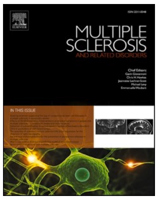
Multiple Sclerosis and Related Disorders 47 (2021) 102608

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard



Original article

Speech discrimination impairments as a marker of disease severity in multiple sclerosis

Pippa Iva [a,*], Joanne Fielding [b], Meaghan Clough [b], Owen White [b], Gustavo Noffs [c], Branislava Godic [a], Russell Martin [a], Anneke van der Walt [b], Ramesh Rajan [a]

[a] *Neuroscience Discovery Program, Biomedicine Discovery Institute, Department of Physiology, Monash University, Melbourne, Australia*
[b] *Department of Neurosciences, Central Clinical School, Alfred Hospital, Monash University, Melbourne, Australia*
[c] *Centre for Neuroscience of Speech, University of Melbourne, Melbourne, Australia*

ARTICLE INFO

Keywords:
Multiple sclerosis
Speech discrimination in noise
Daily communication
Auditory processing deficits
Disease severity

ABSTRACT

Background: Multiple Sclerosis (MS) pathology is likely to disrupt central auditory pathways, thereby affecting an individual's ability to discriminate speech from noise. Despite the importance of speech discrimination in daily communication, it's characterization in the context of MS remains limited. This cross-sectional study evaluated speech discrimination in MS under "real world" conditions where sentences were presented in ecologically valid multi-talker speech or broadband noise at several signal-to-noise ratios (SNRs).

Methods: Pre-recorded Bamford-Kowal-Bench sentences were presented at five signal-to-noise ratios (SNR) in one of two background noises: speech-weighted noise and eight-talker babble. All auditory stimuli were presented via headphones to control ($n = 38$) and MS listeners with mild ($n = 20$), moderate ($n = 16$) and advanced ($n = 10$) disability. Disability was quantified by the Kurtzke Expanded Disability Status Scale (EDSS) and scored by a neurologist. All participants passed a routine audiometric examination.

Results: Despite normal hearing, MS psychometric discrimination curves which model the relationship between signal-to-noise ratio (SNR) and sentence discrimination accuracy in speech-weighted noise and babble did not change in slope (sentences/dB) but shifted to higher SNRs (dB) compared to controls. The magnitude of the shift in the curve systematically increased with greater disability. Furthermore, mixed-effects models identified EDSS score as the most significant predictor of speech discrimination in noise (odds ratio = 0.81; $p < 0.001$). Neither age, sex, disease phenotype or disease duration were significantly associated with speech discrimination performance in noise. Only MS listeners with advanced disability self-reported audio-attentional difficulty in a questionnaire designed to reflect auditory processing behaviours in daily life.

Conclusion: Speech discrimination performance worsened systematically with greater disability, independent of age, sex, education, disease duration or disease phenotype. These results identify novel auditory processing deficits in MS and highlight that speech discrimination tasks may provide a viable non-invasive and sensitive means for disease monitoring in MS.

1. Introduction

Multiple Sclerosis (MS) has a heterogeneous clinical course and symptomology which includes disruption of motor, cognitive and sensory systems (Fielding and Clough, 2019). Despite the importance of hearing to communication, characterization of auditory deficits in people with MS (pwMS) remains inconsistent and elusive (Furst and Levine, 2015). Auditory processing networks are highly integrated and widespread (Musiek, 1986) and MS-related neurogenic injury at any anatomical level (s) will impact on the person's ability to navigate the world, build relationships, and socialize, all directly impacting quality of life (Amaral et al., 2019).

Abbreviations: MS, multiple sclerosis; SNR, signal-to-noise ratio; EDSS, Expanded Disability Status Scale; dB, decibel; pwMS, people with Multiple Sclerosis; AEP, auditory evoked potential; SiN, speech in noise; HREC, Human Research Ethics Committee; Hz, hertz; dB HL, decibel hearing level; ISO, International Organization for Standardization; BKB, Bamford-Kowl-Bench; SWN, speech-weighted noise; BN, babble noise; AADQ, Auditory Attention and Discomfort Questionnaire; RR, relapsing-remitting; SP, secondary progressive; VIF, variance inflation factor; AIC, Akaike information criterion.

[*] Corresponding author.

E-mail address: pippa.iva@monash.edu (P. Iva).

https://doi.org/10.1016/j.msard.2020.102608
Received 8 September 2020; Received in revised form 17 October 2020; Accepted 29 October 2020

Although cochlear hearing loss is uncommon in pwMS (Doty et al., 2012), reports of abnormal wave amplitude and latency in auditory evoked potentials (AEP) from brainstem, subcortical and cortical regions are common (Folmer et al., 2012). Tasks involving later stages of auditory processing, especially psychoacoustic tasks that require binaural hearing and precise neural timing (Levine et al., 1993; Aharonson et al., 1998), can also be impaired. Binaural hearing requires the listener to integrate complementary sound inputs to both ears, and involves detection within millisecond precision; a function particularly susceptible to effects of demyelination on neural timing and conduction velocity (Furst and Levine, 2015). Binaural hearing is vital to many everyday dynamic functions like identifying the location and direction of a sound source (an approaching vehicle), segregating different streams of auditory information (the ringing of a phone from background music), suppressing interference from echoes and reverberations, providing situational awareness (obstacles like workmen drilling in the path), and disambiguating speech in noisy environments (Kohlrausch et al., 2013). We therefore postulate MS individuals will have speech-in-noise (SiN) processing deficits.

How speech processing deficits, especially in real-world conditions, contribute to communication difficulties in MS is poorly studied; communication breakdown in MS is generally reported only in the context of speech production, i.e. dysarthria (Hartelius et al., 2000). This may be due to observations that MS individuals do not have problems repeating speech presented in silence (Olsen et al., 1975; Dayal et al., 1966). However, studies attempting to understand real-life communication should consider the fact that our world is often noisy. Descriptions of speech processing in noise (Olsen et al., 1975; Lewis, 2006; Valadbeigi et al., 2014) are yet to be described in an ecologically relevant context, or are limited in characterizing disease severity in MS listeners. Hence, our objective in this cross-sectional study was to evaluate speech processing in MS under a "real world" perspective of open-set whole sentences in ecologically valid multi-talker speech (“babble”) or broadband noise. To examine the impact of disease severity on these functions, pwMS were segregated according to their Expanded Disability Status Scale (EDSS) score (Kurtzke, 1983), a clinical scale widely used for assessing physical disability in MS. Objective test data were also compared to responses in a questionnaire (Dunlop et al., 2016) for self-reports of difficulties in different daily-life scenarios.

