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Improving speech perception in noise in young and older adults using transcranial magnetic stimulation

Valérie Brisson, Pascale Tremblay *

Département de réadaptation, Université Laval, Québec, Canada
Centre de recherche CERVO, Québec, Canada

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ABSTRACT

Normal aging is associated with speech perception in noise (SPiN) difficulties. The objective of this study was to determine if SPiN performance can be enhanced by intermittent theta-burst stimulation (iTBS) in young and older adults.

Method: We developed a sub-lexical SPiN test to evaluate the contribution of age, hearing, and cognition to SPiN performance in young and older adults. iTBS was applied to the left posterior superior temporal sulcus (pSTS) and the left ventral premotor cortex (PMv) to examine its impact on SPiN performance.

Results: Aging was associated with reduced SPiN accuracy. TMS-induced performance gain was greater after stimulation of the PMv compared to the pSTS. Participants with lower scores in the baseline condition improved the most.

Discussion: SPiN difficulties can be reduced by enhancing activity within the left speech-processing network in adults. This study paves the way for the development of TMS-based interventions to reduce SPiN difficulties in adults.

1. Introduction

Older adults often report difficulties following conversations in noisy environments (e.g., at the restaurant or during family reunions), which can hinder social interactions (Aydelott, Leech, & Crinion, 2010; CHABA, 1988). Several studies have shown that peripheral hearing only partially explains these difficulties, which suggests a contribution of central mechanisms (e.g. Anderson, White-Schwoch, Parbery-Clark, & Kraus, 2013; Dubno et al., 2008; Fostick, Ben-Artzi, & Babkoff, 2013; Humes & Dubno, 2010; Pichora-Fuller & Souza, 2003). One possibility is that speech perception in noise (SPiN) difficulties are triggered by age-related decline in brain regions supporting central auditory mechanisms in the primary auditory cortex (transverse temporal gyrus; TTG). Alternatively, these difficulties could be related to aging of the brain networks supporting speech functions. Indeed, in addition to involving the primary auditory cortex, processing speech also activates regions involved in phonological (e.g., the superior temporal cortex; STC), motor (e.g., the primary motor and premotor cortex; PM) and lexical (e.g., the middle temporal gyrus; MTG) processes, as well as regions of the executive network, such as the middle frontal cortex, cingulate cortex, frontal operculum and anterior insula (e.g. Adank, 2012; Alain, Du, Bernstein, Barten, & Banai, 2018; Eckert, Teubner-Rhodes, & Vaden, 2016).

Consistent with the notion of a role for higher-order processes in age-related decline in SPiN, several brain imaging studies have shown that structural decline in brain areas and white matter tracts that support phonological (e.g., the bilateral STC), motor (e.g., the PM), lexical (e.g., the MTG), and attention-related processes (e.g., the insula) is associated with speech performance decline (e.g. Bilodeau-Mercure, Lortie, Sato, Guitton, & Tremblay, 2015; Eckert et al., 2008; Sheppard, Wang, & Wong, 2011; Tremblay, Brisson, & Deschamps, 2021; Wong, Ettlinger, Sheppard, Gunasekera, & Dhar, 2010). For instance, in a group of older adults, accuracy during a sentence repetition task was found to be predicted by cortical thickness of the left superior frontal gyrus and hemispheric volume of the left pars triangularis gyrus (Wong et al., 2010).

Differences in cerebral activation patterns between young and older adults have also been found during SPiN tasks within auditory, phonological and lexical processing areas (e.g. Du & Alain, 2016; Hwang, Li, Wu, Chen, & Liu, 2007; Manan, Franz, Yusoff, & Mukari, 2015; Manan, Yusoff, Franz, & Mukari, 2017; Tremblay, Brisson, & Deschamps, 2020; Wong et al., 2009), as well as sensorimotor (e.g. Bilodeau-Mercure et al., 2015; Du & Alain, 2016; Eckert et al., 2008; Manan et al., 2017; Peelle,

* Corresponding author at: Département de Réadaptation, Université Laval, 1050 avenue de la Médecine, Québec (QC) G1V 0A6, Canada.
E-mail address: Pascale.Tremblay@fmed.ulaval.ca (P. Tremblay).

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Troiani, Wingfield, & Grossman, 2010) and attention-related areas (e.g. Bilodeau-Mercure et al., 2015; Du & Alain, 2016; Eckert et al., 2008; Peelle et al., 2010; Vaden, Kuchinsky, Ahlstrom, Dubno, & Eckert, 2015; Wong et al., 2009). For instance, a study from our group showed a detrimental indirect effect of age on syllable repetition errors (Bilodeau-Mercure et al., 2015). In that study, aging was associated with lower activation in the left anterior insula, which in turn was associated with decreased accuracy. In a recent study, it was found that when performance in a syllable identification task was matched between younger and older adults, older adults showed higher activity in areas including the bilateral STG, MTG, MFG and precentral gyrus, as well as the left ventral premotor cortex (PMv) and left IFG, suggesting that compensation within speech processing areas contributed to maintaining performance (Du & Alain, 2016). Another study found that the bilateral anterior cingulate cortex (ACC) and the left MFG were more engaged in older adults during degraded word recognition for correct compared to incorrect answers (Eckert et al., 2008). Together, brain imaging studies show that the network supporting SPiN declines with age, and that this decline is associated with a decline in performance. The question that we address here is whether SPiN performance can be enhanced using non-invasive brain stimulation methods.

Non-invasive brain stimulation methods, such as transcranial magnetic stimulation (TMS), can induce beneficial short and longer-term plasticity in the brain, which can lead to enhanced performance in a variety of domains, including motor performance (e.g. Hoyer & Celnik, 2011; Lüdemann-Podubecká, Bösl, & Nowak, 2015; Schambra, 2018), cognition (e.g. Guse, Falkai, & Wobrock, 2010; Kim, Hong, Kim, & Yoon, 2019; Widhalm & Rose, 2019), hearing (e.g. Chen et al., 2020; Schoisswohl et al., 2019; Soleimani, Jalali, & Hasandokht, 2016), and speech/language (e.g. Devlin & Watkins, 2007; Li, Zeng, Lin, Xian, & Chen, 2020). Intermittent theta-burst stimulation (iTBS), a repetitive TMS (rTMS) protocol that can increase cortical excitability, is a promising method to enhance performance during speech tasks in healthy adults and in those with communication disorders. Consistent with this notion, one study has shown that iTBS over the pIFG increased accuracy in sentence repetition in healthy young adults (Restle, Murakami, & Ziemann, 2012). Another study showed enhanced vocal pitch regulation in healthy young adults after iTBS over the right somatosensory laryngeal cortex, during a pitch-matching singing task with masked feedback (Finkel et al., 2019). Several studies of post-stroke aphasic patients have shown that language functions (e.g., semantic fluency, picture naming, auditory comprehension) can be improved by applying iTBS over the left IFG or left temporal cortex in young and older adults (Griffis, Nenert, Allendorfer, & Szaflarski, 2016; Szaflarski et al., 2018; Szaflarski et al., 2011; Versace et al., 2019; Vuksanović et al., 2015). Together, these studies suggest that the adult speech/language system is plastic, and that performance can be boosted using faciliatory rTMS such as iTBS.

To our knowledge, iTBS has never been used to induce changes in the speech network in healthy older adults. A limited number of studies have shown that iTBS applied to the motor cortex can successfully increase cortical excitability in healthy older adults (e.g. Dickins, Sale, & Kamke, 2015; Gedankien, Fried, Pascual-Leone, & Shafi, 2017; Young-Bernier, Tanguay, Davidson, & Tremblay, 2014). Yet, a recent meta-analysis reported reduced motor evoked potential (MEP) amplitudes and longer latencies in older compared to younger individuals after single-pulse, paired pulse or rTMS was applied (Tang et al., 2019). Specifically, the analysis of 20 studies using electromyography to measure cortical excitability in the primary motor cortex showed that MEP responses to TMS had a significantly lower amplitude in elderly compared to younger adult groups, though the MEP responses were significant in both groups. Another analysis including seven studies showed that post TMS MEP latency was delayed in the elderly group compared to the younger group. Although MEP activity measures can be influenced by age-related factors other than brain plasticity itself (e.g., skin and skull characteristics), at least one study has shown that MEP amplitude changes after motor cortex iTBS correlate with TMS-evoked EEG potentials. This suggests that post-iTBS MEP changes are representative of brain activity changes (Gedankien et al., 2017). Together with findings from clinical populations, these findings suggest that TMS can induce neuroplasticity in the aging brain, though the potential for plasticity may be reduced in older compared to younger adults. Additional evidence is needed regarding the potential for plasticity within specific functional systems such as the speech/language system in the aging brain.

