

Audiometric hearing status of individuals with and without multiple sclerosis

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Abstract—The purpose of the present investigation was to determine whether differences exist in audiometric hearing status between individuals with and without multiple sclerosis (MS) and between individuals with relapsing-remitting MS (RRMS) and individuals with secondary progressive MS (SPMS). Forty-seven subjects with MS (26 with RRMS and 21 with SPMS) and forty-nine control subjects without MS completed both a comprehensive case-history questionnaire and a conventional hearing evaluation. Statistical analyses, accounting for the potential confounding factors of age, sex, noise exposure, and use of ototoxic medications, revealed significant differences in hearing thresholds between subjects with and without MS at select audiometric test frequencies ($p < 0.05$). At these audiometric test frequencies, the subjects with MS had poorer hearing thresholds. Additional analyses revealed significant differences in hearing sensitivity at select audiometric frequencies between the subjects with RRMS and the subjects with SPMS, such that those with SPMS had poorer hearing thresholds. These findings have significant clinical implications for practitioners working with patients with MS.

Key words: audiometric hearing status, auditory function, hearing, hearing loss, multiple sclerosis, pure tone thresholds, relapsing-remitting multiple sclerosis, secondary progressive multiple sclerosis, speech reception threshold, word recognition.

INTRODUCTION

The prevalence and nature of audiometric hearing loss associated with multiple sclerosis (MS) are not completely understood. The estimates regarding the prevalence of pure tone hearing loss in this patient population vary greatly. Noffsinger et al., after reviewing multiple studies, suggested that the prevalence ranges anywhere from 1 to 86 percent [1]. Most articles, though, reported that the prevalence was about 50 percent. Typically, when

Abbreviations: ANOVA = analysis of variance, CID = Central Institute for the Deaf, EDSS = Expanded Disability Status Scale, HL = hearing level, MS = multiple sclerosis, RR&D = Rehabilitation Research and Development, RRMS = relapsing-remitting MS, SPMS = secondary progressive MS, SRT = speech reception threshold, VA = Department of Veterans Affairs, VAMC = VA medical center, WRS = word recognition score.

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a loss in hearing did occur, the loss was considered mild (i.e., ≤ 40 dB hearing level [HL]) [2]. Noffsinger et al., in a seminal investigation of auditory function in patients with MS, reported that only 25 out of 122 ears (21%) in their study exceeded a mild degree of hearing loss at one or more audiometric test frequencies [1].

It is important to consider the audiometric hearing status of the population with MS in relation to the general population. The prevalence of pure tone audiometric hearing loss in the general population varies depending on the criteria used to define hearing loss and on the age of the population sampled. When using a criteria of ≥ 25 dB HL for the average of the hearing thresholds obtained at the audiometric frequencies of 500, 1,000, 2,000, and 4,000 Hz (i.e., the frequencies most important for understanding speech) in one ear and looking at the population aged 15 to 20 years and older, estimates regarding the prevalence of hearing loss range from 16.1 to 27.2 percent [3–5]. When considering a hearing loss being any one audiometric test frequency that is ≥ 25 dB HL and when evaluating the older adult population, prevalence rates are notably higher [6–8].

Comparisons between studies evaluating only individuals with MS and studies evaluating only the general population suggest that hearing sensitivity may differ between these two samples. Only three studies have directly compared the audiometric hearing status of individuals with and without MS [9–11]. These three studies reported significant differences in pure tone hearing sensitivity between these two study populations, such that Cohen and Rudge reported poorer low frequency hearing thresholds for the individuals with MS in comparison with the control group without MS [9], Dayal and Swisher reported poorer hearing thresholds in the right ear only for females with MS versus females without MS [10], and Zeigelboim et al. reported better extended high frequency (i.e., frequencies above 8,000 Hz) hearing for females with MS versus females without MS [11]. While these three studies suggest that hearing sensitivity may differ between individuals with and without MS, the findings across the three investigations were not consistent. Additionally, these three studies had several limitations that we must consider. First, none of these studies controlled for other contributing factors for hearing loss differing between individuals with and without MS, such as noise exposure and use of ototoxic medications. Second, Dayal and Swisher failed to report at what audiometric test frequencies significant differences between study

