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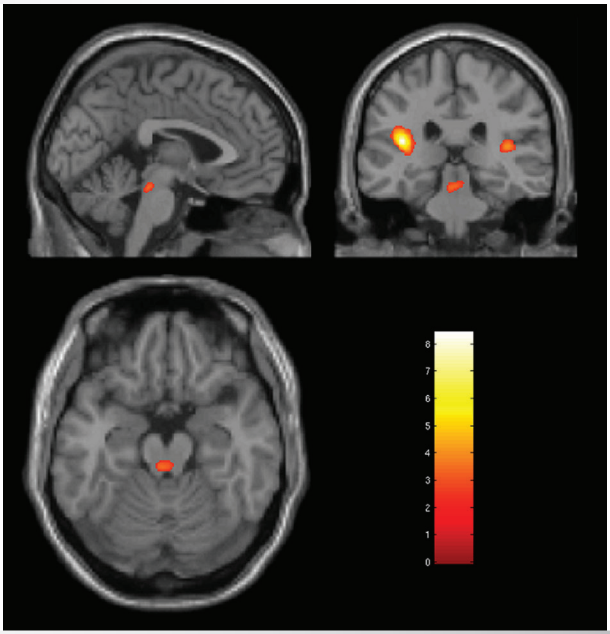
Improved Auditory fMRI Imaging Using Toshiba Scanner With Pianissimo



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Auditory experiments are typically conducted in sound booths to avoid any interfering background sounds. However, for decades, with the advent of Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI), there has been a desire to "brain map" regions of neuronal activity in response to presented auditory stimuli, taking the subject out of the sound booth.

Auditory imaging has been used for basic auditory experiments and to investigate hearing disorders such as Tinnitus and Central Auditory Processing Disorder. Early auditory imaging experiments used PET, and while the environment was noisier than that of a sound booth, it was similar to that of a computer fan and could be effectively reduced with headphones[1]. In comparison, MRI scanners are typically very loud.

With PET H_2O^{15} imaging, only five or six image volumes can be collected in an hour, and a team of researchers and clinicians is needed to make and inject the dose for each scan. With fMRI, hundreds or thousands of image volumes can be collected in an hour, with only the MRI operator being strictly needed. Because of the reduced interdependence of personnel compared to PET, MRI research scans can often be performed during non-peak hours and only add minimal staffing costs. However, with fMRI the environment can, in some cases, have extreme levels of background noise. The noise level of some MRI sequences can be similar to that of construction work, requiring the participant to wear ear protection.

Because of the tremendous amount of background noise generated from MRI imaging, an fMRI study using auditory stimuli is among the most difficult to perform, since the noise of the MRI can be overpowering. In fact, the noise of the scanner itself was shown to cause brain activation even in very early work using fMRI[2]. So while PET is much quieter, the utility of fMRI is overwhelmingly apparent: many more image volumes can be collected, fewer personnel are needed and research experiments can be effectively performed during off-hours. Furthermore, the Vantage Titan™ 3T from Toshiba America Medical Systems comes standard with the necessary sequences and scanning protocols can be easily set up without additional cost.

Toshiba's Pianissimo Minimizes Noise

Currents passing through the gradient coils, which are within the static magnetic field of the MRI, will have a Lorentz force applied to them. This force causes a vibration of the coil and the components that it is attached to. This causes the loud "banging" noise that is typically associated with MRI scanning.

To address the issue of noise, Toshiba engineers took several steps to minimize sound levels as part of the Pianissimo™ noise-reduction technology. Pianissimo provides a vacuum chamber that surrounds the gradient coil and the mounting support of the chamber and gradient coil is separated from the magnet. Additionally, acoustic insulation dampens any mechanical energy from the vacuum chamber[3]. Innovative sequences also help to reduce the originating noise of the gradient coil. The result is EPI sequences with sound levels similar to that of a noisy street.