2. Methods

All procedures were approved by the Monash University Human Research Ethics Committee (8170) and Melbourne Health HREC (2015.069). The study conformed to guidelines of the National Health and Medical Research Council of Australia and the Helsinki Declaration protocols for experiments involving human participants.

2.1. Participants

Forty-six people with confirmed MS by revised McDonald criteria (McDonald et al., 2001) were recruited through the Royal Melbourne Hospital Australia. Thirty-eight neurologically healthy controls were recruited from the local community. All participants provided informed written consent. The main exclusion criterion for all participants was hearing loss (Section 2.3 Audiometry for definition of hearing loss) and no pwMS experienced recent (within 30 days) relapses and/or steroids administration. All participants reported English as their native language.

PwMS were grouped according to Expanded Disability Status Scale (EDSS) score (Kurtzke, 1983) as rated by a neurostatus certified neurologist at study entry. PwMS with EDSS scores ≤ 1.5 were classified as ‘mild’; between 2–4.5 as ‘moderate’ and between 5–7 as ‘advanced’ disability.

2.2. Study overview

All participants completed an assessment battery of audiometry, speech discrimination tasks, and an auditory questionnaire, in a quiet room over a single session lasting 35–45min.

2.3. Audiometry

Hearing status was determined using a Beltone Model 110 Clinical Audiometer and calibrated TDH headphones to test sensitivity one ear at a time, at standard audiometric frequencies of 500 hertz (Hz), 750 Hz, 1000 Hz, 1500 Hz, 2000 Hz, 4000 Hz, 6000 Hz and 8000 Hz, using a modified Hughson-Westlake procedure (Jerger et al., 1959). Hearing thresholds, recorded as decibels Hearing Level (dB HL) relative to normal sensitivity (ISO 8253–1, 1989), were defined as the lowest level at which the tone was perceived 50% of the time. Pure tone averages (PTAs) of the hearing threshold levels at 500, 1000, 2000 and 4000 Hz were obtained for all participants to describe hearing status, and only participants with a bilateral four tone average < 25 dB HL were used in this study.

2.4. Speech in noise (SiN) discrimination tasks

The general procedures and stimuli for the SiN task have been outlined previously (Dunlop et al., 2016; Mann et al., 2013; Cainer et al., 2008), and details are provided within the “Data in Brief” journal (Iva et al., 2020). In brief, speech stimuli, derived from a standard battery of clinically used sentences called the Bamford-Kowal-Bench (BKB) sentence lists (Bench et al., 1979), were each four to six words long with three keywords (Supplementary Figure A.1). Sentences were presented in speech-weighted noise (SWN) or babble noise (BN). SWN was shaped to the long-term average spectrum of the target sentences. BN consisted of eight simultaneous voices generated by doubling over and temporally offsetting a recording of four people reading nonsense text.

Speech and masker stimuli were presented binaurally through Sennheiser HD535 headphones. Sentences were presented at a constant level of 70 dBA, whilst the masker level was varied to generate signal-to-noise ratio (SNRs) of 3, 1, −1, −3, and −5 dB in BN; and 1,−1,−3,−5, and −7 dB in SWN. Prior to each noise condition, participants completed ten practice trials (ten unique target sentences) at an ‘easy’ SNR of +5 dB for acclimatization to stimuli. Subsequent SNR blocks were presented in random order. At each SNR, ten unique sentences were presented one at a time and the listener asked to repeat each sentence or indicate inability to do so. A correct response was scored when all three keywords were correctly repeated in correct order. No time limit was placed on response and feedback was not provided. The experimenter recorded the responses and presented the next sentence after 1.5 second delay.

2.5. Auditory attention and discomfort questionnaire (AADQ)

The AADQ was developed by Dunlop, Enticott and Rajan (2016) and based on validated inventories for specific adult clinical populations with abnormal auditory processing (Schow and Nerbonne, 1980; Ventry and Weinstein, 1982; Meijer et al., 2003). The 33-item AADQ consisted of statements about daily life events involving hearing and had three subscales; the Audio-Attentional Difficulty subscale measured difficulties attending to speech in noisy environments; the Auditory Discomfort (Non-Verbal) subscale measured discomfort to non-verbal environmental sounds; and the Auditory Discomfort (Verbal) subscale measured discomfort to verbal sounds. Refer to Supplementary Figure A.2 for the questionnaire items and the “Data in Brief” journal (Iva et al., 2020) for scoring procedures and details.

2.6. Generalised linear mixed model

To identify factors that significantly influenced speech discrimination accuracy on any given trial (0=incorrect; 1=correct), two binomial generalized linear mixed effects model (glme) with logit link functions were generated. One model was based on all participants, whilst the other focused on pwMS only. To build the models, considered variables included: disability groups, SNR, masker type (SWN vs. BN), trial order, age (years), sex (male vs. female), education (years), average pure-tone thresholds (dB HL), EDSS score, disease duration (years), disease phenotype (relapsing-remitting (RR) vs. secondary-progressive (SP)) and theoretically relevant interactions. Supplementary Table A.1 specifies how the categorical/ordinal variables were coded, and the mean ± SD and range for continuous variables. Potential fixed-effects were explored with a subject-specific random intercept representing between-subject heterogeneity. All variables had variance inflation factors (VIF) < 3, below the recommended cut off VIF of 5, indicating no problematic levels of multicollinearity amongst predictors.

Models were validated using the ‘hold-out method’, with a 70:30 split into training and validation data sets, and confusion matrices were generated to determine sensitivity (true positive rate) and specificity (true negative rate).

