

Silent and Continuous fMRI Scanning Differentially Modulate Activation in an Auditory Language Comprehension Task

Conny F. Schmidt,^{1,2,3} Tino Zaehle,² Martin Meyer,^{2,4*} Eveline Geiser,²
Peter Boesiger,¹ and Lutz Jancke²

¹Institute for Biomedical Engineering, University and ETH, Zurich, Switzerland

²Department of Neuropsychology, University of Zurich, Zurich, Switzerland

³Singapore Bioimaging Consortium (SBIC), BioMedical Sciences Institutes, Singapore

⁴Institute of Neuroradiology, University Hospital of Zurich, Zurich, Switzerland

Abstract: Sparse temporal acquisition schemes have been adopted to investigate the neural correlates of human audition using blood-oxygen-level dependent (BOLD) based functional magnetic resonance imaging (fMRI) devoid of ambient confounding acoustic scanner noise. These schemes have previously been extended to clustered-sparse temporal acquisition designs which record several subsequent BOLD contrast images in rapid succession in order to enhance temporal sampling efficiency. In the present study we demonstrate that an event-related task design can effectively be combined with a clustered temporal acquisition technique in an auditory language comprehension task. The same fifteen volunteers performed two separate auditory runs which either applied customary fMRI acquisition (CA) composed of continuous scanner noise or “silent” fMRI built on a clustered temporal acquisition (CTA) protocol. In accord with our hypothesis, the CTA scheme relative to the CA protocol is accompanied by significantly stronger functional responses along the entire superior temporal plane. By contrast, the bilateral insulae engage more strongly during continuous scanning. A post-hoc region-of-interest analysis reveals cortical activation in subportions of the supratemporal plane which varies as a function of acquisition protocol. The middle part of the supratemporal plane shows a rightward asymmetry only for the CTA scheme while the posterior supratemporal plane exposes a significantly stronger leftward asymmetry during the CTA. Our findings implicate that silent fMRI is advantageous when it comes to the exploration of auditory and speech functions residing in the supratemporal plane. *Hum Brain Mapp* 29:46–56, 2008. ©2007 Wiley-Liss, Inc.

Key words: functional MRI; sparse temporal sampling; auditory perception; speech comprehension; auditory cortex

Conny Schmidt and Tino Zaehle equally contributed to this work.

Contract grant sponsor: Swiss National Foundation (projects 46234101, 46234103) ETH Zurich (Strategic Excellence Project TH 7/02-02).

*Correspondence to: Martin Meyer, Department of Neuroradiology, University Hospital of Zurich, Frauenklinikstrasse 10, CH-8091 Zurich, Switzerland. E-mail: mmeyer@access.unizh.ch

Received for publication 3 February 2006; Revised 23 November 2006; Accepted 28 November 2006

DOI: 10.1002/hbm.20372

Published online 22 February 2007 in Wiley InterScience (www.interscience.wiley.com).

© 2007 Wiley-Liss, Inc.

INTRODUCTION

Since the advent of neuroimaging techniques approximately twenty years ago, our understanding of the cerebral organization of speech functions has substantially changed and improved. However, customary functional magnetic resonance imaging (fMRI) is hampered by acoustic noise produced during operation of the MR system, which affects the experimental integrity of auditory fMRI studies [Amaro et al., 2002; Haller et al., 2005; McJury and Sherlock, 2000; Moelker and Pattynama, 2003]. In particu-

lar, the MR acquisition inevitably produces bursts of acoustic noise up to 120 dB SPL, which obscure the quality of auditory stimulus presentation. At the perceptual level, recognition of spoken utterances is distorted by acoustic masking of the stimulus when its spectral components overlap with the scanner acoustic noise as well as by psycho-acoustic effects, such as a stapedius muscle reflex that alters the perceived sound level and spectral characteristics of the presented stimulus.¹ At the physiological level, the ambient scanner noise is tied to a saturation of the neuronal population residing in auditory cortices in the supratemporal plane. At the cognitive level the extraction of an auditory stimulus in an obscuring acoustic background is affected by foreground-background decomposition processes and attentional effort which may provoke additional functional responses in extra-auditory frontal areas. This slew of deleterious issues imperatively required the development of new devices and strategies to overcome the drawback of noisy fMRI, especially in the realm of auditory cognition. Hardware-based attempts to alleviate acoustic scanner noise at its very source, for example, engineering of Lorentz force-balanced gradient coils, selection of gradient coil material with high stiffness in order to minimise mechanical vibration, implementation of acoustically damped mounting systems as well as special sound insulation have been successfully applied [Edelstein et al., 2002; Katsunuma et al., 2002; Mechefske et al., 2002]. Moreover, the acoustic features of the scanner noise could be changed so that they are less disruptive [Hennel et al., 1999; Seifritz et al., 2006]. However, neither of these approaches can be considered as an optimal solution since both fail to reduce acoustic noise sufficiently nor do they eliminate it. In addition, recent evaluation of one experimental design to reduce scanner noise, the sparse temporal acquisition technique (STA) demonstrates the advantages of this approach in auditory experiments [Amaro et al., 2002; Edmister et al., 1999; Gaab et al., in press, a,b; Hall et al., 1999, 2001; Talavage and Edmister, 2004; Talavage et al., 1999]. Using this technique, the interval between single volume scans is enhanced and the physiological delay between the onset of the stimulation and the succeeding hemodynamic response is used to separate the functional responses evoked by the scanner acoustic noise and the auditory stimulus at issue. Thus, the STA scheme allows insertion of relatively long silent intervals between function image acquisitions during which auditory stimuli are presented. Hence the aforementioned detriments affecting the perceptual, physiological, and cognitive level are reduced.

To investigate the cerebral substrates of auditory speech perception, it has become convenient to use scanning pro-

¹The stapedius reflex is a reflexive contraction of the stapedius muscle in response to loud sound. The reflex threshold varies across individuals between 70–100 dB sound pressure level in normal hearing subjects, and hence is relevant for fMRI experiments [Olsen, 1999].

ocols that are reliant on the sparse sampling technique to avoid interference with ambient scanner noise. Evidently, the functional response to an auditory stimulus as measured with a STA was magnified in terms of amplitude of the response and spatial extent of significant clusters of activation. Moreover, it has been shown that functional activation was localised with enhanced spatial and functional specificity [Yang et al., 2000]. However, compared with continuous scanning, these acquisition schemes require longer total imaging time in order to collect sufficient data for powerful statistical analyses. Hence, “silent” event-related sparse temporal acquisition designs have been further elaborated upon to produce clustered-sparse temporal acquisitions (CTA).² In this acquisition design, multiple volume scans are acquired in rapid succession after each trial (therefore “clustered”), in order to combine advantages of “silent” scanning with time-efficient data collection. Incorporating long acquisition intervals, such schemes have been employed in a variety of studies, such as investigation of functional activation evoked by scanner noise itself [Bandettini et al., 1998], motor activation [Bandettini et al., 1998; Eden et al., 1999], and in the context of short sine wave tone perception [Di Salle et al., 2001] as well as in fMRI-studies on syllable processing [Zaehle et al., 2004], auditory imagery [Bunzeck et al., 2005], and short sentence stimuli [Schwarzbauer et al., 2006].

