Quantitative Assessment of Auditory Cortex Responses Induced by Imager Acoustic Noise

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Abstract: A clustered volume acquisition functional MRI pulse sequence was modified to assess the response to the acoustic noise of echo-planar imaging in the auditory cortex and to determine whether it is possible to obtain data which is relatively free of acoustic contamination. The spatial location and strength (percent signal change) of cortical responses to the imager noise were examined by introducing extra gradient readouts, without slice excitation, to provide acoustic stimulation immediately prior to acquisition of a cerebral volume. The duration of acoustic stimulation was controlled by varying the number of extra gradient readouts. Slice acquisitions were clustered at the end of the repetition time (TR) period to prevent a response from being induced by the volume acquisition itself ("Intra-Acquisition Response"). The cerebral volumes were acquired using a long TR in order to limit the integration of the cortical response across volume acquisitions ("Inter-Acquisition Response"). Cortical responses were observed to be largest and most significant on the medial two-thirds of Heschl's gyrus, the location of primary auditory cortex. Mean signal changes induced by the imager noise were observed to be as high as 0.95%. A 2 sec delay prior to onset of the BOLD response was empirically determined. These results demonstrate that clustered volume acquisitions may be utilized for up to 2 sec of volume acquisition without inducing an appreciable Intra-Acquisition Response and can be used, with a sufficiently long TR, to provide data which are similarly free of any Inter-Acquisition Response. *Hum. Brain Mapping* 7:79–88, 1999. © 1999 Wiley-Liss, Inc.

Key words: fMRI; pulse sequence; brain mapping; stimulus masking; response suppression

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INTRODUCTION

Loud acoustic noise levels inherent in the functional MRI echo-planar imaging (EPI) process [Ravicz and Melcher, 1998; Counter et al., 1997] have been demonstrated to generate responses in the auditory pathway [Bandettini et al., 1998; Scheich et al., 1998], affecting the dynamic range of responses to desired stimuli

[Edmister et al., 1999]. The dominant element of echo-planar imaging noise is the rapidly changing gradient during readout of the image. The gradient readout sequence for a GE/ANMR imager is 32 msec in duration, but the transient decay of the resonance coupled with reverberation of the sound lead to a 50 msec duration burst of imaging noise ("beep") associated with each slice acquisition. The readout gradient switches at 1 kHz resulting in a beep that is a tone complex with a fundamental frequency of 1 kHz and significant harmonics out to 8 kHz [Ravicz and Melcher, 1998]. The interaction of this beep and the presented stimulus can change the spatial extent of the fMRI-observable response, reducing the accuracy of traditional stimulus vs. no stimulus paradigms [Shah et al., 1997; Edmister et al., 1999]. These changes are probably due to the non-linearity of the BOLD response in auditory cortex. The physiological responses in the auditory centers may also be affected by acoustic masking and a reduction in the ability of the subject to attend to the desired stimulus [e.g., Woodruff et al., 1996].

Direct functional responses to the imaging noise have been qualitatively demonstrated in auditory cortex by Bandettini et al. [1998]. Responses to the noise of the imager were observed by comparing the initial images of experiments preceded by gradient readouts without slice excitation (extra beeps) to the initial images of experiments not preceded by gradient readouts (no extra beeps). In this experimental paradigm, the response to auditory stimulation by the beeps is superimposed on the transient approach to steady-state magnetization. Therefore, quantitative assessment of the strength of the response is non-trivial as the comparison of conditions (extra beeps vs. no extra beeps) assumes that both image noise and signal levels are stationary across experiments.

Representative quantitative measurements of the functional response induced in auditory cortex by the noise of EPI fMRI were obtained in this study through the use of the "Sledgehammer" imaging sequence. Sledgehammer is based on a clustered volume acquisition (CVA) sequence and is used to measure the functional response due to extra beeps inserted prior to a volume acquisition. These additional beeps can effect a change in the cortical BOLD response by changing the duty cycle of the imager noise within a fixed TR. The inclusion of both imaging conditions within a single experiment in the Sledgehammer sequence and the presence of steady-state magnetization in the slices of interest throughout the experiment readily permit accurate quantification of signal changes, something that was not possible in the experiment of Bandettini et al. [1998].