3. Results

3.1. Participant groups

Basic demographics and disease details of the participant groups are reported in Table 1. Twelve controls (24%) and eleven MS (26%) participants were excluded for bilateral hearing loss (PTAs $\geq$ 25 dB HL). The remaining participants (Table 1) had bilaterally normal hearing between 500–4000 Hz except for 5% of participants from each group with small hearing losses (of 5–10 dB) at higher frequencies of 6000 and 8000 Hz in one ear only. Controls and MS groups had similar hearing sensitivity within normal ranges; the PTAs are presented in Supplementary Figure A.3. Additionally, the thresholds measured at every frequency tested are reported in the “Data in Brief” journal (Iva et al., 2020).

3.2. Speech discrimination in noise

In both noise conditions, sentence recall decreased as SNR decreased. SiN discrimination appeared to be easier in SWN than BN as a floor effect occurred in BN at an SNR of −5, at which point sentence recall was poor for all listener groups, however, at the same SNR of −5 in SWN, no such floor effect was observed. A direct comparison between the noise conditions is described in a mixed effects model described in Section 3.4.

Table 1
Participant characteristics.

	Control	Mild MS	Moderate MS	Advanced MS
Number of participants	38	20	16	10
Sex F (M)[*]	35(3)	17(3)	13(3)	9(1)
Phenotype RR (SP)[**]	–	20 (0)	13(3)	2(8)
Age (yrs)				
Mean (SD)	45.66 (10.43)	44.3 (9.52)	44.83 (11.69)	49 (6.56)
Range	28 - 60	24 - 63	28 - 64	36 - 58
Disease duration (yrs)				
Mean (SD)	–	10.7 (5.77)	13 (7.24)	18.5 (7.07)
Range		1 - 22	1 - 32	10 - 31
EDSS[*]				
Median	–	0	2.5	6
Range	–	0–1.5	2–4.5	5–7
Disease modifying therapy (%)	–	90	81	80

[*] F = female; M = male.

[**] RR = Relapsing-remitting; SP = Secondary progressive.

[*] EDSS = Expanded Disability Status Scale Score determined by a neurologist within 6 months of audiological testing.

3.2.1. Identification of sentences in speech-weighted noise

Mean ± SEM sentences in SWN correctly recalled by controls and pwMS at various SNRs is presented in Fig. 1A. A 4 × 5 [(control, minimal, moderate and advanced MS)] × (SNR = 1, −1, −3, −5, and −7)] two-way mixed ANOVA confirmed a significant interaction between listener group and SNR on sentence recall [F (12, 12 308)=2.45,p = 0.005]. There was also a significant main effect for listener group [F (3,77)=16.66, $p < 0.0001$] and SNR [F (4, 308)=372.1, $p < 0.0001$]. A Tukey’s post hoc analysis confirmed that significantly fewer sentences were recalled by moderate ($p = 0.0004$) and advanced ($p < 0.0001$), but not mildly impaired pwMS ($p = 0.46$) compared to controls.

3.2.2. Identification of sentences in multi-talker babble

BN degraded speech intelligibility for all MS listener groups more than controls except at an SNR of −5, at which a floor effect was observed (refer to Fig. 1B). A 4 × 5 two-way mixed ANOVA confirmed a significant interaction effect between listener group and SNR [F (12, 320)=3.445, $p < 0.0001$]. Main listener group effects were also significant [F (3,80)=16.86,$p < 0.0001$]; and as expected, the SNR also had a significant effect on sentence recall in BN [F (4, 320)=595.6, $p < 0.0001$]. A Tukey’s post hoc analysis confirmed that significantly fewer sentences were discriminated by all MS listener groups ($p < 0.05$) compared to controls.

3.3. Estimating psychometric functions

To quantify MS effects on SiN discrimination, Boltzmann sigmoidal functions were fitted to each participant’s discrimination curves, using GraphPad PRISM 8. From each psychometric curve the slope and midpoint data were extracted, the details of which are specified in the “Data in Brief” journal (Iva et al., 2020). A one-way ANOVA revealed no significant difference in slopes (sentences/dB) between the listening groups in SWN [F (3, 77)=1.70,p = 0.18] and BN [F (3,80)=0.3,p = 0.83]. In contrast, the midpoints of the curves were significantly different amongst listener groups in SWN [F (3,77)=7.48,p = 0.0002] and BN [F (3,3,80) = 14.84, $p < 0.0001$]. The midpoints represent the SNR±SEM (dB) at 50% discrimination and are visually graphed for the SWN (Fig. 1C) and BN task (Fig. 1D), note: higher SNRs indicated poorer discrimination performance.

A Tukey’s honestly significant difference (HSD) post hoc test confirmed that in SWN, the SNR at 50% discrimination for moderate and advanced pwMS was significantly higher than controls ($p < 0.05$). However, no statistical difference was found between controls and minimally impaired pwMS ($p = 0.55$). In BN, the SNR at 50% discrimination for all MS groups was significantly higher than controls ($p < 0.05$). Minimal, moderate, and advanced pwMS had 0.7 ± 0.35 dB, 1.14 ± 0.26 dB and 1.84 ± 0.31 dB greater SNRs than controls, respectively.

3.4. Modelling the factors that impact on SiN discrimination

To explain the impact of MS on SiN discrimination, we adopted a holistic approach to build a model that incorporates all variables needed for explanatory power. Model-building started with a ‘constrained model’ with fixed effects being disability group, SNR, masker type, and the interaction between SNR and masker. Additional theoretically important variables such as trial order number, age, sex (male vs. female), education (years) and average pure-tone thresholds (dB HL) were then incorporated and the model evaluated (see Supplementary Table A.1 for details on how variables were coded). Thirteen theoretical regression models (Table 2) were generated using MATLAB Statistic Toolbox Release 2019b and compared to the constrained model to