The main objectives of this two-part study were (1) to investigate the mechanisms underlying age-related SPiN decline, and (2) to determine if SPiN performance in young and older adults can be enhanced by excitatory rTMS to two areas involved in processing sublexical speech: the left posterior superior temporal sulcus or pSTS, and the left ventral premotor cortex or PMv. The selection of these areas was based on knowledge of their role in SPiN, and prior evidence that TMS to these regions can successfully induce behavioural changes in healthy young adults. The left pSTS is involved in sublexical phonological processing (e.g. Hickok & Poeppel, 2007; Turkeltaub & Coslett, 2010). For instance, a recent study has shown that inhibitory TMS to this region is associated with phonological errors during auditory word comprehension, syllable repetition, syllable identification and pseudo-word repetition (Murakami, Kell, Restle, Ugawa, & Ziemann, 2015). Another study found that rTMS applied to the anterior STS led to poorer performance during sentence repetition in noise (Kennedy-Higgins, Devlin, Nuttall, & Adank, 2020). The left PMv is involved in speech perception and comprehension (e.g. McGettigan & Tremblay, 2018; Pulvermuller & Fadiga, 2010; Tremblay & Small, 2011; Walenski, Europa, Caplan, & Thompson, 2019). Although the specific contribution of this region is still unclear and a subject of debate, previous studies have shown that inhibitory rTMS to this region is associated with reduced speech perception performance (Krieger-Redwood, Gaskell, Lindsay, & Jefferies, 2013; I. G. Meister, Wilson, Deblieck, Wu, & Iacoboni, 2007; Sato, Tremblay, & Gracco, 2009) or enhanced selective adaptation to speech during speech perception (Grabski, Tremblay, Gracco, Girin, & Sato, 2013).

The specific objectives of Experiment 1 were to develop and test an age-sensitive sub-lexical SPiN test and to examine the impact of cognition and hearing on performance at this test. Our main hypothesis was that aging would be associated with reduced SPiN performance operationalized as lower accuracy and longer reaction times (RT), after controlling for hearing and cognition. The specific objective of Experiment 2 was to determine whether excitatory rTMS can enhance SPiN in younger and elderly adults via stimulation of the left pSTS and/or left PMv. We hypothesized that performance gain would be more limited in older compared to younger adults because of known reduced plasticity in the aging brain. An effect of target (pSTS, PMv) would suggest that one region has a stronger functional contribution to SPiN and might represent a better option to reduce or prevent SPiN decline in aging using non-invasive brain stimulation.

2. Experiment 1

2.1. Method

2.1.1. Participants

22 healthy native Canadian French speakers were recruited through the laboratory database, emails, posts on the lab website (www.speechneurolab.ca), lab Facebook page (https://www.facebook.com/speechneurolab/) and flyers distributed in various institutions, including shops and retirement homes throughout Québec City. One participant was excluded from the analyses due to inability to complete the main task. The remaining participants were aged 20–85 years (mean 53.33 ± 20.52 years). A telephone interview was conducted to verify inclusion criteria. Participants reported no history of speech, language, hearing, psychiatric or neurological disorder. All participants were schooled primarily or exclusively in French. The French version of the

Montreal Cognitive Assessment (MoCA, version 8) (Nasreddine et al., 2005) was administered to evaluate general cognitive level. All participants were considered clinically normal (Larouche et al., 2016). Participants' characteristics are presented in Table 1. Participants were screened for depression using the Geriatric Depression Scale (GDS) (Yesavage et al., 1982), and for anxiety using the Geriatric Anxiety Index (GAI) (Pachana et al., 2007). One participant had a GAI score higher than the cut-off, and another one had GDS and GAI scores higher than the cut-off. All statistical analyses were done with and without these participants. Because this comparison yielded no difference, these two participants were kept in the final analyses. All participants gave their informed consent and received a monetary compensation. This study was approved by the *Comité d'éthique de la recherche sectoriel en neurosciences et santé mentale, Institut Universitaire en Santé Mentale de Québec* (#1495–2018).

2.1.2. Hearing Assessment

Hearing assessments are reported in Table 1. Participants reported no hearing problem (including tinnitus) and did not wear hearing aids or cochlear implants. Pure tone audiometry was used to assess hearing for each ear separately (clinical audiometer AC40, Interacoustic, Denemark). Hearing thresholds were measured in dB HL at 0.25, 0.50, 1, 2, 4 and 6 kHz and are presented in Supplementary Material 1. Pure tone averages (PTAs) were calculated in each ear separately. All participants had PTAs lower than 35 dB in each ear and averaged interaural differences of lower than 15 dB at 0.5, 1 and 2 kHz (the main speech frequencies) (Stach, 2008). Ten participants had a threshold of ≥40 dB HL (up to 75 dB), at frequencies of 3 kHz, 4 kHz and/or 6 kHz. Although these frequencies are outside the main speech frequencies, higher thresholds at high frequencies have been associated with brain changes (e.g. Eckert, Cute, Vaden, Kuchinsky, & Dubno, 2012; Mudar & Husain, 2016). Thus, an extended best ear PTA (i.e., the ear with the lowest averaged thresholds at 0.25 to 6 kHz) was computed and used in all statistical analyses as a covariate. Finally, self-perception of hearing abilities was measured using the questionnaire "*Entendez-vous bien*" (EVB) (Caron, 2007). As detailed in Table 1, participants' scores were on average of 8.88 ± 5.81/60, indicating that, on average, participants did not perceive important difficulties related to their hearing abilities.

Table 1
Participants' characteristics.

	Experiment 1 (N = 21; 11F)			Experiment 2 (N = 34; 17F)		
	M	SD	Range	M	SD	Range
Age	53.33	20.71	20 – 85	57.35	14.69	32–79
Handedness	66.90	70.60	−100–100	93.97	9.60	70–100
Number of languages [a]	2	0.77	1 – 3	2.26	0.86	1 – 4
Education (years)	14.24	4.16	0 – 21	15.38	2.76	6 – 23
GDS (/30) [b]	3.02	2.65	0 – 10	1.97	3.85	0 – 22
GAI (/20) [c]	2.38	3.61	0 – 12	1.14	2.52	0 – 13
MoCA (/30) [d]	27.00	2.26	23–30	27.38	2.61	21–30
EVB (/62) [e]	8.88	5.81	2 – 26	5.76	3.90	0 – 18
Best ear PTA [f]	15.61	11.10	1.43 – 34.29	16.23	10.33	1.25 – 36.88

Note. N = number of participants; F = number of female participants; M = Mean; SD = standard deviation; PTA = pure tone average (in dB HL). [a] Number of languages spoken, including French. [b] Geriatric Depression scale (30 questions). A score of 11 or more indicates possible depression. [c] Geriatric Anxiety Inventory (20 questions). A score of 10 or more indicates possible anxiety disorder. [d] Montreal Cognitive Assessment (12 questions). A score of 25 or less indicates possible mild cognitive impairment. [e] "*Entendez-vous bien*" (15 questions). This is an informal evaluation of a person's perceived hearing abilities. A consultation in audiology is recommended for those with scores ≥ 15. [f] Best ear pure tone thresholds at 0.25, 0.5, 1, 2, 3, 4, 6 kHz (+8 kHz for Experiment 2).

2.1.3. Speech perception in noise (SPiN)

2.1.3.1. Stimuli. To evaluate SPiN, syllable pairs were presented as part of an auditory discrimination task. The syllables were selected from SyllabO+, a corpus and database of spoken Quebec French (Bédard et al., 2017). The syllables had a consonant–vowel-consonant (CVC) structure, which is one of the most common structures in Quebec French (Bédard et al., 2017). The syllables were recorded in a double-walled soundproof room (Génie Audio. Inc, Canada) by a native male speaker of Québec French trained in linguistics. Each syllable was recorded through a high-quality headset microphone (Microflex Beta 53, Shure, USA) connected to a USB audio interface (Quartet, Apogee Electronics, USA). The recording was made using sound Studio Software (v 4.8, Felt Tip Software, USA) for Mac, at a sampling rate of 44 kHz with 16-bit digitization. Each syllable was repeated three to five times at the end of the sentence "Maintenant je dis ___" (Now I say ____) to ensure a constant descending (neutral) intonation. The amplitude of the stimuli was normalized using Praat v 6.0 (Boersma & Weenink, 2011) at a mean intensity of 70 dB SPL. Syllables were segmented using Praat and the best pairs were selected by two judges. The selected syllables were listened to and transcribed into phonetic alphabet by a linguistics student to further validate.

A multi-talker's babble noise (Perrin & Grimault, 2005) that consisted of four native French speakers (two males and two females) aged 25 to 45 years reading newspapers was used as background noise. The noise file was normalized at different intensities to examine the impact of different signal-to-noise ratios (SNR; Pressure $_{\text{signal}}$ / Pressure $_{\text{noise}}$: −5 dB, −3 dB, 0 dB, 3 dB, 5 dB SPL) on speech perception. These SNRs were selected based on the results of previous studies using speech tasks in a babble noise that suggested that speech reception thresholds (i.e., the SNR at witch performance reaches 50%) is around −2 dB SPL in young adults and −1 dB SPL in older adults (e.g. Anderson, Parbery-Clark, Yi, & Kraus, 2011; S. Kim, Frisina, Mapes, Hickman, & Frisina, 2006; Schoof & Rosen, 2016).