The Present Study

The current study investigates the effects of ambient scanner noise bound to continuous fMRI on hemodynamic responses to spoken sentences. For this purpose, we compare data collected from two differential scanning protocols that systematically vary the emission of acoustic scanner noise while the total amount of scanning time and auditory stimulation is kept constant. As outlined above, scanner noise affects auditory processing at the perceptual, physiological, and cognitive level. In terms of the perceptual level, noise is meant to acoustically mask stimulus recognition. Hence we hypothesise that behavioural performance is slower and less accurate during “noisy” CA relative to “silent” CTA. As for the physiological level, persistent acoustic scanner noise comes along with a steady saturation of neural ensembles in the auditory cortex and hence reduces the functional modulation range with which the cortex can respond to an auditory stimulus. Thus, we hypothesise that in the presence of continuous scanner noise, the functional response to an auditory

²Importantly, we would like to emphasise that in the context of our study, we relate the term “clustered temporal acquisition” to clustered acquisitions of scans, as opposed to the clustered volume acquisition (CVA), which is the clustered acquisition of slices within one volume scan [Edmister et al., 1999]. The clustered temporal acquisition and the continuous acquisition techniques are referred to as CTA and CA techniques, respectively, through the remainder of the article.

stimulus is reduced in primary and secondary auditory areas whereas cortical association areas supporting higher linguistic processing are not affected. Furthermore, the presence of acoustic scanner noise demands additional cognitive processing. Thence, we predict a stronger involvement of extra-auditory, in particular frontal brain regions when participants undergo the experimental task in the noisy environment.

MATERIALS AND METHODS

Subjects

Fifteen healthy volunteers (eight males, seven females, age $26 \pm SD 5$ years), all consistently right-handed as determined by the Annett-Handedness Questionnaire [Annett, 1992; Jancke, 1996], participated in the study. All participants were native speakers of German and had not been familiar with the stimuli prior to scanning. They had no neurological or psychiatric history, nor did they have any hearing disorder. Written informed consent was obtained prior to the examination. The study was in accordance with Zurich Medical Faculty Ethical guidelines.

Stimuli and Design

Stimulus material consisted of normal and pseudo sentences of 3.4 ± 0.4 s duration. In the normal speech condition, participants heard normal German sentences while the pseudo speech condition was composed of grammatically correct nonsense sentences with all content words having been replaced by pseudo-words adhering to the phonotactical rules of the German language (for details see Friederici et al., [2000]). We decided to include normal and pseudo-sentences to offer participants a larger variability of controlled speech material.

For example, a sentence from the normal speech condition was:

*Die besorgte Mutter sucht das weinende Kind.
The anxious mother searches for the crying child.*

Likewise, an example sentence from the pseudo speech condition was:

*Das mumpfige Folofel hongert das apoldige Trekon.
The mumpfy folofel hongers the apoldish trekon.*

In both normal and pseudo speech condition, half the stimuli were active voice sentences and half were passive voice sentences. We controlled all normal and pseudo sentences for syntax, mean duration, and mean amplitude. All sound files were digitised at a 16 bit/44.1 kHz sampling rate and were volume balanced using Volume Balancer software (Version 1.3, www.delback.co.uk/volbal/).

Task

Throughout the experiment, participants were asked to indicate whether each sentence had an active or passive

syntactic structure and gave their response by button press (only using the right hand) as soon as they identified the sentence structure. Prior to scanning, participants underwent brief training during which they were presented with spoken normal and pseudo sentences specifically recorded for practice purposes.

Procedure

During scanning the room lights were dimmed and a fixation cross was projected via a forward projection system onto a translucent screen placed at the end of the magnet's gurney. Subjects viewed the screen through a double mirror attached to the head coil. Stimuli were controlled using Presentation[®] software (Version 0.70, www.neurobs.com). Stimulus presentation was synchronised with the data acquisition by a 5 V TTL trigger pulse. We used an MR-compatible piezoelectric auditory stimulation system incorporated into standard Philips headphones for binaural stimulus delivery.

Each volunteer performed two experimental runs (CA and CTA). We balanced the order of acquisition scheme across the subjects. A total of 60 auditory events and 20 empty trials (silence) was presented in each experimental run in an event-related pseudo-randomised order. Each trial lasted 15 s, leading to a total duration of 20 min for both the CA and the CTA scheme. Therefore, the total amount of scanning time was kept constant between the two acquisition paradigms. Each sentence was only presented once during either CA or CTA. In the CA, we varied the inter-stimulus-interval systematically by moving the onset of the stimulation in three steps of 0.5 s (cf. Fig. 1) [Dale, 1999]. In the CTA, the stimulus was presented 4.0 or 4.5 s prior to the data acquisition. Each trial was initialised visually by a 2 s fixation cross, which directly preceded the auditory stimulus or empty trial. The sound level of the acoustic noise produced by the MR scanner during the CA scheme was ~ 97.1 dB. Considering the level of attenuation provided by the combination of headphones (Phillips Standard SHC headset, attenuation of ~ 15 – 17 dB) and earplugs (attenuation of ~ 30 – 40 dB), participants were exposed to a noise level of ~ 40 – 52 dB during the CA scheme.

Data Acquisition

Measurements were performed on a Philips Achieva 3 T whole body MR unit (Philips Medical Systems, Best, The Netherlands) equipped with an 8-channel Philips SENSE head coil. Functional data were obtained from 14 transverse slices covering the entire perisylvian cortex parallel to the AC-PC plane with high spatial resolution of $1.7 \times 1.7 \times 3$ mm³ using a Sensitivity Encoded (SENSE, [Pruessmann et al., 1999]) single-shot gradient-echo planar sequence (acquisition matrix 128×128 , SENSE acceleration factor $R = 2.7$, FOV = 220 mm, inter-slice gap 0.3 mm, TE = 35 ms). With the CTA scheme, three subsequent volumes

