1-1-2022

# A neural signature of regularity in sound is reduced in older adults

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# A Neural Signature of Regularity in Sound is Reduced in Older Adults

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26

27                                            Abstract

28   Sensitivity to repetitions in sound amplitude and frequency is crucial for sound perception. As with other

29   aspects of sound processing, sensitivity to such patterns may change with age, and may help explain

30   some age-related changes in hearing such as segregating speech from background sound. We recorded

31   magnetoencephalography to characterize differences in the processing of sound patterns between

32   younger and older adults. We presented tone sequences that either contained a pattern (made of a

33   repeated set of tones) or did not contain a pattern. We show that auditory cortex in older, compared to

34   younger, adults is hyperresponsive to sound onsets, but that sustained neural activity in auditory cortex,

35   indexing the processing of a sound pattern, is reduced. Hence, the sensitivity of neural populations in

36   auditory cortex fundamentally differs between younger and older individuals, overresponding to sound

37   onsets, while underresponding to patterns in sounds. This may help to explain some age-related changes

38   in hearing such as increased sensitivity to distracting sounds and difficulties tracking speech in the

39   presence of other sound.

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47   Keywords: magnetoencephalography, regularity processing, aging, hyperactivity, auditory pattern;

48   hearing loss

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50                                             Introduction

51    Many adults aged 50 or older experience challenges understanding speech in the presence of

52    background sound (Pichora-Fuller, 2003; Pichora-Fuller et al., 2016), but the underlying neural sources

53    contributing to such deficits are not fully understood. Speech contains rich, regular patterns, such as

54    quasi-regular amplitude fluctuations at 4–5 Hz (Rosen, 1992; Varnet et al., 2017), and perceptual

55    sensitivity to sound pattern and speech-in-noise perception correlate with each other (Holmes and

56    Griffiths, 2019), suggesting shared mechanisms (Holmes et al., 2021). The perceptual processes through

57    which sensitivity to such patterns may contribute to speech perception likely include the segregation of

58    unique, concurrent sound streams (Schröger, 2005, 2007; Snyder and Alain, 2007; Winkler et al., 2009;

59    Bendixen, 2014) and the recognition and prediction of relevant sound features (Jones and Boltz, 1989;

60    Nobre et al., 2007; Henry and Herrmann, 2014; Nobre and van Ede, 2018). The current study is

61    concerned with the degree to which patterns are represented in the brains of older individuals and

62    whether neural sensitivity to patterns differs between younger and older adults.

63         The detection of a regular pattern in a sound is associated with an increase in a sustained, low-

64    frequency, DC power offset in cortical electroencephalography (EEG) and magnetoencephalography

65    (MEG) recordings (Barascud et al., 2016; Southwell et al., 2017; Herrmann and Johnsrude, 2018b).

66    Sustained neural activity manifests as soon as a pattern, such as repetition of a set of tones, is present

67    (Southwell et al., 2017; Herrmann and Johnsrude, 2018b; Southwell and Chait, 2018; Herrmann et al.,

68    2021). It also manifests for spectrally coherent chord fluctuations (Teki et al., 2016), complex sounds

69    made of isochronous tone sequences (Sohoglu and Chait, 2016), and repeated amplitude or frequency

70    modulations (Gutschalk et al., 2002; Ross et al., 2002; Herrmann and Johnsrude, 2018b; Herrmann et

71    al., 2019). Sustained activity increases with the degree of regularity of a pattern, for example, with

72    increasingly coherent frequency modulation in sounds (Teki et al., 2016; Herrmann and Johnsrude,

73    2018b). The magnitude of sustained activity is thought to reflect prediction-related processes (Heilbron

74    and Chait, 2018).

75         Accumulating evidence suggests that aging and age-related hearing loss are associated with a

76    loss of inhibition throughout the auditory pathway following peripheral decline (Caspary et al., 2008;

77    Rabang et al., 2012; Ouellet and de Villers-Sidani, 2014). This may render neurons in the aged auditory

78    system hyperresponsive to sound (Hughes et al., 2010; Alain et al., 2012; Bidelman et al., 2014; Overton

79    and Recanzone, 2016; Presacco et al., 2016b, a; Herrmann et al., 2018) and shorten the time it takes for

80    neurons to regain responsiveness following adaptation to sound (de Villers-Sidani et al., 2010; Mishra et

81    al., 2014; Herrmann et al., 2016; Herrmann et al., 2019). Changes in inhibition, responsivity, and

82    adaptation associated with aging and hearing loss likely affect all aspects of hearing (Herrmann and

83    Butler, 2021), including sensitivity to sound patterns.

84          Some initial evidence suggests that sustained neural activity may be reduced in older compared

85    to younger people. Many years ago, Pfefferbaum and colleagues (1979) demonstrated that sustained

86    activity elicited by a short sine tone is reduced for older compared to younger adults. More recent work

87    indicates that younger individuals exhibit pattern-related sustained activity in response to amplitude-

88    modulated sounds, whereas older adults do not appear to, although the difference between these

89    groups was not significant (Herrmann et al., 2019). Another study yielded data suggestive of reduced

90    sustained activity in older compared to younger people in response to repeated tone sequences (Al Jaja

91    et al., 2020), but stimulus parameters differed between age groups in this paper. A controlled

92    experiment with sufficient power is thus required to elucidate whether sustained neural activity to

93    regular sound patterns differs between younger and older people.

94          Previous work investigating sustained neural activity in older adults has utilized low-density

95    electroencephalography (EEG; fewer than 20 electrodes; Pfefferbaum et al., 1979; Herrmann et al.,

96    2019; Al Jaja et al., 2020). This type of EEG is not very well suited for the localization of neural sources

97    generating scalp-recorded signals. Magnetoencephalography typically allows for better source

98    reconstruction than EEG, because magnetic fields are less distorted by the skull and scalp than the EEG-

99    recorded electric potentials (Hämäläinen et al., 1993; Hämäläinen and Hari, 2002). Previous MEG source

100   localizations in younger adults suggest that the auditory cortex underlies sustained neural activity (Hari

101   et al., 1980; Pantev et al., 1994; Pantev et al., 1996; Gutschalk et al., 2002; Ross et al., 2002; Okamoto

102   et al., 2011; Barascud et al., 2016; Teki et al., 2016) and that additional brain regions in parietal cortex,

103   frontal cortex, and hippocampus may also contribute (Tiitinen et al., 2012; Barascud et al., 2016; Teki et

104   al., 2016). Whether the neural sources of pattern-related sustained activity differ between younger and

105   older adults is unknown.