populations occurred, which is important information for clinicians to consider when it comes to the diagnosis and remediation of hearing loss [10]. Third, Zeigelboim et al. only evaluated females and extended high frequencies [11]. These results may be different for males and for standard audiometric test frequencies (i.e., where the predominant speech information is located). Fourth, none of these studies adequately described the characteristics of the study sample with MS. In particular, they provided no information regarding the type of MS. Finally, none of these studies assessed speech recognition. When standard testing of speech recognition has been assessed in other investigations of patients with MS, results have been mixed such that two articles reported that their subjects with MS had good word recognition scores (WRSs), whereas another reported some difficulties with word recognition [1,12–13]. Specifically, Noffsinger et al. reported that only 7 percent of the ears tested had WRSs less than 90 percent [1], Rappaport et al. reported that their poorest WRS was 92 percent [12], and Levine et al. reported a significant difference between WRS for their subjects at the standard test level versus a louder testing level such that the standard level was poorer [13].

The purpose of the present investigation was to examine audiometric hearing status, while controlling for the potential confounding factors of age, sex, noise exposure, and use of ototoxic medications, in a large group of individuals with relapsing-remitting MS (RRMS) and secondary progressive MS (SPMS), and a control group of individuals without MS to answer the following questions: (1) Does audiometric hearing status differ between individuals with and without MS? and (2) Does audiometric hearing status differ between individuals with RRMS and individuals with SPMS? To date, no study has compared the audiometric hearing status of individuals with RRMS and individuals with SPMS. We hypothesized that differences would exist in hearing between subjects with and without MS, as well as between subjects with RRMS and subjects with SPMS.

METHODS

Subjects

We recruited subjects with and without MS from the Portland Department of Veterans Affairs Medical Center (VAMC), the Oregon Health & Science University, and the surrounding local community to participate in this

investigation. Control subjects without MS were also recruited from a database of subjects who had participated in other studies at the National Center for Rehabilitative Auditory Research and had indicated an interest in participating in other hearing-related studies. All subjects met the following inclusion criteria:

1. Aged 21 to 65 years.
2. Absence of current major disease or disorder (besides MS).
3. Absence of dementia or other neurological conditions.
4. Fluency in spoken English.
5. Willingness and ability to consent to participation in this investigation as indicated by their signature on the Portland VAMC Institutional Review Board-approved consent form.

Subjects with MS also met the following additional inclusion criteria:

1. Clinical or laboratory diagnosis of “definite” MS [14].
2. Diagnosis of RRMS or SPMS.
3. Kurtzke Expanded Disability Status Scale (EDSS) score of 0.0 to 7.0, inclusive [15].
4. No history of clinical relapse or change in EDSS score for 3 months prior to entering the study.
5. Recent brain magnetic resonance imaging scan showing at least three white-matter lesions consistent with MS on T2-weighted images.

A neurologist, neurology resident, or nurse practitioner, all of whom were trained in evaluating individuals with MS, confirmed the diagnosis of MS and determined the EDSS score. The research audiologist, with consultation from the rest of the research team, evaluated all other inclusion/exclusion criteria by a review of the medical record, a comprehensive case-history questionnaire, and an informal interview with the subject.

Case-History Questionnaire

All subjects completed a comprehensive case-history questionnaire. This questionnaire asked the subjects a number of questions regarding their hearing and health status, including their history of noise exposure and current use of medications.

Audiometric Hearing Status

All subjects completed a comprehensive audiometric evaluation. This evaluation included the attainment of pure tone air-conduction and bone-conduction thresholds, speech reception thresholds (SRT), and WRSs in

each ear. We obtained pure tone air-conduction thresholds at 250, 500, 750, 1,000, 1,500, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz bilaterally and bone-conduction thresholds at 500, 1,000, 2,000, and 4,000 Hz. We conducted this testing using standard procedures recommended by the American Speech-Language-Hearing Association [16]. We tested the SRT in each ear by using an adaptive procedure and the Central Institute for the Deaf (CID) W-1 spondee word list [17]. We obtained WRSs by using a presentation level of 25 dB above the SRT (dB HL according to American National Standard Institute standards [18]) for the test ear and recorded CID W-22 word lists [17]. We conducted all audiometric testing in a double-walled sound-treated chamber that was adjoined to a single-walled control room and using an audiometer (model 320, Virtual Corporation; Portland, Oregon). We used insert earphones (model ER-3A, Etymotic Research, Inc; Elk Grove Village, Illinois) to test the pure tone air-conduction thresholds, the SRT, and the WRS in each ear.