Patient Comfort Means Better Images

Typically, having an MRI is not considered an enjoyable experience. Previous research on a scanner without Pianissimo required subjects to be in the scanner for more than an hour while having the motion of their head severely restricted. Noise from the MRI can not only be distracting to the subject trying to listen to auditory stimuli in the scanner, but a high noise level will affect a person's mood and comfort level. Not surprisingly, a subject's level of cooperation can also deteriorate in a noisy environment. Rerunning the experiment using a Toshiba scanner with Pianissimo would improve subject comfort and lead to results that better represent changes in physiology due to the presented auditory stimuli, not the acoustic noise of the scanner.

As a patient or subject is exposed to high levels of noise, they will often fidget and have an increasingly hard time remaining still. This can be problematic, as motion during the scan collection can cause artifacts to appear within the image. Even a very small movement during the actual acquisition can cause a subtle artifact. To guard against this in both the previous and current studies, a method is used that models the response of each voxel for each session. This allows for the intensity difference between a measured voxel's value and what is predicted based on other scans from the same or similar conditions to be determined. If the difference is greater than two standard deviations, that voxel is classified as an outlier. So for each scan the number of voxels that are outliers can be calculated. A large spike in the number of voxels classified as outliers is likely caused by (even small) patient motion, or perhaps a system transient. In this case, that particular collection can be discarded and the remaining image volumes would be used. Subjects will be more comfortable in the Toshiba scanner and will therefore be more compliant, leading to fewer image volumes classified as outliers and rejected.

Better Quiet Conditions

fMRI typically contrasts images collected under different conditions. In this case, we will be comparing images collected while no auditory stimuli is presented together with stimuli of a band-pass noise and a pure tone signal. A "quiet" or "no stimuli" condition is especially useful in auditory imaging since it provides a baseline activity. In addition to imaging the effect of our stimuli, we will unavoidably be imaging other aspects of what the subject is experiencing. We believe that by using a scanner that is much quieter than we used previously, our "quiet" condition collected using the Toshiba scanner will be more reflective of a "true" quiet condition. If our assumption is true, it should be evident by a stronger (improved) contrast between when conditions presented acoustic stimuli and the quiet condition.