The BOLD response to the noise generated by the imager can interfere with stimulus-induced activation in auditory cortex by two mechanisms. The first is a short-term effect in which the beep associated with the acquisition of the first slice of a volume induces a BOLD response that is observed in a slice imaged later within the same volume acquisition. We shall refer to this response as an "Intra-Acquisition Response" in this paper. An Intra-Acquisition Response should be observed when a slice is acquired subsequent to the first slice of a volume acquisition at a delay greater than the onset time of the BOLD response, provided that the time between slice acquisitions is less than the time it takes the BOLD response to return to baseline. The second mechanism that may alter a response is a long-term, integrative effect across volume acquisitions. In this "Inter-Acquisition Response," the beep train generated by one volume acquisition leads to a BOLD response that does not decay prior to subsequent volume acquisitions and is thus observed as a signal change. An Inter-Acquisition Response should occur when any slice of a given volume acquisition is acquired after the onset, but prior to the decay, of the BOLD response to the slice acquisitions of a preceding volume acquisition.

Given knowledge regarding the time-course of the BOLD response, we may make predictions regarding when both Intra- and Inter-Acquisition Responses will be present in fMRI data. First, we know that the onset delay of the BOLD response is approximately 2 sec [Buckner et al., 1996; Savoy et al., 1994; Kwong et al., 1992]. Second, we know that the rise and fall times for the BOLD response, as observed in visual and frontal cortex, are 4–10 sec [Buckner et al., 1996; Bandettini et al., 1993]. From our previous description of the two noise-induced responses, an Intra-Acquisition Response should be observed when a slice is acquired within a volume acquisition of at least 2 sec in duration, and in which the time between slice acquisitions is less than the combined rise and fall times of the BOLD response—approximately 8–16 sec for short duration (1 sec) stimuli [Buckner et al., 1996; Bandettini et al., 1993]. The limits on the onset and duration of the BOLD response further imply that an Inter-Acquisition Response may be observed when volume acquisitions are separated by less than 8–16 sec.

Clustered volume acquisition sequences (e.g., Siemens EPI) allow for the possibility of acquiring functional data that is free of the effects of the imager noise. A CVA sequence should permit the elimination of the Intra-Acquisition Response by clustering all slices to be acquired into a period of time that is shorter than the 2 sec onset delay of the fMRI response to the

Figure 1.

A clustered volume acquisition (CVA) sequence shown for $TR = 4$ sec and using a reverse-centric acquisition order. A typical axial slice ordering, numbered inferior to superior, is shown to the left of the sequence. The period during each slice acquisition (white boxes) in which the imaging noise (beep) occurs is depicted by the black boxes.

noise of imaging. The Inter-Acquisition Response may be minimized through appropriate choice of a TR that is sufficiently long (e.g., 8 sec or longer) for the response to the imager noise to decay significantly between volume acquisitions.

In this paper we use data obtained with the Sledgehammer sequence to demonstrate that the acoustic noise (beeps) generated by the echo-planar functional MR imaging procedure can effect substantial percent signal changes in particular locations within auditory cortex, specifically primary auditory cortex. The data also suggest that the CVA imaging sequence can be used, for up to 2 sec duration volume acquisitions, to yield functional activation maps that are almost free of contamination by the acoustic noise of the imaging procedure.

METHODS

Imaging sequence

The “Sledgehammer” pulse sequence was implemented on a General Electric (Milwaukee, WI) 1.5 T Signa system retrofitted for echo-planar imaging (EPI) by Advanced NMR Systems, Inc. (Wilmington, MA). The sequence was developed as an extension of a clustered volume acquisition (CVA) imaging sequence (Fig. 1). Sledgehammer alternated stimulus conditions in epochs of three volume acquisitions, maintaining a fixed TR between volume acquisitions. Odd epochs included three clustered volume acquisitions as per a normal CVA sequence. Even epochs likewise included three clustered volume acquisitions, but each volume acquisition was preceded by a fixed number of extra gradient readouts and associated beeps (Fig. 2). Activa-

tion was assessed by comparison of selected volume acquisitions from odd and even epochs.

