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Neural Signatures of Working Memory in Age-related Hearing Loss

Stephanie Rosemann a,b* and Christiane M. Thiel a,b

Abstract—Age-related hearing loss affects the ability to hear high frequencies and therefore leads to difficulties in understanding speech, particularly under adverse listening conditions. This decrease in hearing can be partly compensated by the recruitment of executive functions, such as working memory. The compensatory effort may, however, lead to a decrease in available neural resources compromising cognitive abilities. We here aim to investigate whether mild to moderate hearing loss impacts prefrontal functions and related executive processes and whether these are related to speech-in-noise perception abilities. Nineteen hard of hearing and nineteen age-matched normal-hearing participants performed a working memory task to drive prefrontal activity, which was gauged with functional magnetic resonance imaging. In addition, speech-in-noise understanding, cognitive flexibility and inhibition control were assessed. Our results showed no differences in frontoparietal activation patterns and working memory performance between normal-hearing and hard of hearing participants. The behavioral assessment of further executive functions, however, provided evidence of lower cognitive flexibility in hard of hearing participants. Cognitive flexibility and hearing abilities further predicted speech-in-noise perception. We conclude that neural and behavioral signatures of working memory are intact in mild to moderate hearing loss. Moreover, cognitive flexibility seems to be closely related to hearing impairment and speechin-noise perception and should, therefore, be investigated in future studies assessing age-related hearing loss and its implications on prefrontal functions. © 2020 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: hearing loss, functional MRI, cognitive processing, working memory, cognitive flexibility.

INTRODUCTION

Age-related hearing loss or presbycusis refers to a decrease in hearing abilities for high frequencies in older adults (Lin, 2012; Cardin, 2016). The disorder itself goes beyond sensory impairment as hard of hearing people have difficulties in understanding and processing speech, particularly in adverse listening situations. Further, the additional effort needed to compensate the reduced auditory input may have negative consequences (Wingfield et al., 2005; Lin et al., 2011; Rönnberg et al., 2011; Wingfield and Peelle, 2012; Humes et al., 2013; Cardin, 2016; Peelle and Wingfield, 2016; Gillingham et al., 2018; Peelle, 2018). For example, recent evidence from longitudinal studies supports a relationship between hearing loss and cognitive decline - primarily affecting learning and memory (Lin et al., 2011, 2013; Gurgel et al., 2014; Armstrong et al., 2018; Pronk et al., 2019).

On the other hand, the decrease in hearing abilities can partly be compensated for by linguistic knowledge and verbal intelligence (Wingfield et al., 1995; Thiel et al., 2016). Moreover, an increased working memory capacity has often been associated with increased speech-intelligibility in hard of hearing people with and without hearing aids (Anderson et al., 2013; Arehart et al., 2013; Rönnberg et al., 2013; Moradi et al., 2014; Souza and Arehart, 2015). Hence, intact executive functions may help to maintain successful communication in age-related hearing loss. Cognitive flexibility also seems to be related to speech perception as it is a good predictor of vocoded speech learning (Rosemann et al., 2017) and the interpretation of complex sentences (Vogelzang et al., 2019) in healthy volunteers. Further, speech understanding in cochlear implant patients can be predicted by cognitive flexibility (Hua et al., 2017; Sonnet et al., 2017). However, how individual differences in speech-in-noise perception relate to cognitive abilities in hard of hearing individuals remains to be unknown so far.

Less clear are also the neural implications that the compensatory efforts may have. Although several studies have shown changes in auditory brain regions in age-related hearing loss, there is also evidence for

^a Biological Psychology, Department of Psychology, School of Medicine and Health Sciences, Carl von Ossietzky Universität Oldenburg, 26111 Oldenburg, Germany

^b Cluster of Excellence "Hearing4all", Carl von Ossietzky Universität Oldenburg, 26111 Oldenburg, Germany

^{*}Correspondence to: S. Rosemann, Biological Psychology, Department of Psychology, School of Medicine and Health Sciences, Carl von Ossietzky Universität Oldenburg, 26111 Oldenburg, Germany. E-mail address: Stephanie.rosemann@uni-oldenburg.de (S. Rosemann).

frontal cortical changes. For example, grey matter reduction was found in the middle frontal gyrus in hard of hearing compared to normal-hearing participants (Husain et al., 2014) and poorer speech-in-noise perception abilities were related to grey matter decrease in frontal regions (Rudner et al., 2019). Decreases in functional resting-state connectivity in frontal areas were also associated with an increase in daily listening effort in elderly participants (Rosemann and Thiel, 2019). Contrarily, several studies have shown an increased frontal recruitment as a compensatory mechanism to improve speech understanding under difficult listening situations (Harris et al., 2009; Peelle et al., 2011; Hervais-Adelman et al., 2012; Campbell and Sharma. 2013: Erb et al., 2013: Erb and Obleser, 2013; Vaden et al., 2013, 2015; Lee et al., 2016: Glick and Sharma. 2017: Rosemann and Thiel. 2018). Increased pupil dilation as well as cognitive load was also associated with increased frontal brain activity (Zekveld et al., 2014).

Hence, there is evidence that age-related hearing loss leads to structural and functional changes in frontal brain regions – primarily due to decreased auditory input and increased listening effort. It is, however, unclear, whether mild to moderate hearing loss has wider consequences on prefrontal functions during cognitive processing and whether potential prefrontal changes are related to speech-in-noise perception abilities. A recent study regarding deafness showed weaker recruitment of frontoparietal regions and additional recruitment of superior temporal cortex during a visual working memory task in young deaf compared to hearing individuals (Cardin et al., 2018). These findings indicate a reorganization of cognitive networks.