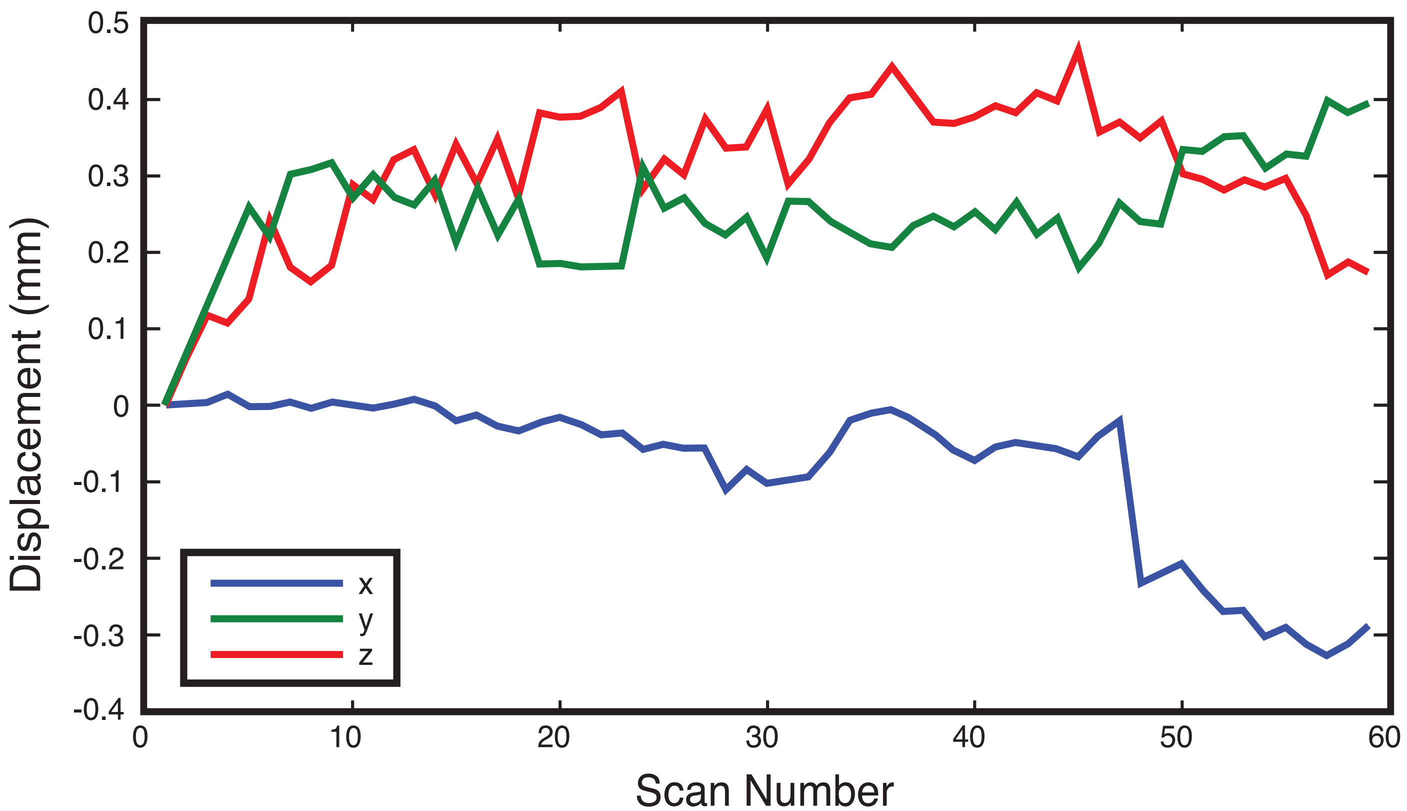

Figure 1: Motion in the x (left – right), y (anterior – posterior) and z (inferior – superior) directions during the last fMRI scan session for a single subject. There was a noticeable sudden change at scan 47, but only ~0.2 mm in the x direction and much smaller in the other directions.

To summarize, we believe that by using the Toshiba Titan 3T scanner:

1) Fewer scans will be rejected due to artifact since subject compliance will be higher.

2) Contrasts between the auditory noise and signal conditions and the quiet condition will yield stronger results because of a truer quiet condition with the Toshiba scanner.

Method Details

Twenty subjects who underwent informed consent were enrolled and approved by the University at Buffalo's Institutional Review Board. Auditory and fMRI testing closely followed the protocol used in the previous study[4].

Subjects were presented with 10 different auditory conditions that were combinations of the band-pass noise and pure tone signal presented both in and out of phase, together with the no-stimuli condition. The auditory stimuli presented were used to calculate Masking Level Differences (MLDs), which are the differences in the detection threshold of the pure tone signal when either the noise masker or pure tone signal is presented out of phase, subtracted from the detection level when both signal and masker are in phase between ears. When either the noise or signal is out of phase, the detection levels are typically 10-15 dB lower (better) than when both noise and signal are in-phase.

Scanning

Each subject underwent a high-resolution T1 scan acquisition (approximately five minutes) and four sessions of fMRI scans each lasting roughly 12.5 minutes. Each fMRI session presented 10 different auditory stimuli, six times each in a pseudo-random manner that assured balanced placement of each of the stimuli within the session. Time of acquisition for each image volume was three seconds, whereas Repetition Time was 12 seconds. Between active acquisitions there were nine seconds of relative quiet from scanner noise during which the stimuli could be presented[5,6].