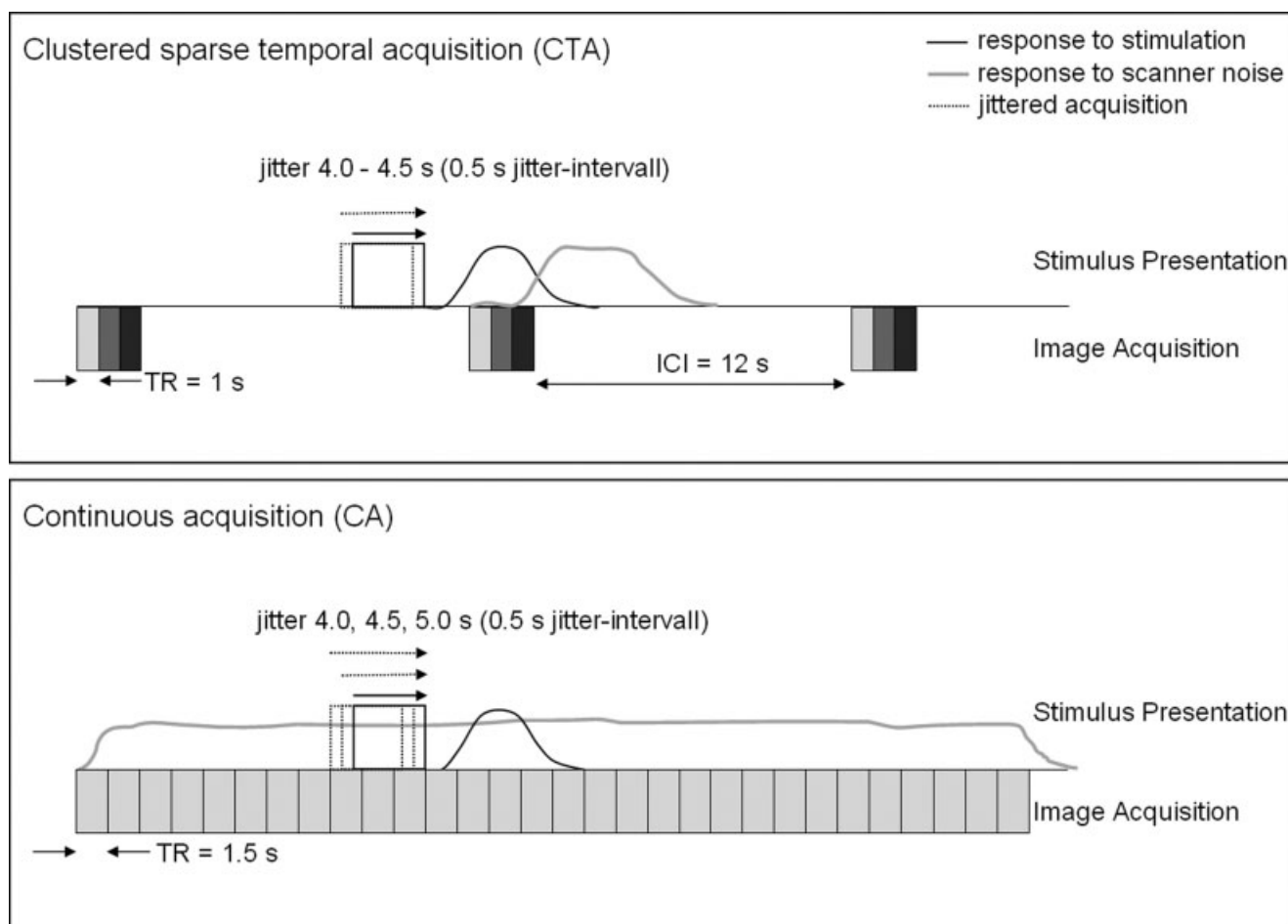


Figure 1.

Clusters temporal and continuous acquisition (CTA and CA). With the CTA, the auditory stimulus was presented during silence, followed by three volume scans (each with a TR = 1 s). Trial duration was 15 s with a 12 s inter-cluster-interval (ICI). Stimulus presentation started 4.0 s or 4.5 s. The stimulus induced functional signal (thin black line) was sampled at the pre-

sumed amplitude of the response and was separated from the scanner-noise induced functional response (thick grey line). During continuous data acquisition volume scans were acquired with a TR = 1.5 s. The stimulus presentation was jittered by 0 s, 0.5 s, and 1 s respectively, forming a 0.5 jitter interval.

were acquired per trial with a TR = 1 s, flip angle 90° (decay sampling), and a 12 s inter-cluster-interval (ICI) resulting in 240 dynamic scan volumes.

With the CA scheme, a total of 800 dynamic scan volumes were continuously acquired with a TR = 1.5 s (flip angle 72°). Three dummy scans preceded the experiment to allow the magnetization to reach a steady state.

We additionally collected a standard 3D T1-weighted scan for anatomical reference with 1 × 1 × 0.8 mm³ spatial resolution (acquisition matrix 224 × 224, TE = 2.30 ms, TR = 20 ms, flip angle 20°).

Data Analysis

Artifact elimination and image analysis was performed using MATLAB 6.5 (Mathworks, Natick, MA), the SPM99

software package (Institute of Neurology, London, UK; <http://www.fil.ion.ucl.ac.uk>) and the MarsBar toolbox for SPM (<http://marsbar.sourceforge.net/>) [Brett et al., 2002]. All volumes were realigned to the first volume to account for movement artifacts, normalised into standard stereotactic space (voxel size 2 × 2 × 2 mm³, template provided by the Montreal Neurological Institute), and smoothed using a Gaussian kernel with 8 mm full-width-at-half-maximum. Condition and subject effects were estimated using the General Linear Model (GLM) [Friston et al., 1995a,b]. For CA scheme, condition of interest corresponding to the verbal condition was modeled using the appropriate stimulus function (box-car) convolved with a canonical hemodynamic response function (HRF). Low-frequency drifts were removed using a temporal high-pass filter (cut-off of 210 s). Additionally, the time series was temporally

smoothed with a moving Gaussian kernel (FWHM = 4 s). Similar, for the CTA scheme, condition of interest corresponding to the verbal conditions were modeled using a box-car function without convolving with the canonical haemodynamic response function as reference waveform. Low-frequency drifts were removed using a temporal high-pass filter (cut-off of 42 s). Because of the very low sampling frequency in this sparse temporal sampling design, low-pass filter was not applied. One characteristic of the CTA design is that the longitudinal magnetization does not reach its steady state within the acquisition of one cluster. Thus, each of the three scans collected for one trial is influenced by different T1 saturation effects. To account for T1-decay related changes in the MR-signal, we included two additional regressors of no interest into the single subject analyses. These regressors model the means of different MR signal intensities at the three time points of acquisition along the T1-decay curve. Considering a constant amount of noise within the signal of these images and no T1-effects on BOLD-induced signal changes, we can assume a constant Contrast-to-Noise-Ratio (CNR) over the three consecutive images. Thus, the use of regressors should be considered an appropriate device to partial out the influence of T1-decay related signal changes. After estimation of model parameters for each subject, an analysis of variance was calculated for the whole group using the individual contrast images for the main effects. To test hypotheses about regionally specific condition effects, linear contrasts were employed in the context of a random effects procedure [Friston et al., 1999]. In a first step, we calculated the effects of auditory stimulation separately for the CA and CTA scheme. In a next step, we directly compared the data of the CA and CTA schemes. Results of all analyses were thresholded at $T = 5.52$ ($P = 0.05$, corrected for multiple comparisons) and a spatial extent of $k = 20$ voxels.

Region of Interest Analysis

In order to quantify functional hemispheric differences of local brain activity in auditory fields stretching along the entire supratemporal plane (STP) as a function of the acquisition technique, a set of six distinct regions of interest (ROI) was placed for each subject in Heschl's gyrus (HG, middle STP), the planum polare (PP, anterior STP) and planum temporale (PT, posterior STP) of each hemisphere. Regions of interest were anatomically defined based on macroanatomical landmarks [Rademacher et al., 2001; Steinmetz et al., 1990].³ The left and right HG ROI were centred at MNI coordinates $x = \pm 49$, $y = -15$, $z = 5$, size 4.16 cm^3 , the left and right PP ROI at $x = \pm 46$, $y = -4$, $z = -7$, size 3.22 cm^3 and the PT ROI comprised 3.22 cm^3 at $x = \pm 54$, $y = -30$, $z = 12$. Mean *beta*-values were

³The supplementary materials include an illustration of size and position of ROIs (www.psychologie.unizh.ch/neuropsych/home_mmeyer/HBM-06-0027/).

collected for each subject from each ROI (HG, PP, PT), and acquisition technique (CTA and CA), and were subjected to a repeated-measure within-subjects ($2 \times 3 \times 2$) ANOVA with factors *acquisition scheme* (CTA, CA), *ROI* (HG, PP, PT), and *hemisphere* (left, right). All main effects or interactions with two or more degrees of freedom in the numerator were adjusted due to the Greenhouse-Geiser correction. Subsequently, we computed a (2×2) ANOVA with the factors design and hemisphere for each ROI. The threshold for significance was set at $P < 0.05$.