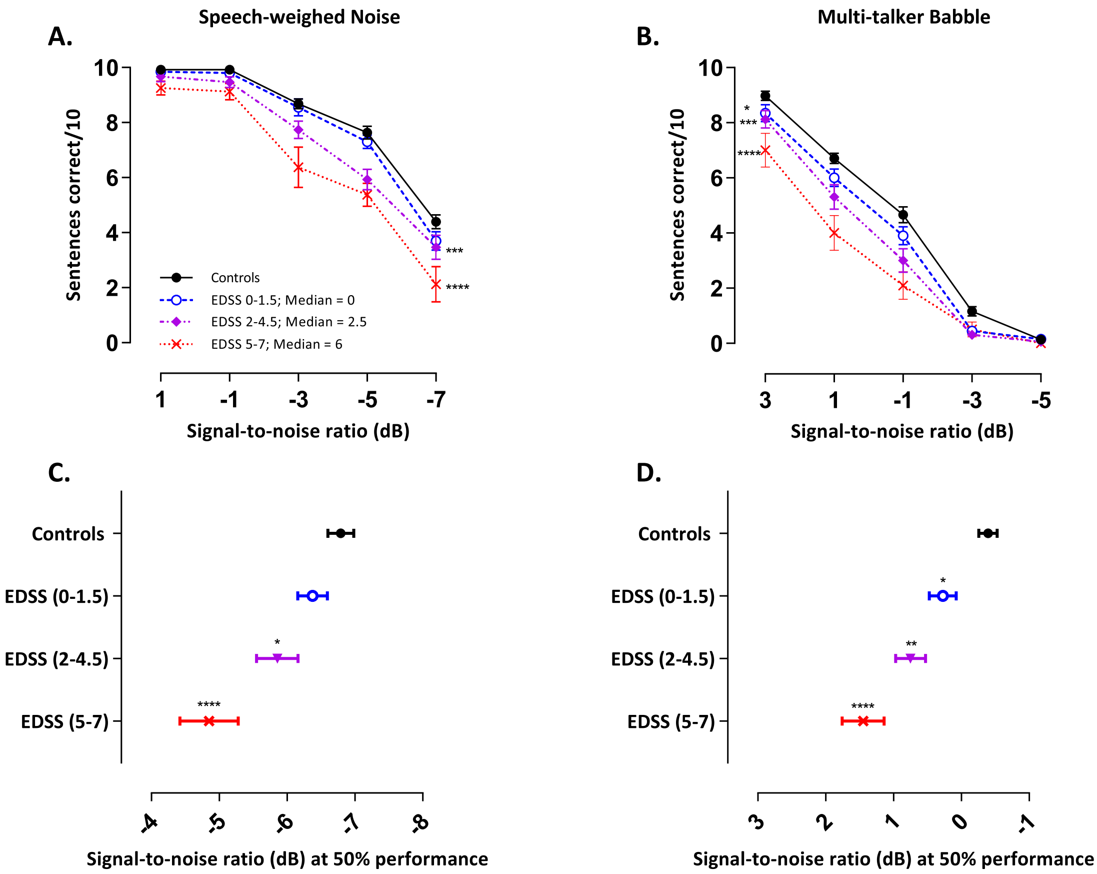


Fig. 1. Sentence recall was systematically worse in MS participants with greater disease severity as measured by the Expanded Disability Status Scale (EDSS) score. Sentence recall by controls (filled circle, $n = 38$); and pwMS with mild (EDSS 0–1.5, open circle, $n = 20$); moderate (EDSS 2–4.5, diamond, $n = 16$); and advanced disability (EDSS 5–7, cross, $n = 10$) in speech-weighted noise (SWN; left-hand column) and multi-talker babble (BN; right-hand column). Mean ± SEM sentences correctly discriminated (out of a possible total score of10 at each signal to noise ratio) in SWN (A) and BN (B). Mean SNRs ± SEM (dB) at 50% discrimination in SWN (C) and BN (D). * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; ****$p < 0.0001$ compared to controls. (A&B: two-way ANOVAs; C, D: one-way ANOVA).

determine the difference in Akaike's Information Criterion (AIC:ΔAIC). Models were based on 8250 trials as nearly all participants ($N = 84$) completed 100 trials each (10 trials x 5 SNRs x 2 masker types). The model with the lowest AIC was used to select the final model as it explains the greatest amount of variation using the fewest possible independent variables. Tests of fixed effects were also confirmed with likelihood ratio (LRT) tests to compare the constrained model with nested models.

The addition of demographic variables did not significantly improve the constrained model. The model with the lowest AIC value included the addition of 'trial order' as a fixed effect (model 6 in bold in Table 2). Therefore, the constrained model was rejected in favour of the final model 6.

Parameter estimates of fixed effects in model 6 are listed in Table 3, along with the t statistic, degrees of freedom and p-values for each fixed effect to test the null hypothesis that the coefficient equals zero. The odds ratio (OR) and confidence intervals (CI,95%) are also included to quantify the magnitude of the association between the fixed effect and the outcome.

Changes in all fixed effects are significantly associated with changes in sentence recall accuracy ($p < 0.05$). To quantify this association, the ORs were interpreted. The OR of correctly discriminating a sentence was 0.72 (0.56 – 0.92) for mild pwMS, i.e. 28% lower odds (1- $e^{-0.33}$) compared to controls when all other factors were constant. A decrease in odds ratio corresponded to the severity of disability as moderately and advanced pwMS had 51% and 73% lower odds compared to controls, respectively.

There was also a positive association of trial order on speech discrimination as the odds of correct speech discrimination was 1.03 (95% CI, 1.01–1.06) times greater compared to the previous trial. Finally, a one-unit increase in SNR increased the odds of correct sentence recall by 84% in SWN but only by 11% in BN.

3.5. *Disease factors that impact SiN discrimination*

A second model was built to investigate the impact of various disease factors on SiN discrimination, this time, with a specific focus on characteristics and clinical measures in pwMS only. In an exploratory approach, all theoretically important variables were included. The model was based on 4450 trials as nearly all participants ($N = 46$; with the exception of one participant who did only 50 trials) completed 100 trials each (10 trials x 5 SNRs x 2 masker types). A total of 11 variables were identified for inclusion in the generalized linear mixed effects model, and were classified into four groups: experimental, demographic, disease characteristics and 'other'. Experimental fixed-effects were: trial order, SNR, masker type, and the interaction between SNR and masker; demographic variables were: age (years), sex (female: male) and education (years); disease characteristic variables were: duration (years), EDSS score and disease type (RR:SP); and the 'other' variable was: the average pure-tone threshold (dB HL). Refer to Supplementary Table A.1 for details on how variables were coded.