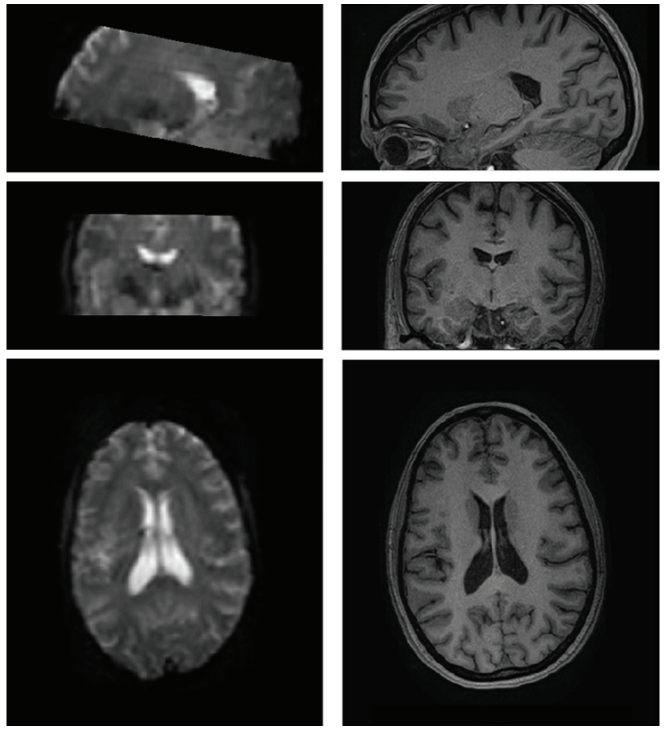

Figure 2: fMRI images shown in left-hand column are from a single subject and are co-registered to images from a T1 – weighted sequence, shown in the right-hand column.

Results

fMRI data was corrected to compensate for any small motion using Statistical Parametric Mapping[7] (SPM) realignment tool. Unsurprisingly, after a subject has been in a scanner for a long period of time they are more likely to exhibit movement. In **Figure 1**, we show an example of motion during the last session for our first subject scanned in the Titan 3T scanner. Despite the subject having been in the scanner for approximately an hour before the start of the session shown, the subject's movement was still less than 0.5 mm in any direction across the entire 12.5-minute session. After realignment correction using SPM, the data was co-registered with a high-resolution T1 scan, which was used for spatially normalizing all of the scans to a common template. The iterative segmentation routine within SPM was used to calculate the normalization transform parameters. Examples of the T1 and fMRI images are provided in **Figure 2**.

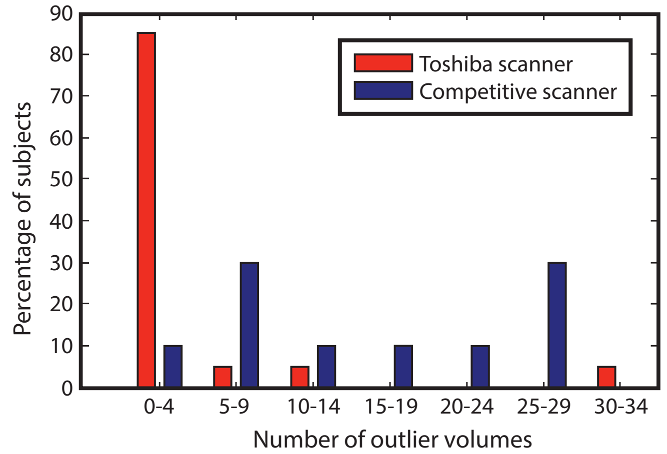

Figure 3: Histogram showing the percentage of subjects by the number of the subjects' scans that were classified as outliers. There is a much higher percentage of number of subjects with less than 4 outlier scan volumes in the current study than with the previous study.

Reduced Scan Outliers

As with the previous study, we followed the method of SPMd[8] and the fitting parameters of the General Linear Model were calculated individually for all sessions and subjects. At this stage, residual images were created for each scan time point which displays the error between the modeled fit and the actual data. By calculating the number of outlier voxels in each scan, we can determine whether a particular scan was unduly influenced by motion of the subject or some other system transient. Overall, there was a great reduction in the number of scan volumes that were classified as outliers when using the Toshiba Titan 3T with Pianissimo. The one exception is a participant who was observed to have persistent body motion while in the scanner. This participant was offered the opportunity to end the scanning early with no consequence, but wanted to continue. This participant did eventually settle their motion as the scanning continued. A histogram of the percentage of subjects with varying numbers of outlier scans is given in **Figure 3**.