The main aim of the present study was to investigate the impact of untreated mild to moderate age-related hearing loss on neural signatures of working memory. We expected decreased prefrontal cortex activity in hard of hearing compared to normal-hearing participants similar to the results shown in deaf participants (Cardin et al., 2018). In addition, we tested whether speech-innoise perception in mild to moderate hearing loss can be predicted by cognitive abilities similar to research in cochlear implant patients (Hua et al., 2017; Sonnet et al., 2017). Here, we expected that superior speechin-noise perception in hard of hearing participants is related to an increased working memory performance but also to an increased, compensatory frontal lobe recruitment (Anderson et al., 2013; Arehart et al., 2013; Rönnberg et al., 2013; Moradi et al., 2014; Souza and Arehart. 2015).

EXPERIMENTAL PROCEDURES

Participants

Participants were recruited via newspaper advertisements as well as through the database of the local hearing clinic (Hörzentrum Oldenburg) from the University. Participants with mild to moderate agerelated hearing loss affecting the higher frequencies as well as participants with age-appropriate hearing, defined by less than 30 dB at low frequencies

(125–2000 Hz) and less than 30 dB for the mean frequencies of high thresholds between 2 kHz and 8 kHz (cf. WHO, 2001 definition of hearing loss; von Gablenz and Holube, 2015) participated in the study. Asymmetrical (≥15 dB difference between left and right ear for more than three frequencies) as well as low-frequency hearing loss was excluded. Most of the hard of hearing participants were not aware of their mild to moderate decrease in hearing abilities before study participation/registration in the database, therefore reliable assessment of duration of hearing loss was not possible.

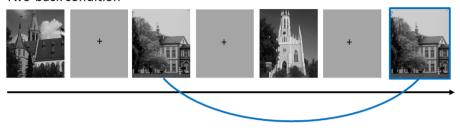
Forty-four volunteers participated in the study. Two participants were excluded due to excessive movement during the experiment (>3 mm absolute movement as well as >1.5 mm scan-to-scan movement). Further, four participants were excluded due to problems with the response buttons during the experiment (no button presses were recorded). Half of the remaining participants (n=19) showed mild to moderate agerelated hearing loss and the other half showed normal age-appropriate hearing. No participant reported current or previous use of hearing aids. The mean age of the hard of hearing participants was 64.63 (\pm 6.3) years and 63.32 (\pm 5.4) years for the normal-hearing participants. Age did not significantly differ between both groups (p > 0.1).

All participants were right-handed. Apart from exclusion criteria regarding hearing abilities, further exclusion criteria for participation were previous or current psychiatric or neurological disorders. Approval for the study was obtained from the local ethics committee of the University of Oldenburg "Kommission für Forschungsfolgenabschätzung und Ethik" (Committee for research outcome assessment and ethics). The study was carried out in accordance with the Declaration of Helsinki and with the EU General Data protection Regulation. All subjects signed a written informed consent form and were paid for participation.

Working memory task

We used an n-back task with 0-back and 2-back conditions (design depicted in Fig. 1). N-back working memory tasks are often used in fMRI studies and reliably activate a frontoparietal network independent of the stimuli used (Mencarelli et al., 2019). We choose a 2-back condition that represents a moderate working memory load in elderly subjects and a 0-back condition with minimal working memory load in which subjects had to identify a predefined stimulus. Stimuli used in both conditions were greyscale pictures of faces and buildings. These stimuli were chosen based on previous research showing functional brain reorganization for face processing in the deaf (Stropahl et al., 2015; Benetti et al., 2017). The experiment was a block design with eight blocks of the 0-back condition and eight blocks of the 2-back condition. Each block consisted of either only faces or only houses and there were four blocks of houses and four blocks of faces in each 0-back and 2-back condition. Within each block, 15 pictures were presented for one second with a one-second inter-stimulus-interval, in which a fixation cross was shown. Each block included four

Two-back condition



Zero-back condition



Fig. 1. Experimental design. Each condition consisted of either face or house stimuli within a block of 15 pictures. In the 2-back condition, the task was to press the response button whenever the current picture was the same as the one two pictures before. In the 0-back condition, participants had to identify a predefined target stimulus (in this example the famous building). Targets are framed in blue. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

targets. In the 2-back condition, three lures were presented as well. The distracting lures were repeated images with a different gap from one another, greater or less than two. Distracting lures were introduced to increase task difficulty since participants had to attend carefully whether the image was only repeated in general or repeated with the correct gap of two pictures. An additional rest condition, where only the fixation cross was present, was presented eight times. Blocks of rest, 0-back and 2-back conditions were presented pseudorandomized with a fixed presentation order for all participants. The presentation of stimuli and targets within each block was randomized. The blocks for the rest condition were 20 s and the blocks for the 0-back and 2-back conditions had a duration of 30 s. At the beginning of each block, the instruction of whether the 0-back or 2-back task should be performed was presented for three seconds. In the 0-back condition, two greyscale pictures of a famous person and a famous building served as the target the participants had to identify. In the 2-back condition, participants had to press the response button whenever the current picture was the same as the one two pictures before. Stimuli were presented with the Presentation® software (Version 18.3, Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com) via a projector behind the bore of the MRI (DATAPixx2, VPixx Technologies Inc.).