The beep-induced responses in the cortex were not superimposed upon a transient approach to steady-state magnetization as in Bandettini et al. [1998], permitting direct statistical interpretation of the data obtained in these experiments. The extra gradient readouts used in the even epochs to generate the extra beeps lacked excitation pulses, but otherwise presented gradient patterns and timing identical to those of the gradient readout sequence used to acquire the first slice of the imaged volume. Because these extra gradient readouts lacked slice excitation (i.e., no RF transmit), they did not affect the magnetization of the slices and resulted in steady-state imaging of the desired volume. All experiments also involved the use of at least one volume excitation and readout without data acquisition prior to the commencement of the paradigm. Through the use of these preceding excitations and readouts, steady-state magnetization was achieved in the imaging volume prior to the initial volume acquisition of the experiment. This eliminated the need to discard the initial volume acquisitions prior to data analysis.

Steady-state imaging conditions in Sledgehammer

Sledgehammer imaging of a DQA phantom produced consistent patterns of artifactual activation ($t > 2.68$) in the first seven to 10 slices of a given volume when acquisitions from even epochs (extra gradient readouts) were compared to acquisitions from odd epochs (no extra gradient readouts). The most significant effects due to the presence of the extra gradient readouts were observed in the first slice, with the effect

Odd Epochs: Regular Volume Acquisition

Even Epochs: Extra Gradients + Volume Acquisition

Figure 2.

Example of the Sledgehammer sequence ($TR = 7$ sec). Odd epochs are identical to a clustered volume acquisition. In even epochs, each clustered volume acquisition is preceded by extra gradient readouts, with no RF transmit, that generate extra acoustic noise (“beeps”) without disturbing the magnetization of the slices. Volume acquisition occurs at the same elapsed time in each TR interval, with or without extra gradient readouts, permitting statistical comparison across epochs. Intra-Acquisition Responses, signal changes observed in a slice that are induced by the beeps associated with the acquisition of slices earlier in the same volume

acquisition, are assessed by comparing Acq 3 to Acq 4. Signal increases observed in auditory cortex are responses to the extra beeps associated with the extra gradient readouts (shaded portion of Acq 4). Inter-Acquisition Response differences are computed by comparing Acq 4 to Acq 6, with signal changes due to longer-term, integrative responses of auditory cortex to the extra beeps. For these experiments, 12 or 16 slice volumes were acquired. Between four and 20 extra gradient readouts were used in the even epochs to generate total beep train durations of 2–4 sec (Table I).

decaying thereafter. Beyond the 10th slice, the statistical maps ceased to have observable structure relating to the underlying physical structure of the phantom. No significant activation ($t > 2.68$) was observed when a t -test was used to compare volume acquisitions obtained under identical conditions (even or odd epochs) within a single experiment on a phantom. Statistical comparisons were made by randomly assigning each of the 24 images obtained under like conditions to one of two populations and then computing a t -statistic for each voxel in the images. The lack of activation implies that steady-state conditions exist within each epoch type, and indicates that the CVA sequence itself is free of any artifacts.

Signal variations due to the presence or absence of preceding gradient readouts coupled with the internal consistency of the CVA sequence imply that the acquisition of a given slice is dependent upon the history of the volume acquisition (i.e., the gradients are a time-varying system). As an example, let us consider the case of a 16 slice volume acquired with eight extra gradient readouts in each even epoch. In this case, activation is observed in the first slice because the slice acquisition performed as the first gradient readout of a

sequence acquires information from a different volume than the same slice acquisition performed as the ninth element of a CVA sequence. Similarly, for the second slice, the second readout performed differs from the 10th, the third from the 11th (slice 3), and so forth. Beyond the seventh to the 10th slice acquisition, steady-state conditions exist and artifacts cease to be observed (i.e., identically prescribed slices acquired as the 11th and 19th readouts are equivalent under a t -test).

While there was some day-to-day fluctuation in the number of contaminated slices, this number was found to be independent of both the quantity of extra gradient readouts and the number of slices acquired in the volume. We therefore conclude that Sledgehammer data from slices prior to the 11th should not be used without confirmation of steady-state imaging conditions using a phantom. It is likely that the boundary condition for achievement of steady-state imaging will vary across machines and imaging coils. The issue of steady-state imaging conditions could be avoided by using an acoustic-only reproduction of the gradient readout beep, but this will not lead to measurement of

the response to the full character of the beep, including reverberation and physical vibration.