Statistical Analyses

We fit a general linear model to the observed audiometric test results. This model generalizes the repeated-measures analysis of variance (ANOVA) commonly used in audiological research to include continuous covariates and more general response covariance structures [19]. The model included a 3-level MS type factor (RRMS, SPMS, and control), 2-level noise exposure factor (yes and no) and 2-level use of ototoxic medication factor (yes and no). The model also included a 2-level sex factor (male and female) and age as a continuous covariate. We fit separate models to the pure tone thresholds, SRT, and WRS results. The pure tone threshold model included a 10-level stimulus frequency factor (250, 500, 750, 1,000, 1,500, 2,000, 3,000, 4,000, 6,000, and 8,000 Hz) and an MS type \times audiometric test frequency interaction to test for differences in mean pure tone air-conduction thresholds at different test frequencies. The model of mean SRT and mean WRS did not include a frequency factor, since we only used one stimulus (speech) to elicit each of these outcomes. Each of the fitted models provided estimates of the effect of MS type on mean outcomes after adjusting for age, sex, noise exposure, and use of ototoxic medications.

We computed separate Fisher exact tests to evaluate differences between subjects with and without MS in terms of the number of ears affected in each subject and

the type of hearing loss (i.e., sensorineural vs conductive vs mixed) present in each ear. We computed additional Fisher exact tests to compare these same factors between the subjects with RRMS and the subjects with SPMS.

RESULTS

Subjects

Forty-seven subjects with MS, of whom 26 had RRMS and 21 had SPMS, and 49 control subjects participated in this investigation. **Table 1** summarizes subject characteristics. A one-way ANOVA, Fisher exact tests, and a Kruskal-Wallis test revealed no significant differences ($p \geq 0.05$) between the three subject groups in terms of age, sex, exposure to noise, or education level. We did, however, note a significant difference ($p = 0.01$) between groups in use of ototoxic medications, with the subjects with MS reporting using more medications that have the potential to be ototoxic.

Audiometric Hearing Status

Figure 1 shows the mean pure tone air-conduction thresholds obtained at each audiometric test frequency for each subject group. This figure shows clear evidence for differences between the subjects with SPMS and the control subjects. The former have considerably higher thresholds across all frequencies. The difference between the subjects with RRMS and the control subjects is not as apparent in the middle frequencies, though the highest and lowest frequencies show differences between these groups. The subjects with RRMS and the subjects with SPMS have relatively similar thresholds at the lower audiometric test frequencies. Large differences between MS types (RRMS and SPMS) are apparent at the higher audiometric test frequencies, with the subjects with SPMS having overall worse hearing than the subjects with RRMS.

Results of the general linear model fit to the pure tone threshold measurements indicated significant effects of frequency ($F_{2,312} = 10.8$; $p < 0.001$) and age ($F_{1,82.7} = 22.6$; $p < 0.001$), but no significant effects of sex

Table 1.
Subject characteristics.

Characteristic	Subject Group			All Subjects
	RRMS	SPMS	Control	
No. of Subjects	26	21	49	96
Age (years)				
Mean	50.5	52.7	51.3	51.4
Minimum	36	35	22	22
Maximum	65	63	64	65
Sex, <i>n</i> (%)				
Male	11 (42.3)	15 (71.4)	24 (49.0)	50 (52.1)
Female	15 (57.7)	6 (28.6)	25 (51.0)	46 (47.9)
Ototoxic Medications, <i>n</i> (%)				
Yes	22 (84.6)	15 (71.4)	25 (51.0)	62 (64.6)
No	4 (15.4)	6 (28.6)	24 (49.0)	34 (35.4)
Noise Exposure, <i>n</i> (%)				
Yes	22 (84.6)	18 (85.7)	44 (89.8)	84 (87.5)
No	4 (15.4)	3 (14.3)	5 (10.2)	12 (12.5)
Years Since Disease Onset				
Mean	12.6	23.2	—	17.3
Minimum	2	8	—	2
Maximum	43	50	—	50
EDSS Score				
Mean	3.1	5.4	—	4.1
Minimum	1	3	—	1
Maximum	6	7	—	7

EDSS = Expanded Disability Status Scale, MS = multiple sclerosis, RRMS = relapsing-remitting MS, SPMS = secondary progressive MS.

