Influence of Acoustic Masking Noise in fMRI of the Auditory Cortex During Phonetic Discrimination

N. Jon Shah, PhD,[1] Lutz Jäncke, PhD,[1,2] Maria-Liisa Grosse-Ruyken, RTA,[1] and Hans Wilhelm Müller-Gärtner, MD[1]

The application of functional magnetic resonance imaging (fMRI) to study activation of auditory cortex suffers from one significant confounding factor, namely, that of the acoustic noise generated by the gradient system, which is an integral part of the imaging process. Earlier work has shown that it is indeed possible to distinguish cortical activation resulting from presentation of auditory stimuli despite the presence of background noise from the gradient system. The influence of acoustic noise from the gradient system of the MRI scanner on the blood oxygen level-dependent (BOLD) response during functional activation of the auditory cortex has been investigated in six healthy subjects with no hearing difficulties. Experiments were performed using gradient-echo echoplanar imaging (EPI) and a verbal, auditory discrimination paradigm, presented in a block-wise manner, in which carefully aligned consonant-vowel syllables were presented at a rate of 1 Hz. For each volunteer the experiment was repeated three times with all parameters fixed, except slice number, which was 4, 16, or 64. The positioning of the central four slices in each experiment was common. Thus, the fraction of TR during which the stimulus is on but no imaging is being performed, varies from almost zero, in the case of 64 slices, to over 8 seconds, in the case of four slices. Only the central four slices were of interest; additional slices simply generated acoustic noise and were discarded. During the four-slice experiment, all subjects showed a robust BOLD response in the superior temporal gyrus covering the primary and secondary auditory cortex. The spatial extent and the z-scores of the activated regions decreased with longer duration of gradient noise from the scanner. For a phonetic discrimination task, the results indicate that presentation of the stimulus during periods free from scanner noise leads to a more pronounced BOLD response. J. Magn. Reson. Imaging 1999;9:19–25. © 1999 Wiley-Liss, Inc.

Index terms: cerebral blood flow; auditory cortex; acoustic noise; gradient noise; functional magnetic resonance imaging

FUNCTIONAL magnetic resonance imaging (fMRI) of the brain, based on the generation of blood oxygen level-dependent (BOLD) contrast (1), employing a variety of acquisition techniques, has been successfully applied to study cortical activation in response to an increasingly large range of stimulation paradigms. The success of the method has been due largely to the inherent flexibility and non-invasiveness of MRI. Improvements in hardware and image analysis software, and the use of more sophisticated statistical tests, have facilitated the introduction of more complex paradigms designed to study not only primary activation, but also higher cognitive function. However, for questions relating to primary activation of auditory cortex or higher cognitive function such as language, the use of auditory stimulation paradigms suffers from one significant confounding factor, namely, the acoustic noise generated by the gradient system that is an integral part of the imaging process. Acoustic gradient noise may differ depending on the method of choice for image acquisition [echoplanar imaging (EPI), fast low-angle shot (FLASH), BURST, spiral, etc.) and hardware (reduced-bore gradient coils or whole-body gradient coils) but is nevertheless significant.

Earlier work (2–7) has shown that it is indeed possible to distinguish cortical activation resulting from the presentation of auditory stimuli despite the presence of background noise from the gradient system. Notwithstanding the success of the earlier work, attempts have been made to minimize the acoustic noise generated by the gradient coils by implementing reduced bandwidth FLASH sequences (8) and by using the BURST sequence (9), for example. Recent work from Bandettini and colleagues (10), however, has shown that the acoustic noise from the gradient system does induce activation, which was shown through careful experimental set-up and appropriate data post-processing.

The aim of the present study is to examine in detail the influence of acoustic scanner noise on the BOLD activation produced by the processing of auditory information by varying, in three separate experiments of fixed TR of 9 seconds, the duration of the scanner noise by imaging either 4, 16, or 64 slices. The influence of gradient-generated acoustic noise of varying duration during presentation of an auditory stimulus (a phonetic discrimination task) is thus evaluated.

Contract grant sponsor: Deutsche Forschungsgemeinschaft; contract grant number: DFG JA 735/5–1, 735/4–1.

A preliminary version of this work was given as an oral presentation at the 5th ISMRM (1997).

[1]Research Center Jülich, Institute of Medicine, D-52425 Jülich, Germany.

[2]Institute of General Psychology, Otto-von-Guericke University, D-39112 Magdeburg, Germany.

Address reprint requests to: N.J.S., Institute of Medicine, Leo-Brandt-Strasse, Research Center Jülich, D-52425 Jülich, Germany.

Received February 2, 1998; Accepted June 2, 1998.