Imaging parameters

Data acquisition for all experiments described in this paper was performed on the 1.5 T system using asymmetric spin-echo (ASE) echo-planar imaging (TR = 7 sec, TE = 70 msec, $\tau = -25$ msec, 128×64 collection matrix, $40 \text{ cm} \times 20 \text{ cm}$ FOV). Contiguous, (axial) oblique, 4 mm thick slices were obtained such that the central slices passed through the body of Heschl's gyrus. The in-plane resolution for all studies described was $3.1 \text{ mm} \times 3.1 \text{ mm}$. A surface receive coil positioned around the left ear was used to maximize signal from Heschl's gyrus and the rest of the auditory cortex. The body coils of the magnet were used for transmit. Functional images were acquired with the coolant compressor turned off to eliminate the dominant, periodic component of the non-EPI background noise, producing a condition of quiet between clusters of beeps.

Peak noise levels generated in echo-planar imaging (EPI) at our facility range from 117 dB Sound Pressure Level (SPL) on a 1.5 T machine to 133 dB SPL on a 3.0 T imager [Ravicz and Melcher, 1998]. These values are consistent with other reports [Counter et al., 1997]. Such noise levels are typically reduced through the use of passive attenuation measures such as earmuffs and earplugs. Our imaging coil is integrated into a passive attenuation system that reduces the level of the EPI noise by 30 dB to 85–90 dB SPL [Ravicz and Melcher, 1998].

Experiments

Seven volunteers (one female, six male; ages 22–29 years) were imaged, after providing informed consent, using the Sledgehammer sequence in conditions of quiet. No stimuli were presented to the subject other than the beeps associated with the imaging process. Forty-eight images were acquired of each slice in each experiment (24 images with and without extra beeps) using an epoch duration of three volume acquisitions (21 sec). The functional location of auditory cortex in these slices was verified through one run of an On vs. Off paradigm in which instrumental music was presented binaurally to the subject (eight slices, TR = 4 sec, CVA sequence).

All seven subjects were imaged using a 16 slice volume with 16 extra beeps in the even epochs (32 beeps vs. 16 beeps). Six subjects were imaged using a 16 slice volume with eight extra beeps. Five of the

TABLE I. Duration of imager noise stimulus (beep train) generated by the Sledgehammer sequence

Number of slices in imaged volume	Extra gradient readouts	Beep train duration (sec)	
		Imaged volume plus gradient readouts	Imaged volume
16	16	3.776	1.888
16	8	2.832	1.888
12	20	3.776	1.416
12	12	2.832	1.416
12	4	1.888	1.416

volunteers were further imaged using a 12 slice volume preceded by 4, 12, and 20 extra beeps in the even epochs. The additional beeps were selected to compare the response to the imaging noise inherent in the volume acquisition (2 sec for 16 slices; 1.5 sec for 12 slices) to the response to the extended duration of imaging noise due to the extra beeps (2, 3 or 4 sec). The actual durations of the trains of beeps were slightly different from these theoretical values, because the acquisition time for each slice was just less than 118 msec (see Table I for the maximal beep train duration times for each experimental condition). Two subjects were imaged with the 16 slices and eight extra beeps using TR = 6 sec, but all other studies utilized a constant TR = 7 sec to permit accurate comparisons of activation levels across imaging noise durations.

In all cases, a reverse-centric slice ordering was used in order to obtain the slices of greatest interest (primary auditory cortex and areas immediately surrounding Heschl's gyrus) at the end of the acquisition so that they were free of imaging artifact. This ordering also permitted assessment of the effect of the maximal duration of the train of beeps.

Data analysis

Prior to statistical analysis, the central eight slices of each baseline volume were motion corrected to the first image of the first run of the imaging session using SPM95 [Friston et al., 1995]. Images were spatially smoothed using a three-point Hamming filter and drift corrected on an individual voxel basis using a minimum mean-square error fit.

A *t*-statistic was computed to compare all volume acquisitions in even epochs (extra beeps) to all volume acquisitions in odd epochs (no extra beeps). Voxels that achieved $t > 2.68$ (uncorrected significance level of $P < 0.01$) and were located on or in the vicinity of Heschl's gyrus were defined as activated and included in a

region of interest (ROI) for subsequent analysis. Separate ROIs were generated for each of the combinations of imaging volume size and extra beeps (e.g., 12 slices with 12 extra beeps). The ROIs generated for the runs using a given slice volume (12 or 16 slices) were combined to maximize the number of voxels analyzed.