384 syllables were used to create 192 pairs that differed only by one feature (voice, manner or place of articulation) on the first (50%) or the last consonant (50%) (e.g., /niz/ /miz/ or /sit/ /sid/). 192 identical pairs were also included (e.g., /maz/ /maz/). The final list of stimuli included six runs of 64 pairs (32 identical and 32 different), each representing a noise condition (one in quiet and five in various SNRs from −5 dB to + 5 dB). A two-way ANOVA was performed to ensure that the average spoken frequency of the pairs was not significatively different across experimental conditions. Within-subject factors were the noise condition and the type of pair (identical or different). The results of this analysis showed no effect of noise condition ($F_{(5,372)} = 0.04$, $p = 0.999$) or type of pair ($F_{(1,372)} = 0.03$, $p = 0.860$), and no interaction ($F_{(5.372)} = 0.03$, $p = 0.999$). The final syllables had an average duration of 496 (SD = 48) ms. A similar ANOVA was performed on average syllable duration to ensure that the average duration of the pairs was not significatively different across experimental conditions. No effect of noise condition ($F_{(5,372)} = 1.12$, $p = 0.352$), type of pair ($F_{(1,372)} = 0.05$, $p = 0.823$), and no interaction ($F_{(5,372)} = 0.80$, $p = 0.552$), reached significance. All experiment files and stimuli are publicly available on the Scholar Portal Dataverse (https://doi.org/10.5683/SP2/9H31OY).

2.1.3.2. Procedure. Participants were sitting approximately 50 cm away from a 27-inch monitor (HP, E272q) in a double-walled soundproof room (Génie Audio. Inc, Canada). Stimuli were first played binaurally through high quality headphones (DT 770 Pro, Beyer Dynamic Inc., DE), to adjust intensity to a comfortable level. Participants were presented with pairs of syllables binaurally in quiet or in one of the following SNR conditions: −5 dB, −3 dB, 0 dB, 3 dB, 5 dB SPL. Each run took approximately 5 min to complete. At the beginning of each trial, a fixation cross appeared simultaneously with the speech noise in the middle of a black background. The syllables were presented 1000 ms after the presentation of the noise and were followed by a green question mark presented visually on the monitor. The syllables were presented at an interval of 300 ms to minimize working memory demands. Participants were asked to indicate as quickly as possible whether pairs of syllables were identical or different, by pressing a button on a response box (RB-840, Cedrus Corporation, USA) with their right hand (one button for "identical" and a different button for "different"). Trials were terminated immediately following a response or after three seconds if no response was provided. The inter-trial interval was 1000 ms. The stimuli and responses were presented using Presentation Software 20.0 (Neuro-Behavioural Systems Inc., USA) on a desktop computer running Windows 10, 64 bits. 16 pairs of syllables (8 different, 8 identical) were presented in four noise conditions (quiet, SNR + 5, SNR 0, SNR-5) as practice trials prior to the main task. The main task included 64 pairs (32 identical, 32 different) presented for each noise condition, for a total of 384 pairs.

2.1.4. Analyses

Statistical analyses were performed using R (version 3.4) with a two-tailed significance level set at 0.05 (the r scripts for the main analyses are available on the Scholar portal Dataverse (https://doi.org/10.5683/SP2/9H31OY). The dependent variables were accuracy, calculated as the percentage of correct answers, and reaction time (RT).

2.1.4.1. Age and noise effects on SPiN performance. To determine whether age and noise level affect performance, linear mixed model (LMM) analyses were computed, with age as a continuous between-subject independent variable and noise level as a within-subject factor (SNR −5, SNR −3, SNR 0, SNR +3, SNR +5), separately for accuracy and RT.

As part of the model selection process, different models were tested to verify if the inclusion of hearing (best ear PTA) and/or cognition (MoCA score) as covariates improved model fit. Models with or without SNR as a random slope were also tested. Participants were always included as a random factor in the model (random intercept). The model with the best overall fit (i.e., with the lowest akaike information criterion) was selected. The final model for accuracy included no covariates and no random slope. The final model for reaction times included PTA and a random slope.

The normality of the residuals and the homogeneity of the variances were visually assessed for each dependent variable (accuracy, RT) in each noise condition using Q-Q plots and histograms. The silent condition showed non-normal distribution of the accuracy score residuals; it was thus excluded in the final accuracy analyses. All dependent variables were linearly distributed as assessed using Q-Q plots. To ensure that the statistical model did not suffer from collinearity issues, the variance inflation factors (VIF) were calculated for each independent variable (Harrison et al., 2018; Zuur, Ieno, & Elphick, 2010). All factors had a VIF value ≤3, which indicates the absence of a collinearity issue (Zuur et al., 2010). We calculated semi-partial correlations R^2_β as estimates of the effect size for all predictors (Edwards, Muller, Wolfinger, Qaqish, & Schabenberger, 2008).

2.1.4.2. Age and phonetic contrast effects on SPiN performance. An additional, exploratory analysis was computed to examine whether the difficulty level was similar across the different types of phonetic contrasts (voice, manner and place of articulation). For this analysis, performance scores (accuracy, RT) were computed separately for each phonetic contrast, across all noise conditions. LMM were computed to determine the effects of age (as a continuous variable) and contrast (voice, manner, place) on performance (accuracy, RT), while controlling for hearing (best ear PTA) and cognition (MoCA score). Model selection was based on the same procedures detailed in section 1.1.4.1, but "phonetic contrast" was used as a main independent variable instead of SNR. The final model for accuracy included no covariates and no random slope. The final model for RT included the PTA measure and the random slope for the phonetic contrast.

2.2. Results

2.2.1. Age and noise effects on SPiN performance

Percentages of correct answers ranged from 82.81 to 100% in the quiet condition and from 40.63% to 98.44% across noise conditions. The mean accuracy was 97.32 ± 3.93% (Quiet), 90.10 ± 5.98% (SNR + 5), 84.38 ± 8.30% (SNR + 3), 76.79 ± 11.71% (SNR 0), 73.07 ± 9.16% (SNR −3) and 68.38 ± 10.80% (SNR −5). Complete descriptive statistics are presented as Supplementary Material 2.1.

For accuracy, the LMM analysis (Table 2; Supplementary Material 3.1) revealed a main effect of SNR ($F_{(4,76)} = 58.29$, $p < .001$, $R^2_\beta = 0.75$); responses were more accurate at higher compared to lower SNRs. A main effect of age was also found ($F_{(1, 19)} = 10.68$, $p = .004$, $R^2_\beta = 0.36$). Accuracy was lower in older adults. An interaction between age and SNR was also found ($F_{(4, 76)} = 4.24$, $p = .004$, $R^2_\beta = 0.18$) (Fig. 1). To decompose this interaction, linear regression analyses were computed to examine the effect of age on accuracy for each SNR separately. These analyses revealed that age significantly impacts accuracy in all SNRs (SNR + 5: β = −0.20, SE = 0.05; SNR + 3: β = −0.30, SE = 0.06; SNR 0: β = −0.45, SE = 0.08; SNR −3: β = −0.36, SE = 0.06; SNR −5: β = −0.48, SE = 0.05; all *p*-values were < 0.001). Importantly, the effect size of the model (R^2) increased as SNR decreased (from 0.46 for the SNR +5 to 0.85 for the SNR −5; see Supplementary Material 3.3 for details). For reaction time (RT), the LMM analysis revealed a main effect of SNR ($F_{(4, 76)} = 11.48$, $p < .001$, $R^2_\beta = 0.38$): shorter RT were found at higher compared to lower SNRs. There were no age effects on RT ($F_{(1, 18)} = 0.69$, $p = .418$, $R^2_\beta = 0.04$). However, a main effect of hearing was found ($F_{(1, 18)} = 8.17$, $p = .01$, $R^2_\beta = 0.31$); higher hearing thresholds were associated with longer RT.

2.2.2. Age and phonetic contrast effects on SPiN performance

An additional exploratory analysis was conducted to determine if age effects vary for different phonetic contrasts (place, manner and voice). This analysis was conducted to guide the selection of stimuli for Experiment 2. Prior to running this analysis, the main characteristics of the stimuli for each phonetic contrast were verified (i.e., the distribution of the pairs across different noise conditions, the average duration and the average frequency of the pairs). A chi-square test was run to verify that the number of pairs for each contrast was distributed similarly across all noise conditions. The results demonstrated that the distribution was similar ($\chi^2_{(10)} = 8.70$, $p = .561$). Next, a one-way ANOVA was run to determine if the average duration of the pairs was similar across the different contrasts. The analysis confirmed that duration did not vary as a function of contrast ($F_{(2, 189)} = 1.12$, $p = .329$). Finally, a one-way ANOVA was conducted to determine if the average spoken frequency of the pairs differed across contrasts. Results did not show a significant difference across contrasts ($F_{(2, 189)} = 2.38$, $p = .095$).

