Cortical fNIRS Responses Can Be Better Explained by Loudness Percept than Sound Intensity

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Objectives: Functional near-infrared spectroscopy (fNIRS) is a brain imaging technique particularly suitable for hearing studies. However, the nature of fNIRS responses to auditory stimuli presented at different stimulus intensities is not well understood. In this study, we investigated whether fNIRS response amplitude was better predicted by stimulus properties (intensity) or individually perceived attributes (loudness).

Design: Twenty-two young adults were included in this experimental study. Four different stimulus intensities of a broadband noise were used as stimuli. First, loudness estimates for each stimulus intensity were measured for each participant. Then, the 4 stimulation intensities were presented in counterbalanced order while recording hemoglobin saturation changes from cortical auditory brain areas. The fNIRS response was analyzed in a general linear model design, using 3 different regressors: a non-modulated, an intensity-modulated, and a loudness-modulated regressor.

Results: Higher intensity stimuli resulted in higher amplitude fNIRS responses. The relationship between stimulus intensity and fNIRS response amplitude was better explained using a regressor based on individually estimated loudness estimates compared with a regressor modulated by stimulus intensity alone.

Conclusions: Brain activation in response to different stimulus intensities is more reliant upon individual loudness sensation than physical stimulus properties. Therefore, in measurements using different auditory stimulus intensities or subjective hearing parameters, loudness estimates should be examined when interpreting results.

Key words: Cortical brain activation, Functional near-infrared spectroscopy, Loudness perception, Sound intensity.

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INTRODUCTION

Functional near-infrared spectroscopy (fNIRS) is a noninvasive brain imaging method that uses near-infrared light to measure changes in hemoglobin oxygenation that are related to neural activity. fNIRS has been shown to be useful in detecting cortical activations in response to auditory stimulation. In fact, this technique is particularly suitable for hearing studies, as it runs silently, is applicable to all age groups, and does not interfere with hearing devices (e.g., cochlear implants). Furthermore, in contrast with functional magnetic resonance imaging (fMRI), fNIRS recordings can be set up in a normal sound-treated booth, a vital prerequisite for the reliable and standardized performance of hearing examinations.

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In a previous study, we demonstrated that auditory stimuli presented at high stimulus intensities lead to higher fNIRS response amplitudes in auditory and auditory associated fields compared with stimuli presented at low intensities (Weder et al. 2018). These findings might eventually enable the development of an fNIRS-based clinical tool for hearing assessment. In populations where direct behavioral feedback is not possible or complicated (e.g., babies and infants), fNIRS could help evaluate cortical auditory activation (does a certain sound intensity lead to a cortical response?) and might even assist with adjusting hearing devices (e.g., cochlear implants).

However, the relationship between fNIRS response amplitude and stimulus intensity is not well understood. Although intensity is the physical property of sound (measured in decibel sound pressure level, dB SPL), loudness describes the perceptual counterpart and signifies the magnitude of an auditory sensation (Florentine et al. 2011). Previous fMRI studies looking into this matter have suggested that, at the cortical level, neural activity appears to be a reflection of subjective loudness sensation rather than physical sound intensity (Hall et al. 2001; Röhl & Uppenkamp 2012; Uppenkamp & Röhl 2014). Röhl and Uppenkamp (2012) demonstrated that the percentage signal change of the blood oxygenation level–dependent response almost linearly increased with the perceived loudness. This effect was also replicated with stimuli at a fixed sound intensity but with varying bandwidths (and therefore differing loudness correlates, Röhl et al. 2011). Langers et al. (2007) compared fMRI activation maps of normal-hearing and hearing-impaired listeners and found that subjects with hearing loss demonstrated a much steeper growth function of the brain activation compared with the normal-hearing group. This effect was attributed to the loudness recruitment that is present in this subpopulation and is another indicator that auditory cortical activation is more closely correlated to perception than stimulus properties.

In fNIRS, a small number of studies have investigated intensity or loudness-related responses. Bauernfeind et al. (2016, 2018) presented stimuli at two different intensities and found, with the higher stimulation level, increased saturated hemoglobin amplitudes in bilateral middle and superior temporal gyri as well as in Broca's area. Chen et al. (2015) used two different stimulus intensities for which they also measured loudness estimates. There were two stimuli in that study. The first consisted of a pure tone that alternated in frequency every 500 msec from 440 to 554 Hz. The second was a 1 kHz carrier tone that was frequency-modulated by a complex modulator (the modulator was a 10 Hz sinusoid modulated by a 4 Hz sinusoid). Loudness estimates were gathered by applying a categorical loudness scale with seven subdivisions. However, the exact procedure was not further explained (stimulus presentation and repetition). The authors described a significant change of the hemodynamic

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responses near the primary auditory cortex by perceived loudness, but not by sound intensity (Chen et al. 2015).

In our previous study, we demonstrated that fNIRS responses in bilateral superior temporal gyri were significantly larger for high compared with low-intensity stimuli (Weder et al. 2018). Sound intensities at 40, 65, and 90 dB SPL showed an increase of saturated hemoglobin levels (and a simultaneous decrease of desaturated hemoglobin levels) in ascending order. We also found that sound intensities near the hearing threshold elicited no response or even a negative response of saturated hemoglobin levels. However, it remains unclear whether these changes can be primarily explained by stimulus properties or rather by individually perceived attributes (i.e., loudness estimates).

The aim of our study was to better understand the relationship between auditory stimulus intensity and fNIRS response amplitude in auditory regions of the brain. This was done by comparing the fit of different general linear model (GLM) regressors to the measured fNIRS response. First, we examined whether higher sound intensities led to increased fNIRS responses to reassess earlier findings. Then, we analyzed whether cortical responses could be better explained by a model that used fixed (i.e., intensity regressor) or individually adapted increments (i.e., loudness regressor).

MATERIALS AND METHODS

Study Participants

Twenty-six normal-hearing adults (15 males, 11 females; mean = 30 years, range 20 to 39 years) participated in the experiment. Only subjects below the age of 40 years were included in this study, as in the preprocessing step of the fNIRS data, a differential path-length factor has to be specified which can vary with age (Scholkmann & Wolf 2013). Four subjects had to be excluded from further analysis as most channels of the fNIRS experiment were lost due to insufficient scalp contact. All of them had thick dark hair.