MATERIALS AND METHODS

Six healthy subjects (four men and two women), without any history of neurological or audiological illness, were studied while performing a phonetic discrimination task. Subjects gave informed, written consent following a full explanation of the nature and risks of the research, according to a protocol approved by the Ethics Committee of the Heinrich-Heine University of Düsseldorf. High-resolution, T1-weighted anatomical images of the entire brain were obtained in three dimensions using the magnetization-prepared, rapid acquisition gradient-echo (MP-RAGE) pulse sequence with the following parameters: TR 11.4 msec; TE 4.4 msec; θ (flip angle) 15°; 1 excitation; field of view (FOV) 230 mm; matrix 200×256; 128 sagittal slices with 1.41 mm slice thickness. The fMRI paradigm consisted of a preceding baseline of 81seconds ($9 \times$ the (TR) followed by four repetitions of a 54 second activation period (6TR) and a 54 second rest period (6TR). EPI was performed on a Magnetom Vision 1.5 T scanner (Siemens, Erlangen, Germany) equipped with a gradient booster system; the standard radiofrequency head coil was used for transmission and reception. Pulse sequence parameters were as follows: gradient-echo EPI; TR 9 seconds; TE 66 msec; FOV 200×200 mm; θ 90°; matrix size 64×64; pixel size 3.125×3.125 mm; slice thickness 3.0 mm; inter-slice gap 0.3 mm.

Three consecutive experiments were performed on each volunteer. Using a left hemispheric, sagittal slice from the anatomical MR images, showing the course of the sylvian fissure, four oblique slices were oriented along it. The experiment was repeated twice with all parameters fixed, except slice number, which was 16 and 64, respectively. The set-up of the three paradigms is shown schematically in Fig. 1.

The central four slices were common in each experiment. Thus, the fraction of TR during which the stimulus is on but no imaging is being performed varies from almost zero, in the case of 64 slices, to over 8 seconds, in the case of 4 slices. Only the central four slices were of interest; the additional slices were simply there to generate acoustic noise and were discarded.

During scanning the room lights were dimmed and the subjects kept their eyes open. Auditory stimuli were presented binaurally using a digital playback system, a magnetically shielded transducer system, and air conduction through paired plastic tubes. The air conduction system terminated in tightly occlusive headphones allowing unimpeded conduction of the stimulus with good suppression of ambient scanner noise by about 15 dB. The sound pressure level (SPL) of the stimulus was 85 dB SPL for the three experiments and remained constant across subjects. This stimulus intensity was chosen based on previous experiments that demonstrated excellent auditory cortex activation with the same paradigm (11). The intensity of the stimuli was determined outside the scanner using an artificial head (Bruel & Kjaer KA637) by measuring the mean signal intensity during a 30 second epoch. The average intensity of the scanner noise was approximately 75 dB SPL after attenuation by the headphones.

Auditory Stimuli and Experimental Conditions

Stimuli were 16-bit, digitally sampled, consonant-vowel (CV) syllables (/ka/, /ta/, /pa/, /ga/, /da/, /ba/) recorded by a trained phonetician. The onset, duration, intensity, and fundamental frequency of the stimuli were edited and synchronized by means of a speech editor. The criterion for temporal alignment of the syllables was the onset of articulatory release. Each syllable started with zero intensity of 100 msec duration before start of the articulation and stopped with zero