Next, the main LMM analysis revealed a main effect of age ($F_{(1,19)} = 28.44$, $p < .001$) and contrast on accuracy ($F_{(2,38)} = 101.89$, $p < .001$), but no interaction ($F_{(2,38)} = 0.36$, $p = .702$) (Supplementary Material 3.4). The results showed that accuracy declines with age (see Supplementary Material 2.2). Post-hoc comparisons revealed differences between all contrasts ($p < .05$), with the lowest accuracy associated with the voice contrast and the highest accuracy associated with the manner contrast. For RT, a main effect of contrast was found ($F_{(2,38)} = 12.14$, $p = <0.001$), but there was no main effect of age ($F_{(1,18)} = 0.636$, $p = .435$). Post-hoc comparisons revealed higher average RT for manner compared to place and voice contrasts ($p < .05$), but no differences between place and voice ($p = .238$). The PTA score did not show a significant effect ($F_{(1,18)} = 0.514$, $p = .651$).

Table 2
LMM analyses on accuracy (% correct) and reaction time (ms) (marginal effects) (Experiment 1).

Variable	Accuracy				Reaction time			
	DF	F	*p*	R^2_β	DF	F	*p*	R^2_β
(Intercept)	1, 76	5537.62	**< 0.001**		1,76	43.77	**< 0.001**	
Age	1, 19	10.68	**0.004**	0.36	1, 18	0.69	0.418	0.04
SNR	4, 76	58.29	**<0.001**	0.75	4, 76	11.48	**<0.001**	0.38
SNR × Age	4, 76	4.24	**0.004**	0.18	4, 76	0.95	0.119	0.05
Hearing					1, 18	8.17	**0.010**	0.31

Note. SNR = signal-to-noise ratio (noise condition); Hearing = Best ear PTA;
Cognition = MoCA score; DF = degrees of freedom; Bold = $p < .05$; R^2_β = semi-partial correlations (estimates of the effect size).

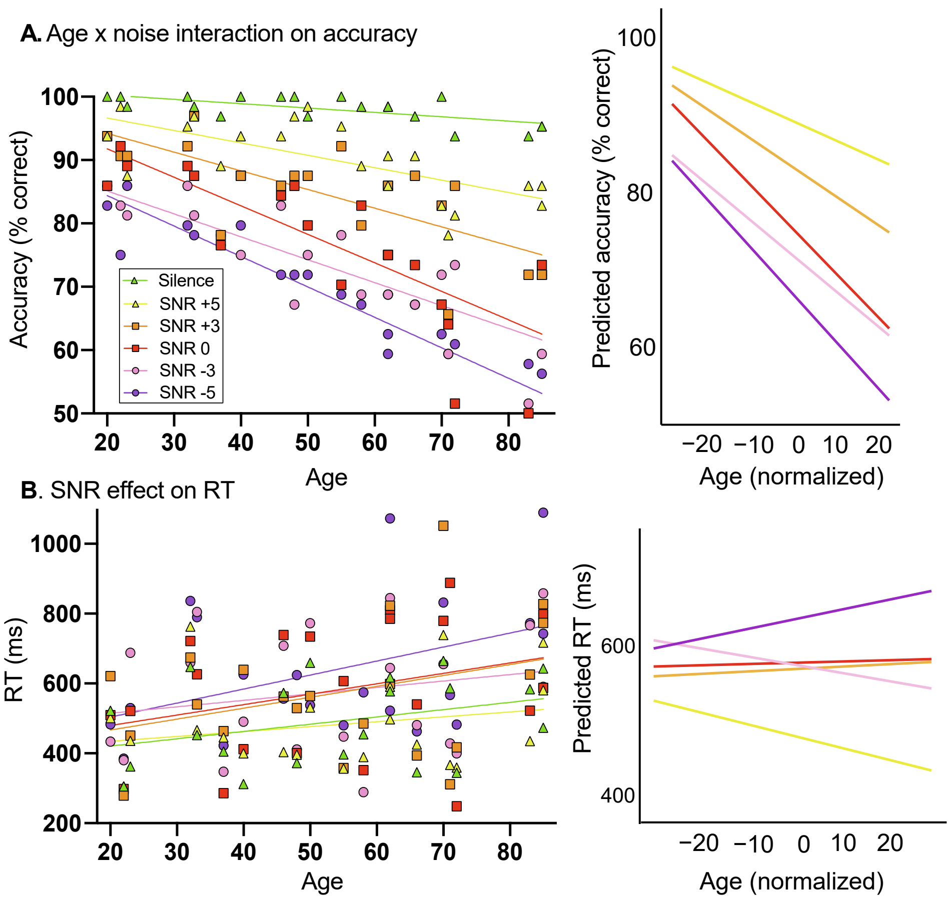

Fig. 1. *Experiment 1 results,* A. The left scatterplot shows the relationship between age and accuracy (% correct answers), separately for each SNR condition (silence, SNR +5 dB, SNR +3 dB, SNR 0 dB, SNR −3 dB, SNR −5 dB). The right scatterplot shows the marginal effects, i.e., the relationship between age and accuracy controlled for all other factors included in the model, separately for each SNR condition. B. The left scatterplot illustrates the relationship between age and RT (ms), separately for each noise condition. The right scatterplot illustrates the marginal effects of age reaction times (ms), separately for each SNR condition.

2.3. *Interim discussion*

As part of Experiment 1, we developed a syllable discrimination task to use in Experiment 2 (TMS). Syllables were used as stimulus materials (as opposed to words or sentences) to minimize the involvement of lexical processes that can mask SPiN deficits. A discrimination task was chosen to minimize the involvement of other cognitive processes, such as speech production or categorization that are present in identification and repetition tasks.

Our main finding is that our task is sensitive to age, even after controlling for one measure of hearing acuity and a measure of overall cognitive level (i.e., MoCA). Although these measures do not account for all of hearing and cognition, this result replicates prior studies showing that hearing and cognition only partially predict SPiN performance (e.g. Anderson et al., 2013; Benichov, Cox, Tun, & Wingfield, 2012; Bilodeau-Mercure et al., 2015; Dubno et al., 2008; Frisina & Frisina, 1997; H. Meister et al., 2013; Tremblay et al., 2021; Tremblay et al., 2019), suggesting a more complex etiology. For instance, in a longitudinal study with 256 adult participants, Dubno and colleagues showed that age-related decline in word recognition is steeper than what is predicted by speech audibility reductions alone—a measure of hearing acuity that takes into account the relative influence of each frequency on the speech spectrum (Dubno et al., 2008).

Another important finding is that the strength of the association between age and performance is stronger when intelligibility is low (i.e., lower SNRs), consistent with other studies (e.g. Bilodeau-Mercure et al., 2015; Helfer & Freyman, 2008; Wong et al., 2009). Based on these results, we decided to use the SNR −3 dB in Experiment 2 to avoid ceiling effects in young adults and maximize age differences (β = −0.84), while avoiding floor effects in older adults.

The exploratory analysis of phonetic contrasts revealed no interaction between age and contrast on either accuracy or RT. This suggests that SPiN decline affects perception of consonants with various phonetic properties rather than specific phonetic properties. This result is in line with a study that observed lower syllable identification scores, but similar consonant confusion matrices for hearing impaired compared to normal hearing older adults (Gordon-Salant, 1987). Despite the absence of an age by contrast interaction, the different phonetic contrasts affected accuracy and RT distinctly. The voice contrast was associated with the lowest accuracy, but with the fastest reaction time. A previous study in healthy young adults using one-syllable words presented in noise found that recognition scores were higher for the voice contrasts than for the place or manner of articulation contrasts (Meyer, Dentel, & Meunier, 2013). This inconsistency may be related to the finding that, in the present study, the average spoken frequency of the voice contrast pairs was lower compared to the other contrasts, which could have negatively affected accuracy. However, participants age was also different across the two studies (participants were aged 18–30 years in the Meyer et al. study, compared to 20–85 years in the present study), which could have affected the results. Further studies are needed to determine whether voice contrasts are indeed more difficult to discriminate in noise compared to the manner and place contrasts, for young and older adults. Nevertheless, because the voice contrast was most difficult to discriminate in this study, this contrast was used in Experiment 2.

3. Experiment 2

3.1. Method

3.1.1. Participants

A sample of 34 healthy right-handed healthy native French speakers aged 32–79 years (M = 57.35, SD = 14.69) was recruited through emails sent to the university community and the *Centre intégré universitaire de santé et des services sociaux de la Capitale-Nationale*, posts on the lab website (www.speechneurolab.ca) and Facebook page (https://www.facebook.com/speechneurolab/) and flyers distributed in various institutions, including shops and retirement homes throughout Québec City, as well as from the laboratory participant database (n = 18). Handedness was assessed using the Edinburgh Handedness Inventory (Oldfield, 1971). Participants reported normal or corrected-to-normal vision, no history of language, neurological or psychiatric disorder, no hearing aids or cochlear implant, and no contraindication to MRI or TMS (Wassermann, 1998). The French version of the Montreal Cognitive assessment (MoCA v8) (Nasreddine et al., 2005) was used to evaluate general cognitive level. The scores, which ranged from 21 to 30 (M = 27.39; SD = 2.61), were used as a covariate in all analyses. The French version of the Geriatric Depression Scale (Yesavage et al., 1982) and the Geriatric Anxiety Inventory (Pachana et al., 2007) were used to assess depression and anxiety symptoms. One participant had GDS and GAI scores over the cut-off. Participants' characteristics are presented in table 1. All participants gave their informed consent and received a monetary compensation. The study was approved by the *Comité d'éthique de la recherche sectoriel en neurosciences et santé mentale, Institut Universitaire en Santé Mentale de Québec* (#1495-2018).