Experimental procedure

First, pure-tone audiometry was performed in a soundproof chamber. Subjects qualifying for participation were then screened for general cognitive abilities (Montreal Cognitive Assessment: MOCA; Nasreddine et al., 2005), processing speed, cognitive flexibility (Comprehensive Trail Making Test: CTMT;

Reynolds, 2002) and inhibition control (Stroop Task; Bäumler, 1984). Subsequently, each participants' speech-in-noise intelligibility at 80% was assessed with a matrix sentence test (Oldenburger Satztest; OLSA; Wagener et al., 1999). Before entering the MR scanner. a training of the n-back task outside the MRI was performed. Inside the MRI. another task was conducted first (reported elsewhere) and the n-back task followed as the second measurement. After a short break outside the MRI, a resting state MRI, diffusion tensor imaging and an anatomical MRI were performed. Both scanning sessions had a duration of approximately 30 minutes each. After scanning, subjects filled out questionnaires on handedness (Oldfield, 1971), verbal intelligence (Wortschatztest: WST; Schmidt and Metzler, 1992), daily life listening effort ("H

öranstrengungsbogen"; Schulte et al., 2015) and depression (Geriatric Depression Scale: GDI; Sheikh and Yesavage, 1986).

Data acquisition

Data were acquired with a 3T whole-body Siemens Magnetom Prisma MRI system with a 20-channel head coil. Functional images were acquired using a descending echo-planar imaging (EPI) sequence with BOLD contrast (TR = 1800 ms, TE = 30 ms, flip angle = 75° , df = 20, slice thickness: 3 mm, field of view = 192×192 , 33 slices). The task comprised 428 volumes. Anatomical images were acquired with a 3-D T1-weighted sequence (MP-RAGE, TR = 2000, TE = 2.07, flip angle = 9° , voxel size = 0.75 mm, field of view = 240×240 , 224 sagittal slices).

fMRI data analysis

The fMRI data were analyzed with the Statistical Parametric Mapping software package (SPM12. Welcome Department of Imaging Neuroscience. London, UK) running under MATLAB 2016a. The preprocessing pipeline of each dataset included slicetiming offset correction, realignment estimation, normalization to the Montreal Neurological Institute (MNI), stereotactic using normalization space parameters obtained from a segmentation of the image, anatomical T1-weighted and Gaussian smoothing (full width half maximum = 8 mm). In a first level analysis, the five different conditions (0-back faces, 0-back houses, 2-back faces, 2-back houses and rest) were individually modeled as boxcar functions and convolved with a canonical hemodynamic response

function. Head movement parameters were entered as regressors. A temporal high pass filter (128 s) and an AR (1) model were applied to remove temporal autocorrelations. At the second level, we performed a full factorial model in order to explore the main effect of group, the main effect of working memory (2back versus Oback condition) and the interaction of both. In addition, we explored the interaction of group, working memory and stimulus type (faces versus houses). We further computed an additional region of interest analysis using coordinates from the meta-analysis of Mencarelli et al. (2019) with 15 mm spheres in superior frontal gyrus (-4, 16, 52), middle frontal gyrus (-46, 26, 32) and inferior parietal lobule (-40, -48, 52) (fronto-parietal activation peaks for n-back face tasks). As a second step. multiple linear regression analyses were computed for testing the relation between speech-in-noise perception (dependent variable), hearing loss and frontal brain activity (independent variables) in hard of hearing as well as normal-hearing participants. Betas for frontal brain activity were extracted from peak coordinates that were obtained in the 2-back versus 0-back contrast for all participants (supplementary motor cortex (-4, 18, 50); right middle frontal gyrus (40, 6, 50); left middle frontal gyrus (-46, 22, 34)). For all fMRI analyses, effects were determined to be significant when passing a threshold of p < 0.05(FWE cluster size inference with p < 0.001 clusterforming threshold). Peak coordinates are reported in MNI space.

Behavioral data analysis

The performance for the 0-back and 2-back conditions was computed for each subject (% accuracy). An ANOVA served to explore differences between the hearing and hard of hearing group with respect to both conditions (2-back and 0-back) and stimulus types (faces and houses). Performance in the cognitive tasks and corresponding T-values were compared between hard of hearing and normal-hearing participants using two-sample t-tests. In order to assess cognitive flexibility in the trail making task, the time to complete trail 1 (linking the numbers 1 through 25 in order) was subtracted from the completion time of trail 5 (linking numbers 1 through 13 and letters A through L in alternating order). By that, general processing speed is cancelled out. Inhibition control was gauged by the median speed for the color word interference task of the Stroop test (T-value). In addition, the individual highfrequency hearing loss was computed for each participant from thresholds determined in the pure-toneaudiometry (average hearing threshold between 2 and 8 kHz). A multiple linear regression analysis in hard of hearing and normal-hearing participants served to significant predictors of speech-in-noise identify perception apart from hearing loss (cognitive variables obtained in executive tasks) in order to explore the relationship between hearing abilities and possible compensatory cognitive abilities. Data analysis was performed in SPSS Statistics 25 (IBM, Armonk, NY, USA).

RESULTS

Behavioral data

Demographics and audiological variables. Age, depression scores, audiological variables, general cognitive status and verbal intelligence are depicted in Table 1. We assessed mean high-frequency hearing loss (2-8 kHz), speech-in-noise perception and listening effort experienced in daily life as audiological variables. The mean value for high-frequency hearing loss was 41.4 dB (±9.14) for the hard of hearing group and 19.9 dB (\pm 6.76) for the normal-hearing participants. The mean audiograms for each group are depicted in Fig. 2. The mean value of speech-in-noise reception thresholds was -8.35 SNR (± 0.9) in the hard of hearing participants and -9.18 SNR (± 0.87) in the normal-hearing participants. Listening effort determined by the daily life questionnaire was rated as 2.88 (± 1.17) for hard of hearing and 2.53 (± 1.05) for normal-hearing participants - which corresponds to a low effort in both groups. High-frequency hearing loss (T (36) = 8.242.p < 0.001) and speech-in-noise perception (T(36) = 2.916, p = 0.006) significantly differed between hard of hearing and normal-hearing participants. The listening effort experienced in daily life did not significantly differ between both groups. General cognitive status and verbal intelligence were within the normal range and did not significantly differ between both groups. None of the participants showed depressive symptoms (cut off value: 5) and scores did not significantly differ between both group.