106         In the current study we recorded MEG from younger and older adults while they listened to

107   sound sequences. Sequences were made by taking pure tones at different frequencies and either

108  repeating the same small set of these in the same order, so that a regular pattern is heard, or by

109  presenting them pseudo-randomly so that no pattern is present. We investigate whether sustained

110  neural activity to a regular sound pattern differs between younger and older individuals. We also

111  examine whether auditory cortex is generally more responsive to sound in older, compared to younger

112  adults, as has been previously reported (Bidelman et al., 2014; Herrmann et al., 2018).


## Methods and Materials

*Participants*

115  Twenty-six younger (mean: 26.7 years; range: 21–33 years; 13 males and 13 females) and twenty-five

116  older adults (mean: 63.9 years; range: 53–73 years; 11 males and 14 females) participated in the current

117  study. Participants reported no neurological disease or hearing impairment, gave written informed

118  consent, and were paid for their participation. None of the participants wore a hearing aid or reported

119  having been prescribed a hearing aid. We focused on a typical sample of older individuals, allowing for

120  the possibility of some degree of hearing impairment. The study was conducted in two sessions on

121  separate days (range: 1-43 days apart; median: 7 days apart; no age-group difference: $t_{49} = 0.99$, p =

122  0.327). The study was conducted in accordance with the Declaration of Helsinki, the Canadian Tri-Council

123  Policy Statement on Ethical Conduct for Research Involving Humans (TCPS2-2014), and was approved

124  by the local Nonmedical Research Ethics Board of the University of Western Ontario (protocol ID:

125  106570).

*Hearing assessment and hearing thresholds*

127  Pure-tone audiometric data were acquired for each participant (Figure 1). The pure-tone average

128  hearing threshold (i.e., the mean across the 0.25, 0.5, 1, 2, and 4 kHz frequencies) was larger for older

129  compared to younger adults ($t_{49} = 7.79$, $p = 4 \times 10^{-10}$, $r_e = 0.744$; Figure 1, right). This indicates a mild-to-

130  moderate hearing impairment in many of the older adults and is consistent with the high-frequency

131  sloping loss characteristic of age-related hearing impairment (Moore, 2007; Plack, 2014) as well as with

132  previous electrophysiological studies that investigated differences in sound processing between younger

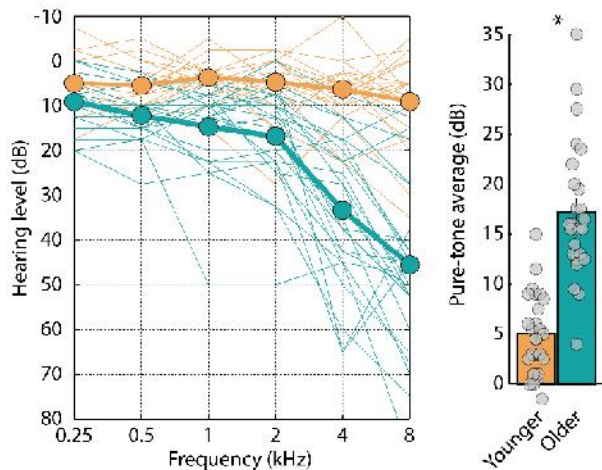133  and older adults (Presacco et al., 2016b; Herrmann et al., 2018).

Figure 1: Audiograms and pure-tone average hearing threshold. Left: Audiograms for each participant. Thin lines reflect individual participant data. Thick lines reflect the mean across participants. Right: Pure-tone average hearing threshold (mean across 0.25, 0.5, 1, 2, and 4 kHz). Gray dots reflect the threshold for individuals.

134    For each participant, we measured the hearing threshold (i.e., sensation level [SL]) using a

135    method-of-limits procedure (Herrmann and Johnsrude, 2018a; Herrmann et al., 2019) as a reference

136    threshold in MATLAB software for sound presentation. Participants listened to a 12-s pure tone with a

137    frequency of 1323 Hz that changed continuously in intensity at a rate of 5 dB/s (either decreased [i.e.,

138    starting at suprathreshold levels] or increased [i.e., starting at subthreshold levels]). Participants pressed

139    a button when they could no longer hear the tone (intensity decrease) or when they started to hear the

140    tone (intensity increase); the sound stopped after button press. The sound intensity at the time of the

141    button press was noted for 6 decreasing sounds and 6 increasing sounds (decreasing and increasing

142    sounds alternated), and these were averaged to determine the individual hearing threshold. The mean

143    hearing threshold was elevated for older compared to younger adults ($t_{49}$ = 5.208, p = 3.7×10$^{-6}$, $r_e$ =

144    0.597), which was expected given the audiograms (Figure 1).

145    All acoustic stimuli described below were presented at 55 dB above each individual's hearing

146    threshold – that is, at 55 dB sensation level – in order to control for audibility across age groups. Because

147    hearing thresholds were on average elevated for older compared to younger adults, sounds during the

148    MEG recordings were on average more intense in sound-pressure level (SPL) in older compared to

149    younger individuals. Higher sound levels can lead to larger brain responses to sound onsets (Picton et

150    al., 1974; Picton et al., 1978; Pfefferbaum et al., 1979; Polich et al., 1988; Schadow et al., 2007; Herrmann

151    et al., 2018) as well as for sustained activity (Picton et al., 1978; Pfefferbaum et al., 1979). Because we

152    hypothesized that regularity-related sustained activity would be smaller for older compared to younger

153    adults, playing sounds at a higher level for older adults only works against this hypothesis. Presenting

154    sounds at sensation level was thus favorable in the current study. However, a higher sound level for

155    older compared to younger adults could bias statistical analyses for investigations of age-related

156    hyperresponsivity to sound, for which we expect larger responses in older compared to younger adults.

157    Hence, for these analyses, we also used a subgroup of 14 participants of each age group for which the

158    hearing threshold – and thus the sound level of the acoustic presentation – did not differ ($t_{26}$ = 0.956, p

159    = 0.348, $r_e$ = 0.184; younger mean [±sd]: -94.16 dB ±1.39, older mean [±sd]: -93.36 dB ±2.65[1]) to confirm

160    our results.