Fig. 3 displays the ORs for the demographic, disease characteristics and pure-tone average variables that were included in the model. Although the fixed effects of trial order, SNR, masker, interaction

Table 2

Comparisons of fixed effects combinations in a generalized linear mixed effects model (with a logit link function) used to predict correct sentence recall on each trial.

Constrained model (nested model):	AIC	ΔAIC	X^2	Δdf	p
(1)(Disability group + SNR + Masker + SNR*Masker + (1| participant)	6615.7	0			
Additional covariates:					
(2) Disability group*SNR	6618.3	2.6	3.37	3	0.34
(3) Disability group*Masker	6619.9	4.2	1.77	3	0.62
(4) Disability group*SNR + Disability group*Masker	6621.1	5.4	6.59	14	0.36
(5) Disability*SNR*Masker	6624.3	8.6	9.34	9	0.41
(6) Trial order	**6610.3**	**−5.4**	**7.38**	**1**	**0.007****
(7) Trial order + Trial order*Disability group	6615.3	−0.4	8.42	4	0.08
(8) Trial order + Age + Sex + Education + Pure tone average	6617.1	0.4	7.41	5	0.21
(9) Pure tone average	6617.5	1.9	0.08	1	0.78
(10) Pure tone average*Disability group	6617.6	0.9	7.10	4	0.13
(11) Age	6617.7	2	0.01	1	0.92
(12) Age*Disability group	6622.4	6.7	1.31	4	0.86
(13) Sex	6617.8	2	0.05	1	0.82

Based on 8250 observations (84 participants).

The estimate of the variability of the random effects (σ_b^2) for all models = 0.32.

The last three columns show the chi squared statistic (X^2), difference in the degrees of freedom and p value from the likelihood ratio (LRT) tests.

SNR = signal-to-noise ratio.

AIC = Akaike's Information Criterion.

df = degrees of freedom.

between SNR and masker, and the intercept were significant predictors of the model, they are not displayed in Fig. 3 as it was not informative to repetitively display experimental variables that have previously been established as significant contributors to speech discrimination performance (refer to Table 3). EDSS score was the only predictor identified as the most significant predictor of speech discrimination in noise (OR 0.81; $p < 0.001$). There were no associations between any of the other patient characteristics and SiN discrimination.

3.6. Noise and daily life events

Data for the three AADQ domains probing subjectively perceived difficulty in different facets of daily life events are presented in Fig. 4. ANOVA revealed significant differences between groups on Audio-Attentional difficulty [F (3, 77) = 7.05, $p = 0.0003$; $\eta^2 = 0.22$], but no significant differences on the Auditory Discomfort scales for both non-verbal [F (3, 77) = 1.30, $p = 0.28$, $\eta^2 = 0.05$] and verbal stimuli [F (3, 77) = 2.09, $p = 0.11$; $\eta^2 = 0.08$]. Tukey's post-hoc analysis confirmed that only the advanced MS group reported significantly greater difficulty in attentionally demanding environments than controls ($p < 0.001$), mild ($p < 0.01$) and moderately impaired ($p < 0.05$) pwMS.

4. Discussion

We have uniquely investigated sentence discrimination under 'real-world' conditions to report deficits in MS listeners in discriminating open-set natural whole sentences in noise, including ecologically valid noise. This worsened systematically with disease severity but the absent slope changes coupled with the shift to higher SNRs for 50% performance in MS psychometric curves show that MS participants required a more favourable SNR for equal performance but otherwise conducted SiN processing in the same way as control listeners.

Successful extraction of speech from noise requires disentangling a complex auditory scene to develop neural representations that maintain the integrity of distinct sound sources (Sussman et al., 2007). Given audiometric normal hearing, MS-related SiN difficulties must reflect centralised auditory processing (CAP) disorders (Furst and Levine, 2015) in higher-order mechanisms that preserve, analyse, organise and interpret information. Temporal processing, an important component of CAP, is impaired in MS (Rappaport et al., 1994); posited to be related to the delays of signal transmission within the auditory pathways affected by demyelinating lesions that impact on neural synchrony (Rappaport et al., 1994; Mustillo, 1984). Temporal acuity is critical for speech perception processes like detection of rise/fall time, voice onset, and the transient onset of syllables (Nair and Basheer, 2017), and it also facilitates 'glimpsing' in which an individual takes advantage of momentary 'dips' in noise energy where the target signal is more audible (Li and Loizou, 2007). This ability appears impaired in MS listeners who have been previously reported to perform worse than controls in a words-in-noise paradigm when a wideband background noise had randomised silent periods, but not for continuous noise (Rappaport et al., 1994).

Sound input parsed by spectral/temporal cues is modified at cortex to sharpen stream segregation by attentional systems that filter irrelevant inputs so the listener can focus on a single target stream (Sussman et al., 2007). This becomes more difficult when SNRs are smaller and

Table 3

Parameter estimates of fixed effects of the final generalized linear mixed effects model (with a logit link function) used to predict correct sentence recall on each trial.

						95% C.I for e^{β}	
Name	Estimate (β)	SE β	tStat	*P*	OR (e^{β})	Upper	Upper
Intercept + $N(0, \sigma_b^2)$	3.88	0.15	26.15	**<0.0001**	48.26	36.09	64.54
Trial	0.03	0.01	2.72	**<0.01**	1.03	1.01	1.05
SNR	0.59	0.02	27.08	**<0.0001**	1.81	1.73	1.89
Masker type	−3.86	0.12	−30.94	**<0.0001**	0.02	0.02	0.03
Disability group							
Control	Reference group		–	–	1	–	–
Mild (EDSS 0–1.5)	−0.33	0.12	−2.66	**<0.01**	0.72	0.56	0.92
Moderate (EDSS 2–4.5)	−0.71	0.13	−5.27	**<0.0001**	0.49	0.38	0.64
Advanced (EDSS 5–7)	−1.30	0.16	−7.92	**<0.0001**	0.27	0.20	0.38
SNR x Masker type	0.11	0.03	3.62	**<0.0001**	1.11	1.05	1.18

Based on 8250 observations ($N = 84$ participants).