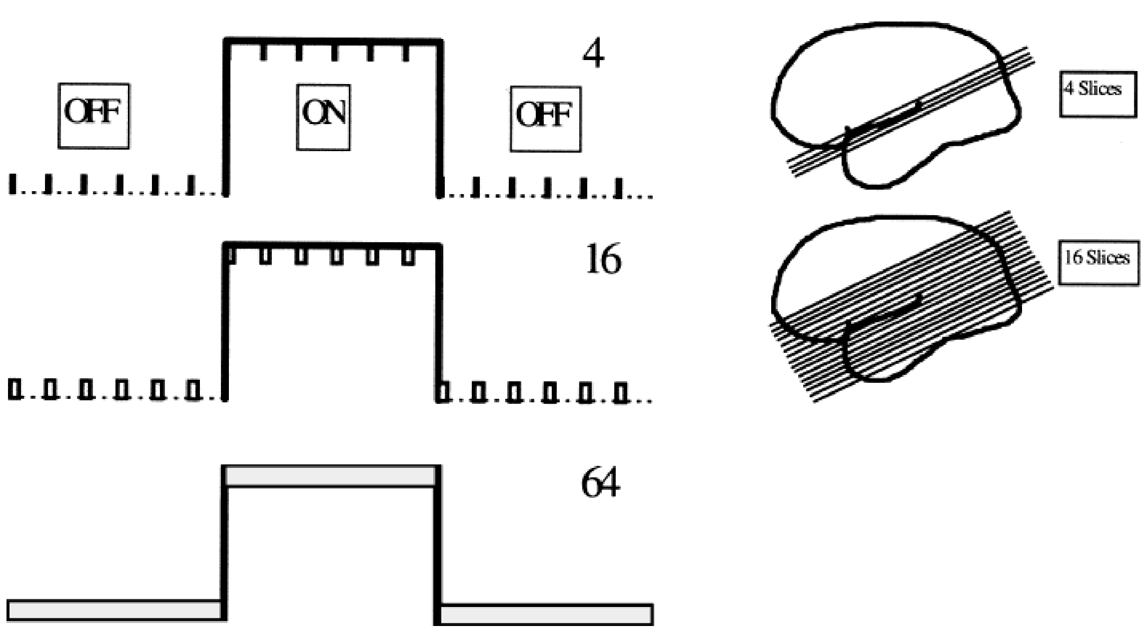

Figure 1. Schematic representation of the paradigm and slice positions; the shaded regions show the periods of gradient noise.

intensity of 50 msec duration after vowel end. This manipulation served to remove clicks at the beginning and end of digital-to-analogue (D/A) conversion. Depending on voice onset times, the duration of syllables ranged from 310 to 360 msec with a vowel duration of 300 msec. Voice onset times (in msec) for the stops were approximately k = 60, t = 50, p = 40, g = 20, d = 15, b = 10. The duration of the entire signal (syllables, leading and end interval of zero intensity) ranged from 460 to 510 msec. These syllables were randomized and arranged in blocks containing 30 syllable pairs. Each of the 30 possible pairwise permutations of the six CV syllables occurred with equal frequency. Since all possible CV pairs were equi-probable, one-third of the trials consisted of pairs containing the syllable /ta/, which served as a target syllable in the experiments. The interval between syllable pairs was 1 second. The simultaneous presentation of two syllables at one time was used in order to increase task difficulty. Subjects were instructed to respond to any occurrence of the target syllable /ta/ by briefly lifting the index finger of their left hand. Because a plethysmograph was fixed on the index finger, finger movement in the magnetic field of the scanner produced a signal on a monitor outside the magnet enabling registration of subject responses.

The order of experimental conditions was 4-slice, 16-slice, 64-slice across the six subjects. For two subjects, immediately following these three experiments, a further three experiments were performed in reverse order. In order to investigate possible magnetization transfer effects, in a subsequent experiment on one subject, the firing order of the slices was changed from the usual ascending to that of the central four slices firing first.

Image Analysis

Image analysis was performed on a SPARC 20 workstation (Sun Microsystems) using MATLAB (version 4.2c, The Mathworks, Natick, MA) and SPM96 software (Statistical Parametric Mapping, The Wellcome Department of Neurology, London, UK) (12–15). Additional region-of-interest (ROI) analysis was performed using the DPA (16) software package. The first three images of each time-series, during which the MR signal reaches a steady state, were discarded. The 48 remaining volume data sets of each condition were automatically realigned to the first image to correct for head movement between scans. All data sets were motion-corrected using the coregister and reslice algorithms in SPM96 (12–15). Given the reduced number of slices and to avoid loss of portions of the top and bottom slices resulting from the reslice algorithm, motion correction for the four-slice images was performed in two dimensions. Following image registration, the two-dimensional slices were then concatenated into a single three-dimensional data set and subjected to further image analysis. Motion correction in three dimensions is more robust than in two dimensions and since it corrects in one extra dimension, it produces superior results. Therefore, motion correction on the 16-slice and 64-slice data sets was performed in three dimensions because partial loss of the upper and lower slices could be tolerated since they did not encompass the auditory cortex. Further analysis of these data sets was expedited by discarding, immediately after motion correction, the unwanted slices.

Statistical Parameter Mapping

The first three images of each time-series were discarded from all analysis not only to allow the MR signal to reach equilibrium, but also because subjects often jerk their heads in response to the sudden noise of the scanner; the first image if included in the data analysis has the potential to be a serious confound. Given the relatively low spatial resolution of the EPI images, bilinear interpolation was employed during the motion correction procedure; on one data set, the more time-intensive sinc interpolation method yielded similar motion corrections. Significantly activated voxels were found by using SPM96 software based on the "general linear model" approach for the analysis of time-series data (12,13). The time-course of each voxel was compared with a user-specified reference vector (a box-car with exponential rise and decay, time constant 9 seconds, to model the hemodynamic response). The same user-defined reference vector was used throughout the analysis with both software packages. Data were spatially smoothed (4 mm) but were not temporally smoothed or high-pass filtered. Thus, the z-scores were used as descriptive measures of the effect induced by auditory stimulation. Given the number of scans and the repeat time, no correction for spin-history effects was performed. Since it is well-known that the images acquired with the EPI sequence can suffer from geometrical distortions (17), the resultant z-maps (which have the same distortions as the EPI images) are depicted on the native EPI images.