The study was approved by the local ethical committee (Human Research Ethics Committee, Royal Victorian Eye and Ear Hospital, project number 16/126H) and all participants had given written consent. All experiments (behavioral and fNIRS) were performed on the same day. Otoscopy and pure-tone audiometry showed normal findings (all participants had hearing thresholds ≤20 dB HL at frequencies 125 to 8000 Hz).

Acoustic Stimuli

Insert earphones (ER-3A, E-A-RTONE 165 GOLD) were used to deliver acoustic stimuli binaurally. In the behavioral and fNIRS part, an amplitude-modulated broadband noise (mBBN; Dreschler et al. 2001) was applied. This stimulus has been proven to generate reliable and strong activation in auditory and auditory associated cortical fields, as shown in our previous functional imaging study (Weder et al. 2018). During the experiments, 5 different variations of the broadband noise (with an on-offset ramp of 10 msec) were randomly played to account for the variability of the stimulus. Calibrations of the auditory stimuli were done by using an artificial ear (G.R.A.S., Denmark) and the Norsonic sound level meter (Norsonic, Norway) and calibrated as suggested by its authors (Dreschler et al. 2001). All experiments (behavioral and fNIRS, see later) were performed in a sound-treated booth.

Hearing Thresholds and Loudness Estimates

First, we measured hearing thresholds (in dB SPL) of the amplitude mBBN by using a 3 alternative forced-choice AXB method (Amitay et al. 2006). The test was complete when nine turning points had been reached. Second, to determine the discomfort level of the noise stimulus, we applied and verified an ascending method of limits by repeating this process three times (Warner & Bender 2002). If levels lay above 105 dB SPL, further measurements were terminated. Third, we measured the loudness correlates of the four sound intensities (Fig. 1A) which were used later in the fNIRS part of the experiment (i.e., 15, 40, 65, and 90 dB SPL). We used an unbound and continuous absolute magnitude estimation scale (Marks & Florentine 2011). Participants' instructions were given in a written form and were exactly as described by Marks and Florentine (2011). Interleaved with the mBBN stimuli, a 1 kHz pure tone at 40 dB SPL was delivered. The stimulus duration of both types of stimuli was 1 second. Literature has shown that, for nonsteady state sounds, short stimulus durations can affect loudness estimation. Stimulus duration of 1 second or longer, however, should lead to similar loudness estimations (Kuwano & Namba 2011). After a trial period of 20 stimuli, stimuli at each sound intensity (mBBN segments and the pure tone) were repeated 5 times in a counterbalanced manner. The median magnitude estimation value for each intensity was calculated individually. For each participant, the magnitude estimates were then converted into a sone scale by comparing them to the magnitude estimates for the 1 kHz pure tone, as described by Florentine et al. (2011). A sone scale bears the advantage of enabling interindividual comparison.

fNIRS Measurements

A continuous-wave fNIRS system with 16 LED light sources and 16 detectors was used (NIRScout, NIRX, Germany; wavelengths 760 and 850 nm). The channel setup of our experiment was identical to our previous study (Weder et al. 2018). For each channel, corresponding brain regions were determined by applying the method of Tsuzuki and Dan (2014). Our aim was to cover primary and secondary auditory cortices and auditory associated brain regions (Fig. 4B). The fNIRS cap was adjusted compliant with electroencephalography positions T7, T8, and Cz (Klem et al. 1999). On each side of the head, 12 long channels (3 cm source-detector distance, Fig. 4A) and 2 short channels (11 mm source-detector distance, shown by * in Fig. 4A) were available. Short channels were used to measure the extracerebral component of the fNIRS signal (Sato et al. 2016).

Presentation software (Neurobehavioral Systems) was employed to deliver acoustic stimuli. Stimulus duration was 18 seconds as suggested by (Skudlarski et al. 1999). The stimuli were presented in a counterbalanced manner at the 4 different sound intensity levels (Fig. 1B). Stimuli at each sound intensity were repeated 10 times in total. During the experiment, participants were sitting in an armchair. To reduce head movements, they were told to maintain their gaze on a white cross displayed on a PC monitor directly in front of them. They were further instructed to pay attention to the acoustic stimuli and confirm the end of a stimulus with a button press. After every stimulus, a randomly chosen rest period of 25, 30, or 35 seconds allowed the fNIRS signal to return to baseline. To help participants focus on the task, a break of flexible chosen duration was included