The estimate of the variability of the random effects (σ_b^2) for all models = 0.32.

Model was validated using the 'hold-out method', with a 70:30 split into training and validation data sets.

Note: Sensitivity = 82.7%. Specificity = 80.5%. Overall accuracy = 81.25%.

SNR = signal-to-noise ratio.

SE = standard error.

OR = odds ratio.

C.I = confidence interval.

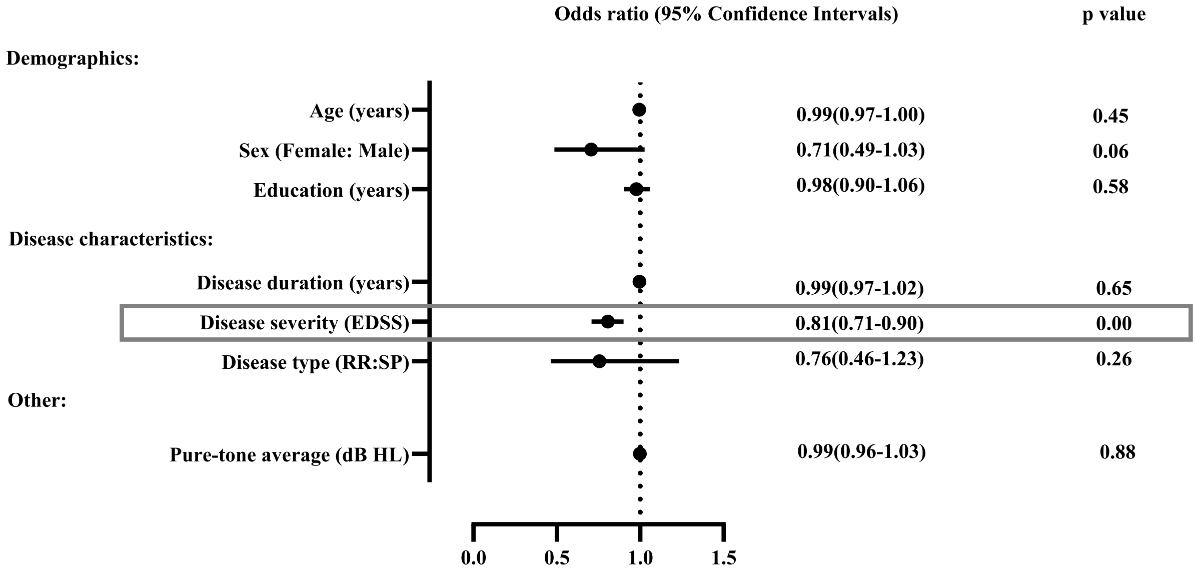


Fig. 3. Disease severity, as measured by the Expanded Disability Status Scale (EDSS) score, was the only significant predictor for correct speech discrimination in noise at any given trial. A generalised linear mixed-effects model (with a logit link function) was used to determine significant predictors of speech discrimination in people with multiple sclerosis; the grey box highlights the significant predictor. An odds ratio of 1 = no effect; < 1 is associated with lower odds of correctly discriminating a sentence from noise. EDSS: Expanded Disability Status Scale Score; RR: Relapsing Remitting; SP: Secondary Progressive; dB HL: decibels hearing level. Black dots indicate odds ratio and lines indicate the 95% confidence interval. Refer to Supplementary Table A.1 for details on how variables were coded.

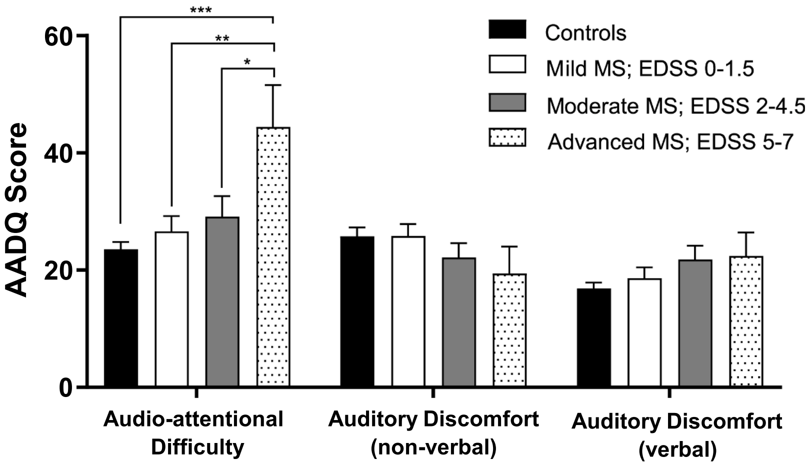


Fig. 4. MS participants with advanced disability reported significant audio-attentional difficulty in the Auditory Attention and Difficulty Questionnaire (AADQ). Mean total score (±SEM) for controls (black; $n = 38$), mild (white; $n = 20$), moderate (grey; $n = 15$) and advanced MS (patterned; $n = 7$) on the three components of the questionnaire: audio-attentional difficulty, auditory discomfort (non-verbal) and auditory discomfort (verbal). Audio-Attentional Difficulty had a possible range of 14–98, Auditory Discomfort (Non-Verbal) had a possible range of 8–56, and Auditory Discomfort (Verbal) had a possible range of 5–35. (* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; One way ANOVA; Tukey's Honestly Significant Difference (HSD) Test).

stimuli are similar. Multi-talker babble will elicit confusion because of its similarity to speech and its saliency which will involuntarily capture attention. This perceptual interference is known as informational masking and similarity between talkers is a particularly strong feature of such masking (Bronkhorst, 2000). In contrast, SWN is an energetic masker that diminishes target audibility only through masking and blending of acoustic signals at the periphery (Bronkhorst, 2000). The difference in difficulty of the two tasks is apparent in our modelling: when all other factors were constant, a one-unit improvement in SNR increased the odds of correct sentence recall by 84% in SWN but only 11% in babble. However, there was no differential degradation between the disability groups.