RESULTS

Behavioural Data

The mean accuracies with which the subjects identified active and passive sentence structures in the presented auditory sentence material were 98% and did not differ between CTA and CA. As for the reaction times, a paired sampled t-test uncovered that mean reaction times were significantly faster during "silent" clustered (RT = $2.98 \pm \text{SE } 0.73 \text{ s}$) than during continuous scanning (RT = $3.22 \pm \text{SE } 0.73 \text{ s}$; $t(14) = -3.74$, $P < 0.005$).

Imaging Data

Akin to former studies using the same stimulus corpus [Friederici et al., 2000; Heinke et al., 2004; Meyer et al., 2002] we collected significant functional activation in response to auditory speech stimuli⁴ as compared to silence from bilateral perisylvian regions, in particular along the supratemporal plane, including Heschl's gyrus (HG), the plana temporale (PT) and polare (PP), from the lateral and deep fronto-opercular region (FOR), and from the insula regardless of the selected design. Furthermore, we also observed activation in extrasylvian brain sites, namely the middle temporal gyrus, the cuneus, and subcortical structures (basal ganglia, thalamus).

To exemplify the individual acquisition main effects Figure 2 shows data of 6 out of 15 volunteers.⁵ In terms of the CTA scheme, hearing sentences compared to empty trials evoked considerably stronger responses in bilateral superior temporal and inferior frontal regions relative to the CA scheme.

As shown in Figure 3 and listed in Table I, the direct comparison of the CTA and CA scheme showed that the former corresponds to more significant activation bilaterally.

⁴We did not look at the contrast "normal" with "pseudosentences" (or vice-versa) as it is beyond the scope of this study. This contrast and its related neural and psycholinguistic implications have been extensively addressed by former publications of the corresponding author ([Friederici et al., 2000; Heinke et al., 2004; Meyer et al., 2002, 2003]) or others [Mazoyer et al., 1993; Roder et al., 2002]. We simply included pseudo sentences for reasons of a highly desirable variability of speech input.

⁵The supplementary materials include an illustration of SPMs of all subjects (www.psychologie.unizh.ch/neuropsych/home_mmeyer/HBM-06-0027/).

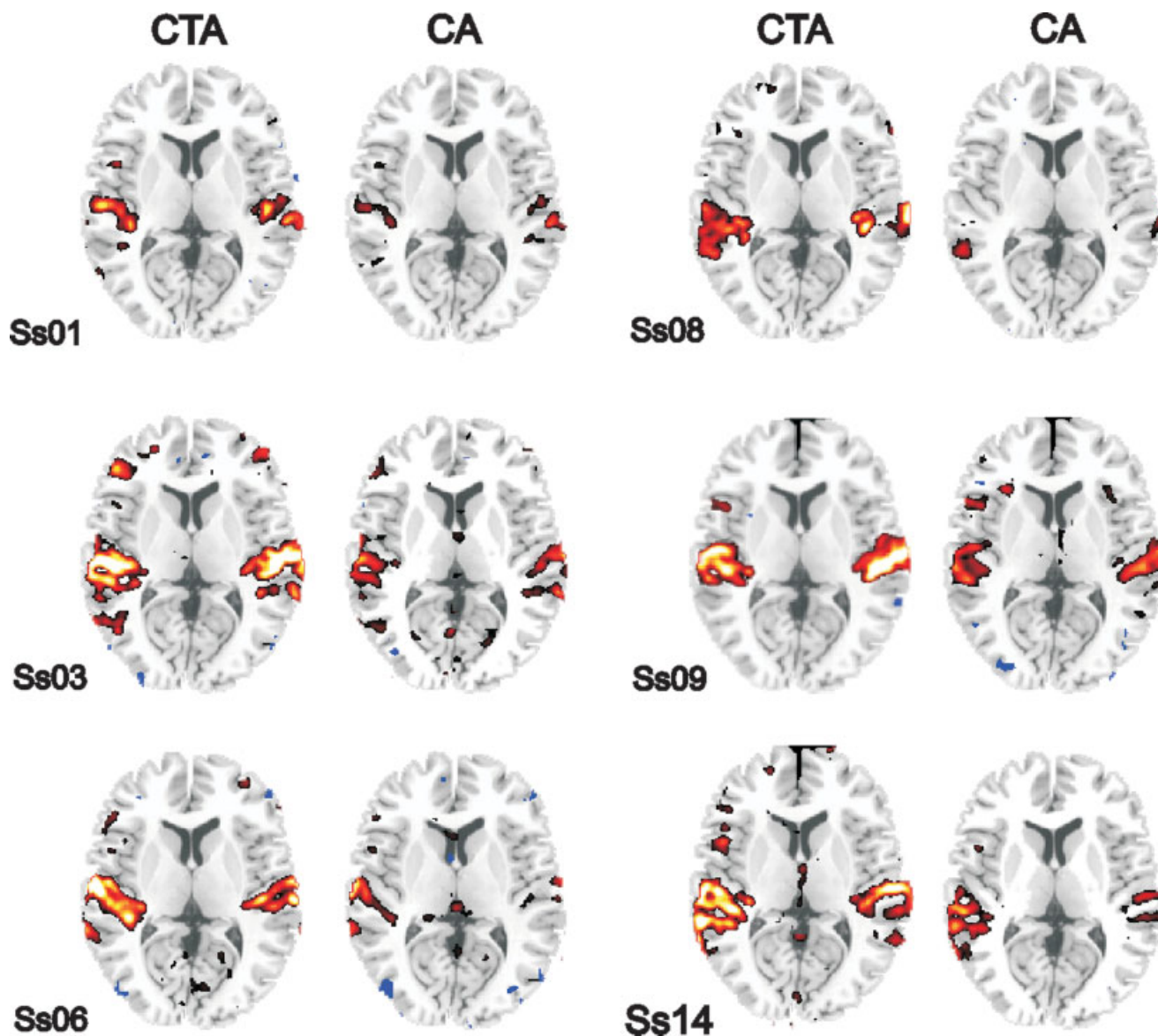


Figure 2.

Individual acquisition main effects. Illustration of main effect (CA vs. CTA) in six individuals. Stronger responses to CTA are colour-coded at a red-yellow scale. Stronger responses to CA are colour-coded at a blue-petal scale. Individual functional results

are superimposed onto a horizontal section ($z = 8$) of a standard anatomical template and are thresholded at $T = 5.03$ ($P = 0.05$, corrected for multiple comparisons). Data is plotted in neurological convention.

ally in superior temporal cortex and in the left lateral convexity of inferior frontal gyrus. For the complementary comparison of CA scheme with the CTA scheme we did not find significant activation with the given threshold. By applying a lower threshold ($T = 3.30$, $P = 0.001$, uncorrected for multiple comparisons, extent threshold $k = 20$ voxels), the analysis exposed an involvement of the left and right insula and the superior occipital cortex for the CA in comparison to CTA scheme.

ROI Analysis

We computed an additional ROI analysis to reveal local differences and interaction effects between acquisition scheme, ROI, and hemisphere in the supratemporal response pattern.