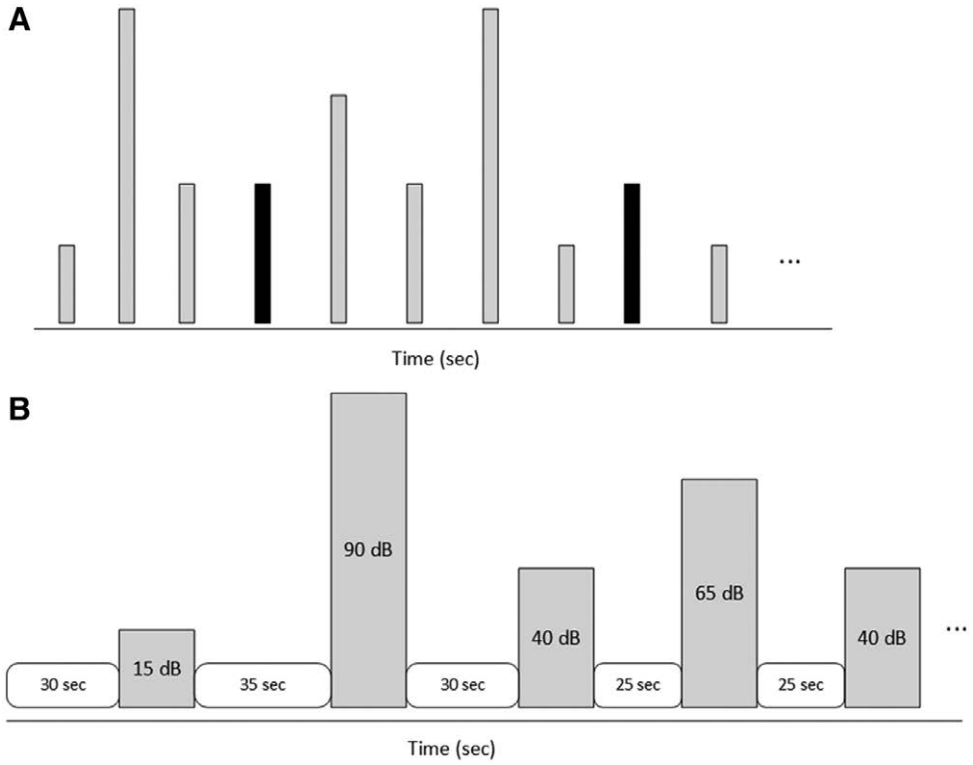


Fig. 1. Schematic illustration exemplifying the measurement of the loudness estimation part (A) and the fNIRS part (B). In the loudness estimation part (A), 4 different intensity levels (15, 40, 65, 90 dB SPL) of the mBBN (gray boxes) and 1 level (40 dB SPL) of the 1 kHz pure tone (black box) were applied in a counterbalanced fashion. The stimulus duration of both types was 1 sec. Participants had to indicate the loudness of all stimuli. In the fNIRS part (B), the experiment started off with 30 seconds resting period. Then, 4 different intensity levels (15, 40, 65, 90 dB SPL) of mBBN were applied in a counterbalanced fashion. During stimulating blocks, randomly assigned resting periods of 25, 30, and 35 seconds were interleaved. Stimulus duration was 18 seconds. During the fNIRS measurement, participants were instructed to pay attention to the stimuli and confirm the end of a stimulus with a button press. fNIRS indicates functional near-infrared spectroscopy; mBBN, modulated broadband noise.

after 8 stimulations (7 minutes = 1 block). The total recording time without breaks was 35 minutes.

fNIRS Data Preprocessing and Analysis

We used Matlab (MathWorks, version R2017b) to process and analyze the data. Custom-made scripts were complemented by open, accessible Homer2 functions (Huppert et al. 2009). Preprocessing of the data included the steps below:

Only channels with good contact to the scalp (scalp coupling index higher than 0.75; Pollonini et al. 2014) were included in further analysis. Then, raw data were converted into optical densities. We used wavelet transformation to reduce motion artifacts using the Homer2 function hmrMotionCorrectWavelet (function parameter set to 1.5) (Molavi & Dumont 2012). Signals were band-pass filtered between 0.01 and 0.5 Hz using zero-phase 3rd-order Butterworth low-pass and 5th-order Butterworth high-pass filters, respectively (Homer2 function *hmrBandpassFilt*, Huppert et al. 2009). By applying the modified Beer-Lambert Law (Delpy et al. 1988), concentration changes of oxygenated hemoglobin (HbO) were calculated. Finally, the extracerebral component of the fNIRS signal was removed for each hemisphere separately as described by Sato et al. (2016): The first principal components from the two short channels on each side (which we assumed to originate from extracerebral tissue) were calculated. For each side separately, we used a GLM, consisting of the hemodynamic response functions (HRFs) and the first principal component to fit the signals in long channels (Kamran et al. 2015). Finally, we subtracted the extracerebral response, that is, PC1 multiplied by its beta coefficient from the GLM, from the signal in each long channel. A more detailed description of the preprocessing steps is outlined in our previous article (Weder et al. 2018).

Saturated hemoglobin responses were modeled using a parametric modulated GLM (Friston et al. 1995; Plichta et al. 2007). Thereby, three different regressors (on-off regressor, intensity-modulated regressor, and loudness-modulated regressor) were compared for each participant individually (fNIRS data and the 3 regressors from an example participant are shown in Fig. 2). The expected responses of each regressor were defined using canonical HRFs consisting of 2 gamma functions as described by Kamran et al. (2015). These HRFs were then adjusted depending on the nature of the regressor: whereas the non-modulated/on-off regressor did not account for changes of the stimulus (i.e., the amplitude of the HRF stayed the same for all sound intensity levels), the intensity and loudness regressors were modulated depending on the stimulation level. While the amplitude increase of the intensity regressor was fixed for all subjects, the loudness regressor was adjusted individually, according to the sones scale from the behavioral part (loudness measurement). For each participant, the three regressors were

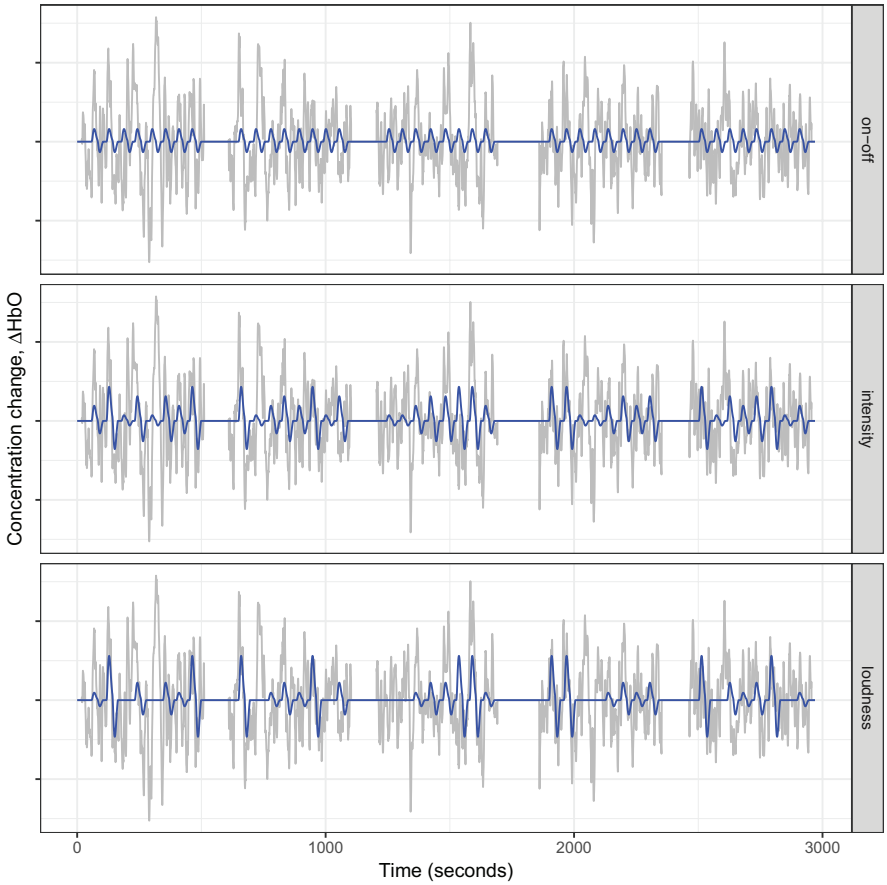


Fig. 2. Data from an example participant and channel. The *x* axis is time in seconds; the *y* axis is concentration changes of HbO. fNIRS measurements are depicted as gray lines in all three rows. Overlying are the regressors in blue. The first row shows the on-off regressor, the second row shows the intensity-modulated regressor, and the third row shows the loudness-modulated regressor. fNIRS indicates functional near-infrared spectroscopy; HbO, oxygenated hemoglobin.