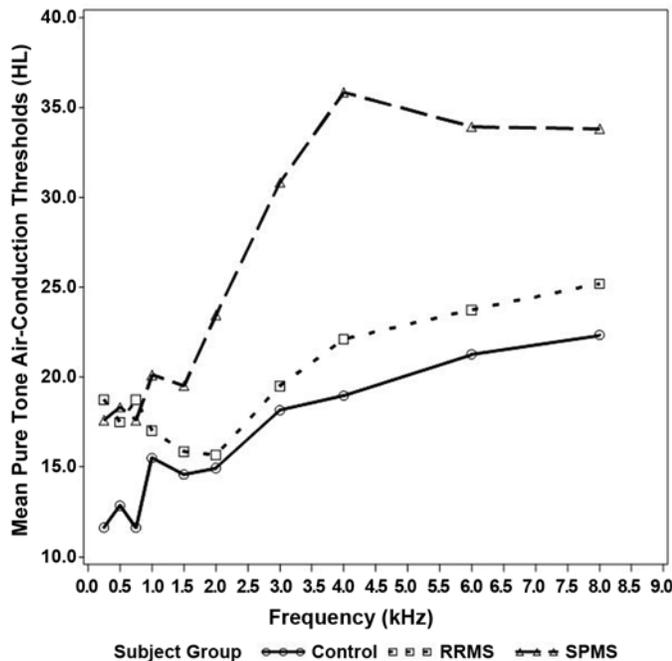


Figure 1.

Pure tone air-conduction thresholds obtained at each audiometric test frequency for each subject group. HL = hearing level, RRMS = relapsing-remitting multiple sclerosis, SPMS = secondary progressive multiple sclerosis.

($F_{1,85.1} = 1.2$; $p = 0.28$), use of ototoxic medications ($F_{1,81.1} = 0.02$; $p = 0.90$), or noise exposure ($F_{1,85.5} = 0.31$; $p = 0.58$). The test of overall differences in pure tone thresholds between subjects with MS and control subjects, after accounting for all of these potential effects, was statistically significant ($F_{10,414} = 3.18$; $p < 0.001$).

Figure 2 shows model-based estimates of mean pure tone air-conduction thresholds and 95 percent confidence intervals among subjects with MS minus the thresholds among control subjects. Positive values indicate higher thresholds (worse hearing) among subjects with MS compared with control subjects. Confidence intervals that do not span 0, indicated by the dashed reference line, are frequencies showing statistically significant differences ($p < 0.05$) between subjects with MS and control subjects. Results are consistent with the unadjusted averages shown in **Figure 1**. Subjects with MS have significantly higher thresholds in the lowest audiometric test frequencies (250, 500, and 750 Hz) and the highest audiometric test frequencies (3,000, 4,000, 6,000, and 8,000 Hz). Within these frequencies, the subjects with MS have

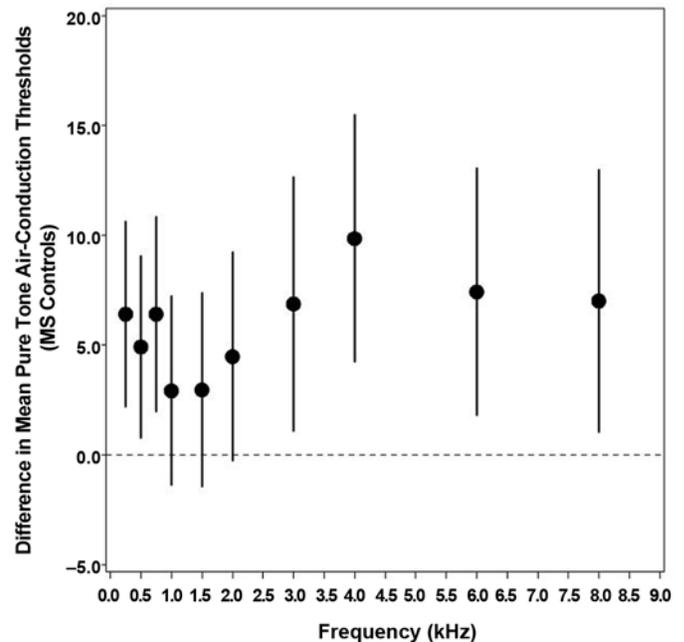


Figure 2.