RESULTS

The functionally active regions, resulting from data processed using SPM96, from a typical volunteer are shown in Fig. 2.

An arbitrary threshold of z = 0.4 was chosen in order to eliminate a considerable portion of noise but still be sensitive enough to detect small effects evoked by the stimulation paradigm. Voxels surviving this thresholding have been superimposed onto the slices from one time-point of the original data set acquired using the EPI sequence described earlier in this paper. The four-slice experiment (top row of Fig. 2) shows activation that extends over three consecutive slices covering auditory and non-auditory cortices (the remaining slice did not show any activation above the threshold of z = 0.4). The single voxel that had the highest z-score (z = 6.85) was located in left auditory cortex.

Concomitant with an increase in the duration of the acoustic noise, the 16-slice experiment (Fig. 2, middle row) shows a reduced extent of the activated regions. The z-score of the maximally activated voxel, located in left auditory cortex, is also reduced slightly (z = 6.27). In

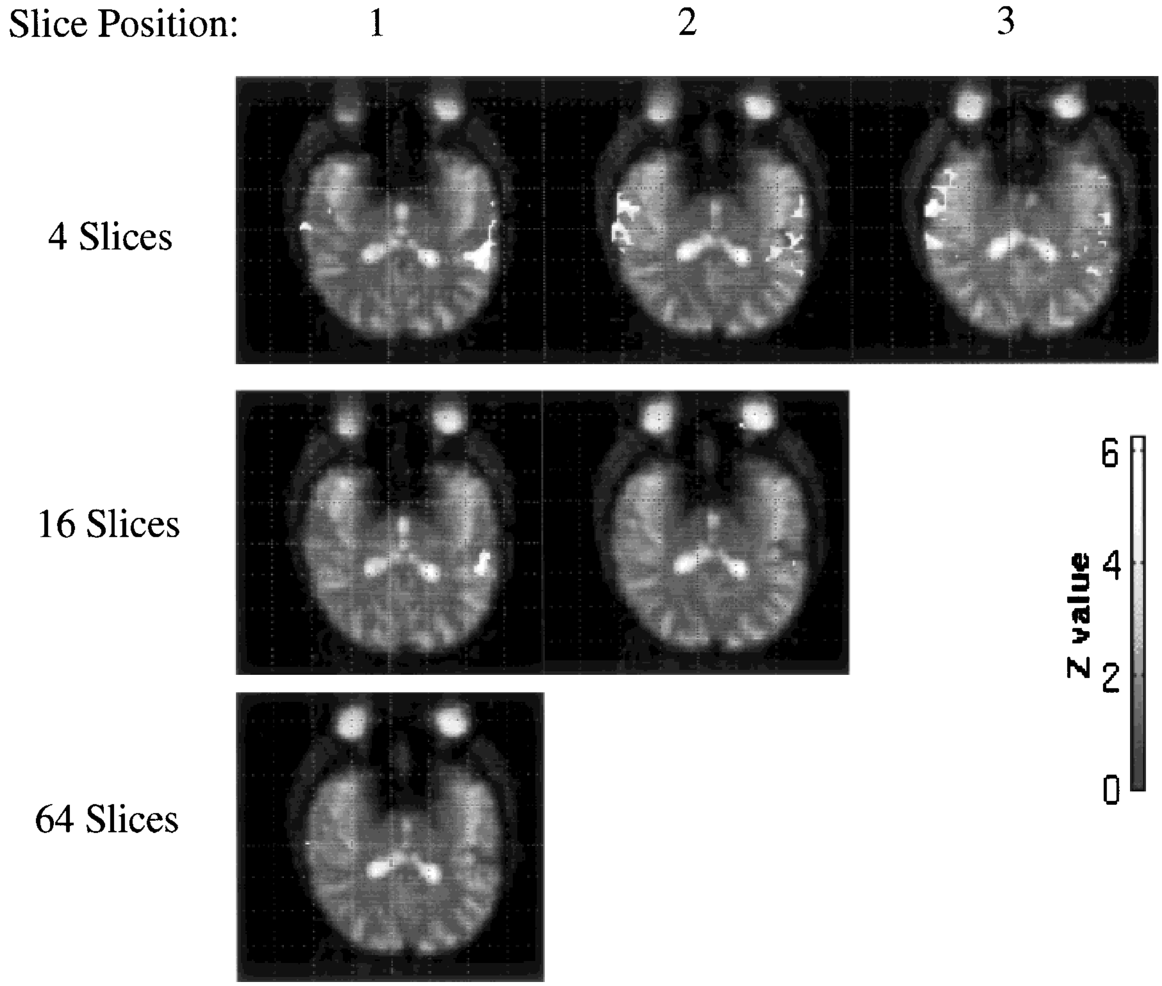

Figure 2. Results from a single, representative subject showing the decrease in the number of activated voxels in the auditory cortex as duration of background acoustic noise increases. Slice position of consecutive slices is indicated across the top of the figure; slice position 2 is oriented according to the sylvian fissure.