entered into the model independently which was then solved by using least-square curve fitting. Coefficients of determination (R^2) of all regressors and channels were calculated. R^2 is a scale-free measure of goodness-of-fit that relies on the sum of squared residuals. Values typically lie between 0 and 1 and indicate the variability of the data explained by the regressor. The distribution of R^2 coefficients was statistically compared between the three different regressors to determine which model had the best fit to the measured fNIRS response.

Statistics

Shapiro-Wilk's test ($p > 0.05$, Royston 1993) was applied to determine whether the assumption of normality was met. If required, nonparametric statistical tests were employed. R^2 coefficients were statistically compared for all channels individually. First, the intensity regressor was compared with the on-off regressor. In this way, we could answer the question of whether the measured fNIRS response could be better explained by a modulated regressor or not. In a second step, we compared the fit of the intensity regressor to the fit of the loudness regressor to determine whether fNIRS response amplitude was better predicted by stimulus properties (intensity) or individually perceived attributes (loudness). To account for multiple comparisons, false discovery rate correction was employed (Benjamini & Hochberg 1995).

RESULTS

Hearing Thresholds and Loudness Estimates

Ambient noise in the experiment room was measured at 19.5 dBA. Median group hearing thresholds for mBBN lay at 11 dB SPL (range 6 to 15.5 dB SPL). The lowest stimulation level (i.e., 15 dB SPL) was therefore near and in one case slightly below perception level. Discomfort levels lay for 14 participants above 105 dB SPL (for 3 at 105 dB SPL, for 4 at 100 dB SPL, and for 1 at 95 dB SPL). It can therefore be assumed that even for the highest stimulation level in our experiment, loudness estimates and fNIRS measurement were not significantly influenced by hearing discomfort.

For the loudness estimates, the range of individual responses increased with higher sound intensity. Although loudness estimates for lower sound intensities (i.e., 15 and 40 dB SPL) were closely clustered, estimates for the 2 higher levels had a wider range between participants: for 90 dB SPL, loudness estimates extended from 1.8 to 15.8 sones (Fig. 3).

fNIRS Measurements

Participants' Attention • As attention has been shown to modulate the activation of primary and secondary auditory cortices (Jäncke et al. 1999; Woods et al. 2009), we (1) intentionally kept the task simple and clear, (2) included regular breaks of participants' own chosen duration, and (3) examined the button press

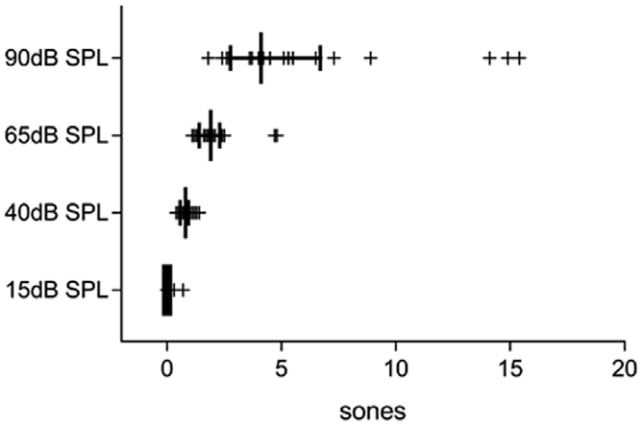


Fig. 3. Individual loudness estimates in sones (*x* axis) for the 4 stimulation levels in dB SPL (*y* axis). For every level, median and interquartile ranges are shown. The range of individual loudness estimates increased with higher sound intensity; loudness estimates for lower sound intensities (i.e., 15 and 40 dB SPL) were closely clustered, estimates for the two higher levels had a wider range between participants.

response times. For every participant individually, the reaction times of the four stimulation blocks were evaluated using a one-way analysis of variance. For all participants, reaction times between the four blocks did not significantly differ ($p > 0.05$).

Results From Parametric Regressors • R^2 coefficients for the three parametric regressors were calculated for every participant. In Table 1, median R^2 coefficients across participants for every regressor and channel are shown, respectively. In many channels, the on-off regressor could not predict the measured fNIRS response very well (Table 1). However, with the intensity regressor and even more with the loudness regressor, higher median R^2 coefficients could be noted. Highest median R^2 coefficients were recorded in channels 1 to 3, 6, 7, 10, and 23 which lay above the inferior frontal gyrus and the superior temporal gyrus. Channels 11, 16, 19, 20, 21, and 22 had low values for all 3 types of regressors. These channels were overlying the middle temporal gyrus and the supramarginal gyrus. For these channels, the predicted hemodynamic response function did not explain the measured fNIRS response very well.

The distribution of R^2 coefficients was compared between different regressors. First, the goodness-of-fit between the on-off and the intensity regressor was compared using the Wilcoxon signed-rank test. Thereby, after correction for multiple comparisons, in channels 3, 5, 8, and 13 (Table 1 and Fig. 4C), the measured fNIRS response could be explained significantly better by the modulated model than by the on-off regressor. These channels were overlying the superior temporal gyrus (temporal pole), the inferior frontal gyrus and the postcentral near the belt and para-belt region of the auditory cortex.

In a second step, the intensity regressor was compared with the loudness regressor. R^2 coefficients calculated with the loudness regressor were in most cases higher than with the intensity regressor (Table 1). With the loudness regressor, test statistics of the Wilcoxon signed-rank test showed a significant increase of R^2 coefficients in channels 8 and 10 on the right side (adjusted $p = 0.01$ for both channels; Fig. 4D). These two channels were overlying the anterior aspect of the superior temporal gyrus as well as the inferior frontal gyrus.