Executive functions

Apart from assessing working memory performance in the MRI, we applied two further tasks of executive functions tapping on cognitive flexibility and inhibition control. Inhibition control (assessed by the STROOP task) and cognitive flexibility (assessed by the comprehensive trail making test) were both in the normal range (see Table 2). Cognitive flexibility significantly differed between groups: Hard of hearing subjects showed less flexibility in the trail making test (CTMT subtest 5 versus subtest 1; T(36) = 2.261; p = 0.03). No differences were found for inhibition control and working memory. There was no interaction between group and condition

Table 1. Mean values (±standard deviation) for demographic and audiological variables

Demographics	Hard of hearing	Normal-hearing
Age (years)	64.63 (±6.3)	63.32 (±5.4)
GDS (depression) MOCA (score)	$1.34 (\pm 1.42)$ $26.53 (\pm 2.29)$	1.11 (±1.1) 26.47 (±1.68)
WST (score)	32.89 (±2.4)	33.79 (±2.97)
Hearing loss*** (2–8 kHz)	41.4 (±9.14)	$19.9 (\pm 6.76)$
Speech-in-noise** (SNR) Listening effort (score)	$-8.35 (\pm 0.9)$ 2.88 (±1.17)	$-9.18 (\pm 0.87)$ 2.53 (±1.05)
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p < 0.001; p < 0.01 (significance of between-group comparison).

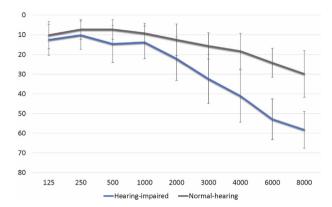


Fig. 2. Pure-tone audiometry for the hard of hearing (blue) and normal-hearing (grey) participants [mean values and standard deviation for each group averaged over left and right ear]. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

(0back or 2back), nor between group and stimulus material (faces or houses).

Neuroimaging data

Neural activity related to working memory in hard of hearing and normal-hearing subjects. fMRI data were analyzed with a full factorial model to explore the main effect of group, the main effect of working memory (2back versus 0back condition) and the interaction of both. In addition, we explored the interaction of group, working memory and stimulus type (faces versus houses). We found a main effect of working memory and stimulus type (Table 3). The model did however not reveal any significant main effect of group nor an interaction with working memory. An interaction between group, working memory and stimulus type was also not obtained. Brain regions showing a main effect of working memory (2back versus 0back) in each group are displayed in Fig. 3. Normal-hearing participants showed a widespread pattern of brain activity covering superior parietal lobule, superior and middle frontal gyrus, supplementary motor area, occipital cortex, fusiform gyrus, as well as the cerebellum and brain stem. Hard of hearing participants showed similar albeit less widespread activity in brain regions covering frontal

and parietal areas, in addition to the cerebellum, brain stem and the insula. The visual cortex – apart from the fusiform gyrus – was not significantly activated in this contrast for hard of hearing participants. Note that the additional region of interest analysis did not reveal any significant main effect of group nor group by condition interaction.

Relationship between speech-in-noise perception, executive functions and frontal brain activity in hard of hearing participants. In order to identify significant predictors of speech-in-noise perception in hard of hearing participants, we computed a multiple linear regression analysis between speech-in-noise perception (dependent variable), hearing loss and executive function using the scores of the working memory task, STROOP interference task and trail making test as independent variables. This regression showed that two predictors explained 57.5% of the variance ($R^2 = 0.575$: F(4,18) = 4.74, p = 0.013). Both, hearing loss $(\beta = 0.455, p = 0.025)$ and cognitive flexibility – as measured by the trail making test ($\beta = 0.576$, p = 0.016) – had a significant influence on speech-innoise perception. In normal-hearing participants, this regression analysis was not significant. Hence, only in hard of hearing participants speech-in-noise perception could be significantly predicted by hearing and cognitive variables.

A second multiple linear regression analysis was computed to assess whether increased frontal lobe recruitment during working memory processing may compensate for decreased hearing abilities. Again, speech-in-noise perception served as the dependent variable while hearing loss and frontal brain activity (peak beta values of supplementary motor cortex, right and left middle frontal gyrus) were included as independent variables. This analysis did, however, not yield any significant result (p > 0.1). Hence, our results suggest that cognitive flexibility but neither working memory nor frontal lobe recruitment predict speech-innoise perception in hard of hearing participants.

DISCUSSION

The current study aimed to investigate the influence of mild to moderate age-related hearing loss on neural signatures of working memory. We hypothesized that

Table 2. Mean values (± standard deviation) for executive functions (cognitive flexibility, inhibition control and working memory performance)

Task	Hard of hearing	Normal- hearing
CTMT flexibility (seconds)*	33.57 (±23.7)	19.99 (±11.11)
STROOP interference (<i>T</i> -value)	$61.63 (\pm 6.34)$	$61.11 (\pm 7.55)$
Accuracy 2-back (total; %)	$91.84 (\pm 3.72)$	$93.49 (\pm 3.68)$
Accuracy 2-back (faces; %)	93.29 (±0.86)	93.64 (±0.83)
Accuracy 2-back (houses; %)	$92.54 (\pm 0.87)$	$93.46 (\pm 0.92)$
Accuracy 0-back (total; %)	99.34 (±0.68)	98.97 (±1.38)
Accuracy 0-back (faces; %)	99.91 (± 0.09)	$99.43 (\pm 0.31)$
Accuracy 0-back (houses; %s)	99.87 (±0.10)	99.56 (±0.22)

^{*}p < 0.05 (significance of between-group comparisons).