161    *Acoustic stimulation and procedure*

162    Acoustic stimuli were 4-s long sequences that each consisted of 96 pure-tone pips arranged in twelve

163    sets of eight tones each (see also Barascud et al., 2016; Herrmann and Johnsrude, 2018b; Southwell and

164    Chait, 2018; Herrmann et al., 2021). Each set had a duration of 0.333 s. Pips were 0.0417 s in duration

165    with attack and decay times of 0.007 s, and no gap between tones, or sets. The frequency of each tone

166    was one of 150 possible values between 700 and 2500 Hz (logarithmically spaced).

167          Acoustic stimuli were presented in two conditions, 'Pattern-Absent' and 'Pattern-Present', which

168    occurred with equal probability (50%). In the 'Pattern-Absent' condition, tones with different

169    frequencies were presented in pseudo-random order without a pattern, whereas in the 'Pattern-

170    Present' condition, tones transitioned from random to a regular pattern 1 s (3 sets) after sound onset.

171    For the 'Pattern-Absent' condition, 8 new frequency values were randomly selected for each of the 12

172    sets (Figure 2, top). In the 'Pattern-Present' condition, 8 new frequency values were randomly selected

173    for each of the first 3 sets (0–1 s; similar to 'Pattern-Absent'), and then 8 new random frequency values

174    were selected and repeated in the same order for the remaining 9 sets, thereby creating a regular

175    pattern (Figure 2, bottom). These conditions are similar to the sounds used in previous studies that

176    investigated sustained neural activity (Barascud et al., 2016; Southwell et al., 2017; Herrmann and

177    Johnsrude, 2018b).

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[1] The dB values are derived from MATLAB. More negative values reflect softer sound intensities. These dB values can be interpreted relative to each other, whereas the absolute magnitude is related to hardware and software conditions, such as sound card, transducers, and MATLAB internal settings.
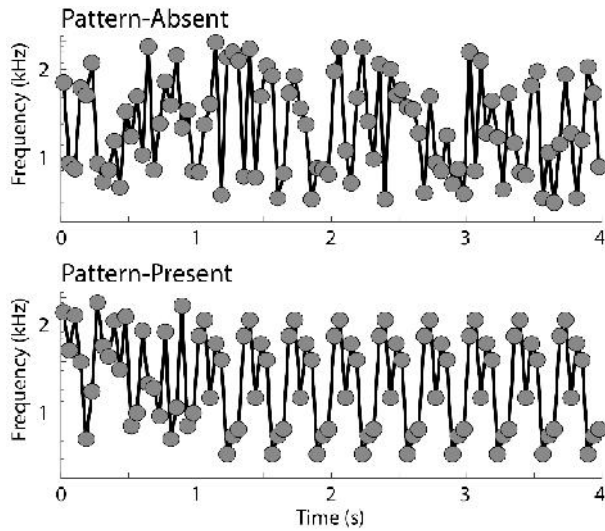
Figure 2: Schematic of acoustic stimulation for 'Pattern-Absent' and 'Pattern-Present' conditions. Sound frequency is displayed on the y-axis and dots reflect the sound frequency of individual tones of the tone sequence.

178    In each of the two recording sessions, participants were presented with one 12-min block of

179    stimulation as part of recording sessions for an additional project not presented here. The data from the

180    experimental blocks reported here were recorded in the beginning of the recording sessions.

181    Participants listened passively to sixty 4-s sound sequences of each condition per session, while watching

182    a muted movie of their choice, with subtitles, that was projected into the electromagnetically shielded

183    room via a mirror system. Trials of the Pattern-Absent and the Pattern-Present conditions were

184    presented pseudo-randomly throughout the block, such that each condition could occur maximally

185    three times in direct succession. Across both sessions, participants listened to 120 trials per condition.

186    Trials were separated by a 2-s inter-stimulus interval.

187    *Magnetoencephalographic recordings and initial preprocessing*

188    Magnetoencephalographic data were recorded using a 306-channel Neuromag Vectorview MEG

189    (MEGIN Oy, Helsinki, Finland; sampling rate: 1000 Hz, online filter: DC–330 Hz) at the Max Planck

190    Institute for Human Cognitive and Brain Sciences in Leipzig, Germany. Data were recorded in an

191    electromagnetically shielded room (AK3b, Vacuumschmelze, Hanau, Germany). The signal space

192    separation (SSS) method (maxfilter© version 2.2.15; default parameter setting $L_{in} = 8$; $L_{out} = 3$) was used

193    to suppress external interference, interpolate bad channels, and transform each person's individual data

194    to the sensor space of the first block of the first session to ensure the data are in a common space (Taulu

195    et al., 2004; Taulu et al., 2005).

196 *Combination of magnetometer and gradiometer channels*

197 The Vectorview MEG device records magnetic fields using 102 magnetometers and 204 gradiometers in

198 102 locations distributed around the head. In order to account for all data that were recorded, we

199 combined signals from magnetometer and gradiometer channels (Herrmann et al., 2018).

200 Magnetometers and gradiometer differ in their configuration, such that magnetometers measure

201 magnetic fields in Tesla (T), while gradiometers (a coupled pair of magnetometers) measure differences

202 in the same magnetic fields over a distance of 0.0168 m in Tesla per meter (T/m). The combination of

203 channel types requires accounting for their different units. We transformed all channels into

204 magnetometer channels, because such a model only requires a linear interpolation that results in the

205 same unit for all channels. To this end, we applied the following transformation matrix to each of the

206 102 sensor triplets (i.e., one triplet comprises two gradiometer channels and one magnetometer

207 channel):

208 $$X_{S_i} = S \times X$$

209 where X consists of a 3 × n matrix (with n being the number of data samples over time). The three

210 rows of X refer to the two gradiometers and one magnetometer (i.e., one triplet). S refers to a 5 × 3

211 scaling matrix with the following elements:

212 $$S = \begin{matrix} -0.0084 & 0 & 1 \\ 0.0084 & 0 & 1 \\ 0 & -0.0084 & 1 \\ 0 & 0.0084 & 1 \\ 0 & 0 & 1 \end{matrix}$$

213 The value 0.0084 reflects half of the distance between the two gradiometer loops measured in

214 meters, and the transformation constitutes a linear approximation of the magnetic field at each of the

215 triplets. The transformation replaces the sensor triplet by a sensor quintet of magnetometers. The

216 columns of S refer to the triplet of two gradiometers and one magnetometer and the rows of S refer to

217 the resulting five magnetometers. This procedure resulted in signals from 510 magnetometer channels

218 centered on and around 102 locations around a participant's head (Herrmann et al., 2018).