When testing for laterality of the fNIRS response by comparing corresponding channels on each hemisphere, the goodness-of-fit measures showed no statistical difference in the Wilcoxon signed-rank test for all three types of regressors.

Finally, we tested whether individually determined loudness estimates would be better predictors of the fNIRS responses than the group-level loudness estimates (median loudness estimates across participants). The group median loudness estimates for each stimulus level were 0, 0.78, 1.7609, and 4.0297 sones. Considering all 24 channels, R^2 values for the models calculated using individually determined loudness estimates were equal or higher for most participants compared with the group median loudness estimates (median: in 19.5 participants). When comparing loudness regressors against on-off and intensity regressors statistically, individually adjusted loudness regressors showed significance in more channels and lower p values (compared with group loudness regressors).

TABLE 1. HbO measurements

Left Hemisphere				Right Hemisphere			
CH No.	On-Off	Intensity	Loudness	CH No.	On-Off	Intensity	Loudness
1	5.9	10.8	10.3	2	6.3	7.2	4.2
3	7.51*	14.9†	17.6	4	1.8	1.8	1.7
5	0.0*	1.0†	2.3	7	1.5	5.7	6.3
6	1.0	12.7	13.4	8	0.0*‡	0.2†‡	1.7*†
9	0.0	0.2	0.7	10	0.0	1.5	3.5
11	0.0	0.0	0.2	13	0.0*‡	0.3†	1.0†
12	0.0	0.2	0.8	14	0.0	0.0	0.5
15	0.0	0.2	0.7	17	1.5	1.6	1.1
16	0.1	0.2	0.1	18	0.0	0.0	0.6
19	0.0	0.0	0.0	21	0.0	0.0	0.0
20	0.0	0.0	0.1	22	0.2	0.4	0.3
23	0.3	4.4	5.8	24	1.1	0.6	0.2

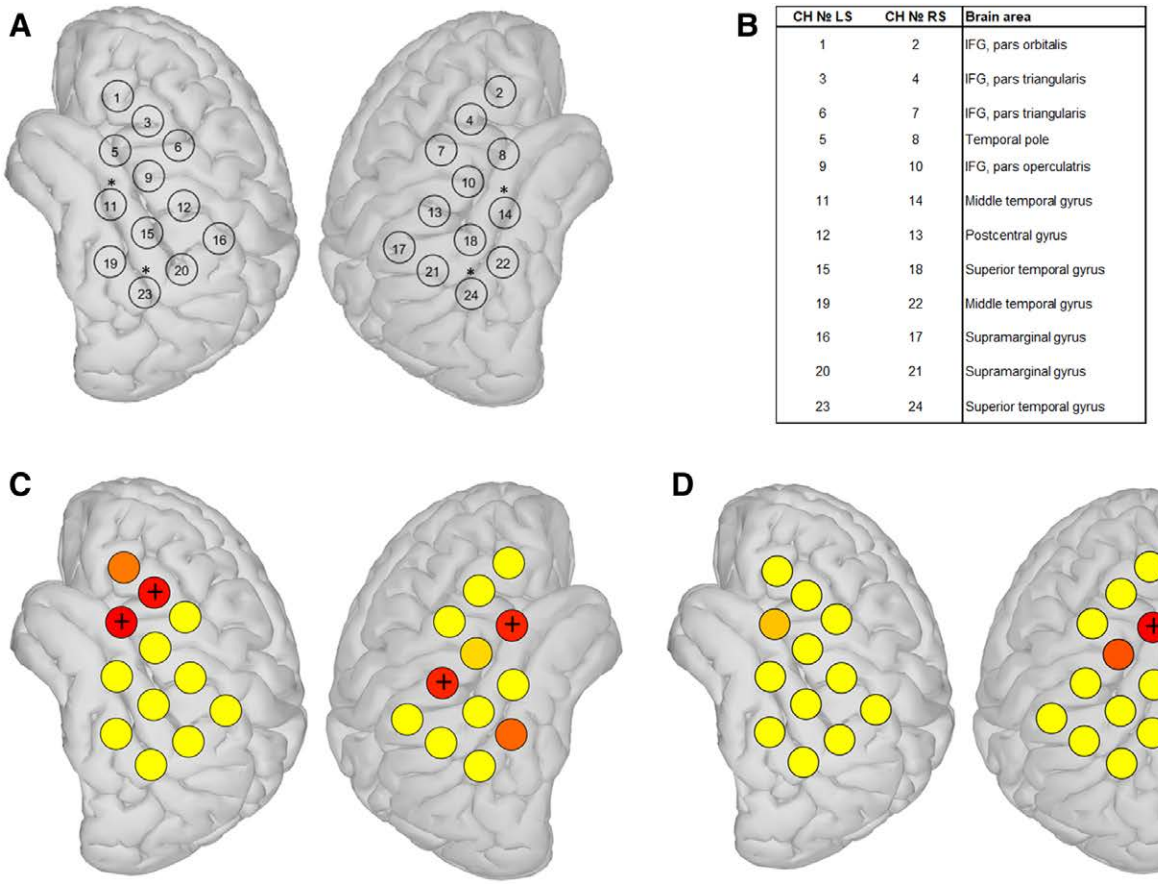
For every regressor and channel, the median coefficient of determination (scaled by factor of 10^3) is shown. Channel positions can be found in Figure 4A and B and are allocated to the lft and right hemispheres. Symbols designate statistical significance after correction for multiple comparisons ($p < 0.05$ considered significant).

**Significant difference to the intensity R.*

†Significant difference to the on-off R.

‡Significant difference to the loudness R).

CH, channel; HbO, oxygenated hemoglobin.