Table 3. Peak coordinates for the main effects in the full factorial model

Effect	Peak coordinates (x, y, z)	Z-value	Cluster size	Brain region
Main effect of working memory	32, 11, -4	> 8	39,287	Right insula
	-34, 48, 12	6.72	1322	Left middle frontal gyrus
Main effect of stimulus	28, -42, -12	> 8	74,332	Right fusiform gyrus
	-60, -8, -14	5.7	509	Left middle frontal gyrus
Main effect of group	n.s.			

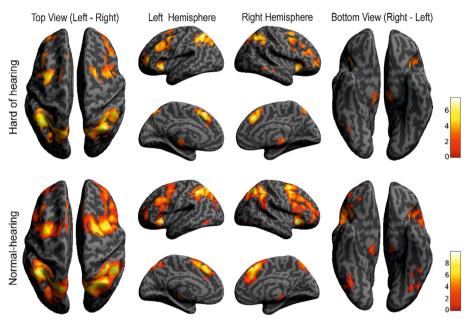


Fig. 3. Activation pattern for 2-back versus 0-back conditions in hard of hearing participants (top) and normal-hearing participants (bottom). Areas of activation include superior parietal lobule, superior and middle frontal gyrus, supplementary motor area, occipital cortex, fusiform gyrus, cerebellum and brain stem [p < 0.05; FWE corrected on the cluster level]. Activation patterns did not differ significantly between groups.

hard of hearing participants exhibit decreased brain activity in the prefrontal cortex compared to normal-We further hearing participants. explored relationship between hearing loss, speech-in-noise perception and frontal lobe recruitment during working memory processing. We expected that the hard of hearing participants who are better in speech-in-noise perception may show increased frontal lobe recruitment. Additionally, we investigated whether speech-in-noise perception in hard of hearing participants can be predicted by better working memory or other executive abilities, such as cognitive flexibility and inhibition control. At the neural level, both hard of hearing and normal-hearing participants showed increased brain activity in frontoparietal networks with no significant difference between both groups suggesting that mild to moderate uncompensated age-associated hearing loss does not impact on cognitive brain networks. Our behavioral data suggest that speech-in-noise perception in hard of hearing participants was significantly predicted by hearing loss and cognitive flexibility. A regression analysis with hearing loss, speech-in-noise perception and frontal lobe activity, however, did not yield any evidence that frontal lobe recruitment may contribute to this prediction.

The working-memory related activations that were present in both groups are in line with the known involvement of frontoparietal brain regions, insula and cerebellum across different types of n-back tasks (Mencarelli et al., 2019). Studies in healthy volunteers often analyzed workingmemory related activations as a function of increasing working memory load (i.e., comparing different n-back levels) and have shown that increases in load result in increased neural activity in frontoparietal areas (Mencarelli et al., 2019). The logic here was however to use a design that reliably activates in every subject the whole network of working-memory related brain regions to have maximum sensitivity to detect group differences and/or individual variability. We therefore chose to compare the 2-back task condition with a 0back task condition which poses

minimal demands on working memory as subjects have to identify a predefined target stimulus. Such approach is comparable to the prior study in the deaf by Cardin et al. (2018) and to large scale neuroimaging approaches such as the human connectome project (Barch et al., 2013). Contrary to our hypothesis, mild to moderate age-related hearing loss was however not associated with decreased brain activity in the prefrontal cortex during working memory processing. Further, we did not see any significant relation between hearing loss, frontal lobe recruitment and speech-in-noise perception. Weaker recruitment of frontoparietal regions and additional recruitment of superior temporal cortex for a working memory task was shown in young deaf compared to hearing individuals (Cardin et al., 2018). Thus, deafness seems to be associated with changes in cortical reorganization for cognitive processes. However, these participants were congenitally severely-to-profoundly deaf individuals using sign language. Our data in participants with mild to moderate hearing loss indicate that neural signatures of working memory may not (yet) be affected. Consequently, it seems that in mild to moderate stages

of hearing loss, significant neural alterations are only observed during sensory stimulation (Campbell and Sharma, 2013; 2014), particularly those requiring substantial effort with respect to listening (Erb and Obleser, 2013; Peelle et al., 2011; Reuter-Lorenz and Cappell, 2008; Rosemann and Thiel, 2018; Tyler et al., 2010; Wong et al., 2009; Vaden et al., 2013, 2015).

Further, neither a significant impairment nor difference to normal-hearing participants in cognitive abilities such as general cognitive status, inhibition control and working memory (n-back task in the MRI) was observed in our sample of mild to moderate hard of hearing flexibility participants. Cognitive was. however. significantly worse and predicted speech-in-noise perception in hard of hearing participants. Hence, cognitive flexibility may play a significant role already early in the course of hearing loss. Previous research has shown that cognitive flexibility is a good predictor of noise-vocoded speech learning and could, therefore, serve to predict hearing aid outcomes in cochlear implant patients (Rosemann et al., 2017). Other studies demonstrated that cochlear implant patients with higher cognitive flexibility - also assessed with the CTMT part 5 or the old TMT part B - showed better speech understanding (Hua et al., 2017; Sonnet et al., 2017). We here show, that not only hearing loss but also cognitive flexibility significantly explained variability in speech-in-noise understanding in mild to moderate hard of hearing participants. Thus, cognitive flexibility should not only be assessed in cochlear implant patients but should also be used in studies investigating mild to moderate agerelated hearing loss. Regarding the other cognitive abilities that we assessed, it is possible that in mild stages of hearing loss, these cognitive functions are not yet affected. Another possibility is that the high verbal intelligence (in both groups) was able to compensate for slight decrements in cognition (Wingfield et al., 1995; Thiel et al., 2016). Similarly, Armstrong et al. (2018) did not find an association between hearing and cognition in their baseline assessment, although poorer hearing at baseline predicted worse performance in various executive functions. We suggest that the loss of hearing does not immediately affect cognitive systems, but that effects occur over the course of many years of increased listening effort and load on the executive system. Only if hearing loss gets worse and the executive system is more strongly engaged in adverse listening situations, cognitive abilities may be affected and start to decline (Lin et al., 2011, 2013; Gurgel et al., 2014; Armstrong et al., 2018; Pronk et al., 2019).