Improved Statistical Strength for Comparisons Made with Quiet

In the previous study, we only used 10 participants, so in making the following comparison we used only the last 10 participants from the current study. We formed statistical contrasts of the conditions Noise versus Quiet,

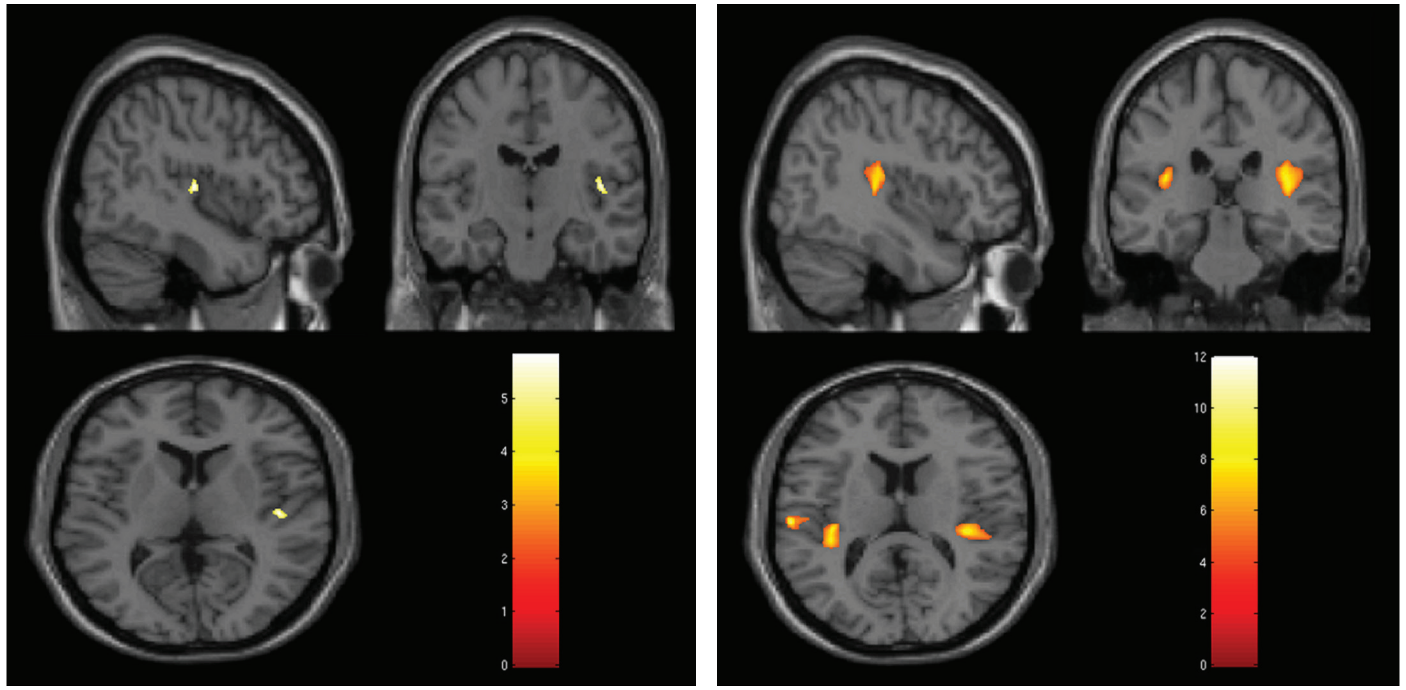

Figure 4: The left-hand side image is from the previous study; the right-hand image is from the current study using the Toshiba scanner. There is a much stronger activation found using the Toshiba scanner for the contrast: Noise – Rest (observe the higher scale used for the Toshiba image).

and expected to see significant activation in both the left and right auditory regions. Both of our studies were fairly ambitious and used 10 different conditions. Therefore, the statistical significance might be somewhat weak since there are a relatively few number of collections for each condition per subject. This was the case in our previous study where we only found a small region of activation located in the right auditory cortex when threshold at p<.001, uncorrected for multiple comparisons (left image, **Figure 4**). However, using only 10 subjects from our current study and the same threshold, the regions of activation were bilateral and larger with the Toshiba scanner as we would expect physiologically (right image, **Figure 4**). Additionally, the strength of SPM t scores can be seen to be considerably higher with the Toshiba study, by observing the maximum color scale value on the previous study was approximately six, and is 12 for the current study. Furthermore, with our current study we were able to detect activation in the very small region of the inferior colliculus for individual subjects (**Figure 5**).