CH № LS	CH № RS	Brain area
1	2	IFG, pars orbitalis
3	4	IFG, pars triangularis
6	7	IFG, pars triangularis
5	8	Temporal pole
9	10	IFG, pars operculatris
11	14	Middle temporal gyrus
12	13	Postcentral gyrus
15	18	Superior temporal gyrus
19	22	Middle temporal gyrus
16	17	Supramarginal gyrus
20	21	Supramarginal gyrus
23	24	Superior temporal gyrus

Fig. 4. Statistical comparison between channel-specific regressors. fNIRS channel positions (A) and anatomical brain regions (B). On each side of the head, 12 long channels and 2 short channels (*) were available. Wilcoxon signed-rank test was used to compare coefficients of determination between the on-off and intensity regressor (C) and the intensity and loudness regressor (D). Color codes with the corresponding scale beside are the *p* values (D). Significant channels after multiple comparison correction are marked with a (+). Significant results were measured above the superior temporal gyrus and the inferior frontal gyrus on both sides. fNIRS indicates functional near-infrared spectroscopy; LS, left side; RS, right side.

DISCUSSION

Our results show that higher sound intensities lead to increased fNIRS responses overlying auditory and auditory associated cortices and that the relationship between stimulus and fNIRS amplitude is best characterized when the stimulus level is coded in terms of individual loudness perception, rather than stimulus intensity.

Effect of Sound Intensity

In the existing literature, only few fNIRS articles have investigated cortical activation in response to auditory stimulation levels (Chen et al. 2015; Bauernfeind et al. 2016, 2018; Weder et al. 2018). These three studies found enhanced cortical activation in response to higher sound intensity levels. Chen et al. (2015) additionally included loudness perception to their statistical model and found a significant influence of the hemodynamic responses by perceived loudness, but not by altered sound intensity. However, this finding contradicts earlier fMRI observations (and also the existing fNIRS literature cited earlier) where higher sound intensities lead to increased cortical responses (Mohr et al. 1999; Hart et al. 2003; Sigalovsky & Melcher 2006; Langers et al. 2007; Röhl & Uppenkamp 2012). In our study too, a fixed modulated regressor (i.e., intensity regressor) explained the measured fNIRS response significantly better than an unmodulated on-off regressor. As a side note, it also has to be considered that Chen et al. (2015) as Bauernfeind et al. (2016, 2018) used only two stimulation levels in their studies. Although two stimuli allow the calculation of a difference map, only multiple stimulation levels allow the determination of a coding pattern.

Loudness Correlation

It must be taken into account that the technique of fNIRS has restricted depth resolution: this neuroimaging technique is therefore only capable of picking up signals from superficial cortical regions. It has often been debated if fNIRS is even capable of measuring responses from the primary auditory cortex (which lies in the depth of the lateral sulcus) or if it picks up responses from the para-belt region, instead (Wiggins et al. 2016). Overall, it can be stated that fNIRS responses originate from superficial cortical regions and not from deeper brain regions. fMRI findings indicate that brainstem activation in response to different stimulation levels is reliant on fixed stimulus properties (i.e., sound intensity; Röhl & Uppenkamp 2012). In contrast with that cortical brain areas are activated depending on individual loudness sensation rather than sound intensity (Langers et al. 2007; Röhl & Uppenkamp 2012). It therefore must be assumed, that transformation of sensation into

conscient perception is completed at cortical level. Congruently with these findings, in our results, individually adjusted loudness regressors better explain the measured fNIRS response. Compared with the intensity regressor, the loudness regressor showed higher median beta values above the superior temporal gyrus on both sides. In our parametric test statistics and after multiple comparison correction, channels 8 and 10 on the right side were statistically significant.

Activated Cortical Regions

Compared with fMRI, fNIRS has only a limited spatial resolution. In our experiment, a broad region overlying the superior temporal gyrus responded well to different sound intensity and loudness levels. This stands in accordance with previous fMRI findings where sound intensity–related activation could be found in the superior temporal gyrus, the transverse temporal gyrus, and the planum temporale (Mohr et al. 1999; Brechmann et al. 2002; Hart et al. 2003; Sigalovsky & Melcher 2006; Langers et al. 2007).

In our results, when comparing the intensity and loudness regressor, statistical significance was reached in channels 8 and 10 overlying the anterior aspect of the superior temporal gyrus of the right hemisphere. This is also the brain region that was activated most in our previous article (Weder et al. 2018) and where Bauernfeind et al. (2016, 2018) found most prominent intensity-related effects. In the latter cited study and in contrast with our results, slightly higher and broader activation of the left hemisphere could be noted. However, congruently with our results, no statistical evidence of laterality could be proven.

Stimulus Selection and Loudness Testing

As in our previous study, we used an amplitude-modulated noise stimulus (Weder et al. 2018). Compared with a simple tone stimulus, noise stimuli have more stable loudness precepts. In sinusoids, incoming and reflecting traveling waves in the cochlea have been shown to influence loudness perception (Mauermann et al. 2004).

In pre-existing neuroimaging studies, different approaches have been chosen to estimate loudness percept: Röhl and Uppenkamp (2012) used a categorical loudness scale, Langers et al. (2007) performed a matching task, and Hall et al. (2001) calculated a loudness model. In our study, we used a magnitude estimation scale of loudness, which is an unbounded and continuous scaling procedure (Florentine et al. 2011). This method has the advantage of not having an edge resolution effect (Berliner & Durlach 1973). The edge resolution effect is commonly present in bounded loudness scales, where the highest and lowest stimulus levels show lesser variability compared with stimulus levels in between.

It is well known that, even between normal-hearing listeners, considerable differences exist in loudness perceptions (Brand & Hohmann 2001). This observation was confirmed by our findings, where a large spread of loudness estimates was present, especially for the highest sound intensity (Fig. 3). Interindividual differences in loudness estimates have been correlated with auditory and nonauditory factors: Uppenkamp and Röhl (2014) hypothesized that in normal-hearing participants, individual reference frames could be related to previous noise exposure. Furthermore, context effects (Arieh & Marks 2011) and personality traits like anxiety (Stephens 1970; Ellermeier et al. 2001) can act on perceived loudness.

Limitations

There was a slightly unequal gender distribution in our study. This could potentially affect loudness estimation. However, a recent study performed by Hamamura and Iwamiya (Reference Note 1) found that, when using magnitude estimation scales, no gender difference was observed. Furthermore, the number of participants in our study was small but comparable to similar fMRI trials, which have investigated the topic (Hall et al. 2001; Langers et al. 2007; Röhl et al. 2011). In the future, more data are needed to confirm our results.

fNIRS recordings measure extra- and intracerebral hemoglobin changes at the same time. Despite our short channel correction, there might still be an extracerebral component of the signal. This could potentially influence the fNIRS signal during higher intensity stimuli as these might evoke a systemic physiological response.