Our sample size was based on two studies that applied rTMS to the PMv or STS in young adults and successfully induced accuracy changes during a phonological task (Kennedy-Higgins et al., 2020; Meister et al., 2007). In the first study, comparing performance in a sentence repetition task pre-and post 10 Hz STS rTMS revealed a large effect size (d = 0.91). In the second study, comparing performance in a syllable identification task pre-and post 1 Hz PMv rTMS revealed a medium effect size (d = 0.78). The projected sample size, with a two-tailed 5% type 1 error rate and 80% power, was 10 to 15 participants. Our sample of 34 was thus adequate to detect performance improvement.

3.1.2. Procedures

All procedures took place in a double-walled soundproof room. The active motor threshold (aMT) was determined, and three TMS sessions (two experimental and one baseline (sham)) were performed, each followed by a syllable decision task in noise. The duration of the experiment was 2.5 to 3 h, including breaks (Fig. 2).

3.1.2.1. Hearing assessment. Hearing was measured with pure tone audiometry following a procedure similar to the one described in Experiment 1, for the following frequencies: 0.25, 0.50, 1, 2, 4, 6 and 8 kHz. An additional frequency (8 kHz) was measured so that the overall PTA would better reflect common hearing loss at higher frequencies in older adults (e.g. Chao & Chen, 2009; Pedersen, Rosenhall, & Møller, 1989), and because some studies have shown a correlation between audiometric thresholds at 4–8 kHz and SPiN performance (e.g. Holmes & Griffiths, 2019). PTAs of speech-related frequencies (0.5, 1, 2 kHz) were ≤35 dB HL for each participant in each ear. One participant had thresholds of 40 dB HL in the left ear and 45 dB HL in the right ear at 0.5 kHz. 16 participants had a threshold ≥40 dB SPL at higher frequencies (3–8 kHz). The thresholds are shown in Supplementary Material 1. To

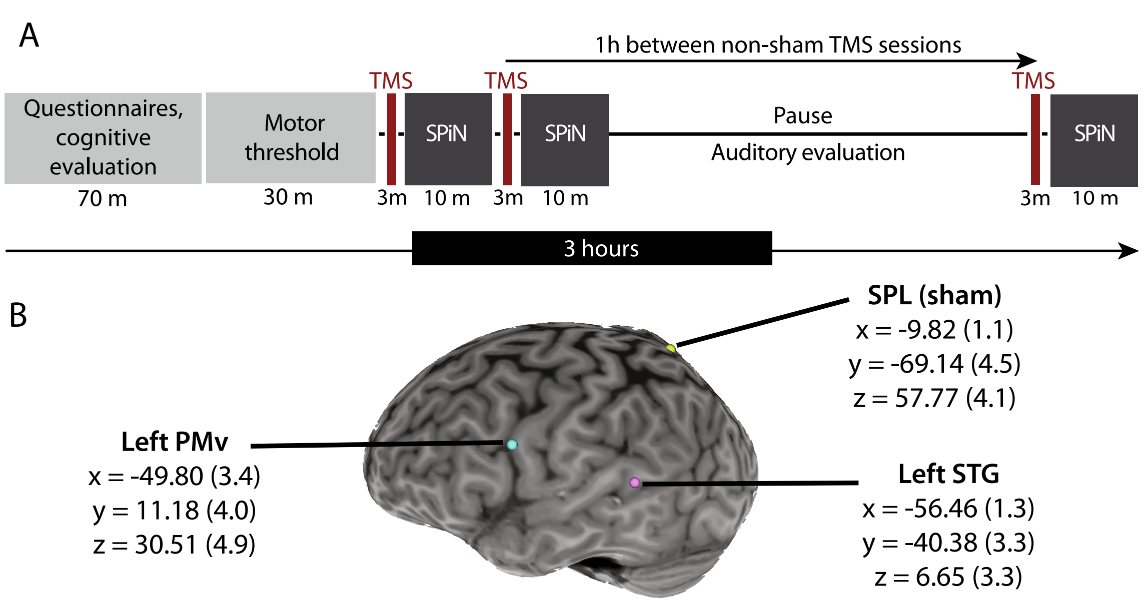

Fig. 2. *Experiment 2 design,* Panel A illustrates an example of the experimental design in which the sham stimulation is administered first. Stimulation order was not the same for all participants. Panel B illustrates the average stimulation sites *(left PMv, left STG, SPL)* across participants, with the corresponding average MNI coordinates (x, y, z) and standard deviations (in parentheses).

control for peripheral hearing, the best ear PTA (i.e., the average threshold from 0.25 to 8 kHz of the ear with the lowest average) was computed and used in all statistical analyses as a covariate. Finally, self-perception of hearing abilities was measured using the questionnaire "*Entendez-vous bien*" (EVB) (Caron, 2007). As detailed in Table 1, participants' scores were on average of 5.57 ± 3.9/60, indicating that, on average, participants did not perceive important difficulties related to their hearing abilities. The descriptive statistics for the best ear PTA are provided in Table 1.

3.1.2.2. SPiN: Stimuli and task. 367 unique syllables were used to create 216 pairs of syllables that were divided into 3 runs. Syllables within a pair differed only in terms of voicing of the first or final consonant. The voiced consonant appeared on the first syllable of the pair during 50% of the trials. The syllables were not repeated within a run. The final stimuli consisted of 3 runs of 144 pairs (72 identical and 72 different pairs presented at an SNR of −3 dB SPL. In each run, 14 pairs (7 different and 7 identical pairs) were repeated to measure response reliability. The repeated pairs were not included in the main analyses.

To ensure that syllable pairs were comparable across runs, a two-way ANOVA was conducted on the average syllable frequency for each pair, with type of pair (different—identical) and run (1,2,3) as within-subject factors. The analysis revealed no significant effect of run ($F_{(2,426)} = 0.01$; $p = .995$), type ($F_{(1,426)} = 0.01$; $p = .938$), and no run × type interaction ($F_{(2,426)} = 0.01$; $p = .988$). The same results were obtained with syllable duration as dependent variable (run: $F_{(2,426)} = 0.09$; $p = .911$; type: $F_{(1,426)} = 0.22$; $p = .643$; run × type: $F_{(2,426)} = 0.373$; $p = 0.689$). 28 pairs were presented as part of a short practice session prior to the main experiment. The three experimental runs (each corresponding to a TMS session) lasted 7 min each. The task was identical to the one described in Experiment 1. Prior to the main task, participants were asked to listen carefully to a one-minute recording of syllables with a CVC structure to familiarize them with the stimuli. These syllables were different from the syllables used in the main task.

3.1.2.3. Transcranial magnetic stimulation. T_1-weighted structural MRI images were acquired on a separate day at the Clinic IRM Québec in Quebec City using an Achieva 3.0 T TX MR scanner, (Philips Healthcare, Netherlands) equipped with a 15-channel head coil (matrix: 256 mm × 256 mm, field of view: 80 × 80, 181 slices, 1 mm^3, no gap). For 18 participants, the MRI images were acquired as part of previous projects and the images were recovered from the laboratory's databank BACH (#360-2014). These MRI images were acquired one to four years prior to the experiment (M = 1.92 years, SD = 0.91). Skin and brain reconstructions were individually generated using Brainsight 2 (Rogue Research, CA). Four anatomical landmarks were identified to register the position of the head for the neuro-navigating system (tip of the nose, bridge of the noise, left ear and right ear tragus). The PMv was defined as the part of the precentral gyrus that intersects with the precentral sulcus and the posterior part of the inferior frontal sulcus (IFS) (Fig. 2). Previous studies have shown that TMS stimulation on this site during syllable discrimination and categorial decision tasks can modify speech perception performance (Grabski et al., 2013; Sato et al., 2009). The second stimulation site was defined based on coordinates reported in the meta-analysis conducted by Turkeltaub & Coslett (2010). The target is a region that was found to be more activated during speech tasks requiring a decision (i.e., phoneme discrimination or categorization) compared to passive speech listening tasks. The region corresponding to the coordinates of the ALE peak (x = −52; y = −40; z = 2) lied in the posterior part of the superior temporal sulcus (pSTS). For the baseline (sham) condition, a point on the vertex which lied within the left superior parietal lobule was identified.