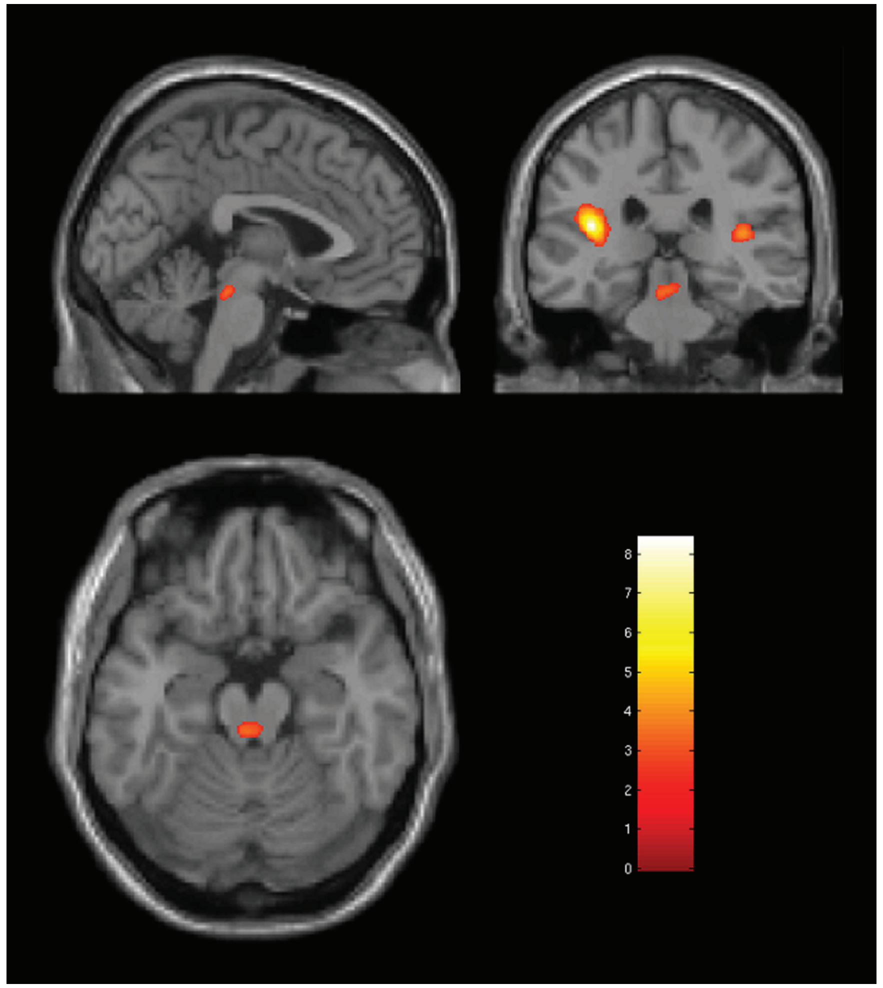

Figure 5: Activation was detected on the Inferior Colliculus using the Toshiba scanner, which was previously undetected on competitive scanner.

Repeat Subjects' Comments

Two subjects were enrolled in both the previous study and the current study. At the end of their scanning session with the Toshiba Titan 3T scanner with Pianissimo, both subjects remarked that the scanning portion of this study was more comfortable than previously.

Conclusion

When conducting research studies, the researcher is dependent upon the subjects to be fully compliant and attentive to the task. This has been difficult with MRI studies, since participants have their head immobilized and are subjected to sound levels from the scanner that are equivalent to power tools, making it easy for a subject to focus on their discomfort rather than a presented task. By improving a subject's comfort, they can be more compliant to the demands of the study. This leads to improved functional imaging studies that are truer measures of the physiology. The Toshiba Titan 3T proves that and MRI can be quiet. The study was conducted using only standard sequences readily available on all Toshiba systems, and demonstrates how easily fMRI imaging can be conducted at any site.

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