BOLD baseline 'activity' of auditory cortex during silence

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Introduction: The perception of voices 'heard' during the lack of an external stimulus to the eardrum can occur in both healthy and disease states including: reduced arousal; hypnosis; drug intoxication; delirium and psychosis. Such auditory hallucinations imply the presence of associated, endogenous neuronal activity that can be present during silence. This study examines the baseline blood oxygen-level dependent (BOLD), hemodynamic response of the human auditory cortex to episodic silence using susceptibility-weighted fMRI.

Methods. *Subjects:* Twelve healthy, right-handed males aged 23 ± 3 years (mean±sd) participated. *Imaging:* All subjects plus a test-object (water melon) were scanned at 1.5T (Eclipse, Philips Medical Systems). Imaging was performed using a 'SPARSE' (1) protocol that consisted a gradient-recalled EPI sequence (TE=50ms; in-plane resolution=1.875mm) which acquired 32 contiguous, 4mm thick, anatomical transaxial slices over 3 seconds followed by a 17 second acquisition delay, giving a repeat-time of 20 seconds. This scheme was repeated to yield 48 dynamic datasets acquired over 16 minutes. The BOLD hemodynamic delay to neuronal activity was used to investigate the T2*-weighted MR signal characteristics that corresponded to periods when the imaging apparatus was not producing noise (during the 17 sec delay). Twenty-four unique speech stimuli were presented during alternate silent periods via headphones (Resonance Technologies, Texas) in an 'A/B' design [30dB headphone passive attenuation affectively cancelling out residual scanner-room noise]. *Analysis:* Statistical interrogation was performed using SPM99 (www.fil.ion.ucl.ac.uk/spm) plus customised software. (i) Comparisons were made between speech and silence conditions using the General Linear Model to define the speech-sensitive components of the auditory cortex for each individual subject; ii) At each 'silence' time point, the number of functionally defined voxels in the left hemisphere that were more than 2 standard deviations above their silence-specific mean ($Z > 2$) was calculated; iii)Time points were ranked in order of total '$Z > 2$ voxels'. The time point with greatest total voxels of $Z > 2$ was defined as a 'spontaneous activation'. Other time points were defined as 'spontaneous activations' if they contained voxels with $Z > 2$ that were common to all higher ranked time points; iv) Models were produced for each subject defining time points of spontaneous activation and time points of no such activation (during silence); v) The main effect of spontaneous activation (versus ordinary silence) was examined across the whole brain in a group average analysis.

Results: As expected, each subject demonstrated extensive bilateral activation of temporal regions in response to speech (versus silence).
In the time-domain: Each subject demonstrated evidence of spontaneous auditory activation ($Z>2$) during silence in both hemispheres (table 1). In the left hemisphere, spontaneous activation occurred at 2 time-points (8% of sampled baseline time) in 11/12 subjects and at 3 time-points (13% sampled baseline) in 1 subject. In the right hemisphere, spontaneous activation occurred at 2 time-points (8% of sampled baseline time) in 8/12 subjects and at 1 time-point (4% sampled baseline) in 4.
In the spatial domain: Contrasting time-points of left hemisphere spontaneous activation with the remainder of the silence baseline revealed significant differences in left lateral and posterior superior temporal gyrus plus transverse temporal gyrus. Contrasting time-points of right hemisphere spontaneous activation with the remainder of the silence baseline also revealed significant differences in left superior temporal gyrus plus transverse temporal gyrus. The right hemisphere spontaneous activation yielded a further focus in the left anterior cingulate / medial frontal gyrus (fig 4).
Control object: The control water melon did not yield any 'spontaneous activation'.

Table 1. Mean auditory activation (speech vs silence) in the 12 subjects. Observed number of voxels with $Z>2$ in the left and right hemispheres at specified time-points during silence is given. The probability of observing these $Z>2$ data under Gaussian assumptions, from the normal approximation to a binomial distribution, is very small (<1x10exp(-6)).

	Left	Right
Functionally-defined voxels	790	779
Mean ±sd EXPECTED $Z>2$ voxels	19.75±4.39	19.48±4.36
Mean OBSERVED $Z>2$ voxels	96	81

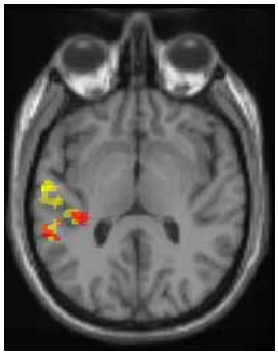

Figure 1. At the group level (n = 12), foci for left (yellow) and right (red) hemisphere. Spontaneous activation phenomena are located in the left primary and association auditory cortices. Functional imaging data in a mixed-effects model are presented. These data show brain regions where statistically defined activation ($p < 0.001$, uncorrected) is associated with high levels of activity in the left (yellow) and right (red) hemisphere speech-sensitive brain volume.

Discussion: The findings of this study show that temporally intermittent, statistically significant increase in susceptibility-weighted BOLD signal occurs during silence within functionally-defined speech sensitive auditory cortex. We define this signal variation as 'spontaneous activation'. In addition to the primary and association auditory cortices, significantly large variance was observed within anterior cingulate cortex and we postulate that endogenous cerebral 'background' variance in BOLD signal may be modulated by this structure. These observations may help to explain why auditory hallucinations are present in healthy as well as disease states. In addition, this technique may help facilitate the anatomical location of other apparently spontaneous cerebral events, such as the focus of neuronal activity that underpins temporal lobe epilepsy.
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Reference:

1) Hall DA et al. Human Brain Mapping 1999; 7:213-223.