After successful registration of the participant's head position using the infrared tracking system (Polaris, Northern Digital, CA), the aMT was determined using a single-pulse TMS session with a high-speech magnetic simulator (Rapid[2], Magstim, USA). Surface electrodes were placed on the first dorsal interosseous (FDI) muscle of the right hand, and a ground electrode was placed on the right cubitus just under the elbow. Participants were asked to produce three maximal voluntary contractions (MVC) of the right hand with their thumb placed inside their fist to measure the average motor evoked potentials (MEPs) recorded in the FDI. Single pulses were delivered by a 70 mm figure-of-eight coil held tangentially to the skull, on the hand knob of the left primary motor cortex. The area that elicited maximal MEPs was first identified. The initial intensity (50% of the simulator output) was increased in 5% steps until the amplitude of the MEPs reached at least 200 μV repeatedly. aMT was established as the minimal intensity of the simulator output needed to elicit MEPs at an amplitude of at least 200 μV, on 5 out of 10 consecutive stimulation, when the right FDI was contracted at 20% of MVC, using visual feedback. Because the intensity of the iTBS stimulation was capped at 50% of the stimulator output for safety reasons, and given that the intensity for iTBS is based on aMT (i.e., 80% of aMT), whenever a person's aMT was ≥65%, the intensity for iTBS was fixed at 50% of the stimulator output. This fixed intensity was used for 12 participants. For one participant, a technical problem occurred, and the electrodes could not detect the electrophysiological responses. However, this participant had participated in a previous TMS study (two years prior) in which his motor threshold was determined with the same procedure and the same machine. His threshold in this prior study was 68%, so the intensity was also set at 50% for this person. Across all participants, the intensity of the stimulator ranged from 32 to 50% (M = 45.38; SD = 4.94). The average coordinates (SD) in which the motor threshold was found were x = −40.00 ± 10.3, y = −22.20 ± 5.8, z = 62.25 ± 11.8. The coil was held tangentially to the skull and positioned on each target site (PMv, pSTS, sham) using the tracking system. The head was immobilized manually, and coil displacements were limited (PMv average 0.33 ± 0.25 mm; pSTS average 0.38 ± 0.38 mm).

An intermittent theta-burst (iTBS) paradigm was used to increase cortical excitability (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005). This protocol consists of trains of three rapid pulses, presented at 50 Hz and repeated at a 5 Hz frequency for 2 s, every 10 s, for 190 s (total of 600 pulses). Stimulation was applied at 80% of the aMT (Rossi, Hallett, Rossini, & Pascual-Leone, 2009), with a predetermined maximum of 50% of the stimulator output (physical limitation of the stimulation). The average intensity was 45.38 ± 4.94% (range: 32–50%). The intensity for the baseline (sham) condition was set at 5% of the stimulator output. The SPiN task was administered ten minutes after each iTBS session. This delay allowed enough time for the participant to be installed in front of the computer and reminded of the instructions. The time frame in which the task was performed (10–17 min after the stimulation) was well within the period were iTBS effects have been found (20–30 min) (e.g. Gedankien et al., 2017; Huang et al., 2005). The active stimulation sessions were separated by 1 h to avoid potential accumulation effects (Fig. 2). During that time, participants performed the SPiN task, an auditory screening, and an auditory attention task (not reported here). Participants were not told that there was a pause between active stimulations. The order of stimulation was counterbalanced across participants.

3.1.3. Analyses

For each analysis, the assumptions of linearity, normality, homogeneity of the variances and multicollinearity were verified with the same procedure as in Experiment 1.

3.1.3.1. Age effect on baseline SPiN performance. First, to replicate the age effects that were found in Experiment 1, two separate multiple regression analyses were performed with accuracy (% correct) and RT in the baseline (sham) condition as the dependent variables, and age, MoCA score, best ear PTA and stimulation order as continuous independent variables. Because the three stimulations were applied consecutively on the same day, order was included to control for possible learning effects. Order was divided into 6 categories, each corresponding to a specific protocol (e.g., 0 = sham first, STS second, PMv third; 6 = PMv first, STS second, sham third). The interaction between order and target was also included to control for the possibility that prior TMS effects would interact with subsequent effect; this risk was also minimized by setting a 1-hour break between the two real stimulations.

3.1.3.2. TMS-induced performance enhancement. Next, to examine the effect of age and TMS target on SPiN performance, a linear mixed model (LMM) analysis was performed using r (R Core Team, 2017). For each participant, one average enhancement score was computed for the pSTS and one for the PMv (average experimental performance – average sham performance), for accuracy and RT. LMM analyses were used to compare the average magnitude of the stimulation effect across regions. Age was used as a continuous independent variable and TMS target (pSTS, PMv) was included as categorical within-subject variable.

Different models were tested to determine if the inclusion of hearing (best ear PTA), cognition (MoCA score), stimulation order and performance scores at baseline (i.e., in the sham condition) as covariates improved model fit. Performance in the sham condition was included as a covariate because TBS effects are often subject to large inter-subject variability (e.g. Hinder et al., 2014; López-Alonso, Cheeran, Río-Rodríguez, & Fernández-Del-Olmo, 2014), and because prior studies have shown that initial brain state or baseline performance can influence TMS-induced behavioural changes (e.g. Siebner et al., 2004; Silvanto, Bona, Marelli, & Cattaneo, 2018). To control for a potential interaction between target and order of the stimulation, we also tested whether the model fit improved when the order*target interaction was included. Each model was tested with or without a random slope for TMS target. Participants were always included as a random factor in the model (random intercept). The model with the best overall fit (i.e., with the lowest akaike information criterion) was selected. The final model with the best fit for accuracy included performance at baseline and the interaction between order and target as covariates but no random slope for TMS. The final model for reaction time included all the covariates (MoCA score, best eat PTA, performance after sham, order*target interaction) but no random slope.

Because an effect of sham performance was found on accuracy, an additional, exploratory analysis was conducted. For this analysis, participants were divided in two groups based on their baseline performance (accuracy) (50% with higher performance, 50% with lower performance). To determine if accuracy and RT improved after the real stimulation, one sample t-tests were computed for each group separately, with the average improvement scores (real stimulation—sham) as the main dependent variable, tested against 0.

3.1.3.3. Task reliability. A Cohen's Kappa was computed to determine response reliability in the SPiN task. Responses for the first and second presentation of the 56 repeated pairs across all participants and all trials were included. Missed trials were excluded from this analysis.

3.2. Results

3.2.1. Age effect on SPiN performance

Baseline accuracy ranged from 52.08 to 87.50% (mean = 73.71, SD = 8.17%). Complete descriptive statistics are presented in Supplementary Material 4.1. One data point was excluded from the RT regression analysis because the score was 3 SD away from the mean. The regression analyses conducted on performance after the sham condition showed a main effect of age on accuracy ($\beta = -0.34$, $p < 0.001$), with older age associated with lower accuracy, but no main effect of age on RT ($\beta = 3.94$, $p = .203$). No other effect reached significance (Supplementary Material 5.1).

3.2.2. Age and target effects on performance improvement scores

For the LMM analyses on enhancement scores, one data point (pSTS target only) was removed (the first participant) because the coordinates of the pSTS were slightly modified after this participant. After verification of the outliers, one data point (pSTS target) was excluded from the accuracy analysis only, because the improvement score was three standard deviations away from the mean, leaving 32 data points in the analyses. Two other data points (PMv target only) were missing because two participants did not complete the TMS session for this specific region, leaving 32 data points in the analyses. Mean performance enhancement was of 0.85% (SD = 5.48%) after iTBS over the pSTS, and of 0.98% (SD = 4.56) after iTBS over the PMv.

The marginal effects are presented in Table 3 (also see Supplementary Material 5). For accuracy, the LMM analysis revealed a main effect of target (Fig. 3), with a stronger gain in accuracy after PMv (mean: 0.98%, SD = 4.56) compared to pSTS (mean: 0.85%, SD = 5.48) ($F_{(1, 24)} = 7.19$, $p = 0.013$, $R^2_\beta = 0.22$). A main effect of initial performance was also found ($F_{(1, 25)} = 6.16$, $p = 0.020$, $R^2_\beta = 0.20$): participants with lower performance in the sham condition showed more improvement than participants with a better performance in the sham condition (Fig. 3). No main effect of age and no interaction between age and region were found (Table 3). The effect size for age was small ($F_{(1, 25)} = 1.37$, $R^2_\beta = 0.05$), and medium to large for target ($F_{(1, 24)} = 7.19$, $R^2_\beta = 0.22$) (Cohen, 1992). There was also an interaction between order and target ($F_{(5, 24)} = 3.02$, $p = 0.029$, $R^2_\beta = 0.11$).

For RT, the LMM analysis revealed no main effect of target ($F_{(1, 24)} = 0.003$, $p = 0.955$, $R^2_\beta < 0.01$) or age ($F_{(1, 24)} = 0.07$, $p = 0.800$, $R^2_\beta < 0.01$) and no interaction ($F_{(1, 24)} = 0.52$, $p = 0.479$, $R^2_\beta = 0.02$). However, a main effect of sham performance was found ($F_{(1, 24)} = 23.70$, $p < 0.001$, $R^2_\beta = 0.50$): participants with longer RTs in the sham condition showed more improvement (i.e., stronger RT decreases) after real stimulations (Fig. 3). There was also an interaction between order and target ($F_{(5, 24)} = 10.86$, $p = < 0.001$, $R^2_\beta = 0.31$).