The Intra-Acquisition Response was assessed through computation of mean percent signal changes within the composite ROIs. The last acquisition of each odd epoch (e.g., Acq 3 in Fig. 2) was compared to the first acquisition of each even epoch (e.g., Acq 4) to examine the immediate effect of the increase in the number of beeps preceding the volume acquisition. Substantial signal changes between these consecutive acquisitions could only be due to the change in the acoustic environment preceding the later acquisition. Analysis involving comparisons of Acq 3 to later acquisitions in the even epoch (e.g., Acq 5 or Acq 6) run the risk of including Inter-Acquisition Responses induced by the first acquisitions within the even epoch. Comparisons involving earlier acquisitions from the odd epoch (e.g., Acq 1 or Acq 2) may not permit recovery of any undershoot resulting from the transition between an even epoch and the subsequent odd epoch.

The integrative Inter-Acquisition Response was analyzed by comparing the first acquisition in each even epoch (e.g., Acq 4) to the last acquisition in the each even epoch (e.g., Acq 6). In this case, signal changes would be due to an accumulation of the increased BOLD response to the longer duration train of beeps. A long TR value (7 sec) was selected to maximize the likelihood of observing an Intra-Acquisition Response while minimizing the Inter-Acquisition Response and maintaining a tolerable experimental duration (5:36). It was assumed a priori that the Inter-Acquisition Response would be small.

RESULTS

Noise-induced response localization

Typical auditory cortex activation induced by the alternating duration of beep trains is shown for all seven subjects in Figure 3. The responses depicted were observed when comparing the auditory cortex response to a 4 sec burst of imaging noise (16 slice volume with 16 extra beeps) to the response to a 2 sec burst of imaging noise (16 slice volume with no extra beeps). The activation maps were generated using all volume acquisitions (24 per condition). The most significant responses (uncorrected *t*-statistic) are located on the medial two-thirds of Heschl's gyrus, the

location of primary auditory cortex [Galaburda and Sanides, 1980].

Noise-induced response strength

The percent signal changes observed for both the Intra- and Inter-Acquisition Responses resulting from the variation in beep train duration are listed in Table II. Statistically significant differences ($P < 0.05$, *t*-test) were found between the Intra-Acquisition Response to 4 sec of noise (32 beeps) and that observed for 2 and 3 sec of noise (16 and 24 beeps) for both the 12 and 16 slice imaging volumes. The responses to a given maximal duration of the beep train did not differ significantly with respect to the size of the imaging volume (12 or 16 slices). Therefore, the Intra-Acquisition Responses were pooled by the duration of the beep train during even epochs, resulting in statistically significant ($P < 0.05$, *t*-test) signal level differences between all three extended durations of imaging noise. The averaged data for the 12 and 16 slice volumes are shown in Figure 4 along with the pooled data and associated 95 percent confidence intervals.

Inter-Acquisition Responses were not significantly affected by either the volume imaged (12 or 16 slices) or the number of extra beeps preceding the acquisitions (Table II). The resulting signal changes were essentially zero for all cases examined in this study.

DISCUSSION

Response characteristics

Maps of the auditory cortex activation induced by the noise of echo-planar imaging suggest that the beeps accompanying prolonged acquisition of image data induce substantial amounts of activation in what is probably primary auditory cortex. While other regions of auditory cortex did not exhibit responses that achieved the $P < 0.01$ statistical significance level threshold of Figure 3, it can not be concluded that secondary auditory cortex did not respond at all to the stimulus. Rather, any responses present were simply sub-threshold based upon our activation criteria.

It has been observed previously [Buckner et al., 1996; Savoy et al., 1994; Kwong et al., 1992] that the onset of the BOLD response exhibits a 2 sec delay after the onset of a stimulus. After this delayed onset, the BOLD response is found to peak after approximately 4–10 sec [Buckner et al., 1996; Bandettini et al., 1993; Kwong et al., 1992]. The Intra-Acquisition Response (Fig. 4) induced in auditory cortex by the beep trains is consistent with this a priori knowledge. The induced

Figure 3.