Electrophysiology shows MS-related impairments in cortical processes that can affect discrimination performance. The cognitive P300 potential is elicited in central processes such as attention, auditory discrimination, memory and decision making (Sur and Sinha, 2009). It is typically measured with an "Oddball Paradigm" requiring a response to deviants within a regular train of repetitive stimuli. Parallels can be drawn to our SiN tasks: background noise forms the repetitive stimulus and target sentences are the deviants requiring detection. In MS, P300 waveform latencies are significantly increased (>2 S.D) (Ivica et al., 2013; Magnano et al., 2006), indicating poorer cognitive performance (Sur and Sinha, 2009). In fact, cognitive impairment is now considered a primary deficit affecting 40–70% of pwMS, manifesting at all disease stages, even onset, and in all subtypes (Chiaravalloti and DeLuca, 2008). MS affects many cognitive domains with most effects on information processing speed, attention and memory, followed by verbal fluency and executive deficits (Fielding and Clough, 2019); cognitive decline worsens with advancing disease. Such cognitive disturbances in MS could contribute to impaired SiN discrimination, however, were not formally tested.

Although SiN discrimination was impaired in all MS groups, only pwMS with advanced disability reported significant audio-attentional difficulty in daily life events. The absence of self-reported auditory difficulty in less severe MS groups could reflect redundant auditory processing (Furst and Levine, 2015), which may be intrinsic (multiple parallel auditory CNS representations (Musiek, 1986)) or extrinsic (syntactic and semantic cues, or multimodal information through (say) lipreading) (Wu et al., 2015). Early pwMS may successfully use compensatory mechanisms to reduce or masque functional deficits (Audoin et al., 2005). Disease progression may degrade compensatory capacity by causing irreversible neurological disability and whole brain volume atrophy (Correale et al., 2016), removing any auditory pathway redundancy. Our subjective measures and psychoacoustic testing serve as complementary tasks to elucidate the difference between a subtle impairment that evades detection and one that greatly impacts on daily life.

Our generalized linear mixed effects model enabled consideration of demographic variables and individual differences (random intercept effect) inherent in human participant trials but even then, disease severity remained a significant factor in predicting speech discrimination accuracy. Thus, our SiN tasks have robust construct validity and merit consideration for monitoring disease changes, with the advantages of speed (approximately 10min per background noise) and being non-invasive, cost effective, easy to administer, and requiring only portable equipment, allowing for home testing. Furthermore, psychoacoustic methodology makes it easy to study many more systematic variations in SNR, sentence difficulty and saliency of background maskers for further refinement. Finally, we acknowledge that our study is cross-sectional and limited to participants with normal hearing. Longitudinal data will provide further confidence that our SiN tasks could be a valid biomarker for disease progression and future studies should investigate SiN performance in pwMS with hearing loss. An investigation into the correlations between SiN performance and CNS lesion location would also provide valuable insight into the pathological underpinnings of SiN deficits in MS.

CRediT authorship contribution statement

Pippa Iva: Formal analysis, Investigation, Data curation, Project administration, Writing - original draft. **Joanne Fielding:** Writing - review & editing. **Meaghan Clough:** Writing - review & editing. **Owen White:** Writing - review & editing. **Gustavo Noffs:** Investigation. **Branislava Godic:** Investigation, Writing - review & editing. **Russell Martin:** Supervision, Writing - review & editing. **Anneke van der Walt:** Investigation, Writing - review & editing. **Ramesh Rajan:** Conceptualization, Methodology, Software, Validation, Resources, Writing - review & editing, Supervision.

Acknowledgements

We are grateful to all participants, the staff of Royal Melbourne Hospital for their assistance and undergraduate students who collected control data.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2020.102608.