219 *Preprocessing of magnetoencephalographic data*

220 Data were high-pass filtered (0.7 Hz; 2391 points, Hann window), low-pass filtered (20.3 Hz, 119 points,

221 Kaiser window), down-sampled to 250 Hz, and divided into 6-s long epochs time-locked to sound onset

222    (from 1 s before to 5 s after sound onset). Independent components analysis (runica method, Makeig et

223    al., 1996; logistic infomax algorithm, Bell and Sejnowski, 1995; Fieldtrip implementation, v20130727,

224    Oostenveld et al., 2011) was used to identify and remove activity related to blinks, horizontal eye

225    movements, muscle activity, and noisy channels. Identification of components related to these non-

226    brain activities was done manually through visual inspection of component time courses, topographies,

227    and frequency spectra by BH. Epochs in which a signal change larger than 8 Picotesla (pT) occurred in

228    any channel were excluded. The remaining data were used to investigate age differences in evoked

229    responses to the onset of the sounds.

230         In order to investigate the sustained neural activity, the same pipeline was computed a second

231    time, with the exception that high-pass filtering was omitted. Omission of the high-pass filter is necessary

232    to investigate sustained activity, because the response is a very low-frequency signal reflecting a DC shift

233    (Barascud et al., 2016; Southwell et al., 2017; Herrmann and Johnsrude, 2018b). Activity related to

234    blinks, horizontal eye movements, muscle activity, and noisy channels was removed using the identified

235    components from the high-pass filtered data. Epochs in which a signal change larger than 8 pT occurred

236    in any channel were excluded.

237    *Analysis of responses to sound onset*

238    High-pass filtered data were used to investigate whether neural responses to the onset of the sounds

239    differed between age groups. This analysis aimed to test whether the auditory cortex of older adults is

240    hyperresponsive to sound, consistent with reduced inhibition (Caspary et al., 2008; Hughes et al., 2010;

241    Juarez-Salinas et al., 2010). Data from the Pattern-Absent and Pattern-Present conditions were averaged

242    because both conditions were identical for the first second of the sound. Epochs ranging from -0.15 s to

243    0.5 s time-locked to sound onset were extracted. Absolute values were calculated for signals of each

244    channel (because magnetic fields have opposite polarities in directions perpendicular to the tangential

245    orientation aspect of the underlying neural source). The mean signal from the pre-stimulus period (-0.15

246    to 0 s) was subtracted from the signal at each time point, separately for each channel (baseline

247    correction). Responses were averaged across channels, resulting in one response time course per

248    participant.

249         For the statistical analysis, differences in response amplitude between age groups were assessed

250    for each time point using independent samples t-tests. False discovery rate was used to account for

251    multiple comparisons (Benjamini and Hochberg, 1995; Genovese et al., 2002). We confirmed the results

252    with two independent samples t-tests that contrasted the amplitudes of the M50 (0.03–0.06 s) and

253    M100 (0.09–0.13 s) between age groups, which have previously been shown to differ between younger

254    and older adults (Sörös et al., 2009; Alain et al., 2012; Herrmann et al., 2018).

255    *Analysis of pattern-related sustained activity*

256    Non-high-pass filtered data were used to investigate whether sustained neural activity associated with

257    a pattern in sounds differs between age groups. The 6-s epochs (-1 to 5 s, time-locked to sound onset)

258    were used. Absolute values were calculated for signals of each channel and the mean signal from the

259    pre-stimulus period (-1 to 0 s) was subtracted from the signal at each time point, separately for each

260    channel (baseline correction). Responses were averaged across channels, resulting in one response time

261    course per condition and per participant.

262         Statistical analysis focused on responses during the last half of each stimulus: the 2–4 s time

263    window. By 2 s, the repeating set of tones would have been presented 3 times (2 full repetitions) in the

264    Pattern-Present condition (Barascud et al., 2016; Teki et al., 2016; Herrmann and Johnsrude, 2018b). An

265    ANOVA with the within-subjects factor Condition (Pattern-Absent, Pattern-Present) and the between-

266    subjects factor Age Group (younger, older) was calculated.

267    *Source localization of magnetoencephalographic data*

268    Anatomically constrained source localization was used to localize the sources underlying the neural

269    activity in sensor space. Individual T1-weighted MR images (3T Magnetom Trio, Siemens AG, Germany)

270    were available for each participant. The MR images were used to construct inner skull surfaces (volume

271    conductor) and mid-gray matter cortical surfaces (source model; using Freesurfer and MNE software;

272    https://surfer.nmr.mgh.harvard.edu/;   http://www.martinos.org/mne/).   The   MR   and   the   MEG

273    coordinate systems were co-registered using MNE software, which included an automated and iterative

274    procedure that fitted the >300 digitized head surface points (Polhemus FASTRAK 3D digitizer) to the MR

275    reconstructed head surface (Besl and McKay, 1992). The inner skull was extracted from the MR images

276    using MNE software and used to calculated lead fields using the boundary element model as

277    implemented in Fieldtrip software (Nolte, 2003). Inverse solutions were calculated using the sLORETA

278    method (Pascual-Marqui, 2002). Neural activity was spatially smoothed across the surface using an

279   approximation to a 6-mm FWHM Gaussian kernel (Han et al., 2006). Individual cortical representations

280   were transformed to a common coordinate system (fsaverage standard brain; Fischl et al., 1999b).

281   Workbench software (v1.4.2; https://www.humanconnectome.org/) was used for visualization of source

282   localizations morphed to the pial cortical surface of the fsaverage standard brain (Fischl et al., 1999a).

283   Source localizations were calculated for onset responses and for sustained neural activity. In order to

284   visualize and analyze pattern-related auditory cortex activity, we averaged source-localization

285   amplitudes across regions of the superior temporal plane (A1, A4, PBelt, MBelt, and LBelt) using the

286   brain parcelations of the Human Connectome Project (Glasser et al., 2016).