Sledgehammer results for seven subjects using odd epoch stimulation of 2 sec (16 slice volume) and even epoch stimulation of 4 sec (16 slice volume with 16 extra beeps). Statistical overlay (uncorrected t -test, $P < 0.01$ threshold) was computed using all volume acquisitions and represents the complete response (including both Intra- and Inter-Acquisition) to the extra beeps. Underlying

T1-weighted images (grayscale) were acquired parallel to the Sylvian fissure, cutting through Heschl's gyrus. The strongest (statistical and percent signal change) responses were observed on the medial two-thirds of Heschl's gyrus, the location of primary auditory cortex [Galaburda and Sanides, 1980]. The white boxes encompass the approximate extent of auditory cortex.

response does not achieve a detectable level (with respect to the level after a 1.5 sec duration beep train) until after 2 sec of beeps have been presented to the subject. The response is detectable after 3 sec (0.25%),

but rises sharply to a substantial level (0.95%) by the time the beeps have been present for 4 sec.

The lack of significant differences in the percent signal changes observed for the Inter-Acquisition Re-

TABLE II. Average percent signal changes for Sledgehammer sequence

Subject	Intra-Acquisition Response (Slices/extra gradient readouts)					Inter-Acquisition Response (Slices/extra gradient readouts)				
	16/16	16/8	12/20	12/12	12/4	16/16	16/8	12/20	12/12	12/4
1	1.19	-0.26	—	—	—	-0.15	-0.73	—	—	—
2	1.11	0.36	—	—	—	0.04	-0.24	—	—	—
3	0.46	0.19	1.03	0.05	0.18	-0.01	0.07	-0.29	0.29	0.22
4	1.19	0.39	0.71	0.52	-0.19	-0.13	-0.31	0.10	-0.26	-0.13
5	0.87	0.04	0.83	0.51	0.02	0.13	-0.37	0.46	0.06	-0.42
6	1.83	—	0.62	0.64	-0.21	-0.37	—	0.10	0.01	0.21
7	0.56	0.55	0.95	0.23	-0.09	0.28	0.00	-0.08	-0.05	0.42
Mean	1.01	0.21	0.83	0.32	-0.06	-0.03	-0.26	0.06	0.01	0.06
S.E.	0.18	0.12	0.08	0.09	0.07	0.08	0.12	0.12	0.09	0.15

Figure 4.

Graph of Intra-Acquisition Response percent signal changes observed for 12 and 16 slice volumes as a function of the net duration of the beep train (slices plus extra beeps) in the activation condition of the Sledgehammer sequence. Composite values across identical beep train durations are also presented in the graph (solid line). The signal changes at 2, 3 and 4 sec after stimulus onset are significantly different (*t*-statistic, $P < 0.05$) from each other. See Table II for mean and standard error values for 12 and 16 slice volume data.

sponses for all Sledgehammer imaging cases indicate that, at a TR of 7 sec, the Intra-Acquisition Response is the dominant response, as was expected a priori.

Implications for auditory fMRI

The strong dependence upon the duration of the train of beeps exhibited by the Intra-Acquisition Response demonstrates that, for experiments involving frequent slice or volume acquisitions, the activation in auditory cortex is likely to be affected by the noise of the imaging process. This interaction may extend beyond the obvious acoustic masking of the desired stimulus to a reduction either in dynamic range available for cortical BOLD response or in the sensitivity to the stimulus-induced response due to an elevated signal level in Off (baseline) experimental conditions.

The strength of the response after 4 sec of beeps is approximately 20–30% of the typical 3–5% signal changes observed in visual cortex. This is potentially a significant reduction in the dynamic range available for a response to the stimulus. We have typically found auditory cortex signal changes, even to robust stimuli such as speech or music, to be smaller (e.g., 1–1.5% in Edmister et al., 1999) than those values reported for visual cortex. The smaller percent signal changes may

be due to reduced dynamic range resulting from the beep-induced response, or the beep-induced response may simply make it more difficult to observe primary auditory cortical responses to auditory stimuli. It should also be noted that the beep-induced response might not have saturated after 4 sec, implying that longer trains of beeps could lead to greater reductions in dynamic range. This would have serious implications for imaging sequences in which slice acquisitions are distributed equally throughout the TR period (distributed volume acquisition, DVA), particularly when many slices are acquired with a short TR value (e.g., 16 slices with TR = 2 sec).