A global $2 \times 3 \times 2$ ANOVA with factors *acquisition scheme* (CTA, CA), *ROI* (HG, PP, PT), and *hemisphere* (left, right) revealed a significant main effect of acquisition scheme

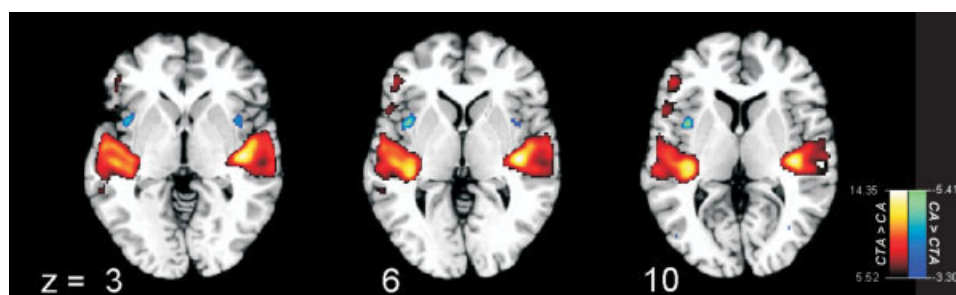


Figure 3.

Group acquisition main effects (CA vs. CTA). Stronger responses to CTA are colour-coded at a red-yellow scale. Starker responses to CA are colour-coded at a blue-petrol scale. Results are superimposed onto horizontal sections of a standard anatomical template. Data is plotted in neurological convention.

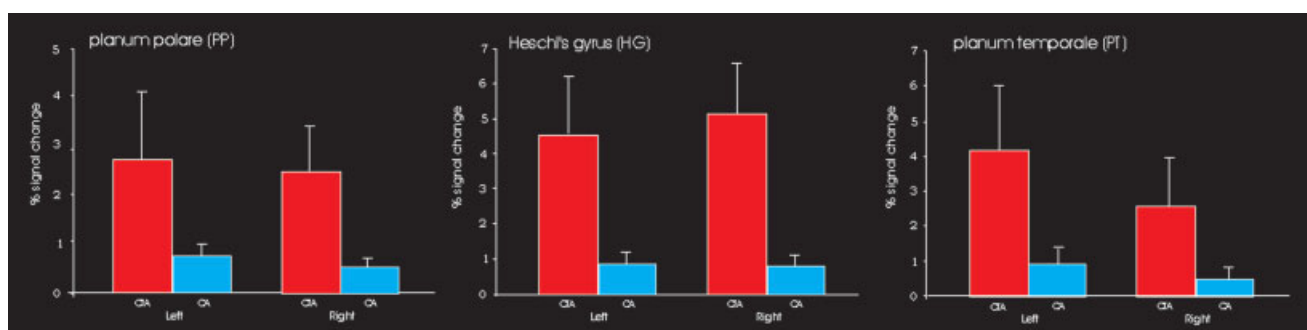


Figure 4.

Analysis of three bilateral superior temporal plane regions for the main effects of acquisition scheme (CA vs. CTA) and hemisphere. Mean *beta*-values were averaged across all subjects within bilateral planum polare (PP), Heschl's gyrus (HG), and planum temporale (PT). Error bars indicate the standard deviation.

($F(1,14) = 153.16$, $P < 0.000$) reflecting stronger responses for the CTA scheme in all regions; hemisphere ($F(1,14) = 8.59$, $P < 0.01$) indicating a general leftward asymmetry, and ROI ($F(2,28) = 13.59$, $P < 0.001$). Furthermore, we identified an interaction between ROI and hemisphere ($F(2,28) = 15.02$, $P < 0.000$), that reflects differential functional asymmetries within the ROIs, a significant interaction between acquisition scheme and ROI ($F(2,28) = 17.64$, $P < 0.000$), and an interaction of acquisition scheme by ROI by hemisphere ($F(2,28) = 14.39$, $P < 0.000$).

To test the statistical significance of regional difference in functional lateralization, we performed a 2×2 ANOVA with factors *acquisition technique* (CA, CTA) and *hemisphere* (left, right) for each ROI separately. The pattern of results for PP, HG, and PT turns out differently: The 2×2 ANOVA for the PP revealed a main effect of acquisition technique ($F(1,14) = 56.85$, $P < 0.000$), but no main effect of hemisphere, and no interaction between acquisition type and hemisphere. The 2×2 ANOVA for the HG uncovered a main effect of acquisition technique ($F(1,14) = 152.66$, $P < 0.000$), no main effect of hemisphere, and a

trend for the interaction of acquisition type with hemisphere ($F(1,14) = 4.51$, $P = 0.052$) indicating a rightward functional superiority for the CTA exclusively. The 2×2 ANOVA for the PT unveiled a main effect of acquisition technique ($F(1,14) = 59.61$, $P < 0.000$), a main effect of hemisphere ($F(1,14) = 35.07$, $P < 0.000$), and an interaction between acquisition type and hemisphere ($F(1,14) = 28.68$, $P < 0.000$) that demonstrates a stronger leftward asymmetry for CTA relative to CA.

Generally, as apparent from Figure 4 we noted consistently larger responses in all ROIs for the CTA as for the CA scheme regardless of hemisphere. More specifically, for the PT the leftward asymmetry was larger for the CTA relative to CA scheme while for the mid STP (HG) we observed a rightward asymmetry for the CTA only.

Taken together, the fMRI results indicate that auditory sentence processing during "silent" CTA generally corresponded to more salient functional responses in auditory fields and inferior frontal sites. The CA, however, appears to lead to stronger brain responses in bilateral insula regions.

TABLE I. Activations observed for the comparison of CTA vs. CA^a

Condition and anatomical labelling	L/R	T-value	x	y	z
CTA vs. CA ^b					
Superior temporal gyrus	R	14.35	44	-18	2
	R	13.98	38	-24	10
Superior temporal gyrus	L	13.33	-36	-28	10
	L	13.12	-38	-36	8
Lingual gyrus	R	8.91	12	-72	4
	R	8.54	18	-66	4
Inferior frontal gyrus	L	8.84	-52	24	-4
	L	7.97	-48	34	10
CA vs. CTA ^c					
Insula	L	5.41	-36	2	12
	L	5.01	-42	6	0
Superior occipital gyrus	L	5.21	-38	-86	18
Superior occipital gyrus	R	5.21	48	-78	14
Insula	R	4.16	40	6	0

^aT-scores and coordinates of clusters according to the MNI stereotactic space are indicated.

^bTo assess the significance of an activation focus, results were thresholded with $T = 5.52$ ($P = 0.05$ corrected for multiple comparisons) and an extent threshold of $k = 20$ voxels.

^cTo assess the significance of an activation focus, results were thresholded with $T = 3.30$ ($P = 0.001$ uncorrected) for multiple comparisons) and an extent threshold: $k = 20$ voxels).

DISCUSSION

In this study, we compared a clustered “silent” acquisition with a continuous fMRI acquisition in order to test the potential advantage of fMRI in a “silent” environment in the context of an auditory speech experiment. We observed that activation in perisylvian regions corresponding to speech perception varied as a function of either the “noisy” CA or the “silent” CTA approach. While auditory sentence processing in a silent fMRI paradigm brought on stronger functional responses of the bilateral supratemporal plane accommodating the entire auditory cortex, the presentation of the identical auditory stimulus material in the context of a traditional continuous acquisition more strongly recruited the bilateral insulae. We also noted that the participants’ behavioural performance significantly slowed down once they were tested in a noisy scanning environment.

