Detection of the Scanner's Genuine Gradient Noise by Functional Echo Planar Imaging

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Introduction

Echo Planar Imaging (EPI) generates considerable acoustic noise by steep gradient pulses at unrestricted bandwidths. In functional neuroimaging, unshielded EPI sounds inevitably activate the auditory system impairing the sensitivity to detect concomitant and successive auditory stimulations. Instead of vanishing the scanner's noise transmission [1], our goal was to utilize it for the functional neuroimaging of audition. In contrast to previous approaches [2-4], which implemented additional gradient switches for sound generation, we focussed on EPI's genuine gradient noise (GGN) of clinical 1.5 T MR scanners to detect auditorily evoked BOLD effects. By taking unique advantage of the delayed rise of haemodynamic response functions, EPI finally ought to detect itself within T2*-weighted signals related to onsets of persistent (A) or intermittently accelerated (B) but otherwise unmodified GGN of the scanning per se.

Material and Methods

Method A (figure 1)

Auditory autodetection of EPI's persistent genuine gradient noise (pGGN):

64 EPI volumes (3 x 3 x 6 mm, DF 0.20, TE 45 / TR 108 ms, FA 40°) were acquired at constant interscan intervals RT of 0.324 seconds avoiding delays between consecutive slices (3 interleaved coronals; G_y H ➞ F) and volumes. Thereupon, scanning was held for 30 seconds to let presumed haemodynamic BOLD responses disappear in silence. Repetition of 30-50 runs separated by these silent intervals was to ensure an in-between fading of BOLD effects evoked by pGGN audition (pGGNA). Discarding the initial 12 volumes to approximate to a steady state, the data were explored model-free by a principal component analysis (PCA) using pca_image confined to the remaining 52 time points in each run [5]. However, the first component still possessed extreme temporal values for the initial volumes and it was included as a confound into further model-driven analysis. Thus, statistical parametric mapping (SPM99) was performed to specifically demonstrate the temporal delay of haemodynamic BOLD activity evoked by pGGNA in an event-related design of finite impulse responses (FIR). In the FIR model, the 52 scans kept of each run were structured into 26 mini-epochs contrasting the final 20 (1/20 x 20 = +1) against the initial 6 (-1/6 x 6 = -1; t-test, see below).

Method B (figure 2)

Auditory autodetection of EPI's intermittent genuine gradient noise (IGGN):

Delays between each of a limited number EPI-repetitions were specified separately: 17 repetitions of axially (parallel to the Sylvian fissure) acquired EPI volumes (5 slices, 3 x 3 x 4 mm, FA 70°) were recorded at an RT of 2.000 seconds, except that the 5th and 6th scan were repeated after 1.000 seconds already. Considering its GGN setting in intermittently, the 5th scanning was discarded from the statistical analyses of the time series but defined as the auditory stimulation of interest. Repeating this protocol at least 12-15 times, data were analysed by Statistical Parametric Mapping (SPM99) in an event-related design. The design matrix contained the HRF and its temporal derivative as basis functions as well as the averaged signal intensity of each image to account for fluctuations of the global signal due to the additional scan.