Secondary analyses were computed to describe how TMS improved performance in low and high baseline performers. The descriptive results show that 76% of the low performers (13/17) had an improvement score higher than 0 (averaged across both targets), compared to 41% of the high performers (7/17). One sample t-tests were used to compare improvements scores (averaged for the pSTS and PMv stimulations) against zero, for the high and low performing groups separately. One extreme outlier (i.e., three standard deviations over the mean) was removed from the accuracy analysis in the low-performing groups. The analysis revealed that only the low performers significantly improved from zero after TMS (low performers: M = 2.52%, SD = 3.17; $t_{(15)} = 3.18$, $p = .006$; high performers: M = −0.96%, SD = 4.52; $t_{(16)} = -0.88$, $p = .395$). Both groups showed no significant improvement on RT (low: M = 2.94, SD = 172, $t_{(16)} = 0.07$, $p = .945$; high: M = 12.57, SD = 50.8, $t_{(16)} = 1.02$, $p = .323$).

3.2.3. Task reliability

The average agreement rate between the test and retest trials was 75%. The Cohen's Kappa analysis revealed a moderate agreement between the test and retest trials ($\kappa = 0.519$; $p < .001$; 95% CI = 0.443 to 0.595).

4. Discussion

The objectives of this study were to determine if SPiN performance in young and older adults can be enhanced by excitatory rTMS to two areas involved in processing sublexical speech (i.e., the left pSTS, and the left PMv). To achieve this goal, we created a reliable syllable discrimination task. The results of Experiments 1 show that older adults are less accurate in our syllable discrimination task. In Experiment 2, we found this same age effect on accuracy in the baseline condition, which confirmed that the task was age sensitive. The main findings of Experiment 2 are that, while rTMS can enhance SPiN performance when applied to both

Table 3
Marginal effects for the LMM analyses on accuracy (% correct) and reaction time (ms) (Experiment 2).

Variable	Accuracy				Reaction time			
	DF	F	*p*	R^2_β	DF	F	*p*	R^2_β
(Intercept)	1, 25	5.62	**0.026**		1, 24	6.06	**0.021**	
Age	1, 25	1.37	0.254	0.05	1, 24	0.07	0.800	<0.01
Target	1, 24	7.19	**0.013**	0.22	1, 24	<0.005	0.955	<0.01
Sham performance	1, 25	6.16	**0.020**	0.20	1, 24	23.70	**<0.001**	0.50
Target × Age	1, 24	0.04	0.848	< 0.01	1, 24	0.52	0.479	0.02
Target × Order	5, 24	3.02	**0.029**	0.11	5, 24	10.86	**<0.001**	0.31
Order	5, 25	2.23	0.083	0.31	5, 24	3.32	**0.020**	0.12
Hearing					1, 24	0.03	0.870	<0.01
Cognition					1, 24	3.81	0.063	0.14

Note. DF = Degree of freedom; Bold = $p < .05$; R^2_β = semi-partial correlations.

pSTS and PMv, the effect was stronger for PMv. Further, those with lower performance at baseline showed more TMS-induced performance gain. These results are discussed below.

4.1. Stimulation site affects behavioural outcomes

The main outcome of this study is that TMS to left PMv lead to stronger gain in performance compared to pSTS in a sublexical speech discrimination task performed in noise. The selection of these regions was based on knowledge of their role in SPiN, and prior evidence that TMS over these regions—primarily inhibitory TMS—can induce behavioural changes in healthy young adults. Inhibitory rTMS over the left PMv has been associated with lower performance or changes in cognitive bias during syllable identification, phoneme discrimination and semantic decision tasks (e.g. Grabski et al., 2013; Krieger-Redwood et al., 2013; Meister et al., 2007; Nuttall, Kennedy-Higgins, Devlin, & Adank, 2018; Sato et al., 2009). Although the contribution of the left PMv to speech processing remains debated (Hickok, 2012; Rauschecker & Scott, 2009), a consensus is beginning to emerge suggesting that the motor system contains articulatory representations that are used to make predictions about auditory inputs, which are then compared with the predictions formed in the auditory processing network to facilitate perception (e.g. see Liebenthal & Mottonen, 2018; McGettigan & Tremblay, 2018; Pulvermuller & Fadiga, 2010; Schomers & Pulvermüller, 2016; Skipper, Devlin, & Lametti, 2017). These articulatory predictions could be particularly relevant to disambiguate speech in challenging listening environments, or when the phonological demand is high (e.g. see Arnal & Giraud, 2012; Bever & David, 2010; Davis & Johnsrude, 2007). Engaging the PMv, compared to the pSTS, could thus be more relevant to perform difficult speech perception tasks. The pSTS, in contrast, is known to be sensitive to speech—especially to sub-lexical speech units—and to tasks that require phonological processing (e.g. Hickok, 2012; Skipper, 2014; Turkeltaub & Coslett, 2010; Vaden, Jr., Muftuler, & Hickok, 2010). Inhibitory protocols applied to the left STS have resulted in lower accuracy or slower RT during sentence and syllable repetition tasks, as well as other phonological, semantic and auditory tasks (Beauchamp, Nath, & Pasalar, 2010; Kennedy-Higgins et al., 2020; Krieger-Redwood et al., 2013; I. G. Meister et al., 2007; Murakami et al., 2015). Consistent with the idea of a greater role for articulatory rather than phonological mechanisms to assist during SPiN, a previous study has shown that inhibitory TMS to the PMv leads to a more pronounced performance decline in healthy young adults during a syllable identification task presented with white noise compared to the TMS to the left STG (Meister et al., 2007). The current finding of a greater performance improvement after PMv compared to STS stimulation is also consistent with this view. This result is also consistent with contemporary versions of the motor theories of speech perception, which suggest a significant contribution of the motor system (motor and premotor cortices) to speech processing (e.g. Davis & Johnsrude, 2007; Galantucci, Fowler, & Turvey, 2006; Skipper et al., 2017). Together, the current and prior studies show that non-invasive stimulation over the left PMv and the left pSTS can successfully modulate speech perception. However, the potential indirect effects of stimulating these regions—which are structurally and functionally connected to other networks—remains unknown. Future studies combining electroencephalography recordings to iTBS could help answer this question.

4.2. iTBS enhances SPiN in adults of all ages

An interesting and unexpected finding of this study is that excitatory iTBS affected SPiN performance in an age-independent manner. To our knowledge, the current experiment is one of the firsts to compare performance improvement in a speech task in young and older healthy adults (Panouilleres & Mottonen, 2018; Rufener, Oechslin, Zaehle, & Meyer, 2016). This preliminary study suggests a similar improvement in young and older adults, a finding that has important implications for rehabilitation research and practice.

This finding is in contrast to our hypothesis, which was that iTBS-induced enhancement would decline with age due to the documented reduced capacity for plasticity in the aging brain. Specifically, studies have found reduced LTP-like responses in the motor cortex of older compared to younger individuals (e.g. Bhandari et al., 2016; Fathi et al., 2010; Müller-Dahlhaus, Orekhov, Liu, & Ziemann, 2008; Tang et al., 2019). One study found that listening to speech was associated with a similar increase of activity within the motor representation of the tongue in younger and older adults, measured by EMG following single-pulse TMS, but a significantly smaller increase for older adults with hearing loss (Panouilleres & Mottonen, 2018), suggesting that the motor system might be under-activated in older adults. Contrary to these prior studies, our result suggests a preserved capacity for plasticity within the adult neural speech system.

An alternative hypothesis would have been that, given that the speech network is less efficient in older adults (e.g. Bilodeau-Mercure et al., 2015; Du & Alain, 2016; Peelle et al., 2010; Sheppard et al., 2011; Tremblay et al., 2019; Vaden et al., 2015; Wong et al., 2010; Wong et al., 2009), there could be more room for improvement; thus older adults could be more sensitive to iTBS than younger adults. A previous study including a voice-onset time categorization task has shown results in line with this hypothesis (Rufener et al., 2016). In that study, after transcranial alternating current stimulation (tACS) was applied to the temporal lobes to enhance brain oscillations at 40 Hz, performance was improved in older adults, but decreased in younger adults, suggesting that older participants with more difficulties are more likely to benefit from excitatory neurostimulation paradigms, or, minimally, that neurostimulation affects the young and older brain distinctly. Our results do not support this alternative hypothesis, since age did not influence TMS gains. We additionally calculated semi-partial correlations as an estimate of the effect size for the age predictor on accuracy enhancement. The size effect was small, suggesting that a larger sample might not have revealed significant age differences.