general, the time courses of the maximally activated voxels, in all subjects, in the 16-slice experiments were somewhat noiser than the corresponding time courses from the four-slice experiments.

The bottom row of Fig. 2 depicts the results from the 64-slice experiment where the presentation of the phonetic task was during almost constant scanner noise. The results show a much reduced spatial extent of the activation above the chosen threshold of $z = 0.4$. The maximally activated voxel has a significantly reduced z-score ($z = 4.71$).

In order to provide a detailed analysis, the data sets were reanalyzed using DPA, which enables cross-correlation analysis to be performed on the average of voxels in a user-defined region. A large region was placed around the activation in the auditory cortex (Fig. 3) and then auto-shrunk to the voxels that had a cross-correlation coefficient of $r > 0.6$ (corresponds approximately to $z = 4.0$). The number of voxels passing this threshold falls sharply with increasing gradient noise duration. It should be noted that in Fig. 3 the auto-shrink region was placed over the primary and secondary cortices, of the left hemisphere (arbitrarily for the purposes of illustration). The results shown in Fig. 3 are typical of other subjects too, irrespective of hemisphere.

Figure 4a depicts the averaged maximum z-scores, and Fig. 4b shows the mean number of voxels passing the threshold of $z = 4.0$, for each of the three experiments, averaged across subjects. For both hemispheres, there is a decrease in the averaged z-score and a decrease in the average number of voxels as the noise from the gradient system increases in duration. The number of active voxels, however, shows a much sharper decline.

Finally, the mean z-score (averaged across both hemispheres) across the three experimental conditions is shown in Fig. 5.

These values were subjected to the Friedman one-way ANOVA revealing a significant difference between all three experimental conditions (χ^2 (df = 2) = 6.5,p = 0.04). A subsequent Jonkhere test revealed increasing z-scores from the 4-slice to the 16-slice to the 64-slice experiments ($P < 0.05$).

The four-slice experiment, during which the phonetic task was presented in the presence of very little acoustic noise from the gradients, showed very strong activation of the primary and secondary auditory cortices, with an

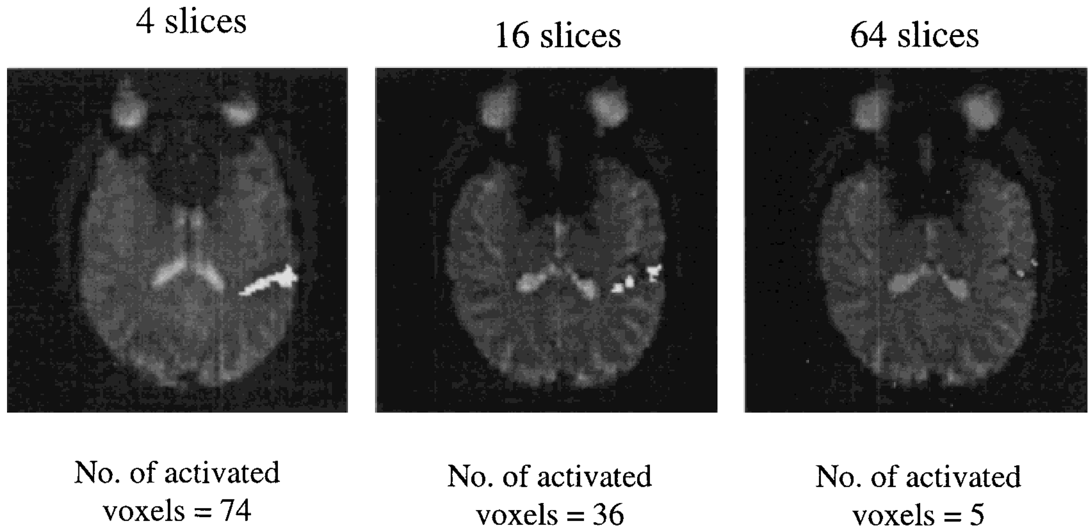

Figure 3. Active pixels in a large, pre-defined region placed over the primary auditory cortex in the left hemisphere. The number of activated pixels in this region is shown.

averaged z-score of 5.6. Strong responses to the CV syllables can be seen in primary and secondary auditory cortices. The 16-slice experiment shows a lower averaged z-score of 5.0, smaller regions of activation, and a noisier response. The size of the activated regions and the averaged z-score (3.71) in the 64-slice experiment are even smaller and the response is significantly noisier. The results, averaged over all subjects, are summarized in Fig. 4.