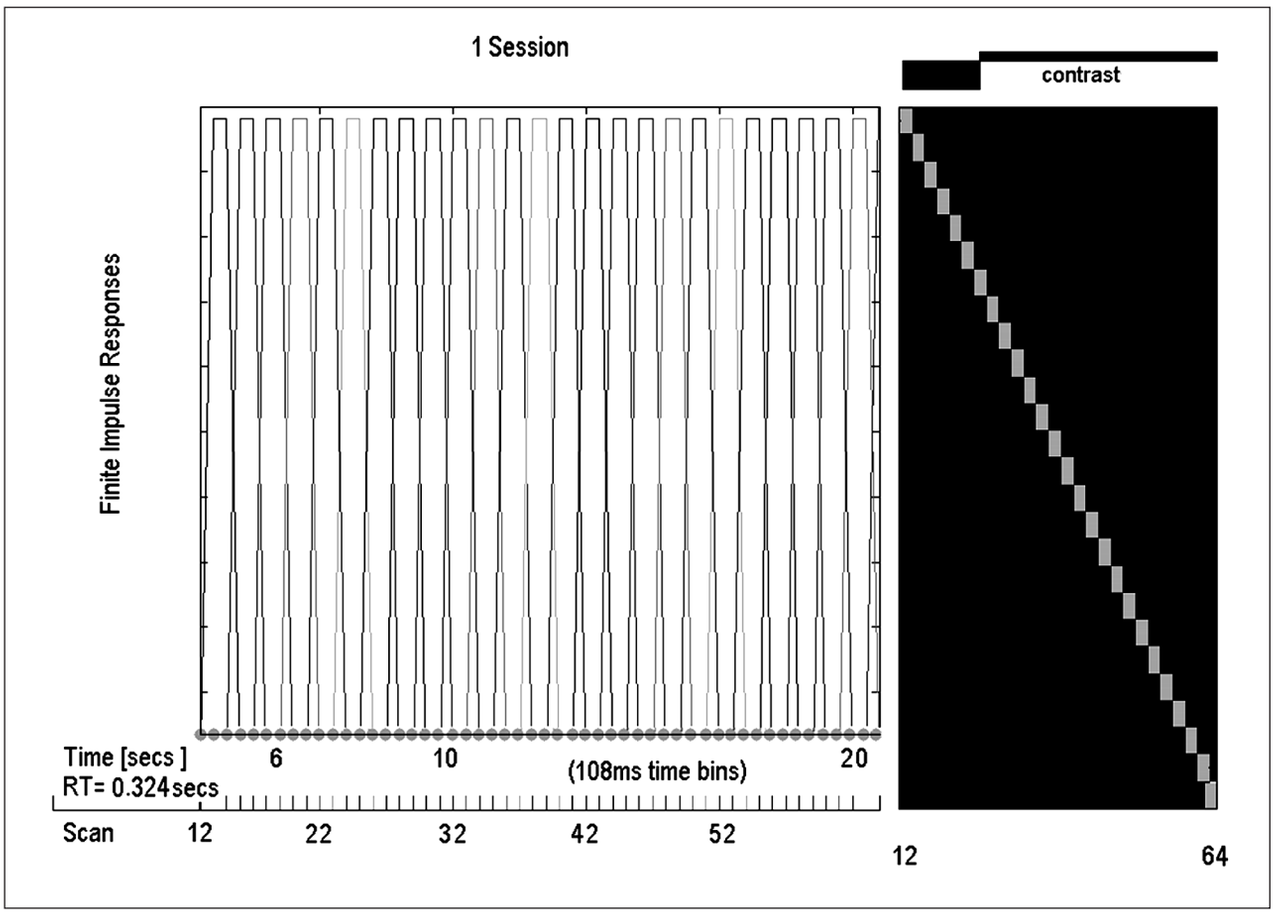

Figure 1 Regressor (left) and design matrix (right) used in the SPM analysis of method A.