287   *Effect sizes*

288   Effect sizes are provided as partial $\eta^2$ for ANOVAs and as $r_e$ ($r_{equivalent}$) for t-tests (Rosenthal and Rubin,

289   2003). $r_e$ is equivalent to the square root of partial $\eta^2$ for ANOVAs.

290   *Data availability*

291   This study was not pre-registered. MEG data in BIDS format (Pernet et al., 2019) are available at

292   https://figshare.com/projects/A_Neural_Signature_of_Regularity_in_Sound_is_Reduced_in_Older_Ad

293   ults/121803.

294                                                   Results

295   *Responses to sound onset are enhanced in older compared to younger adults*

296   Figure 3A displays the neural response time courses elicited by the onset of the sounds. Responses were

297   larger in older compared to younger adults in the M50 and M100 time windows (black line in Figure 3A,

298   FDR-thresholded). Figure 3B/C shows the mean amplitudes and topographical distributions for the M50

299   and M100 time windows. Larger neural responses for older compared to younger adults were also

300   observed for the subgroups of 14 participants per age group for which hearing thresholds – and thus

301   sound-presentation levels – did not differ (M50: $t_{26}$ = 4.812, p = 5.5×10$^{-5}$, $r_e$ = 0.686; M100: $t_{26}$ = 4.257,

302   p = 2.3×10$^{-4}$, $r_e$ = 0.641; all participants: M50: $t_{49}$ = 6.295, p = 8.2×10$^{-8}$, $r_e$ = 0.669; M100: $t_{49}$ = 4.015, p =

303   2×10$^{-4}$, $r_e$ = 0.497). Finally, regressions calculated to predict M50 or M100 responses from age group,

304   while including sensation-level threshold and audiometric pure-tone average as co-variates, also

305 revealed an effect of age group (M50: $t_{47}$ = 3.199, p = 0.002; M100: $t_{47}$ = 2.571, p = 0.013). These results

306 demonstrate that even when sound level does not differ between younger and older adults, older adults

307 exhibit hyperresponsiveness to sound. There was no age difference for the M200 (0.16–0.22 s: $t_{49}$ =

308 1.088, p = 0.282). Source localizations show activity in superior temporal cortex, including auditory

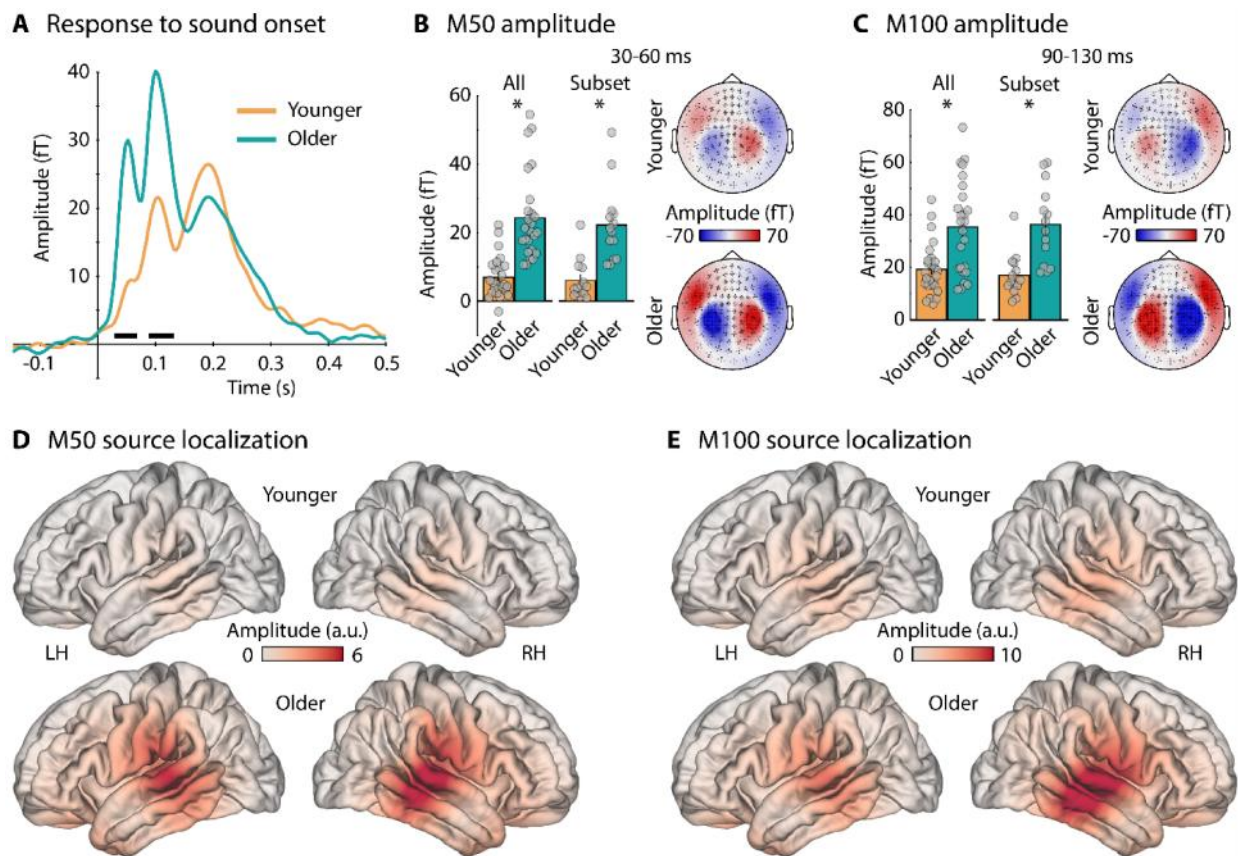309 cortex, underlying M50 and M100 responses in both age groups (Figure 3D/E).