Hearing loss in older adults is a common disorder affecting speech understanding under adverse listening conditions. Consequently, successful communication may be impaired and lead to social isolation and loneliness. Research on cognitive and neural implications of age-related hearing loss and factors contributing to difficulties in speech understanding is therefore highly important. Our study revealed lower cognitive flexibility in mild to moderate hard of hearing compared to normal-hearing participants. Even though cognitive flexibility was still within the normal range, it

predicted speech-in-noise perception in hard of hearing individuals. Hard of hearing participants did not significantly differ from normal-hearing participants in performance or neural activity in a working memory paradigm. Thus, we conclude, that in mild stages of hearing loss, most executive functions are not impaired. These may only be affected in severe stages of hearing loss or due to a concurrent listening effort and cognitive load on the executive system, which may, in turn, lead to cognitive decline. Since cognitive flexibility was shown to be closely related to hearing abilities and speech understanding in older adults, it should be carefully investigated in future studies dealing with hearing impairment. Further, cognitive flexibility may also be highly relevant in predicting hearing aid outcome in age-related hearing loss.

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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AUTHOR CONTRIBUTIONS

SR designed the study, was involved in data acquisition, analysed the data and wrote the manuscript. CT designed the study, was involved in interpretation of the results and revised the manuscript. Both authors approved the final version of the manuscript.

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REFERENCES

Anderson S, White-Schwoch T, Parbery-Clark A, Kraus N (2013) A dynamic auditory-cognitive system supports speech-in-noise perception in older adults. Hear Res 300:18–32. https://doi.org/10.1016/j.heares.2013.03.006.

Arehart KH, Souza P, Baca R, Kates JM (2013) Working memory, age, and hearing loss: susceptibility to hearing aid distortion. Ear Hear 34(3):251–260. https://doi.org/10.1097/AUD.0b013e318271aa5e.

Armstrong NM, An Y, Ferrucci L, Deal JA, Lin FR, Resnick SM (2018) Temporal sequence of hearing impairment and cognition in the baltimore longitudinal study of aging. J Gerontol Ser A Biol Sci Med Sci. https://doi.org/10.1093/gerona/gly268.

- Barch DM, Burgess GC, Harms MP, Petersen SE, Schlaggar BL...Corbetta M, Wu-Minn HCP Consortium (2013) Function in the human connectome: task-fMRI and individual differences in behavior. NeuroImage 80:169–189. https://doi.org/10.1016/ji.neuroimage.2013.05.033.
- Benetti S, van Ackeren MJ, Rabini G, Zonca J, Foa V, Baruffaldi F, Collignon O (2017) Functional selectivity for face processing in the temporal voice area of early deaf individuals. PNAS 114(31):E6437–E6446. https://doi.org/10.1073/pnas.1618287114.
- Bäumler G (1984) Farbe-Wort-Interferenztest Nach JR Stroop: Handanweisung [Color-Word-Interference-Test according to Stroop: Manual]. Boston, MA: Hogrefe.
- Campbell J, Sharma A (2013) Compensatory changes in cortical resource allocation in adults with hearing loss. Front Syst Neurosci 7:71. https://doi.org/10.3389/fnsys.2013.00071.
- Campbell J, Sharma A (2014) Cross-modal re-organization in adults with early stage hearing loss. PLoS ONE 9(2). https://doi.org/10.1371/journal.pone.0090594 e90594.
- Cardin V (2016) Effects of aging and adult-onset hearing loss on cortical auditory regions. Front Neurosci 10:199. https://doi.org/10.3389/fnins.2016.00199.
- Cardin V, Rudner M, De Oliveira RF, Andin J, Su MT, Beese L, Ronnberg J (2018) The organization of working memory networks is shaped by early sensory experience. Cerebral Cortex (New York, N.Y.: 1991) 28(10):3540–3554. https://doi.org/10.1093/cercor/bhx222
- Erb J, Henry MJ, Eisner F, Obleser J (2013) The brain dynamics of rapid perceptual adaptation to adverse listening conditions. J Neurosci 33(26):10688.
- Erb J, Obleser J (2013) Upregulation of cognitive control networks in older adults' speech comprehension. Front Syst Neurosci 7:116. https://doi.org/10.3389/fnsys.2013.00116.
- Gillingham SM, Vallesi A, Pichora-Fuller MK, Alain C (2018) Older adults with hearing loss have reductions in visual, motor and attentional functioning. Front Aging Neurosci 10:351. https://doi.org/10.3389/fnagi.2018.00351.
- Glick H, Sharma A (2017) Cross-modal plasticity in developmental and age-related hearing loss: clinical implications. Hear Res 343:191–201. S0378-5955(16)30139-3.
- Gurgel RK, Ward PD, Schwartz S, Norton MC, Foster NL, Tschanz JT (2014) Relationship of hearing loss and dementia: a prospective, population-based study. Otol Neurotol 35 (5):775–781. https://doi.org/10.1097/MAO.0000000000000000313.
- Harris KC, Dubno JR, Keren NI, Ahlstrom JB, Eckert MA (2009) Speech recognition in younger and older adults: A dependency on low-level auditory cortex. J Neurosci: Off J Soc Neurosci 29(19):6078–6087. https://doi.org/10.1523/JNEUROSCI.0412-09.2009.
- Hervais-Adelman A, Carlyon RP, Johnsrude IS, Davis MH (2012) Brain regions recruited for the effortful comprehension of noise-vocoded words. Lang Cogn Process 27(7–8):1145–1166. https://doi.org/10.1080/01690965.2012.662280.
- Hua H, Johansson B, Magnusson L, Lyxell B, Ellis RJ (2017) Speech recognition and cognitive skills in bimodal cochlear implant users. J Speech Lang Hear Res 60(9):2752–2763. https://doi.org/10.1044/2017 JSLHR-H-16-0276.
- Humes LE, Busey TA, Craig J, Kewley-Port D (2013) Are age-related changes in cognitive function driven by age-related changes in sensory processing? Atten Percept Psychophys 75(3):508–524. https://doi.org/10.3758/s13414-012-0406-9.
- Husain FT, Carpenter-Thompson JR, Schmidt SA (2014) The effect of mild-to-moderate hearing loss on auditory and emotion processing networks. Front Syst Neurosci 8:10. https://doi.org/10.3389/fnsys.2014.00010.
- Lee YS, Min NE, Wingfield A, Grossman M, Peelle JE (2016) Acoustic richness modulates the neural networks supporting intelligible speech processing. Hear Res 333:108–117. https://doi.org/10.1016/j.heares.2015.12.008.
- Lin FR (2012) Hearing loss in older adults: who's listening? JAMA 307 (11):1147–1148. https://doi.org/10.1001/jama.2012.321.