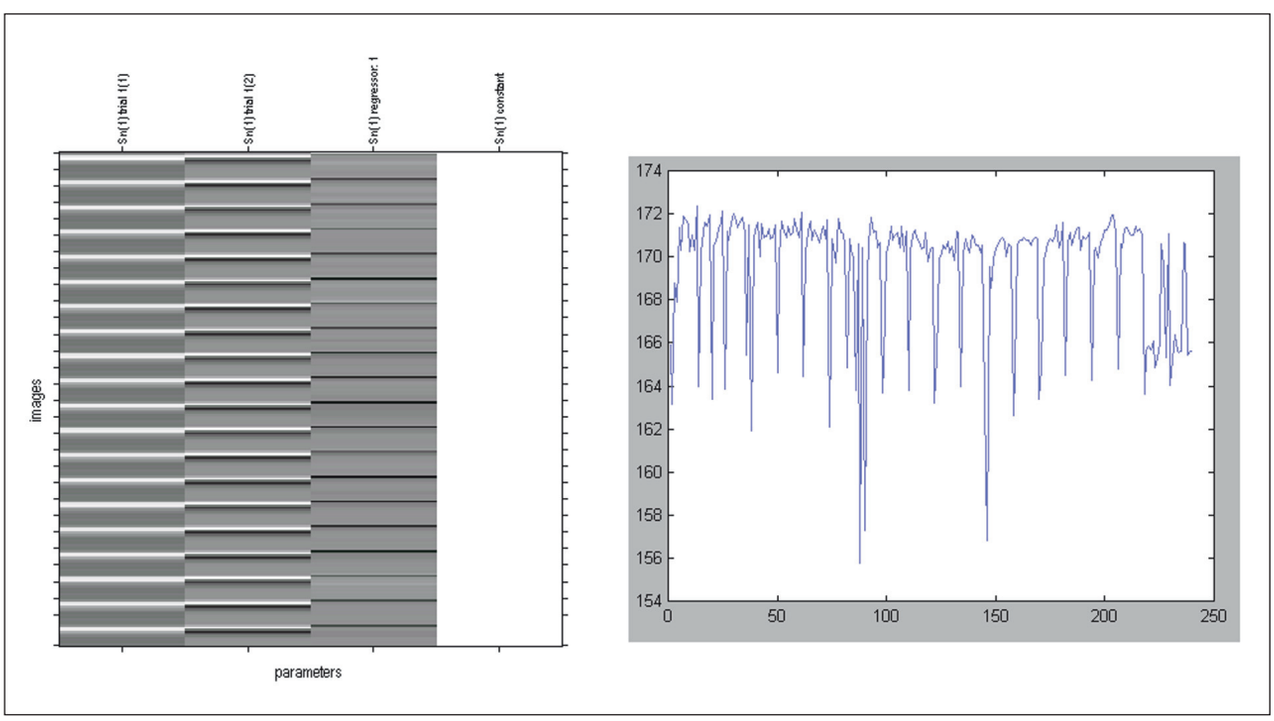

Figure 2 Design matrix (left) and extracted signal (right), which is used as additional covariate in the design matrix of method B.

Method A & B Equipment and Pulse Sequences

Measurements were performed on clinical 1.5 T Siemens MR scanners (A: Magnetom Vision / B: Symphony), running under Numaris 4 and 3, respectively. EPI's genuine gradient noise (GGN) amounted up to 96dB at the level of the auricles unshielded but external foam and muffle pads as well as earplugs were used for fixation purposes and to minimize the subjects motion predominantly due to initial startling. Following TRUFI-localizers, the time series of BOLD-sensitive Mosaic EPIs were acquired. Two methods (A, left, and B, right boxes) were established for auditory EPI autodetection after extensive experimental pretestings. For anatomical inference, a T1-weighted MP-RAGE sequence (≤ 1 x 1 x 1 mm_, TE 4 / TR 12 ms, FA 12°) of the entire brain was recorded.

Subjects and Data Preprocessing

Method A

Five right handed, healthy male volunteers, age 33.2 ± 4.3 years.

Method B

Seven right handed, healthy volunteers (five male, two female), age 30.3 ± 7.7 years.

Method A & B

The functional EPI volumes were spatially realigned by the most accurate rigid body transformations (SPM99) and resliced through a modified Fourier space interpolation. Motion correction parameters were included as confounds into parametric analyses (not shown in the figures). Slice timing was renounced to avoid band-limitation, aliasing, and loss of experimental power at Nyquist's frequency of RT. Considering an interstimulus interval of interest at or below 2 x RT this was particularly warranted by method A. Smoothing was performed by a Gaussian kernel of twice the voxel size. Finally, the structural 3D MP-RAGE image was coregistered to the mean functional by a mutual information algorithm.