Generally, our results are consistent with previous studies having demonstrated the adverse effects of acoustic scanner noise, most strikingly in auditory fields [Bandettini et al., 1998; Bilecen et al., 1998; Gaab et al., in press, a,b; Loenneker et al., 2001; Shah et al., 1999; Talavage et al., 1999]. Basically, the essence of these observations suggests that at the physiological level signal detection in the context of fMRI of auditory research is harmed especially in primary and secondary auditory cortices as continuous gradient noise itself constitutes a persistent acoustic stimulus which evokes a saturation of the neuronal population residing in the supratemporal plane. Furthermore, noisy

continuous fMRI increases the BOLD baseline activation in auditory regions which yields smaller BOLD responses to sound stimuli. As we hypothesised, our present study demonstrates that this reduced functional modulation range determines a decreased hemodynamic response to spoken sentences in the entire auditory cortex. Additionally, our analysis yields that scanner noise modulates the functional hemisphere asymmetry in the mid and posterior STP differentially.

Electrophysiological studies provided evidence for the view that a noisy environment asymmetrically affects neuronal functions in the context of auditory and speech processing. An MEG study on sentence perception reported that noise presented with 75 dB sound intensity disrupted early auditory processing only in the right hemisphere [Herrmann et al., 2000]. Our results underline these findings in that we noticed stronger functional activation in the right relative to the left mid portion of the auditory cortex for the “silent” as opposed to the “noisy” fMRI. However, it should be outlined that right auditory cortex functioning appears to be more complex. According to a combined fMRI and MEG study using scanner noise as auditory stimulus, the right auditory cortex shows higher sensitivity to environmental noise relative to its contralateral homolog [Mathiak et al., 2002]. In other words, a noisy environment more strongly interferes with proper functioning of the right auditory cortex. In addition, in terms of speech perception, it has been shown that in the presence of background scanner noise syllables and speech stimuli are typically perceived as relatively flat sounds due to spectral overlap of typical MR gradient noise and spoken language [Giraud et al., 2000]. This effect might alter the perceived spectral characteristics of the stimulus [Hall et al., 2001] and therefore affects the functioning of the core auditory cortex.

By contrast, the present study further shows that the most posterior compartment of the STP, the planum temporale, displayed a general functional leftward asymmetry for speech perception. More importantly, this leftward asymmetry was significantly stronger when speech was processed under the silent scanning condition. As apparent from recent imaging studies, the left PT appears to be preferentially driven by brief phonological cues which are considered the acoustic foundation of speech [Jancke et al., 2002; Meyer et al., 2005a; Zaehle et al., 2004]. Generally, speech processing corresponds to a functional leftward asymmetry in the human brain [Hickok and Poeppel, 2004; Meyer et al., 2005b; Price et al., 2005; Scott and Johnsrude, 2003; Vigneau et al., 2006], in particular in the PT [Josse et al., 2003]. Here we show that this leftward asymmetry of the posterior supratemporal plane is significantly magnified if “silent” fMRI is applied.

Finally, the contrast of CTA versus CA also revealed stronger activation in the left lateral inferior frontal gyrus (pars triangularis and pars opercularis) for the former acquisition (cf. Fig. 3). Certainly, this finding comes as no surprise as these particular brain regions have long been

considered part of the perisylvian “core language system” [MacSweeney et al., 2002] and have often been reported in the context of sentence comprehension regardless of modality [Friederici et al., 2006a,b]. Because some researchers proposed a preference of these regions for linguistic information [Embick et al., 2000; Suzuki and Sakai, 2003], it is plausible to find the left lateral inferior frontal gyrus involved when subjects are able to process auditory sentences properly in the absence of acoustic scanner noise. However, based on the present experiment we are not able to determine whether responses of left pars triangularis and pars opercularis to auditory sentences reflect the comprehension of grammatical information or represents less specific principles of cognitive processing that are also relevant in linguistic contexts [Bornkessel et al., 2005; Grewe et al., 2005, 2006].

Our comparison between the two acquisition techniques further revealed stronger responses to continuous scanning, particularly in the bilateral insula. A number of recent imaging studies have observed the anterior insula and the adjacent deep frontal operculum as supporting auditory perception, mainly in the context of demanding top-down processing [Binder et al., 2004; Halpern et al., 2004; Jancke and Shah, 2002; Lewis et al., 2004; Wong et al., 2004; Zatorre et al., 1994]. Additionally it has been shown that bilateral damage to the anterior insulae may result in total auditory agnosia [Habib et al., 1995] or in deficient processing of temporal auditory cues [Bamiou et al., 2006]. The authors of the latter study suggest that this region is an integral component of the central auditory pathway. Even though it is widely accepted that this region is (partly) essential for auditory integration and complex sound modulation, its specific functional role still remains elusive [Bamiou et al., 2003]. The present study reports stronger responses of the insula in the context of noisy fMRI. Hence we conjecture that the insular activation particularly observed in the CA mode indicates effortful auditory perception hampered by persistent acoustic scanner noise. Similar observation has been published by Wong et al. [2004; p. 9159], who argued that “the addition of noise introduced an extra cognitive-perception demand (i.e., signal-to-noise extraction)”, which accounts for insular activation. Furthermore, a recent fMRI study demonstrated insula activity in more distractive conventional fMRI relative to a less disruptive scanning protocol [Haller et al., 2005]. A similar scenario can be found in the context of our study: since enhanced effort was necessary in the noisy scanning environment to retrieve intelligible information from the auditory stimuli, it is plausible that this particular region was significantly more engaged during continuous scanning. This observation is additionally supported by the behavioural data, which showed a significantly faster response in “silent” CTA than during continuous scanning.

Summing up, the present study shows that the CTA scheme can successfully be applied to map the functional response to auditory sentence stimuli in a silent environment.

At the perceptual level, faster response times during CTA can be taken as evidence for facilitated auditory sentence processing. Notably, participants performed almost faultless under the two conditions. Evidently, a ceiling effect can be considered the reason we could not find a difference in mean accuracy between the two acquisition schemes. At the physiological level we show that the CTA is generally associated with stronger functional activation in the auditory cortices as this approach is not limited by saturation of the neuronal population evoked by persistent scanner noise. Additionally, we noticed noise dependent modulations of functional hemisphere asymmetry in the mid and posterior STP.

Furthermore, insular regions more strongly responding during CA acquisition may reflect unspecific effort due to compromised perception of inflowing auditory input additionally in a noisy environment.

CONCLUSION

The current study explores an fMRI acquisition scheme that offers the feasibility to deliver auditory stimuli in a silent environment while it allows the acquisition of multiple images to collect sufficient samples in order to efficiently measure the hemodynamic response and thus, limits the total duration of the scanning session to a reasonable duration. Hence, the CTA scheme we have evaluated combines fMRI scanning devoid of interference with scanner acoustic noise and time-efficient data collection.

ACKNOWLEDGMENTS

C.S. and M.M. were supported by the Swiss National Science Foundation grant 46234101. E.G. and T.Z. are supported by the Swiss National Science Foundation grant 46234103. The authors thank Philips Medical Systems for continuing support. They are indebted to the Max Planck Institute of Human Cognitive and Brain Sciences, Leipzig, for providing the stimulus corpus. They also gratefully acknowledge Betina Schnepf and Simon Baumann for motivating discussions.