It is important to note that the strength of the beep-induced activation observed in auditory cortex is likely to be dependent upon the effectiveness of passive attenuation measures and the actual sound levels generated by a given imager. These experiments were conducted with the EPI level reduced to approximately 90 dB SPL by earmuffs and foam rubber padding. The coolant compressor noise was removed from the background in an effort to increase the observed percent signal changes. Despite these experiment-specific variables, we would expect the trends apparent in these results to be representative of those obtained under typical imaging conditions.

Implications for clustered volume acquisitions

It should be possible to use up to a 2 sec beep train duration (16 slice imaging volume on our imager) for a clustered volume acquisition (CVA) to obtain imaging data that are free of Intra-Acquisition Response contamination. The signal change after 3 sec of beeps is significantly different from that at 2 sec and indicates that contamination by imager noise is more likely at this delay, though it will not be as detrimental as after 4 sec of beeps. After 4 sec of beeps images from other slice acquisitions will be significantly contaminated by beep-induced responses (Intra- and/or Inter-Acquisition Responses). The Intra-Acquisition Response curve suggests that the fMRI assessment of activation may be increasingly contaminated by the imager noise as the rate and duration of slice acquisition increases, until the BOLD response in auditory cortex saturates.

The results of these experiments may also be applied to support hypotheses and observations of Edmister et al. [1999]. The potential degradation due to contamination by the increasing rate of imager beeps with decreasing TR would support the hypothesis that variations in the music response maps observed for both CVA and DVA (distributed volume acquisition) were due to increasing contributions by the integrative

(Inter-Acquisition) component of the cortical response. The lack of a significant Inter-Acquisition Response and the probable ability to obtain a 1 sec duration volume acquisition (eight slices in this study) without inducing an Intra-Acquisition Response indicate that the CVA music data obtained using TR = 8 sec was essentially free of noise-induced response contamination. Finally, the sharp rise in the Intra-Acquisition Response between 3 and 4 sec (Fig. 4) may help to explain the peak in statistical power per unit imaging time for the CVA sequence at TR = 3 sec. One hypothesis would be that combined responses induced by the two preceding volume acquisitions (3 and 6 sec previous for TR = 3 sec; 4 and 8 sec previous for TR = 4 sec) are significantly lower for TR = 3 sec than they are for TR = 4 sec. Therefore, TR = 3 sec preserves greater sensitivity to the stimulus-induced response by maintaining a lower steady-state signal level during periods when the stimulus is Off (baseline condition).

CONCLUSIONS

The Sledgehammer data provide quantitative evidence that responses to the beeps associated with the imaging process can interfere with responses to desired stimuli. The beep-induced response partially saturates primary auditory cortex and thereby reduces the dynamic range available for a stimulus-induced response. We may further view this beep-induced response as leading to an increase in the "baseline" signal level to which any stimulus condition will be compared, reducing sensitivity to subsequent signal changes. Therefore, as postulated by Bandettini et al. [1998], a control (Off) period that includes imager noise is quite different from a silent control period because the imager has such a strong stimulatory effect on auditory cortex.

The results obtained across various stimulation conditions indicate that the clustered volume acquisition (CVA) imaging sequence may be used for up to 2 sec worth of data acquisition without inducing an Intra-Acquisition Response, as the onset delay of the BOLD response appears to be at least this long. The lack of an Intra-Acquisition Response for such a sizable volume provides strong support for the use of the CVA sequence over a distributed volume acquisition (DVA) sequence in which slices are acquired periodically throughout the TR. The CVA sequence is preferred because the DVA sequence will have contamination from both inter- and intra-acquisition sources when acquiring slices at rates greater than approximately one every 2 sec. The Inter-Acquisition Response is easily reduced with the CVA sequence by extending

the TR to at least 7 sec, though the amount of contamination present at TR = 3 or 4 sec may be acceptable for many experiments. There appears to be only a slight penalty in statistical power per unit time (On vs. Off paradigm) for the extended TR values [Edmister et al., 1999]. Therefore, it has been demonstrated that CVA sequences may be used to obtain echo-planar fMRI data that are essentially free of acoustic noise contamination.

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