Results

Results for Method A (figure 3)

In all subjects, the first component extracted by PCA regularly detected a decay of the T2*-weighted signal finally approaching its global steady state. Due to the longer T1-values of the cerebrospinal fluid, it centred spatially on the inner and outer liquor-filled spaces. Temporally, reaching a steady state can be fastened by increasing the flip angle (FA) closer to 90°. At latencies of a few seconds, the second or third component caught by PCA commonly exhibited a subsequent rise of the signal amplitude attributable to a BOLD haemodynamic response function (HRF) evoked by pGGNA. In two of the fife subjects measured, however, there were prominent initial startling movements extending over the discarded volumes in most sessions and preventing a meaningful analysis due to the correlation of confounding motions with the effect searched for. In the other three subjects, the component presumably related to pGGNA focussed bilaterally on the subcortical and cortical centres of audition, peaked at around 10 seconds, and then usually attenuated to some extend over time. In SPM, the corrected response fit of the filtered and adjusted data for t-contrasting the initial 6 against the remaining 20 FIRs also detected a delayed signal rise. The signal change amounted to about 2.5% above the global mean of the scaled BOLD-sensitive images. Spatially, this effect was traced by small volume corrections for multiple comparisons performed on anatomically predefined spheres of 10 mm radius to clustered activations covering the primary auditory cortex around the gyri temporales transversi of Heschl and to brainstem centres of audition (nuclei cochleares et corporis trapezoidei, oliva superior, colliculi inferiores et brachium, corpus geniculatum mediale) by the nearest cluster approach (FDR-corrected $p < 0.01$). These results were visualized by AMIRA rendering the activated clusters onto a likelihood voltex of grey matter and an isosurface representation of white matter.

Results for Method B (figure 4)

The method was sensitive enough to detect BOLD responses in the auditory cortex as evoked by scans of the pulse sequence itself intermittently inserted at shortened RTs. Modelling the temporally delayed BOLD effect evoked by GGN, it revealed the increase of the T2*-weighted signal superimposed by a singular stimulus scan. The inclusion of the overall mean intensities captures most of the confounding signal fluctuations. However, the critical point here is that the signal has to be stable at least two scans after the "stimulation scan". Otherwise, the signal fluctuation could be on the same time scale as the expected temporally delayed BOLD response. We observed further that these fluctuations vary profoundly on different scanners (Vision, Symphony, Sonata). Therefore, appropriate adjustments of the flip angle used are mandatory. Removing this global effect and testing for the main effect, i.e. for

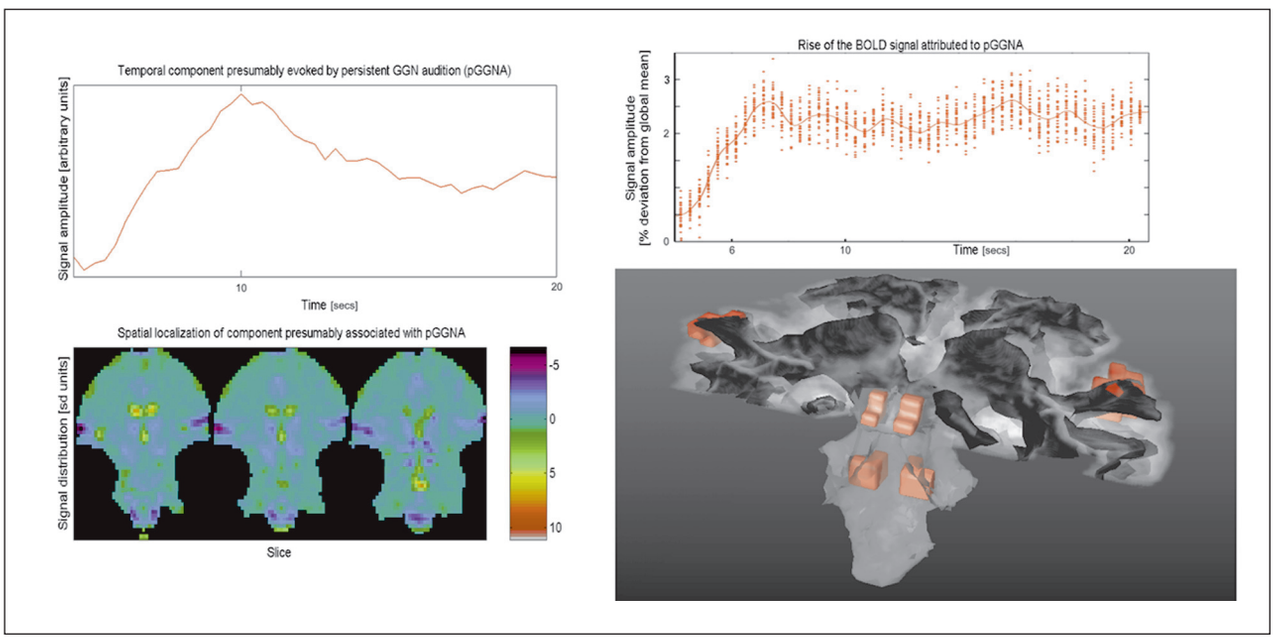

Figure 3 Method A. Left: PCA analysis; right: Fitted response and rendering of the SPM results.