REFERENCES

- Amaro E, Williams SC, Shergill SS, Fu CH, MacSweeney M, Picchioni MM, Brammer MJ, McGuire PK (2002): Acoustic noise and functional magnetic resonance imaging: Current strategies and future prospects. *J Magn Reson Imaging* 16:497–510.
- Annett M (1992): Five tests of hand skill. *Cortex* 28:583–600.
- Bamiou DE, Musiek FE, Luxon LM (2003): The insula (Island of Reil) and its role in auditory processing. Literature review. *Brain Res Brain Res Rev* 42:143–154.
- Bamiou DE, Musiek FE, Stow I, Stevens J, Cipolotti L, Brown MM, Luxon LM (2006): Auditory temporal processing deficits in patients with insular stroke. *Neurology* 67:614–619.
- Bandettini PA, Jesmanowicz A, Van KJ, Birn RM, Hyde JS (1998): Functional MRI of brain activation induced by scanner acoustic noise. *Magn Reson Med* 39:410–416.

- Bilecen D, Radu EW, Scheffler K (1998): The MR tomograph as a sound generator: fMRI tool for the investigation of the auditory cortex. *Magn Reson Med* 40:934–937.
- Binder JR, Liebenthal E, Possing ET, Medler DA, Ward BD (2004): Neural correlates of sensory and decision processes in auditory object identification. *Nat Neurosci* 7:295–301.
- Bornkessel I, Zysset S, Friederici AD, von Cramon DY, Schlesewsky M (2005): Who did what to whom? The neural basis of argument hierarchies during language comprehension. *Neuroimage* 26:221–233.
- Brett M, Anton J-L, Valabregue R, Poline J-B (2002): Region of interest analysis using an SPM toolbox. *Neuroimage* 16(2): Abstract 497 (Presented at the Eighth International Conference on Functional Mapping of the Human Brain, Sendai, Japan, June 2–6, 2002; <http://marsbar.sourceforge.net/>).
- Bunzeck N, Wuestenberg T, Lutz K, Heinze HJ, Jancke L (2005): Scanning silence: Mental imagery of complex sounds. *Neuroimage* 26:1119–1127.
- Dale AM (1999): Optimal experimental design for event-related fMRI. *Hum Brain Mapp* 8:109–114.
- Di Salle F, Formisano E, Seifritz E, Linden DE, Scheffler K, Saulino C, Tedeschi G, Zanella FE, Pepino A, Goebel R, Marciano E (2001): Functional fields in human auditory cortex revealed by time-resolved fMRI without interference of EPI noise. *Neuroimage* 13:328–338.
- Edelstein WA, Hedeem RA, Mallozzi RP, El-Hamamsy SA, Ackermann RA, Havens TJ (2002): Making MRI quieter. *Magn Reson Imaging* 20:155–163.
- Eden GF, Joseph JE, Brown HE, Brown CP, Zeffiro TA (1999): Utilizing hemodynamic delay and dispersion to detect fMRI signal change without auditory interference: The behavior interleaved gradients technique. *Magn Reson Med* 41:13–20.
- Edmister WB, Talavage TM, Ledden PJ, Weisskoff RM (1999): Improved auditory cortex imaging using clustered volume acquisitions. *Hum Brain Mapp* 7:89–97.
- Embick D, Marantz A, Miyashita Y, O’Neil W, Sakai KL (2000): A syntactic specialization for Broca’s area. *Proc Natl Acad Sci USA* 97:6150–6154.
- Friederici AD, Meyer M, von Cramon DY (2000): Auditory language comprehension: An event-related fMRI study on the processing of syntactic and lexical information. *Brain Lang* 74:289–300.
- Friederici AD, Bahlmann J, Heim S, Schubotz RI, Anwander A (2006a): The brain differentiates human and non-human grammars: Functional localization and structural connectivity. *Proc Natl Acad Sci USA* 103:2458–2463.
- Friederici AD, Fiebach CJ, Schlesewsky M, Bornkessel ID, von Cramon DY (2006b): Processing linguistic complexity and grammaticality in the left frontal cortex. *Cereb Cortex* 16:1709–1717.
- Friston KJ, Holmes AP, Poline JB, Grasby PJ, Williams SC, Frackowiak RS, Turner R (1995a): Analysis of fMRI time-series revisited. *Neuroimage* 2:45–53.
- Friston KJ, Holmes AP, Worsley KP, Poline JB, Frith CD, Frackowiak RS (1995b): Statistical parameter maps in functional imaging: A general linear approach. *Hum Brain Mapp* 2:189–210.
- Friston KJ, Holmes AP, Price CJ, Buchel C, Worsley KJ (1999): Multisubject fMRI studies and conjunction analyses. *Neuroimage* 10:385–396.
- Gaab N, Gabrieli JDE, Glover GH (in press DOI: 10.1002/hbm.20298): Assessing the influence of scanner background noise on auditory processing. I. An fMRI study comparing three experimental designs with varying degrees of scanner noise. *Hum Brain Mapp*.
- Gaab N, Gabrieli JDE, Glover GH (in press DOI: 10.1002/hbm.20299): Assessing the influence of scanner background noise on auditory processing. II. An fMRI study comparing auditory processing in the absence and presence of recorded scanner noise using a sparse design. *Hum Brain Mapp*.
- Giraud AL, Lorenzi C, Ashburner J, Wable J, Johnsrude I, Frackowiak R, Kleinschmidt A (2000): Representation of the temporal envelope of sounds in the human brain. *J Neurophysiol* 84:1588–1598.
- Grewe T, Bornkessel I, Zysset S, Wiese R, von Cramon DY, Schlesewsky M (2005): The emergence of the unmarked: A new perspective on the language-specific function of Broca’s area. *Hum Brain Mapp* 26:178–190.
- Grewe T, Bornkessel I, Zysset S, Wiese R, von Cramon DY, Schlesewsky M (2006): Linguistic prominence and Broca’s area: The influence of animacy as a linearization principle. *Neuroimage* 32:1395–1402.
- Habib M, Daquin G, Milandre L, Royere ML, Rey M, Lanteri A, Salamon G, Khalil R (1995): Mutism and auditory agnosia due to bilateral insular damage—Role of the insula in human communication. *Neuropsychologia* 33:327–339.
- Hall DA, Haggard MP, Akeroyd MA, Palmer AR, Summerfield AQ, Elliott MR, Gurney EM, Bowtell RW (1999): “Sparse” temporal sampling in auditory fMRI. *Hum Brain Mapp* 7:213–223.
- Hall DA, Haggard MP, Summerfield AQ, Akeroyd MA, Palmer AR, Bowtell RW (2001): Functional magnetic resonance imaging measurements of sound-level encoding in the absence of background scanner noise. *J Acoust Soc Am* 109:1559–1570.
- Haller S, Bartsch AJ, Radue EW, Klarhofer M, Seifritz E, Scheffler K (2005): Effect of fMRI acoustic noise on non-auditory working memory task: Comparison between continuous and pulsed sound emitting EPI. *MAGMA* 18:263–271.
- Halpern AR, Zatorre RJ, Bouffard M, Johnson JA (2004): Behavioral and neural correlates of perceived and imagined musical timbre. *Neuropsychologia* 42:1281–1292.
- Heinke W, Fiebach CJ, Schwarzbauer C, Meyer M, Olthoff D, Alter K (2004): Sequential effects of propofol on functional brain activation induced by auditory language processing: An event-related functional magnetic resonance imaging study. *Br J Anaesth* 92:641–650.
- Hennel F, Girard F, Loenneker T (1999): “Silent” MRI with soft gradient pulses. *Magn Reson Med* 42:6–10.
- Herrmann CS, Oertel U, Wang Y, Maess B, Friederici AD (2000): Noise affects auditory and linguistic processing differently: An MEG study. *Neuroreport* 11:227–229.
- Hickok G, Poeppel D (2004): Dorsal and ventral streams: A framework for understanding aspects of the functional anatomy of language. *Cognition* 92:67–99.
- Jancke L (1996): The hand performance test with a modified time limit instruction enables the examination of hand performance asymmetries in adults. *Percept Mot Skills* 82:735–738.
- Jancke L, Shah NJ (2002): Does dichotic listening probe temporal lobe functions? *Neurology* 58:736–743.
- Jancke L, Wustenberg T, Scheich H, Heinze HJ (2002): Phonetic perception and the temporal cortex. *Neuroimage* 15:733–746.
- Josse G, Mazoyer B, Crivello F, Tzourio-Mazoyer N (2003): Left planum temporale: An anatomical marker of left hemispheric specialization for language comprehension. *Brain Res Cogn Brain Res* 18:1–14.
- Katsunuma A, Takamori H, Sakakura Y, Hamamura Y, Ogo Y, Katayama R (2002): Quiet MRI with novel acoustic noise reduction. *MAGMA* 13:139–144.