The HRF used in our study consisted of a 2-gamma function model that imitates a broad hemodynamic response starting at stimulus onset and slowly fading after stimulus offset (Kamran et al. 2015). Yet, the waveform morphology of the fNIRS response can alter according to the overlying brain region (Weder et al. 2018). Therefore, a uniform HRF might bear the disadvantage of over-simplification and lead to less significant results.

Compared with fMRI, the spatial resolution of fNIRS is limited. As no simultaneous MRI registration was done in our experiment, the given localization is only an approximation. It must also be highlighted that in fNIRS study designs with many channels, multiple comparison correction can be a problem. Other authors have solved that issue by averaging regions of interest (Chen et al. 2015; Bauernfeind et al. 2018). However, the standard distance of an fNIRS source-detector pair is 3 cm. It is therefore questionable if brain regions separated by such a gap should be functionally summarized. In the present study, we preferred to show the results of all channels separately (and take a stronger effect of multiple comparison correction into account) as not to introduce higher topographical inaccuracy.

Our main analysis displays HbO data. Our calculations with deoxygenated hemoglobin (HbR) measurements are included in the Supplemental Digital Content 1, http://links.lww.com/EANDH/A608. These show a similar pattern as HbO findings; modulated regressors (compared with on-off regressors) can significantly better explain HbR measurements. In the comparison between the intensity and loudness regressor, statistical findings were weaker with no significance between them. This could be a result of the poorer signal to noise ratio of HbR signals compared with HbO signals. Although HbR responses seem to be topographically more accurate (Bauernfeind et al. 2013; Kaiser et al. 2014), they exhibit, at the same time, a lower signal to noise ratio (Huppert et al. 2006; Tak et al., Reference Note 2). Both HbO and HbR signals are closely correlated to the blood oxygenation level–dependent signal from fMRI studies (Steinbrink et al. 2006). Thereby, the correlation of HbO seems to be slightly better (Strangman et al. 2002).

CONCLUSIONS

Our study results substantiate previous fMRI findings: on a cortical level, brain activation of auditory and auditory associated areas is more reliant on individual loudness sensation than physical stimulus properties. This finding has implications on future fNIRS research and clinical applications: in measurements

using different auditory sound intensities or subjective hearing parameters (e.g., discomfort level), loudness estimates should be collected when interpreting its results.

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The authors have no conflicts of interest to disclose.

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REFERENCES

Amitay, S., Irwin, A., Hawkey, D. J., et al. (2006). A comparison of adaptive procedures for rapid and reliable threshold assessment and training in naive listeners. *J Acoust Soc Am, 119*, 1616–1625.

Arieh, Y., & Marks, L. E. (2011). *Measurement of Loudness, Part II: Context Effects Loudness* (pp. 57–87). Springer.

Bauernfeind, G., Haumann, S., Lenarz, T. (2016). fNIRS for future use in auditory diagnostics. *Curr Dir Biomed Eng*, *2*, 229–232.

Bauernfeind, G., Böck, C., Wriessnegger, S., *et al*. (2013). Physiological noise removal from fNIRS signals. *Biomedical Engineering/Biomedizinische Technik* (58 Suppl 1), doi: 10.1515/bmt-2013-4430.

Bauernfeind, G., Wriessnegger, S. C., Haumann, S., et al. (2018). Cortical activation patterns to spatially presented pure tone stimuli with different intensities measured by functional near-infrared spectroscopy. *Hum Brain Mapp, 39*, 2710–2724.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: A practical and powerful approach to multiple testing. *J R Stat Soc Series B (Methodological)* 57, 289–300.

Berliner, J. E., & Durlach, N. I. (1973). Intensity perception. IV. Resolution in roving-level discrimination. *J Acoust Soc Am, 53*, 1270–1287.

Brand, T., & Hohmann, V. (2001). Effect of hearing loss, centre frequency, and bandwidth on the shape of loudness functions in categorical loudness scaling. *Audiology, 40*, 92–103.

Brechmann, A., Baumgart, F., Scheich, H. (2002). Sound-level-dependent representation of frequency modulations in human auditory cortex: A low-noise fMRI study. *J Neurophysiol, 87*, 423–433.

Chen, L. C., Sandmann, P., Thorne, J. D., et al. (2015). Association of concurrent fNIRS and EEG signatures in response to auditory and visual stimuli. *Brain Topogr, 28*, 710–725.

Delpy, D. T., Cope, M., van der Zee, P., et al. (1988). Estimation of optical pathlength through tissue from direct time of flight measurement. *Phys Med Biol, 33*, 1433–1442.

Dreschler, W. A., Verschuure, H., Ludvigsen, C., et al. (2001). ICRA noises: Artificial noise signals with speech-like spectral and temporal properties for hearing instrument assessment. International Collegium for Rehabilitative Audiology. *Audiology, 40*, 148–157.

Ellermeier, W., Eigenstetter, M., Zimmer, K. (2001). Psychoacoustic correlates of individual noise sensitivity. *J Acoust Soc Am, 109*, 1464–1473.

Florentine, M., Popper, A., Fay, R. (2011). *Springer Handbook of Auditory Research: Loudness*. Springer.

Friston, K. J., Holmes, A. P., Poline, J. B., et al. (1995). Analysis of fMRI time-series revisited. *Neuroimage, 2*, 45–53.

Hall, D. A., Haggard, M. P., Summerfield, A. Q., et al. (2001). Functional magnetic resonance imaging measurements of sound-level encoding in the absence of background scanner noise. *J Acoust Soc Am, 109*, 1559–1570.

Hart, H. C., Hall, D. A., Palmer, A. R. (2003). The sound-level-dependent growth in the extent of fMRI activation in Heschl's gyrus is different for low- and high-frequency tones. *Hear Res, 179*, 104–112.

Huppert, T. J., Hoge, R. D., Diamond, S. G., et al. (2006). A temporal comparison of BOLD, ASL, and NIRS hemodynamic responses to motor stimuli in adult humans. *Neuroimage, 29*, 368–382.