Reversal of the order of the experiments from 4, 16, 64 to 64, 16, 4 was found to have no significant effect on the results. Likewise, changing the firing order of the slices did not significantly influence the patterns of activation or the overall decrease in the z-scores with increasing acoustic noise.

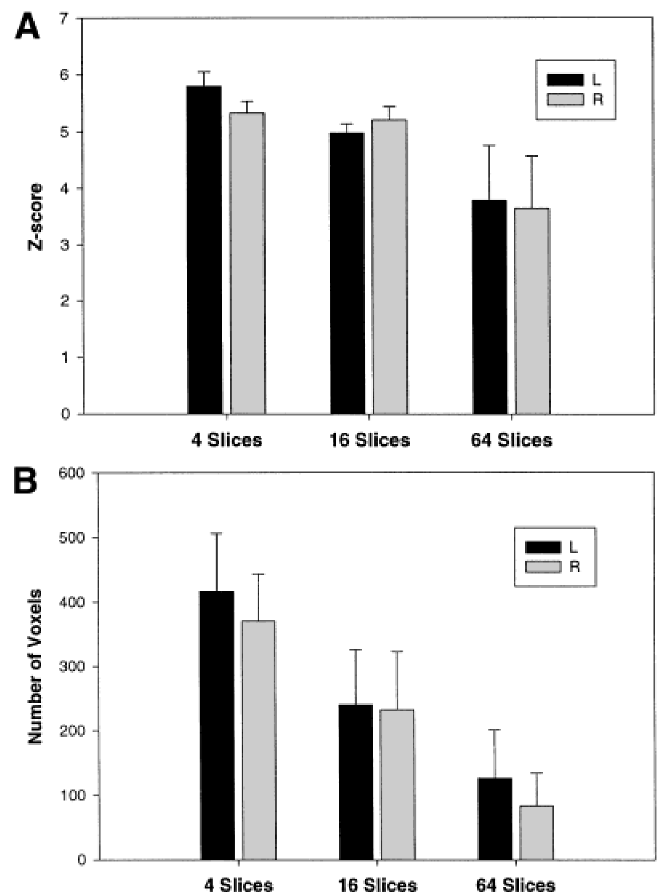

Figure 4. Averaged z-scores (**A**) and number of activated voxels (**B**) for each of the hemispheres for the three experimental conditions. For both hemispheres, there is a decrease in the averaged z-score and a decrease in the average number of voxels as the noise from the gradient system increases in duration. The number of active voxels, however, shows a much sharper decline. The error bars depict the standard error of the mean.

DISCUSSION

With the presentation of a phonetic discrimination task during three distinct periods of acoustic gradient noise from the scanner, we have demonstrated that gradient noise is indeed a factor that must be taken into account in the design of auditory stimulation paradigms for fMRI experiments. By requiring the subjects to attend to the stimulus and to discriminate a target syllable, we have attempted to ensure that attentional factors have been held constant across conditions and across subjects. Although subject performance for these particular experiments was not explicitly recorded, the subjects were under instructions to discriminate the target syllable and were given the impression that performance would be monitored. Performance was monitored by the operator by observing the plethysmograph trace (movement of the wire attached to the finger in the magnetic field can be detected) while listening to the syllables outside the magnet room where the gradient noise was insignificant. Previous experiments in this laboratory with the same stimulus paradigm have shown that subjects can

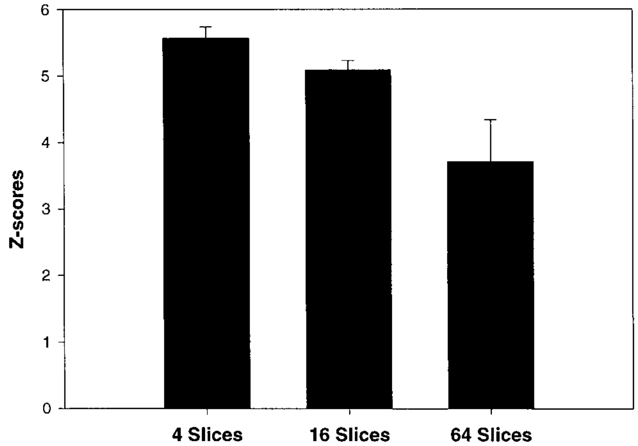

Figure 5. Average whole-brain z-scores across hemispheres for the three experimental conditions. The error bars depict the standard error of the mean. These values were subjected to the Friedman one-way ANOVA analysis, revealing a significant difference between all three experimental conditions [χ^2 (df = 2) = 6.5, P = 0.04]. A subsequent Jonkhere test revealed increasing z-scores from the 4-slice to the 16-slice to the 64-slice experiments ($P < 0.05$).