- Lewis JW, Wightman FL, Brefczynski JA, Phinney RE, Binder JR, DeYoe EA (2004): Human brain regions involved in recognizing environmental sounds. *Cereb Cortex* 14:1008–1021.
- Loenneker T, Hennel F, Ludwig U, Hennig J (2001): Silent BOLD imaging. *MAGMA* 13:76–81.
- MacSweeney M, Woll B, Campbell R, McGuire PK, David AS, Williams SC, Suckling J, Calvert GA, Brammer MJ (2002): Neural systems underlying British sign language and audio-visual English processing in native users. *Brain* 125:1583–1593.
- Mathiak K, Rapp A, Kircher TT, Grodd W, Hertrich I, Weiskopf N, Lutzenberger W, Ackermann H (2002): Mismatch responses to randomized gradient switching noise as reflected by fMRI and whole-head magnetoencephalography. *Hum Brain Mapp* 16:190–195.
- Mazoyer BM, Tzourio N, Frak V, Syrota A, Murayama N, Levrier O, Salamon G, Dehaene S, Cohen L, Mehler J (1993): The cortical representation of speech. *J Cogn Neurosci* 5:467–479.
- McJury M, Shellock FG (2000): Auditory noise associated with MR procedures: A review. *J Magn Reson Imaging* 12:37–45.
- Mechefske CK, Geris R, Gati JS, Rutt BK (2002): Acoustic noise reduction in a 4 T MRI scanner. *MAGMA* 13:172–176.
- Meyer M, Alter K, Friederici AD, Lohmann G, von Cramon DY (2002): fMRI reveals brain regions mediating slow prosodic modulations in spoken sentences. *Hum Brain Mapp* 17:73–88.
- Meyer M, Alter K, Friederici A (2003): Functional MR imaging exposes differential brain responses to syntax and prosody during auditory sentence comprehension. *J Neurolinguistics* 16:277–300.
- Meyer M, Zaehle T, Gountouna VE, Barron A, Jancke L, Turk A (2005a): Spectro-temporal processing during speech perception involves left posterior auditory cortex. *Neuroreport* 16:1985–1989.
- Meyer M, Zysset S, von Cramon DY, Alter K (2005b): Distinct fMRI responses to laughter, speech, and sounds along the human peri-sylvian cortex. *Brain Res Cogn Brain Res* 24:291–306.
- Moelker A, Pattynama PM (2003): Acoustic noise concerns in functional magnetic resonance imaging. *Hum Brain Mapp* 20:123–141.
- Olsen SO (1999): The relationship between the uncomfortable loudness level and the acoustic reflex threshold for pure tones in normally-hearing and impaired listeners—A meta-analysis. *Audiology* 38:61–68.
- Price C, Thierry G, Griffiths T (2005): Speech-specific auditory processing: Where is it? *Trends Cogn Sci* 9:271–276.
- Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P (1999): SENSE: Sensitivity encoding for fast MRI. *Magn Reson Med* 42:952–962.
- Rademacher J, Morosan P, Schormann T, Schleicher A, Werner C, Freund HJ, Zilles K (2001): Probabilistic mapping and volume measurement of human primary auditory cortex. *Neuroimage* 13:669–683.
- Roder B, Stock O, Neville H, Bien S, Rosler F (2002): Brain activation modulated by the comprehension of normal and pseudo-word sentences of different processing demands: A functional magnetic resonance imaging study. *Neuroimage* 15:1003–1014.
- Schwarzbauer C, Davis MH, Rodd JM, Johnsrude I (2006): Interleaved silent steady state (ISSS) imaging: A new sparse imaging method applied to auditory fMRI. *Neuroimage* 29:774–782.
- Scott SK, Johnsrude IS (2003): The neuroanatomical and functional organization of speech perception. *Trends Neurosci* 26:100–107.
- Seifritz E, Di SF, Esposito F, Herdener M, Neuhoff JG, Scheffler K (2006): Enhancing BOLD response in the auditory system by neurophysiologically tuned fMRI sequence. *Neuroimage* 29:1013–1022.
- Shah NJ, Jancke L, Grosse-Ruyken ML, Muller-Gartner HW (1999): Influence of acoustic masking noise in fMRI of the auditory cortex during phonetic discrimination. *J Magn Reson Imaging* 9:19–25.
- Steinmetz H, Rademacher J, Jancke L, Huang YX, Thron A, Zilles K (1990): Total surface of temporoparietal intrasylvian cortex: Diverging left-right asymmetries. *Brain Lang* 39:357–372.
- Suzuki K, Sakai KL (2003): An event-related fMRI study of explicit syntactic processing of normal/anomalous sentences in contrast to implicit syntactic processing. *Cereb Cortex* 13:517–526.
- Talavage TM, Edmister WB (2004): Nonlinearity of fMRI responses in human auditory cortex. *Hum Brain Mapp* 22:216–228.
- Talavage TM, Edmister WB, Ledden PJ, Weisskoff RM (1999): Quantitative assessment of auditory cortex responses induced by imager acoustic noise. *Hum Brain Mapp* 7:79–88.
- Vigneau M, Beaucousin V, Herve PY, Duffau H, Crivello F, Houde O, Mazoyer B, Tzourio-Mazoyer N (2006): Meta-analyzing left hemisphere language areas: Phonology, semantics, and sentence processing. *Neuroimage* 30:1414–1432.
- Wong PC, Parsons LM, Martinez M, Diehl RL (2004): The role of the insular cortex in pitch pattern perception: The effect of linguistic contexts. *J Neurosci* 24:9153–9160.
- Yang Y, Engelien A, Engelien W, Xu S, Stern E, Silbersweig DA (2000): A silent event-related functional MRI technique for brain activation studies without interference of scanner acoustic noise. *Magn Reson Med* 43:185–190.
- Zaehle T, Wustenberg T, Meyer M, Jancke L (2004): Evidence for rapid auditory perception as the foundation of speech processing: A sparse temporal sampling fMRI study. *Eur J Neurosci* 20:2447–2456.
- Zatorre RJ, Evans AC, Meyer E (1994): Neural mechanisms underlying melodic perception and memory for pitch. *J Neurosci* 14:1908–1919.