Huppert, T. J., Diamond, S. G., Franceschini, M. A., et al. (2009). HomER: A review of time-series analysis methods for near-infrared spectroscopy of the brain. *Appl Opt, 48*, D280–D298.

Jäncke, L., Mirzazade, S., Shah, N. J. (1999). Attention modulates activity in the primary and the secondary auditory cortex: A functional magnetic resonance imaging study in human subjects. *Neurosci Lett, 266*, 125–128.

Kaiser, V., Bauernfeind, G., Kreilinger, A., et al. (2014). Cortical effects of user training in a motor imagery based brain-computer interface measured by fNIRS and EEG. *Neuroimage, 85*(Pt 1), 432–444.

Kamran, M. A., Jeong, M. Y., Mannan, M. M. (2015). Optimal hemodynamic response model for functional near-infrared spectroscopy. *Front Behav Neurosci, 9*, 151.

Klem, G. H., Lüders, H. O., Jasper, H., *et al*. (1999). The ten-twenty electrode system of the International Federation. *Electroencephalogr Clin Neurophysiol*, *52*, 3–6.

Kuwano, S., & Namba, S. (2011). Loudness in the laboratory, Part II: Nonsteady-state sounds. In F. Mary, N. P Arthur, R. F Richard (Eds), *Loudness* (pp. 145–168). Springer.

Langers, D. R., van Dijk, P., Schoenmaker, E. S., et al. (2007). fMRI activation in relation to sound intensity and loudness. *Neuroimage, 35*, 709–718.

Marks, L. E., & Florentine, M. (2011). Measurement of loudness, part I: Methods, problems, and pitfalls. In F. Mary, N. P Arthur, R. F Richard (Eds), *Loudness* (pp. 17–56). Springer.

Mauermann, M., Long, G. R., Kollmeier, B. (2004). Fine structure of hearing threshold and loudness perception. *J Acoust Soc Am, 116*, 1066–1080.

Mohr, C. M., King, W. M., Freeman, A. J., et al. (1999). Influence of speech stimuli intensity on the activation of auditory cortex investigated with functional magnetic resonance imaging. *J Acoust Soc Am, 105*, 2738–2745.

Molavi, B., & Dumont, G. A. (2012). Wavelet-based motion artifact removal for functional near-infrared spectroscopy. *Physiol Meas, 33*, 259–270.

Plichta, M. M., Heinzel, S., Ehlis, A. C., et al. (2007). Model-based analysis of rapid event-related functional near-infrared spectroscopy (NIRS) data: A parametric validation study. *Neuroimage, 35*, 625–634.

Pollonini, L., Olds, C., Abaya, H., et al. (2014). Auditory cortex activation to natural speech and simulated cochlear implant speech measured with functional near-infrared spectroscopy. *Hear Res, 309*, 84–93.

Röhl, M., & Uppenkamp, S. (2012). Neural coding of sound intensity and loudness in the human auditory system. *J Assoc Res Otolaryngol, 13*, 369–379.

Röhl, M., Kollmeier, B., Uppenkamp, S. (2011). Spectral loudness summation takes place in the primary auditory cortex. *Hum Brain Mapp, 32*, 1483–1496.

Royston, P. (1993). A pocket-calculator algorithm for the Shapiro-Francia test for non-normality: An application to medicine. *Stat Med, 12*, 181–184.

Sato, T., Nambu, I., Takeda, K., et al. (2016). Reduction of global interference of scalp-hemodynamics in functional near-infrared spectroscopy using short distance probes. *Neuroimage, 141*, 120–132.

Scholkmann, F., & Wolf, M. (2013). General equation for the differential pathlength factor of the frontal human head depending on wavelength and age. *J Biomed Opt, 18*, 105004.

Sigalovsky, I. S., & Melcher, J. R. (2006). Effects of sound level on fMRI activation in human brainstem, thalamic and cortical centers. *Hear Res, 215*, 67–76.

Skudlarski, P., Constable, R. T., Gore, J. C. (1999). ROC analysis of statistical methods used in functional MRI: Individual subjects. *Neuroimage, 9*, 311–329.

Steinbrink, J., Villringer, A., Kempf, F., et al. (2006). Illuminating the BOLD signal: Combined fMRI-fNIRS studies. *Magn Reson Imaging, 24*, 495–505.

Stephens, S. D. (1970). Personality and the slope of loudness function. *Q J Exp Psychol, 22*, 9–13.

Strangman, G., Culver, J. P., Thompson, J. H., et al. (2002). A quantitative comparison of simultaneous BOLD fMRI and NIRS recordings during functional brain activation. *Neuroimage, 17*, 719–731.

Tsuzuki, D., & Dan, I. (2014). Spatial registration for functional near-infrared spectroscopy: From channel position on the scalp to cortical location in individual and group analyses. *Neuroimage, 85*(Pt 1), 92–103.

Uppenkamp, S., & Röhl, M. (2014). Human auditory neuroimaging of intensity and loudness. *Hear Res, 307*, 65–73.

Warner, R. L., & Bender, R. A. (2002). Thresholds of discomfort for complex stimuli: Acoustic and sound-quality predictors. *J Speech Lang Hear Res, 45*, 1016–1026.

Weder, S., Zhou, X., Shoushtarian, M., et al. (2018). Cortical processing related to intensity of a modulated noise stimulus—a functional near-infrared study. *J Assoc Res Otolaryngol*, *19*, 273–286.

Wiggins, I. M., Anderson, C. A., Kitterick, P. T., et al. (2016). Speech-evoked activation in adult temporal cortex measured using functional near-infrared spectroscopy (fNIRS): Are the measurements reliable? *Hear Res, 339*, 142–154.

Woods, D. L., Stecker, G. C., Rinne, T., et al. (2009). Functional maps of human auditory cortex: Effects of acoustic features and attention. *PLoS One, 4*, e5183.

REFERENCE NOTES

1. Hamamura, M., & Iwamiya, S.-I. (2016). *Gender differences in optimal listening levels and loudness perception*. Paper presented at the INTER-NOISE and NOISE-CON Congress and Conference Proceedings.
2. Tak, S., Jang, K. E., Jung, J., et al. (2008). *NIRS-SPM: statistical parametric mapping for near infrared spectroscopy*. Paper presented at the Multimodal Biomedical Imaging III.