Model-based estimates for difference in mean pure tone air-conduction thresholds and 95 percent confidence intervals* between subjects with multiple sclerosis (MS) and control subjects without MS. *Confidence intervals that do not span 0, indicated by the dashed reference line, are frequencies showing statistically significant differences ($p < 0.05$).

about 5 to 10 dB higher thresholds than the control subjects.

The test of overall differences in pure tone thresholds between the subjects with RRMS and subjects with SPMS was also statistically significant ($F_{10,272} = 2.13$; $p = 0.02$). **Figure 3** shows estimates of the mean pure tone air-conduction thresholds among subjects with RRMS and subjects with SPMS. Positive estimates in **Figure 3** indicate audiometric test frequencies at which the subjects with SPMS have worse hearing than the subjects with RRMS. The pattern in **Figure 3** indicates better hearing among subjects with SPMS up to 1,500 Hz, followed by worse hearing at the higher test frequencies. Statistically significant ($p < 0.05$) results are achieved at 3,000 and 4,000 Hz. Other audiometric test frequencies showed no statistically significant differences between groups of subjects with MS, though marginally significant results are achieved at 6,000 Hz ($p = 0.06$).

Table 2 presents the mean SRT and WRS for each subject group. These results suggest that the subjects

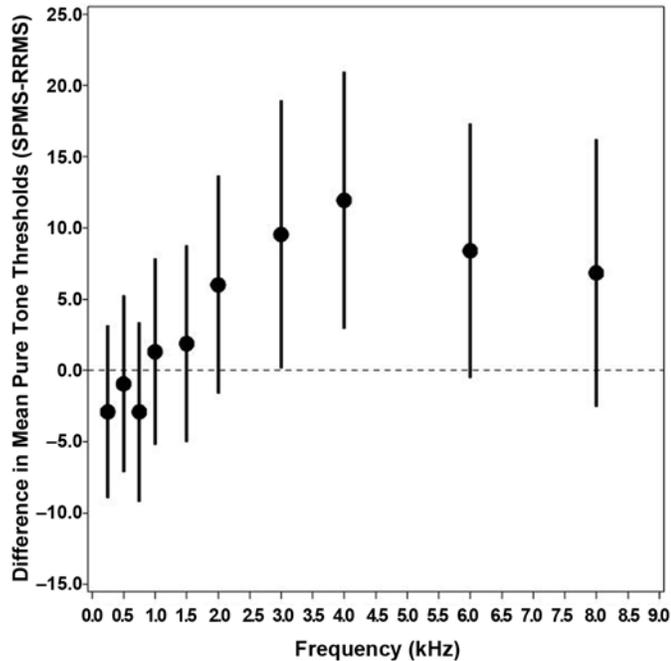


Figure 3.

Model-based estimates of difference in mean pure tone air-conduction thresholds between subjects with relapsing-remitted multiple sclerosis (RRMS) and subjects with secondary progressive multiple sclerosis (SPMS).

with MS have poorer SRT results than do control subjects. Results of the general linear model fit to the SRT measurements indicated significant effect of age ($F_{1,89} = 23.4$; $p < 0.001$) but no significant effects of sex ($F_{1,89} = 0.79$; $p = 0.38$), use of ototoxic medications ($F_{1,89} = 0.13$; $p = 0.72$), or noise exposure ($F_{1,89} = 0.03$; $p = 0.86$). We noted a statistically significant difference in

mean SRT, even after accounting for all these effects, comparing subjects with MS and control subjects ($F_{1,89} = 6.66$; $p = 0.01$). Subjects with MS had on average 4.6 dB higher SRT compared with control subjects (95% confidence interval = 1.1–8.2 dB HL). No statistically significant difference existed in SRT between the subjects with RRMS and the subjects with SPMS ($F_{1,89} = 1.31$; $p = 0.26$). The average difference between these two groups was 2.9 dB HL (95% confidence interval = -2.1 to 7.9 dB HL).