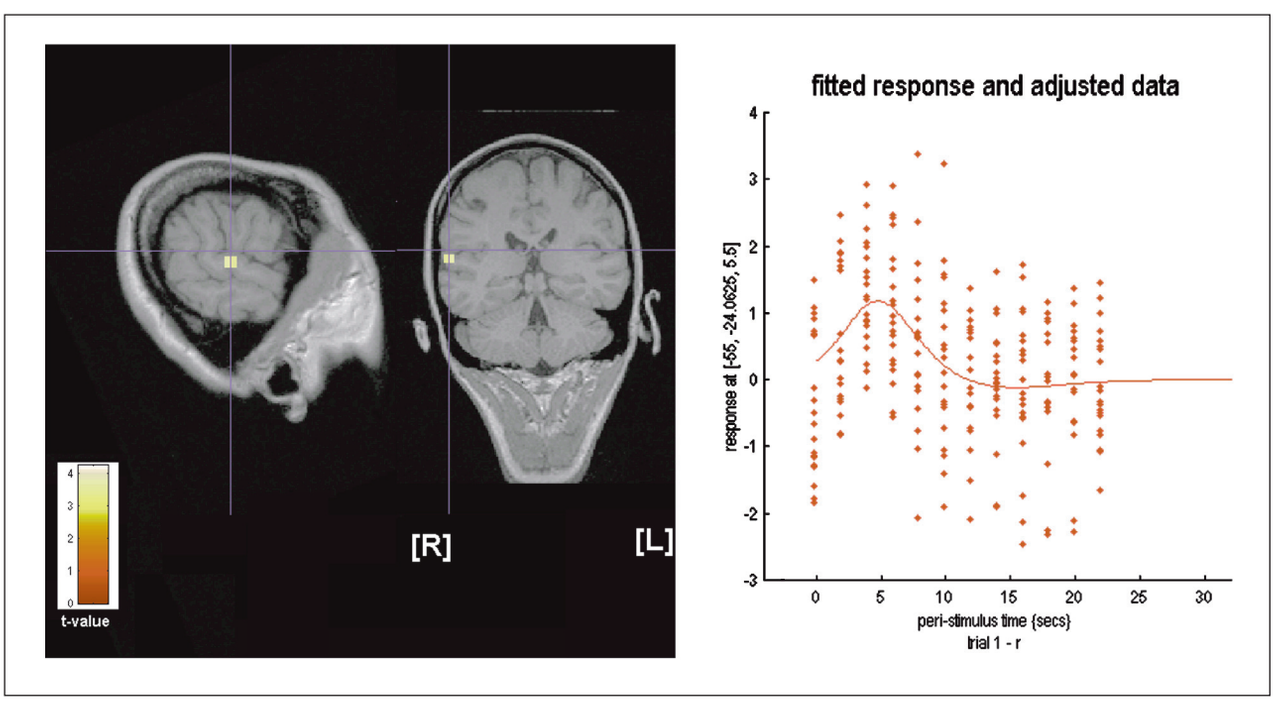

Figure 4 Method B. Overlay of the SPM results onto anatomical sections (left) and the fitted response (right).

the basis function of the HRF, we found significant activations within the primary auditory system. The activated areas were restricted to the gyri temporales transversi (Heschl's gyri). Regions known to be involved in higher order processing of an auditory signal were not detected. Due to the small number of slices (n = 5) and their acquisition parallel to the Sylvian fissure, no brainstem centres of audition were within the field of view. However, in addition to the results above, we were able to demonstrate a lateralized processing of iGGN. In all cases, the

most (or only) significant BOLD signal was detected within the right auditory cortex. The figure below depicts in the left panel the result of a single subject SPM analysis. It shows a significant peak within the auditory cortex, displayed onto the individual anatomy (data not normalized).