perform the task easily with an average success rate of 84%. [This success rate was achieved during an experiment with the same stimulus intensity level (85 dB), 16 slices, but with a TR of 5 seconds.] Given the longer TR used here (TR = 9 seconds) higher success rates during the 4- and 16-slice experiments might reasonably be expected since more target syllables fall in the quiet periods of the paradigm. Upon completion of the experiments, when asked whether they were able to hear the stimuli clearly enough, subjects reported no major difficulties with the 4-slice and 16-slice experiments and some increased difficulty in task performance with the 64-slice experiment although the syllables could still be heard.

Other parameters such as stimulus intensity and rate of presentation of the syllables are known to be important influences in fMRI experiments of the auditory system. Work from our own laboratory (11) has established that presentation of the stimulus paradigm described above with an intensity of 85 dB results in robust and repeatable activation of the primary and secondary auditory cortex. Both these parameters were held constant throughout this study.

In a recent presentation, Bandettini and co-workers (10) showed by means of image subtraction that gradient noise from a reduced-bore gradient set does indeed induce activation in the primary auditory cortex. They obtained two series of images where during the first run, the initial 20 seconds of “imaging” was performed with the RF pulses turned off, after which the RF pulses were turned back on and images acquired as normal. In a second run, the first 20 seconds were omitted, and imaging was performed as normal. By subtracting images from run 1 from those from run 2, they were able to show that there is short-lived activation in the primary auditory cortex. The signal difference falls from about 7% to zero in the first 5 seconds and then remains around zero thereafter. The study was performed at 3 T, where sensitivity is greater than at 1.5 T, but there is no reason to expect dissimilar results at the lower field. The results from Bandettini et al (10) support the notion that acoustic noise from the gradient system is indeed a potential confound and needs to be controlled. However, it is not immediately obvious how this effect would combine with the use of a long TR and a relatively small number of slices, as proposed here.

It may be reasonably argued that the EPI methods employed for the work reported in this paper and that from Bandettini and colleagues (10) are inherently noisier, because of the rapid switching of large readout gradients, and are thus partly the cause of the problem. It is not the intention here to debate the advantages of EPI over other MRI methods for functional studies of the brain, but it should be noted that other methods have been employed (FLASH, BURST) that reduce gradient noise somewhat. Even using these quieter sequences (8), unwanted acoustic noise is a concern. The number of RF pulses being applied during the three experiments reported here differs considerably, namely, from 4 to 16 to 64 in the different experiments. Given this fact, the notion that magnetization transfer (MT) effects may be responsible for the decrease in the number of active voxels needs to be considered. Work by Porter and colleagues (18) where they have compared two-dimensional multi-slice (64 slices) EPI with three-dimensional phase-encoded EPI is instructive in this regard. The acquisition time was held constant for both sequences, but in the former case, the flip angle was 90° and in the latter 30°. They found good agreement between the distribution of activated voxels using the two techniques. For the three-dimensional method, the RF pulses for slab selection are applied on resonance each time, whereas with the two-dimensional method, the RF pulse selecting the first slice will be off-resonance for the bottom slice. Combining this with the larger flip angle, a greater MT effect would be expected in the two-dimensional technique. Their analysis, using SPM96, showed that if there is an MT effect, it is not manifest in the z-score and the distribution of the activated voxels. Our own results where we have changed the firing order of the RF pulses should have revealed the influence of MT; none was seen. For the 16-slice experiment, with ascending order, six RF pulses are employed before the slices of interest are excited. After acquisition of the slices of a given time point, there is a 6 second period without gradient noise before the process is repeated. The six pulses have a moderate frequency offset, and thus a small MT effect would be expected. Based on the above two arguments, the MT effect can be ruled out as a cause of the decrease in the activation ratio seen in the results presented here.

CONCLUSIONS

Using a phonetic discrimination task, we have demonstrated, in keeping with other published work, that despite the presence of significant background acoustic noise from the gradient system of the MRI machine, functional studies of the auditory system produce robust and repeatable activation. Furthermore, it has been shown that the influence of gradient noise can be considerable and leads to a decrease in the z-scores, percentage activation ratios, and number of voxels in the activated regions. The influence of the scanner noise can be minimized by ensuring that a reasonably long part of the TR time is free from gradient noise.