According to **Table 2**, WRSs, on the other hand, were roughly the same across the three subject groups. Results of the general linear model fit to the WRS measurements indicated no significant effects of age ($F_{1,89} = 2.01$; $p = 0.14$), sex ($F_{1,89} = 0.41$; $p = 0.23$), use of ototoxic medications ($F_{1,89} = 0.02$; $p = 0.88$), or noise exposure ($F_{1,89} = 0.80$; $p = 0.37$). Analyses also showed no statistically significant differences between the subjects with MS and control subjects ($F_{1,89} = 2.63$; $p = 0.11$) nor between the subjects with RRMS and subjects with SPMS ($F_{1,89} = 1.64$; $p = 0.20$).

Table 3 summarizes the number of ears affected for each subject and the type of hearing loss present in each ear for each subject group (i.e., subjects with RRMS, subjects with SPMS, and control subjects). A review of this table suggests that few differences exist between the subjects with MS and control subjects. Separate Fisher exact tests revealed no significant difference between the two groups in terms of the number of ears affected ($p = 0.07$) or the type of hearing loss ($p = 0.31$). Additional Fisher exact tests revealed no significant difference between the two groups with MS (RRMS vs SPMS) in the number of ears affected ($p = 0.38$) or the type of hearing loss ($p = 0.20$).

Table 2.

Speech reception threshold (SRT) and word recognition score (WRS) results for each subject group.

Result	Subject Group		
	RRMS	SPMS	Control
SRT (dB HL)			
Mean	19.1	23.8	16.5
Minimum	10.0	10.0	1.7
Maximum	70.0	75.0	35.0
SE	0.6	1.0	1.3
WRS (%)			
Mean	93.7	90.6	94.8
Minimum	38.0	56.0	72.0
Maximum	100.0	100.0	100.0
SE	0.5	1.4	1.4

HL = hearing level, RRMS = relapsing-remitting multiple sclerosis, SE = standard error, SPMS = secondary progressive multiple sclerosis.

Table 3.

Summary of number of ears affected for each subject and hearing loss type for each ear by subject group.

Hearing Loss	Subject Group			
	RRMS	SPMS	Total with MS	Control
No. of Ears Affected, <i>n</i> (%)				
0	13 (50)	6 (29)	19 (40)	28 (57)
1 (unilateral)	6 (23)	7 (33)	13 (28)	5 (10)
2 (bilateral)	7 (27)	8 (38)	15 (32)	16 (33)
Type, <i>n</i> (%)				
None	32 (62)	19 (45)	51 (54)	59 (60)
Conductive	0 (0)	0 (0)	0 (0)	1 (1)
Sensorineural (or likely sensorineural)	19 (37)	20 (48)	39 (42)	37 (38)
Mixed	1 (1)	3 (7)	4 (4)	1 (1)

MS = multiple sclerosis, RRMS = relapsing-remitting MS, SPMS = secondary progressive MS.

DISCUSSION

This study confirmed our hypothesis that differences exist in hearing between subjects with and without MS. Differences in pure tone audiometric hearing thresholds averaged between 5 and 10 dB and the average difference between groups for the SRT, which is an audiometric measure that is highly correlated with pure tone test results, was 4.6 dB. For each of those audiometric test measures, the subjects with MS performed more poorly than the control subjects. While this difference between subjects is not large, there are two likely reasons for this result. First, we completed this study as part of a larger investigation in which the original intention was to find matched-control subjects for the subjects with MS based on sex, age, and audiometric configuration. Despite this intention, differences between groups remained. Differences might have been larger had matching not been part of the original study design. Second, this small difference is consistent with prior investigations [9–10]. Dayal and Swisher reported differences on the order of 10 to 15 dB in the right ear between subjects with and without MS for the female study participants (no frequency information was provided) [10], and Cohen and Rudge reported differences of approximately 4 dB in the right ear between subjects with and without MS at the following frequencies: 500 Hz, 500 Hz in the left ear, and 1,000 Hz in the left ear [9]. In both of these studies, the subjects with MS had poorer hearing thresholds [9–10].