Figure 3: Neural responses to the onset of sounds. A: Time courses of neural activity (root-mean square amplitude, averaged across all channels). The black line indicates a significant difference between age groups (FDR-thresholded). B: Mean activity and topographies for the M50 time window (30–60 ms) for all participants and the subset of 14 participants for which sound level did not differ between younger and older adults. C: Mean activity and topographies for the M50 time window (90–130 ms) for all participants and the subset of 14 participants. D: Source localization for the M50 time window. E: Source localization for the M100 time window. *p ≤ 0.05

310 *Pattern-related sustained activity is reduced in older compared to younger adults*

311 Figure 4A and B show response time courses and topographical distributions for the Pattern-Absent and

312 the Pattern-Present condition for both age groups. The ANOVA for the 2-4 s time window revealed a

313 Condition × Age Group interaction ($F_{1,49}$ = 9.839, p = 0.003, $n_p^2$ = 0.167; also significant for the subset of

314  participants for which sound level did not differ: $F_{1,26} = 6.792$, p = 0.015, $n_p^2 = 0.207$): While both age

315  groups show larger sustained activity for the Pattern-Present compared to the Pattern-Absent condition

316  (younger: $F_{1,25} = 49.692$, p ≤ $1×10^{-6}$, $n_p^2 = 0.665$; older: $F_{1,24} = 6.287$, p = 0.019, $n_p^2 = 0.208$), this difference

317  was larger in younger compared to older adults (Figure 4C). There was no difference between age groups

318  for the Pattern-Absent condition ($F_{1,49} = 0.528$, p = 0.471, $n_p^2 = 0.011$). The main effect of Condition ($F_{1,49}$

319  = 45.185, p ≤ $1×10^{-6}$, $n_p^2 = 0.48$) and the main effect of Age Group ($F_{1,49} = 6.994$, p = 0.011, $n_p^2 = 0.125$)

320  were also significant.

321        In order to explore the relation between the response to sound onset and the regularity-related

322  sustained activity effects in older adults, we calculated the difference between the Pattern-Present and

323  the Pattern-Absent conditions and correlated the response difference with the M50 and M100

324  responses to sound onset. Correlations were not significant (M50: r = -0.075, p = 0.722, df = 23; M100:

325  r = -0.011, p = 0.957, df = 23). However, the relation between hyperactivity in response to sound and

326  hearing loss is non-linear (Qiu et al., 2000; Salvi et al., 2017; Herrmann and Butler, 2021), and we may

327  thus not expect a linear correlation between hyperactivity and changes in regularity-related sustained
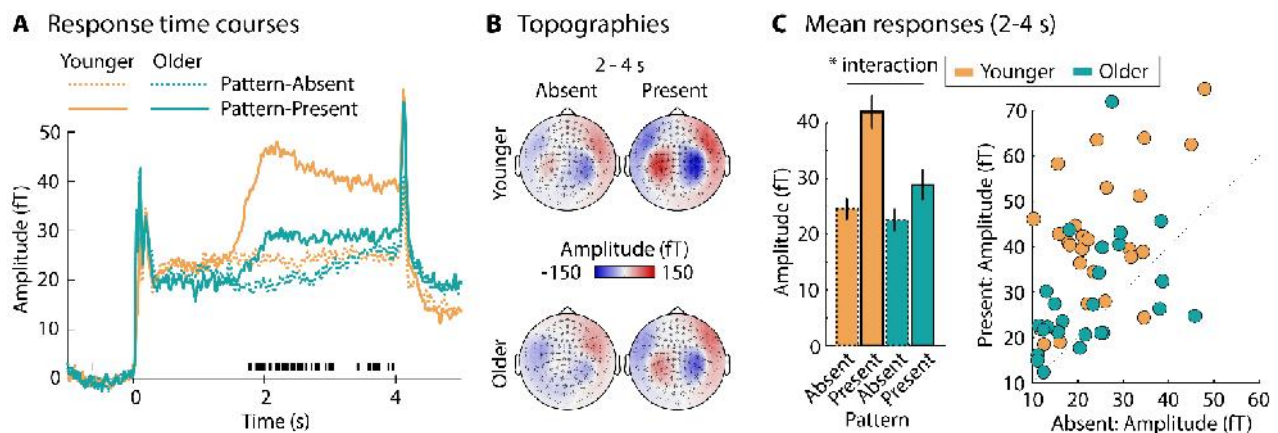
328  activity in older adults.



Figure 4: Pattern-related sustained activity. A: Response time courses (root-mean square amplitude, averaged across all channels). The black markings below the time courses indicate the time points at which the Condition × Age Group interaction was significant (FDR-thresholded). B: Topographical distributions for each condition and age group for the 2-4 s time window. C: Mean responses in the 2-4 s time window. Bar graphs reflect the mean across participants. Error bars are the standard error of the mean. Data points for each participant are shown on the right. Data points above the diagonal (dashed line) reflect a larger response for the Pattern-Present compared to the Pattern-Absent condition.

329

330    Source localizations revealed that the strongest activity associated with pattern-related

331    sustained activity was present in superior temporal cortex and auditory cortex (Figure 5A). Indeed, we

332    observed the same interaction for auditory cortex activity ($F_{1,49}$ = 10.68, p = 0.002, $n_p^2$ = 0.179; Figure

333    5B/C; for the subset of participants: $F_{1,26}$ = 7.299, p = 0.012, $n_p^2$ = 0.219) that we observed in sensor

334    space (Figure 4C), such that the increase in sustained activity for the Pattern-Present compared to the

335    Pattern-Absent condition was significant for both age groups (younger: $F_{1,25}$ = 50.652, p ≤ 1×10$^{-6}$, $n_p^2$ =

336    0.670; older: $F_{1,24}$ = 23.833, p = 5.6×10$^{-5}$, $n_p^2$ = 0.498), with a larger difference in younger compared to

337    older adults. In contrast to the sensor space data of sustained activity, sustained activity in auditory

338    cortex elicited by the Pattern-Absent condition was also larger for younger compared to older adults

339    ($F_{1,49}$ = 4.704, p = 0.035, $n_p^2$ = 0.088; Figure 5B/C), consistent with observations of reduced sustained

340    activity to a sine tone in older compared to younger adults (Pfefferbaum et al., 1979). Main effects of