Although the results presented here have been obtained using a phonetic discrimination paradigm, it is expected that for other auditory paradigms similar results might be obtained. The results suggest that longer periods of gradient-free noise during the presentation of acoustic paradigms are helpful.

Due consideration of the results presented here might reasonably lead one to propose that a 16-slice acquisition with a TR of 9 seconds is a good compromise. Even though the highest z-scores and numbers of activated voxels were obtained with the four-slice sequence, this acquisition mode provides inadequate coverage of the brain and is therefore not recommended. With the 16-slice sequence, the reduction in z-scores (from 5.56 to 5.08) is not dramatic although the drop in the number of activated voxels (393 to 235) is more pronounced. For this paradigm, a long TR of 9 seconds results in lengthy acquisition times, suggesting that a reduction in TR and its influence on the z-score and extent of activated regions needs to be investigated.

ACKNOWLEDGMENTS

We are indebted to Mr. E. Müller (Siemens AG, Germany) for generously providing us with pre-release versions of his echoplanar sequences. Sequence modifications by Dr. Posse are also gratefully acknowledged. We thank Mr. F. Kehren for general assistance with writing additional computer code.

REFERENCES

1. Ogawa S, Lee TM, Nayak AS, Glynn P. Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. Magn Reson Med 1990;14:68–78.
2. Turner R, Jezzard P, Le Bihan D, Prinster A, Pannier L, Zeffiro T. BOLD contrast imaging of cortical regions used in processing auditory stimuli. In: Proceedings of the Society of Magnetic Resonance in Medicine, 1993. p 1411 (abstract).
3. Singh M, Kim H, Kim T, Khosla D, Colletti. Functional fMRI at 1.5T during auditory stimulation. In: Proceedings of the Society of Magnetic Resonance in Medicine, 1993. p 1431 (abstract).
4. Binder JR, Rao SM, Hammeke TA, Frost JA, Bandettini PA, Hyde JS. Effects of stimulus rate on signal response during functional magnetic resonance imaging of auditory cortex. Brain Res Cogn Brain Res 1994;2:31–38.
5. Binder JR, Rao SM, Hammeke TA, et al. Lateralized human brain language systems demonstrated by task subtraction functional magnetic resonance imaging. Arch Neurol 1995;52:593–601.
6. Binder JR, Swanson SJ, Hamecke TA, et al. Determination of language dominance using functional MRI: a comparison with the Wada test. Neurology 1996;46:978–984.
7. Binder JR, Frost JA, Hammeke TA, Cox RW, Rao SM, Prieto T. Human brain language areas identified by functional magnetic resonance imaging. J Neurosci 1997;17:353–362.
8. Tegler C, Gaschler F, Baumgart C, et al. Temporal behavior of a particular human auditory cortex field by masked stimuli. In: Proceedings of the International Society of Magnetic Resonance in Medicine, 1997. p 708 (abstract).
9. Jakob PM, Lovbald KO, Schlaug G, Warach S, Edelman RR. Functional burst imaging. In: Proceedings of the International Society of Magnetic Resonance in Medicine, 1997. p 373 (abstract).
10. Bandettini PA, Jesmanowicz A, Van Kylen J, Birn RM, Hyde JS. fMRI of scanner noise induced auditory cortex activation. In: Proceedings of the International Society of Magnetic Resonance in Medicine, 1997. p 349 (abstract).
11. Jaencke L, Shah NJ, Posse S, Grosse-Ruyken M, Mueller-Gaertner H-W. Intensity coding of auditory stimuli: an fMRI study. Neuropsychologia 1998;36:875–883.
12. Friston KJ, Holmes AP, Poline JB, et al. Analysis of fMRI time-series revisited. Neuroimage 1995;2:45–53.
13. Friston KJ, Jezzard P, Turner R. Analysis of functional MRI time-series. Hum Brain Mapp 1994;1:153–171.
14. Friston KJ, Williams S, Howard R, Frackowiak RS, Turner R. Movement-related effects in fMRI time-series. Magn Reson Med 1996;35:346–355.
15. Poline JB, Worsley KJ, Holmes AP, Frackowiak RS, Friston KJ. Estimating smoothness in statistical parametric maps: variability of p values. J Comput Assist Tomogr 1995;19:788–796.
16. Le Bihan D. Integrated Processing Software for Functional MRI. Hum Brain Mapp 1995;Suppl 1:151.
17. Jezzard P, Balaban RS. Correction for geometric distortion in echo planar images from B_0 field variations. Magn Reson Med 1995;34:65–73.
18. Porter D, Howseman AM, Josephs O, Turner R. A comparison of 2D and 3D echo-planar imaging for whole brain fMRI. In: Proceedings of the International Society of Magnetic Resonance in Medicine, 1997. p 1621 (abstract).