Importantly, our results also revealed the absence of an interaction

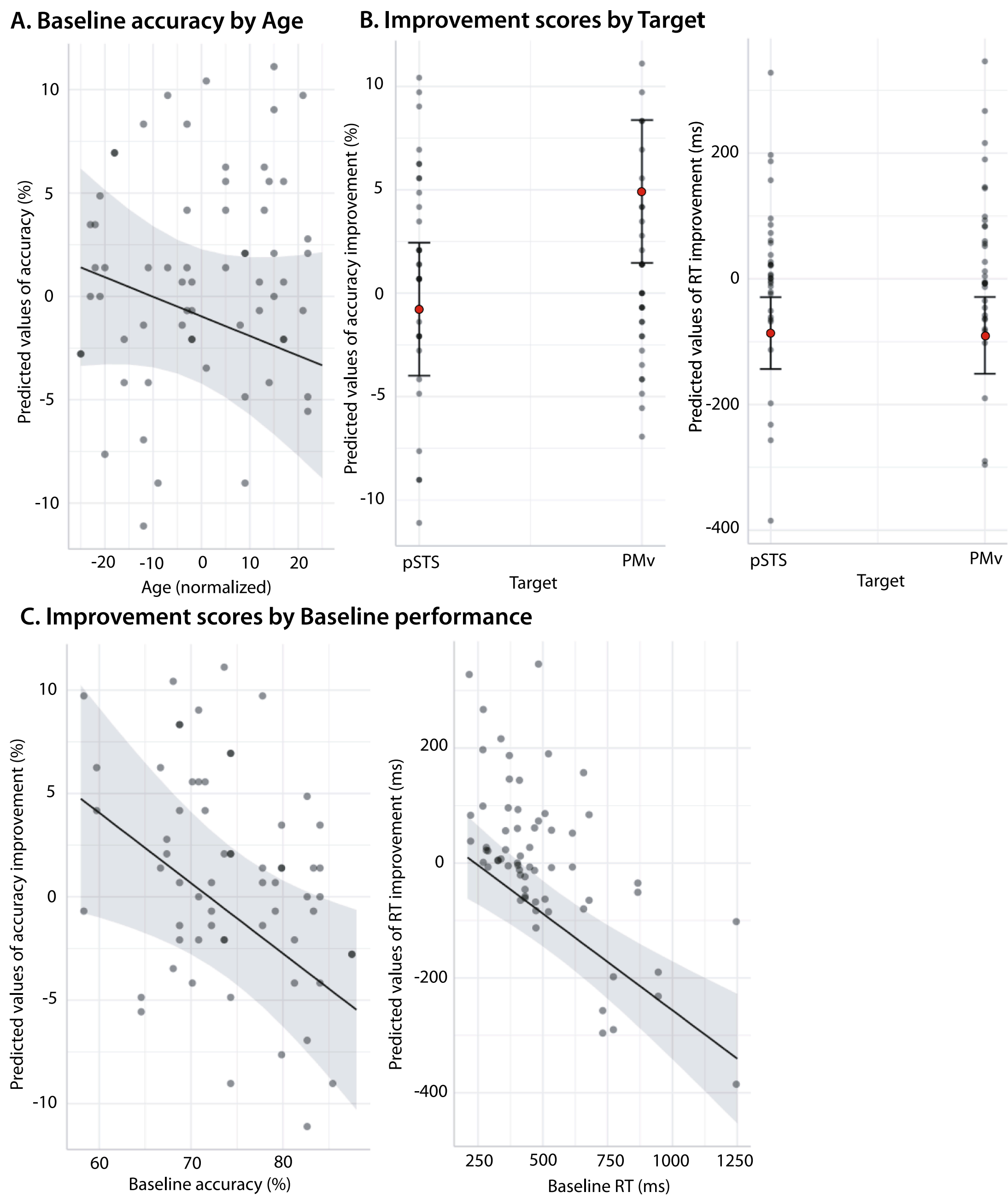

Fig. 3. *Experiment 2 results,* A. Relationship between Age and baseline (sham) accuracy (marginal effect). The scatterplot illustrates the relationship between of age and accuracy (% correct answers) in the baseline condition (sham). The shaded area represents the 95% confidence interval of the regression line. B. Improvement scores (experimental - baseline (sham) performance, separately for accuracy (left) and RT (right). The plots illustrate the marginal effects of target (pSTS, PMv) on accuracy (% correct) and RT (ms) improvement scores (experimental – baseline). The red circles represent the average predicted improvement. The whiskers represent the 95% confidence intervals. C. Relationship between baseline performance and improvement scores. The scatterplot illustrates the predicted relationship between performance in the baseline (sham) condition and improvement in the experimental conditions (experimental – sham), separately for accuracy (left) and RT (right). The shaded areas represent the 95% confidence intervals of the regression lines.

between age and target. The presence of this interaction could have revealed a difference in the functional contribution of the pSTS and PMv to SPiN for young and older adults. A number of neuroimaging studies have shown evidence of structural and functional age-related decline in the superior temporal cortex, as well as the premotor cortex, inferior frontal cortex and other regions (Du & Alain, 2016; Manan et al., 2017; Peelle et al., 2010; Wong et al., 2009), suggesting a global rather than focal change within the speech networks might be responsible for SPiN decline in the elderly, as we recently suggested (Tremblay et al., 2020). Here we hypothesize that the importance of phonological and articulatory processes to SPiN remains similar with aging, although both decline with age. Thus, modulating either region (pSTS, PMv) impacts SPiN performance similarly in young and older adults. It is however possible that iTBS to other regions involved in speech processing or auditory cognition (e.g., the superior temporal gyrus, the inferior parietal lobule or the inferior frontal gyrus) could reveal age differences in the effect of iTBS.

In sum, the present findings suggest that aging does not prevent iTBS-led SPiN improvement, especially when the target site is the left PMv. This result is important, as it opens the door to more studies investigating the use of iTBS in older adults to remediate speech decline as well as other age-related decline.

4.3. iTBS improvements related to initial performance abilities

Although previous iTBS studies have shown faciliatory effects at the group level, the effects of iTBS tend to be heterogeneous (Hinder et al., 2014; López-Alonso et al., 2014). The factors that predict a participant's response to iTBS (and TMS more generally) remain to be identified. Interestingly, our results revealed that improvement scores were sensitive to initial performance level (i.e., performance in the sham condition): participants with longer reaction times and lower accuracy scores showed the most improvement after stimulation of either the pSTS or PMv. Secondary analyses confirmed that lower performers significantly improved their SPiN accuracy, while this was not the case for high performers. This result suggests that the participant's difficulty at the task is a better indicator of TMS response, as opposed to age. This result highlights the importance of considering task difficulty in TMS designs, and in the interpretation of TMS effects. One limit of this experiment was that the average performance improvement across all individuals was small (around 1% increase for accuracy and 135 ms decrease for RT). Although no ceiling effects on accuracy were observed in this experiment (maximal performance was 87.5%), it is possible that presenting the stimuli at a lower SNR could have led to stronger performance improvements. Nevertheless, our results support the potential for iTBS to improve SPiN in adults who experience more difficulties, which is a promising result with important implications for rehabilitation research and practice.

5. Limitations

One potential limitation of this experiment was that TMS sessions were delivered on the same day. While this design has the advantage of eliminating variability related to the participant's health, mood and state of mind during the administration of the tests, the TMS effects could have interacted (i.e., spillover effect). We controlled for this by 1) adding a delay of at least 60 min after a real stimulation before performing a second session (e.g. Chung, Hill, Rogasch, Hoy, & Fitzgerald, 2016), 2) counterbalancing the order of the regions stimulated, and 3) adding the order of the stimulation (e.g., order 1 = PMv, Vertex, pSTS, order 2 = Vertex, PMv, pSTS,…) as well as the order * target interaction to the statistical model used for the analyses. The results revealed a main effect of order on RT improvement scores as well as a target * order interaction on both accuracy and RT improvement scores. This suggests that the order of the stimulation impacted improvement scores. Marginal effects for the interactions are illustrated in Supplementary Materials (Figure 6). A tendency for greater performance improvement can be observed for the region that is stimulated later in the protocol. While it is not impossible that stimulation effects were cumulative (i.e., spillover effect), another potential explanation is a training effect. Crucially, however, the main effect of Target on accuracy remained significant after controlling for this effect in the statistical model.

Another limitation of this study is the use of averaged individual data points to analyze enhancement scores using LMM analyses (i.e., ANOVA-style analysis), which could have underpowered the analyses.

6. Conclusion

Our TMS study is the first to show that hugely prevalent age-related SPiN difficulties can be reduced by enhancing cortical excitability within the speech-processing network, especially when targeting the left PMv. Importantly, initial performance—not age—was the main driving factor for TMS-induced performance improvement. This study paves the way for the development of approaches to enhance speech processing using neurostimulation methods. Future studies are needed to determine how to maximize performance TMS-induced benefits and how to ensure lasting stimulation effects that could allow older adults to enjoy social interactions and actively participate in their communities for more years.

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CRediT authorship contribution statement

Valérie Brisson: Conceptualization, Methodology, Investigation, Project administration, Formal analysis, Visualization, Writing - original draft, Data curation. **Pascale Tremblay:** Conceptualization, Funding acquisition, Methodology, Investigation, Supervision, Resources, Project administration, Writing - review & editing, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bandl.2021.105009.

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