341    Condition ($F_{1,49}$ = 73.205, p ≤ 1×10$^{-6}$, $n_p^2$ = 0.599) and Age Group ($F_{1,49}$ = 10.176, p = 0.002, $n_p^2$ = 0.172)
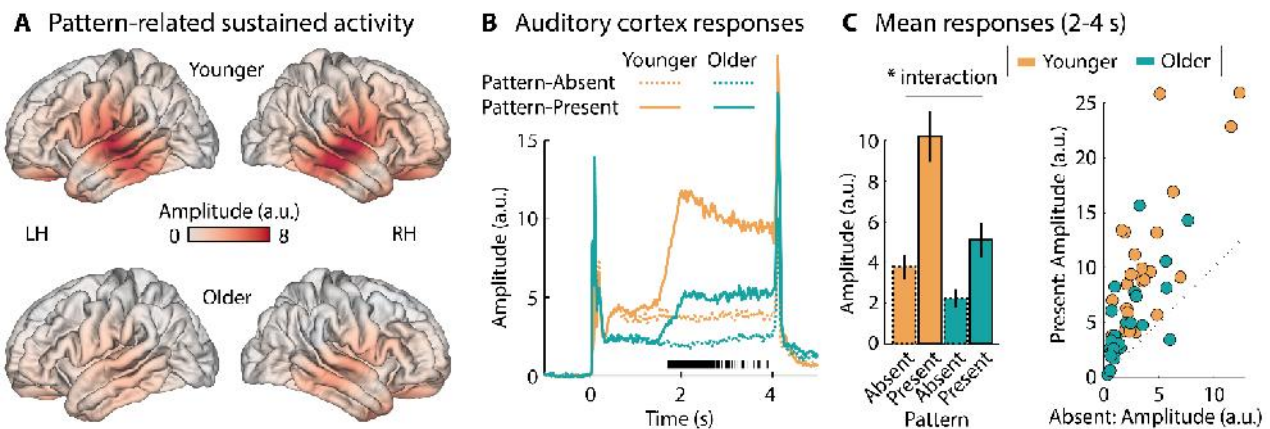
342    were also significant.



Figure 5: Source localization of pattern-evoked sustained activity. A: Source localization of pattern-related sustained activity (difference between Pattern-Present and Pattern-Absent conditions). B: Response time courses from auditory cortex. The black markings below the time courses indicate the time points at which the Condition × Age Group interaction was significant (FDR-thresholded). C: Mean auditory cortex responses in the 2-4 s time window. Bar graphs reflect the mean across participants. Error bars are the standard error of the mean. Data points for each participant are shown on the right. Data points above the diagonal (dashed line) reflect a larger response for the Pattern-Present compared to the Pattern-Absent condition.

343                                                    Discussion

344    The current magnetoencephalography study investigated age-related differences in auditory cortical

345    responsivity to sound onsets and to the presence of a pattern in sounds. We showed that older adults

346    elicit larger responses in auditory cortex to sound onsets compared to younger adults. This response

347    enhancement indicates that auditory cortex of older adults is hyperresponsive to sound. Despite this

348    age-related hyperresponsiveness, sustained neural activity in auditory cortex to sound patterns was

349    diminished in older compared to younger people. Our results suggest that neural responses in auditory

350    cortex are fundamentally altered in older adults such that cortical activity overrepresents sound onsets,

351    whereas it underrepresents temporally coherent structure in sounds.

352    *Hyperresponsiveness of auditory cortex in older adults*

353    We demonstrated that neural responses in the M50 and M100 time window following sound onset are

354    enhanced in older compared to younger adults (Figure 3A-C). We localized the M50 and M100 responses

355    to auditory cortex (Figure 3D/E; consistent with previous work Pantev et al., 1988; Maess et al., 2007;

356    Okamoto and Kakigi, 2014; Herrmann et al., 2018), suggesting that auditory cortex in older adults is

357    hyperresponsive. This is in line with a growing literature showing that neural responses to sound onsets

358    are enhanced in older compared to younger adults (Ross and Tremblay, 2009; Sörös et al., 2009; Lister

359    et al., 2011; Alain et al., 2012; Bidelman et al., 2014; Herrmann et al., 2016; Herrmann and Johnsrude,

360    2018a). Similar observations have been made for aged monkeys (Juarez-Salinas et al., 2010; Recanzone,

361    2018) and aged rodents (Hughes et al., 2010), as well as for non-human mammals whose auditory

362    periphery was damaged through high-intensity sound exposure (Popelár et al., 1987; Syka et al., 1994;

363    Schormans et al., 2019) or ototoxic drugs (Qiu et al., 2000; for detailed reviews see Auerbach et al., 2014;

364    Zhao et al., 2016; Salvi et al., 2017; Herrmann and Butler, 2021).

365         Hyperresponsiveness to sound is thought to result from hyperexcitable neural circuits due to a

366    loss of inhibition in the auditory system following peripheral decline (Caspary et al., 2008; Takesian et

367    al., 2012). The functional role of the loss of inhibition and hyperexcitability is still debated (Zhao et al.,

368    2016; Asokan et al., 2018; Herrmann and Butler, 2021), but likely includes homeostatic processes to

369    regulate excitation (Caspary et al., 2008; Zhao et al., 2016) and a state of increased plasticity that enables

370    cortical reorganization (Cisneros-Franco et al., 2018; Cisneros-Franco and de Villers-Sidani, 2019). A

371    balanced level of excitation and inhibition is crucial for neural function (Wehr and Zador, 2003; Silver,

372    2010; Isaacson and Scanziani, 2011), and the fact that we observed hyperresponsiveness to sound in

373    older compared to younger adults suggests that neural function of auditory cortex was altered in our

374    sample of older individuals. Hyperresponsivity to sharp attacks in sound may underlie increased

375    distractibility by irrelevant sounds in older compared to younger adults (Parmentier and Andrés, 2010)

376    and difficulties comprehending speech in the presence of an interfering, modulated background masker

377    (Millman et al., 2017; Goossens et al., 2018).

378    *Pattern-related activity is reduced in older compared to younger adults*

379    In order to investigate whether neural sensitivity to a pattern in sounds differs between younger and

380    older adults, we presented sounds that either contained a pattern (made of a sequence of a repeated

381    set of pure tones at different frequencies) or did not contain a pattern (made of a sequence of tones at

382    pseudo-randomly selected frequencies; Figure 2). For both younger and older adults, we observed that

383    sustained neural activity increased after the onset of a sound pattern relative to sounds without a

384    pattern. Previous work in younger adults has revealed similar increases in sustained activity for different

385    types of patterns, including tone sequences such as those we have utilized here (Gutschalk et al., 2002;

386    Ross et al., 2002; Keceli et al., 2012; Barascud et al., 2016; Sohoglu and Chait, 2016; Teki et al., 2016;

387    Southwell et al., 2017; Herrmann and Johnsrude, 2018b; Southwell and Chait, 2018; Herrmann et al.,

388    2019; Herrmann et al., 2021).