- Lin FR, Ferrucci L, Metter EJ, An Y, Zonderman AB, Resnick SM (2011) Hearing loss and cognition in the baltimore longitudinal study of aging. Neuropsychology 25(6):763–770. https://doi.org/10.1037/a0024238.
- Lin FR, Yaffe K, Xia J, Xue QL, Harris TB...Purchase-Helzner E, Health ABC Study Group (2013) Hearing loss and cognitive decline in older adults. JAMA Int Med 173(4):293–299. https://doi.org/10.1001/jamainternmed.2013.1868.
- Mencarelli L, Neri F, Momi D, Menardi A, Rossi S, Rossi A, Santarnecchi E (2019) Stimuli, presentation modality, and load-specific brain activity patterns during n-back task. Hum Brain Mapp 40(13):3810–3831. https://doi.org/10.1002/hbm.24633.
- Moradi S, Lidestam B, Hallgren M, Ronnberg J (2014) Gated auditory speech perception in elderly hearing aid users and elderly normal-hearing individuals: effects of hearing impairment and cognitive capacity. Trends Hear 18. https://doi.org/10.1177/2331216514545406.
- Nasreddine ZS, Phillips NA, Bedirian V, Charbonneau S, Whitehead V, Collin I, ...Chertkow H (2005) The montreal cognitive assessment, MoCA: A brief screening tool for mild cognitive impairment. J Am Geriatrics Soc 53(4):695–699. doi: JGS53221.
- Oldfield RC (1971) The assessment and analysis of handedness: The edinburgh inventory, 1971. https://doi.org/10.1016/0028-3932(71)90067-4.
- Peelle JE (2018) Listening effort: How the cognitive consequences of acoustic challenge are reflected in brain and behavior. Ear Hear 39(2):204–214. https://doi.org/10.1097/AUD.00000000000000494.
- Peelle JE, Troiani V, Grossman M, Wingfield A (2011) Hearing loss in older adults affects neural systems supporting speech comprehension. J Neurosci 31(35):12638–12643. https://doi.org/10.1523/JNEUROSCI.2559-11.2011.
- Peelle JE, Wingfield A (2016) The neural consequences of agerelated hearing loss. Trends Neurosci 39(7):486–497. https://doi.org/10.1016/ji.tins.2016.05.001.
- Pronk M, Lissenberg-Witte BI, van der Aa HPA, Comijs HC, Smits C, Lemke U, Kramer SE (2019) Longitudinal relationships between decline in speech-in-noise recognition ability and cognitive functioning: The longitudinal aging study Amsterdam. J Speech Lang Hear Res 62(4S):1167–1187. https://doi.org/10.1044/2018 JSLHR-H-ASCC7-18-0120.
- Reuter-Lorenz P, Cappell KA (2008) Neurocognitive aging and the compensation hypothesis. Curr Dir Psychol Sci 17(3):177–182. https://doi.org/10.1111/j.1467-8721.2008.00570.x.
- Reynolds CR (2002) Comprehensive trail making test. Austin, TX: Pro-Ed. DOI: 10.1177/0734282905282415.
- Rönnberg J, Danielsson H, Rudner M, Arlinger S, Sternang O, Wahlin A, Nilsson LG (2011) Hearing loss is negatively related to episodic and semantic long-term memory but not to short-term memory. J Speech Lang Hear Res 54(2):705–726. https://doi.org/10.1044/1092-4388(2010/09-0088).
- Rönnberg J, Lunner T, Zekveld A, Sorqvist P, Danielsson H, Lyxell B, Rudner M (2013) The ease of language understanding (ELU) model: theoretical, empirical, and clinical advances. Front Syst Neurosci 7:31. https://doi.org/10.3389/fnsys.2013.00031.
- Rosemann S, Giessing C, Ozyurt J, Carroll R, Puschmann S, Thiel CM (2017) The contribution of cognitive factors to individual differences in understanding noise-vocoded speech in young and older adults. Front Hum Neurosci 11:294. https://doi.org/10.3389/fnhum.2017.00294.
- Rosemann S, Thiel CM (2018) Audio-visual speech processing in age-related hearing loss: stronger integration and increased frontal lobe recruitment. NeuroImage 175:425–437. S1053-8119 (18)30319-7.
- Rosemann S, Thiel CM (2019) The effect of age-related hearing loss and listening effort on resting state connectivity 2337-019-38816-z. Sci Rep 9(1). https://doi.org/10.1038/s41598-019-38816-z.
- Rudner M, Seeto M, Keidser G, Johnson B, Ronnberg J (2019)
 Poorer speech reception threshold in noise is associated with
 lower brain volume in auditory and cognitive processing regions. J
 Speech Lang Hear Res 62(4S):1117–1130. https://doi.org/10.1044/2018 JSLHR-H-ASCC7-18-0142.