References

Fielding, J., Clough, M., 2019. Degenerative Disorders of the Brain. Routledge, Taylor & Francis Group, London, pp. 163–186.
Furst, M., Levine, R.A., 2015. Chapter 36 - Hearing disorders in multiple sclerosis. In: Michael, J, Aminoff, FB, Dick, FS (Eds.), Handbook of Clinical Neurology, 129. Elsevier, pp. 649–665.
Musiek, E.F., 1986. Neuroanatomy, Neurophysiology, and Central Auditory Assessment. Part III: corpus Callosum and Efferent Pathways. Ear Hear. 7 (6), 349–358.
Amaral, A., Silva, C., Alves, A., Prata, C., Fernandes, C., Simões, P., et al., 2019. Associations between quality of life and central auditory processing in seniors: preliminary results. Eur. J. Public Health 29 (Supplement_1).
Doty, R.L., Tourbier, I., Davis, S., Rotz, J., Cuzzocreo, J.L., Treem, J., et al., 2012. Pure-Tone Auditory Thresholds Are Not Chronically Elevated in Multiple Sclerosis. Behav. Neurosci. 126 (2), 314–324.
Folmer, R., Hutter, M., Lilly, D., Shannon, J., Casiana, L., Wilmington, D., et al., 2012. Electrophysiological Measures of Auditory Processing in Patients with Multiple Sclerosis. Semin Hear 33 (3), 274–282.
Levine, R.A., Gardner, J.C., Stufflebeam, S.M., Fullerton, B.C., Carlisle, E.W., Furst, M., et al., 1993. Binaural auditory processing in multiple sclerosis subjects. Hear. Res. 68 (1), 59–72.
Aharonson, V., Furst, M., Levine, R.A., Chaigrecht, M., Korczyn, A.D, 1998. Lateralization and binaural discrimination of patients with pontine lesions. J. Acoust. Soc. Am. 103 (5), 2624–2633.
Kohlrausch, A., Braasch, J., Kolossa, D., Blauert, J, 2013. An Introduction to Binaural Processing. editor. In: Blauert, J (Ed.), The Technology of Binaural Listening. Springer, Berlin, Heidelberg, pp. 1–32. Berlin Heidelberg.
Hartelius, L., Runmarker, B., Andersen, O., Nord, L, 2000. Temporal Speech Characteristics of Individuals with Multiple Sclerosis and Ataxic Dysarthria: 'Scanning Speech' Revisited. Folia Phoniatr Logop 52 (5), 228–238.
Olsen, W.O., Noffsinger, D., Kurdziel, S, 1975. Speech Discrimination In Quiet And In White Noise By Patients With Peripheral And Central Lesions. Acta Otolaryngol. 80 (1–6), 375–382.
Dayal, V.S., Tarantino, L., Swisher, L.P, 1966. Neuro-otologic studies in multiple sclerosis. Laryngoscope 76 (11), 1798–1809.
Lewis, M.S., 2006. Some effects of multiple sclerosis on speech perception in noise: preliminary findings. Journal of Rehabilitation Research & Development 43, xiii.
Valadbeigi, A., Weisi, F., Rohbakhsh, N., Rezaei, M., Heidari, A., Rasa, A.R, 2014. Central auditory processing and word discrimination in patients with multiple sclerosis. Eur Arch Otorhinolaryngol 271 (11), 2891–2896.
Kurtzke, J.F., 1983. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 33 (11), 1444–1452.
Dunlop, W.A., Enticott, P.G., Rajan, R, 2016. Speech discrimination difficulties in High-Functioning Autism Spectrum Disorder are likely independent of auditory hypersensitivity. Front. Hum. Neurosci. 10.
McDonald, W.I., Compston, A., Edan, G., Goodkin, D., Hartung, H.P., Lublin, F.D., et al., 2001. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. Ann. Neurol. 50 (1), 121–127.
Jerger, J.F., Carhart, R., Tillman, T.W., Peterson, J.L, 1959. Some Relations Between Normal Hearing for Pure Tones and for Speech. J. Speech Lang Hear Res. 2 (2), 126–140.
Mann, C., Canny, B., Reser, D., Rajan, R, 2013. Poorer verbal working memory for a second language selectively impacts academic achievement in university medical students. PeerJ 1 (1).
Cainer, K.E., James, C., Rajan, R, 2008. Learning speech-in-noise discrimination in adult humans. Hear. Res. 238 (1), 155–164.
Iva, P., Fielding, J., Clough, M., White, O., Noffs, G., Godic, B., Martin, R., van der Walt, A., Rajan, R., 2020. Speech Discrimination in Noise in Multiple Sclerosis Dataset. Data Brief. In Press.
Bench, J., Kowal, A., Bamford, J, 1979. The BKB (Bamford-Kowal-Bench) sentence lists for partially-hearing children. Br. J. Audiol. 13 (3), 108–112.
Sussman, E.S., Horváth, J., Winkler, I., Orr, M, 2007. The role of attention in the formation of auditory streams. Percept. Psychophys. 69 (1), 136–152.
Rappaport, J.M., Gulliver, J.M., Phillips, D.P., Van Dorpe, R.A., Maxner, C.E., Bhan, V, 1994. Auditory temporal resolution in multiple sclerosis. J. Otolaryngol. 23 (5), 307–324.
Mustillo, P., 1984. Auditory Deficits in Multiple Sclerosis: a Review. Audiology 23 (2), 145–164.
Nair, P.G., Basheer, B.M., 2017. Influence of temporal resolution skills in speech discrimination abilities of older subjects. Acta Otorhinolaryngol Ital 37 (1), 58–62.
Li, N., Loizou, P.C., 2007. Factors influencing glimpsing of speech in noise. J. Acoust. Soc. Am. 122 (2), 1165–1172.
Bronkhorst, A., 2000. The Cocktail Party Phenomenon: a Review of Research on Speech Intelligibility in Multiple-Talker Conditions. Acta Acustica united with Acustica 86, 117–128.
Sur, S., Sinha, V.K., 2009. Event-related potential: an overview. Ind. Psychiatry J 18 (1), 70–73.
Ivica, N., Titlic, M., Pavelin, S, 2013. P300 Wave Changes in Patients with Multiple Sclerosis. Acta Informatica Medica 21 (3), 205–207.
Magnano, I., Aiello, I., Piras, M.R, 2006. Cognitive impairment and neurophysiological correlates in MS. J. Neurol. Sci. 245 (1), 117–122.
Chiaravalloti, N.D., DeLuca, J., 2008. Cognitive impairment in multiple sclerosis. The Lancet Neurology 7 (12), 1139–1151.
Wu, C., Stefanescu, R.A., Martel, D.T., Shore, S.E, 2015. Listening to another sense: somatosensory integration in the auditory system. Cell Tissue Res. 361 (1), 233–250.
Audoin, B., Duong, M.V.A., Ranjeva, J.P., Ibarrola, D., Malikova, I., Confort-Gouny, S., et al., 2005. Magnetic resonance study of the influence of tissue damage and cortical reorganization on PASAT performance at the earliest stage of multiple sclerosis. Hum. Brain Mapp. 24 (3), 216–228.
Correale, J., Gaitán, M.I., Ysrraelit, M.C., Fiol, M.P, 2016. Progressive multiple sclerosis: from pathogenic mechanisms to treatment. Brain 140 (3), 527–546.

Schow, R.L., Nerbonne, M.A., 1980. Hearing handicap and Denver Scales: applications, categories and interpretation. J. Acad. Rehabil. Audiol. 13, 66–77.

Ventry, I.M., Weinstein, B.E., 1982. The hearing handicap inventory for the elderly: a new tool. Ear Hear 3 (3), 128–134.

Meijer, A.G., Wit, H.P., TenVergert, E.M., Albers, F.W., Muller Kobold, J.E, 2003. Reliability and validity of the (modified) Amsterdam Inventory for Auditory Disability and Handicap. Int. J. Audiol. 42 (4), 220–226.

Author/s:
Iva, P; Fielding, J; Clough, M; White, O; Noffs, G; Godic, B; Martin, R; van der Walt, A; Rajan, R

Title:
Speech discrimination impairments as a marker of disease severity in multiple sclerosis

Date:
2021-01-01

Citation:
Iva, P., Fielding, J., Clough, M., White, O., Noffs, G., Godic, B., Martin, R., van der Walt, A. & Rajan, R. (2021). Speech discrimination impairments as a marker of disease severity in multiple sclerosis. MULTIPLE SCLEROSIS AND RELATED DISORDERS, 47, https://doi.org/10.1016/j.msard.2020.102608.

Persistent Link:
http://hdl.handle.net/11343/273821

File Description:
Published version