389           We showed that sustained neural activity to a pattern in sounds is reduced in older compared to

390    younger adults. Hence, although neural responses to the onset of sound was enhanced in older adults,

391    neural sensitivity to a pattern in sounds was reduced. Diminished sustained activity for older compared

392    to younger adults is consistent with previous indications of an age-related reduction in sustained activity

393    for short (<1 s) pure tones (Pfefferbaum et al., 1979), amplitude modulations (Herrmann et al., 2019),

394    and repeated patterns in tone sequences (Al Jaja et al., 2020). However, low statistical reliability and

395    differences in stimulus parameters between age groups did not allow drawing firm conclusions from the

396    latter two studies. Our results demonstrate clearly that pattern-related sustained activity indeed is

397    reduced in older adults.

398           Sensitivity to sound patterns is crucial for a variety of auditory functions, enabling a listener to

399    segregate concurrent sound streams (Schröger, 2005, 2007; Snyder and Alain, 2007; Winkler et al., 2009;

400    Bendixen, 2014) and recognize and predict relevant sounds (Jones and Boltz, 1989; Nobre et al., 2007;

Henry and Herrmann, 2014; Nobre and van Ede, 2018). By demonstrating a correlation between perceptual sensitivity to sound patterns and speech comprehension abilities (Holmes and Griffiths, 2019) and common substrates in auditory cortex (Holmes et al., 2021), previous work further indicates a functional relation or common underlying mechanism between the processing of regularities in sounds and speech comprehension. A reduction in sustained activity may thus indicate that sound patterns are processed less well in neural circuits in older compared to younger adults, which may, in part, explain the challenges older adults experience comprehending speech in the presence of background sound.

Participants in the current study were presented with sound sequences while they watched a muted, subtitled movie of their choice. Participants' attention was thus directed away from the sounds, although the degree of attentional focus was not experimentally constrained in the current study. Previous work indicates that regularity-related sustained activity can be increased if participants perform a difficult sound-related task relative to a difficult visual task (Herrmann and Johnsrude, 2018b). Larger regularity-related sustained activity in younger compared to older adults could thus be, in part, the result of younger adults attending more to the sounds than older adults. However, younger and older adults typically enjoy watching a movie in such experiments, where they are not required to perform a sound-related task. Moreover, larger responses in older compared to younger adults to the sound onset may indicate greater attentional capture by sounds for older adults (see also Parmentier and Andrés, 2010; Weeks and Hasher, 2014), but regularity-related sustained activity was decreased for them. Differences in the degree of attention to sounds between age groups are thus unlikely to explain the observed differences in regularity-related sustained activity.

The current source localizations suggest that auditory cortex is the main source underlying pattern-related sustained activity in both younger and older adults (Figure 5A). Previous work in younger individuals also indicated that auditory cortex underlies sustained neural activity (Hari et al., 1980; Pantev et al., 1994; Pantev et al., 1996; Gutschalk et al., 2002; Ross et al., 2002; Gutschalk et al., 2004; Gutschalk et al., 2007; Okamoto et al., 2011; Keceli et al., 2012; Barascud et al., 2016; Teki et al., 2016), but that brain regions in frontal cortex, parietal cortex, and hippocampus may additionally contribute (Tiitinen et al., 2012; Barascud et al., 2016; Teki et al., 2016). However, in the latter work, statistical difference maps were calculated and used to identify neural sources. Statistical difference maps may also capture effects related to activity spread due to volume conduction and may thus not reflect activity

430     originating from these higher-level brain regions (e.g., auditory responses to sound onset were spread

431     to parietal cortex in Teki et al., 2016, suggesting that spread may also affect their sustained activity in

432     parietal cortex related to sound patterns).

433     We further showed that sustained activity in auditory cortex to sounds that did not contain a

434     pattern was also reduced in older compared to younger adults (Figure 5B/C). Sounds without a pattern

435     were made of a sequence of pure tones whose frequency changed randomly for each tone. Such tone

436     sequences are perceptually more structured than noise and the auditory system may treat them as a

437     pattern of low saliency. This is consistent with the observation of reduced sustained activity to short

438     pure tones in older compared to younger adults (Pfefferbaum et al., 1979). Our data thus indicate that

439     the sensitivity of the aged auditory cortex is reduced for sounds containing a pattern (here repetition of

440     a set of tones at different frequencies) as well as for sequences with random tone frequencies.

441     It is clear from previous work that temporally regular – and thus predictable – structure in sounds

442     that forms a pattern elicits sustained neural activity (Gutschalk et al., 2002; Barascud et al., 2016;

443     Herrmann and Johnsrude, 2018b). However, additional work suggests that the magnitude of pattern-

444     related sustained activity is related to the degree of novelty or predictability of a pattern, such that

445     sustained activity decreases when a pattern is frequently, compared to infrequently, heard (Gutschalk

446     et al., 2007; Herrmann et al., 2021). A reduction in sustained activity in older adults may thus result from

447     reduced processing of the pattern as well as from reduced novelty of the pattern, but further behavioral

448     research is needed to investigate the perceptual consequences of the altered cortical sensitivity

449     observed here.

## Conclusions

450

451     In the current study, we recorded magnetoencephalography to characterize differences between

452     younger and older adults in the processing of a pattern in sounds. We presented continuous tone

453     sequences that either contained a pattern (made of a repeated set of tones at different frequencies) or

454     did not contain a pattern (random tone frequencies). We showed that auditory cortex in older adults is

455     hyperresponsive to sound onsets, but that sustained neural activity in auditory cortex, indexing the

456     processing of sound patterns, is reduced. Hence, neural populations in auditory cortex fundamentally

457     differ between younger and older individuals in their sensitivity to sound features, hyperresponding to

458    sound onsets, while underresponding to patterns in sounds. This may help to explain some age-related

459    changes in hearing such as increased sensitivity to distracting sounds and difficulties tracking speech in

460    the presence of other sound.

467                                    Author contributions

468    BH conceptualized and designed the study, recorded data, analyzed the data, interpreted the results,

469    and wrote the manuscript. BM analyzed the data, interpreted the results, and edited the manuscript. ISJ

470    conceptualized and designed the study, interpreted the results, and edited the manuscript.

471                            Declaration of conflicts of interest

472    None.

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