively simple prevention strategy of increasing the consumption of fish and intake of n-3 PUFAs in the diet could be beneficial to preserve cochlear function and reduce the HL associated with increasing age. However, to fully determine the effects of n-3 dietary fats on hearing health, there is a need for
high-quality randomized controlled trials of long duration. Future large prospective studies that explore the links between dietary fatty acids and hearing health may also contribute to the development of public health recommendations and strategies that concern nutrients and foods that were shown to be protective for a healthy auditory system in data from multiple studies.

The authors’ responsibilities were as follows—BG and PM: study concept and design; PM: acquisition of data; BG, VMF, ER, and PM: analysis and interpretation of data; BG: drafting of the manuscript; and BG, VMF, ER, CMM, and PM: critical revision of the manuscript. None of the authors declared a conflict of interest.

REFERENCES