- Schmidt K-H, Metzler P (1992) Wortschatztest: WST. Weinheim: Beltz Test.
- Schulte M, Meis M, Wagener K (2015) Der Höranstrengungs-Fragebogen. 18. Jahrestagung der Deutschen. Gesellschaft für Audiologie.
- Sheikh JI, Yesavage JA (1986) Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. Clin Gerontol 5:165–173.
- Sonnet MH, Montaut-Verient B, Niemier JY, Hoen M, Ribeyre L, Parietti-Winkler C (2017) Cognitive abilities and quality of life after cochlear implantation in the elderly. Otol Neurotol 38(8): e296–e301. https://doi.org/10.1097/MAO.000000000000001503.
- Souza P, Arehart K (2015) Robust relationship between reading span and speech recognition in noise. Int J Audiol 54(10):705–713. https://doi.org/10.3109/14992027.2015.1043062.
- Stropahl M, Plotz K, Schonfeld R, Lenarz T, Sandmann P, Yovel G, Debener S (2015) Cross-modal reorganization in cochlear implant users: auditory cortex contributes to visual face processing. NeuroImage 121:159–170. https://doi.org/10.1016/j.neuroimage.2015.07.062.
- Thiel CM, Ozyurt J, Nogueira W, Puschmann S (2016) Effects of age on long term memory for degraded speech. Front Hum Neurosci 10:473. https://doi.org/10.3389/fnhum.2016.00473.
- Tyler LK, Shafto MA, Randall B, Wright P, Marslen-Wilson WD, Stamatakis EA (2010) Preserving syntactic processing across the adult life span: the modulation of the frontotemporal language system in the context of age-related atrophy. Cereb Cortex 20 (2):352–364. https://doi.org/10.1093/cercor/bhp105.
- Vaden Jr KI, Kuchinsky SE, Ahlstrom JB, Dubno JR, Eckert MA (2015) Cortical activity predicts which older adults recognize speech in noise and when. J Neurosci 35(9):3929–3937. https://doi.org/10.1523/JNEUROSCI.2908-14.2015.
- Vaden Jr KI, Kuchinsky SE, Cute SL, Ahlstrom JB, Dubno JR, Eckert MA (2013) The cingulo-opercular network provides word-

- recognition benefit. J Neurosci 33(48):18979–18986. https://doi.org/10.1523/JNEUROSCI.1417-13.2013.
- Vogelzang M, Thiel CM, Rosemann S, Rieger JW, Ruigendijk E (2019) Cognitive abilities to explain individual variation in the interpretation of complex sentences by older adults. In: Goel AK, Seifert CM, Freksa C, editors. Proceedings of the 41st annual conference of the cognitive science society. Montreal, QB: Cognitive Science Society. p. 3036–3042.
- von Gablenz P, Holube I (2015) Prävalenz von Schwerhörigkeit im Nordwesten Deutschlands. HNO 63(3):195–214. https://doi.org/10.1007/s00106-014-2949-7.
- Wagener KC, Brand T, Kollmeier B (1999) Entwicklung und Evaluation eines Satztests in deutscher Sprache III: evaluation des Oldenburger Satztests [Development and evaluation of a German sentence test Part III: evaluation of the Oldenburg sentence test]. Z Audiol 38(3):86–95.
- Wingfield A, Peelle JE (2012) How does hearing loss affect the brain? Aging Health 8(2):107–109. https://doi.org/10.2217/AHE.12.5.
- Wingfield A, Tun PA, Rosen MJ (1995) Age differences in veridical and reconstructive recall of syntactically and randomly segmented speech. J Gerontol Ser B Psychol Sci Soc Sci 50(5):P257–66. https://doi.org/10.1093/geronb/50b.5.p257.
- Wingfield A, Tun PA, McCoy SL (2005) Hearing loss in older adulthood: What it is and how it interacts with cognitive performance. Curr Dir Psychol Sci 14(3):144–148. https://doi.org/10.1111/ji.0963-7214.2005.00356.x.
- Wong PC, Jin JX, Gunasekera GM, Abel R, Lee ER, Dhar S (2009)
 Aging and cortical mechanisms of speech perception in noise.
 Neuropsychologia 47(3):693–703. https://doi.org/10.1016/ji.neuropsychologia.2008.11.032.
- Zekveld AA, Heslenfeld DJ, Johnsrude IS, Versfeld NJ, Kramer SE (2014) The eye as a window to the listening brain: neural correlates of pupil size as a measure of cognitive listening load. NeuroImage 101:76–86. https://doi.org/10.1016/j.neuroimage.2014.06.069.

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