In this case, only the BOLD signal of the right auditory cortex reached the significance level ($p < 0.001$). The fitted response from that area, which is displayed in the right panel of that figure, demonstrates very nicely the temporal delay of the BOLD response of 5 - 6 seconds.

Discussion and Conclusions

Both methods are sensitive to detect audition of the pulse sequence itself through BOLD activations evoked by EPI's persistent and intermittent genuine gradient noise (p/iGGN), respectively. Lateralized processing observed for iGGN is in good agreement with current models of auditory perceptions of non-verbal auditory stimuli.Essentially, the data- and model-driven analyses correspond well to each other and are consistent with the sampling of a HRF evoked by GGN audition. Obviously, EPI is fast enough to catch the initial but naturally delayed BOLD increase in its own T2*-weighted signal induced by the onset of persistent and intermittently advanced scanning noise. According to the PCA, the mean signal within the initial six seconds of continuous scanning is indeed below the mean of the rest even if the BOLD signal may finally attenuate to some extent. The particular timing of the FIR model emphasizes the temporal features of the component presumably evoked by pGGNA. A peaking of the corresponding signal later than six but not much beyond ten seconds after the onset of persistent scanning clearly supports the notion of single superposed BOLD events. To demonstrate linear superposition of ultrafast stimuli, the HRF (and its temporal derivative) presumably induced by audition of rapid, successive stimulations corresponding to the slice selection gradients (G_z) can be extracted from SPM's design matrix (Sess{s}.bf{i}) set up for a single run. Then, these vectors should be modified to account for the discarded scans, expanded to match the number of runs, and entered as user-specified regressors only into F-tests. Furthermore, nonlinear superposition, i.e. stimulus non-additivity, could be addressed by expansions of the haemodynamic convolution through higher-order Volterra kernels. This may, however, eventually overspecify the effects searched for on cost of considerable loss of sensitivity. In addition, current SPM may not be most efficient for the analysis of our data mainly because it models temporal autocorrelations within the time series by a single parameter of the first order autoregression on the precoloured, i.e. smoothed data which essentially corresponds to a smoothing procedure by a kernel of an infinite FWHM. Local (voxel-by-voxel) pre-whitening with an AR model whose coefficients are smoothed spatially (such as in fmristat) or within tissue types (such as in fsl) is probably more sensible. Modelling by SPM results, however, in very robust estimators. With regards to the data-driven analysis, the PCA presented is to catch the direction of the maximal variance in the data whereas alternative methods of independent component analyses (ICA) represent higher order statistics and can find multiple directions of maximum independence even in non-Gaussian data (see fsl-webpage for further details). Although there may be good reasons for supposing non-Gaussian features in our data, especially of method A, the results of the PCA performed were meaningful interpretable for our purpose. Electrophysiological studies habitually refer to the alleged disadvantage of BOLD imaging to measure epiphenomena but no neural events in real time. We present the single and most outstanding case for which the temporal delay of the BOLD effect is not only of advantage but a prerequisite for the demonstration of the presumed neural response.

This is equivalent to "scanning for the scanner" through auditory autodetection of EPI by sound listening to the temporal characteristics of the BOLD response which otherwise limit temporal resolution and functional sensitivity. Notably, coronal slices are suited to catch both cortical and subcortical auditory activations. Our data show that audition can be investigated by just listening to the scanner. Limiting the bandwidth will increase the signal-to-noise ratio but lower the GGN level. Efficient unilateral earplugging can facilitate lateralized GGN processing. In the future, functional autodetection of EPI may gain clinical value to investigate audition with neither particular soft- nor hardware such as stimulation devices, trigger signals, or designer EPIs. We are working on a customized protocol of parametric iGGNA to increase the sensitivity of the design and to allow for an objective, clinically useful functional assessment of audition within about 6 minutes by just "scanning for the scanner".

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