This study also confirmed our hypothesis that hearing sensitivity differs between subjects with RRMS and subjects with SPMS. In the present investigation, the subjects with SPMS had significantly poorer pure tone hear-

ing thresholds at 3,000 and 4,000 Hz than the subjects with RRMS. This result is reasonable given the disease process of MS, as individuals with SPMS initially start out having RRMS. It is only as the disease progresses and changes, from an inflammatory-disease process to one that is characterized more by nerve damage or loss, that the individual is reclassified as having SPMS. Since SPMS is a more debilitating disease course than RRMS, it is logical that pure tone hearing sensitivity would be worse in these subjects. No study to date has examined the effects of MS factors, such as MS disease course, on audiometric hearing status. This difference between MS disease types is interesting and a future article is planned that will examine the effects of variety of MS factors, such as EDSS score, number of relapses, and years since disease onset, as well as MS disease course, on pure tone hearing thresholds at each audiometric test frequency.

Contrary to our hypothesis, no significant differences existed between the subjects with MS and the control subjects, nor between the subjects with RRMS and the subjects with SPMS in terms of WRSs. This is because all three subject groups generally did well on this audiometric test measure. This result is not unexpected because many individuals do well on word recognition tasks performed in quiet. Many professionals in the audiology community have suggested that audiologists should move away from the standard test protocol of testing word recognition in quiet and instead test speech recognition in noise. Problems recognizing speech in the presence of noise is the primary handicap of individuals with sensorineural hearing loss, and this type of testing better discriminates between individuals with hearing loss and those with normal hearing (e.g., Plomp and

Duquesnoy [20], Pekkarinen et al. [21], Beattie et al. [22]). Further, a prior study we conducted and presented in this journal reported that this type of testing paradigm did show differences in performance between individuals with and without MS [23]. Some of the same study subjects were evaluated in both manuscripts.

The present investigation further showed that no significant differences existed between the subjects with MS and the control subjects in terms of the number of ears affected or in terms of the type of hearing loss. Most subjects had normal hearing in both ears, followed by a bilateral hearing loss, and then a unilateral hearing loss. This is consistent with Noffsinger et al. [1], as well as research on the general population [3,6–7], which suggests that most hearing losses are bilateral rather than unilateral. It does, however, contradict case-study reports of individuals with MS presenting sudden Sensorineural hearing loss [24–36]. In those reports, the loss was typically unilateral but returned to normal or previous HLs after a given period of time (sometime after the exacerbation in symptoms). Note that we conducted the present investigation when the subjects' symptoms were stable and had been stable for at least 3 months prior to participation in the study. The most common type of hearing loss (after normal hearing) for the group of subjects with MS and for the group of control subjects without MS was sensorineural hearing loss. This is the most common type of hearing loss typically reported in articles of both individuals with and without MS. Additionally, this type of hearing loss is consistent with the disease process of MS and prior investigations have suggested that sensorineural hearing loss in individuals with MS is due to swelling and/or scarring in the lower portions of the central auditory pathways or in the cochlear nerve [24,26,28,30,33–34,37–38]

CONCLUSIONS

This study suggests that differences may exist in hearing between individuals with MS and individuals without MS, such that individuals with MS may be more likely to have hearing loss, at least in the low (250–750 Hz) and high (3,000–8,000 Hz) audiometric test frequencies. Additionally, this is the first study to demonstrate that individuals with SPMS may have more hearing loss than do individuals with RRMS (at 3,000 and 4,000 Hz). These differences in hearing based on MS disease status

is an important consideration for practitioners working with this patient population.

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Acquisition of data: D. J. Lilly, M. M. Hutter, D. N. Bourdette, M. A. Fitzpatrick.

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Drafting of manuscript: M. S. Lewis.

Critical revision of manuscript for important intellectual content: D. J. Lilly, D. N. Bourdette.

Statistical analysis: G. P. McMillan, M. S. Lewis.

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Study supervision: D. J. Lilly, M. M. Hutter, S. A. Fausti.

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Institutional Review: The Portland VAMC Institutional Review Board approved this study, and we obtained signed consent forms from all participants.

Participant Follow-Up: The authors plan to inform participants of the publication of this study.

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