Supporting Information

Linke et al. 10.1073/pnas.1102118108

SI Text

Multivoxel Pattern Analysis. Common univariate methods draw on changes in the magnitude of blood oxygenation level-dependent (BOLD) response on an individual voxel basis, identifying differences in overall activation between conditions. Voxels that show a BOLD response that does not reach the predefined significance threshold are ignored in the univariate analysis, although they might still carry meaningful information. Multivoxel pattern analysis (MVPA) compares the distributed activity patterns evoked by different stimuli or conditions across voxels and analyzes the within-subject consistency of these activation patterns (Fig. S1). It is robust to individual differences and can identify important information coding, even when no net overall change in activity is observed (e.g., when some voxels were activated and some were deactivated). This finding makes it possible to work with unsmoothed data and thereby, exploit high spatial frequency information that is usually ignored in conventional functional MRI (fMRI) analyses.

Tonotopic Gradients. From the simple contrast testing for frequencyspecific coding in the MVPA region of interest (ROI) and search light analysis (Figs. 3 and 5), it was observed that sounds close in frequency evoked a more similar activity pattern. To test this observation more explicitly, we ran an MVPA search light using a graded contrast (Fig. S3*A*) and tested for the ordering of the frequencies (Fig. S3 *B–D*). Results of this analysis are shown in the third and fourth columns of Fig. S3. For all four contrasts, auditory cortex was identified as distinguishing between the different frequencies in a way that reflects the tonotopic organization observed in neurophysiology and other fMRI studies (False Discovery Rate (FDR)-corrected at P < 0.05).

Excluding Neural Adaptation as a Reason for Stimulus-Specific Suppression. We modeled the encoding and probe sequence in each trial separately to compare the magnitude of activation in these two phases of the task. If stimulus-specific suppression during maintenance was caused by neural adaptation, we would expect activation to be lower during the probe phase of the task. However, this cause was not the case (Fig. S4).

Impact of Scanner Noise on Task Performance. Many fMRI studies involving auditory stimuli have drawn on sparse MRI sequences with silent intervals to increase the signal. However, in our paradigm, presenting the tones in silence and scanning during the maintenance and ITI periods would have confounded the most relevant contrasts between the different stages of the short-term memory task. Piloting revealed that participants had no problem distinguishing the stimuli from the scanner noise, the BOLD signal in auditory cortex was high, and the frequencies were chosen to coincide as little as possible with peak scanner noise (Fig. S8). Custom-built headphones were used to present sounds with high fidelity and reduce noise. Additionally, all participants wore earplugs throughout the experiment.

Participants consistently performed at a high level but not at ceiling (M = 0.81, SD = 0.09). A repeated-measures ANOVA revealed a significant effect of frequency on performance, with participants performing better in detecting changes in the higher frequency range [F(2.663) = 15.188, P < 0.001]. This behavioral effect was not mirrored in the fMRI results, with response in auditory cortex not varying significantly in magnitude for the four frequency ranges as revealed by an auditory ROI analysis [F(2.83) = 1.5, P = 0.224].

However, performance during an 8-min practice block before entering the scanner was slightly better than performance during the actual experiment [M = 89% vs. M = 81%, t(24) = 5.363, P < 0.001]. We attribute this decrease in performance to the changed environment (although most participants did not rate the scanner noise as distracting them from the task; M = 3.48, SD = 1.29 on a five-point scale, with one being very disruptive and five being not disruptive at all). Additionally, the practice block was relatively short, whereas the experiment lasted ~50 min.

Impact of Repeated Sessions on Task Performance. Twenty-five sessions (nine participants with two sessions each and seven participants with one session each) were analyzed for this study. The question, therefore, arises whether performance improved for the nine participants who completed a second session. This result was not the case [t(16) = 0.17, P = 0.867]. Furthermore, only two subjects reported a switch in strategy: they did not use a strategy in the first session but did in the second session. This consistency in strategy and performance is probably caused by a gap of at least 2 wk between the two sessions.

Predictive Coding as an Explanation for Stimulus-Specific Suppression. We modeled same and different trials separately and compared the magnitude of activation during the encoding and probe phases of the task. The predictive coding explanation for the suppression that we observed during maintenance would predict that activity during the probe phase would be higher for different trials than for same trials, signaling that a change has taken place. Results of this analysis are shown in Fig. S7. Activity was only marginally higher (uncorrected, P < 0.05) in the probe phase when a change had occurred (different trial) vs. when no change had occurred (same trial). Additional experiments need to be carried out to more explicitly test for predictive coding as a possible explanation for the stimulus-specific suppression observed in this experiment.



Fig. S1. MVPA focuses on patterns of activity and thus, can reveal differences between conditions (e.g., conditions A and B) with higher accuracy. Although overall activation in a standard univariate analysis might be the same for two highly similar conditions (such as playing two tones with different frequencies), the fine-grained activation patterns across voxels might be significantly different. Activity patterns generated by repetitions (*k*) of the same condition are correlated to assess pattern similarity within the same condition, and repetitions of condition A are correlated with repetitions of condition B to yield a measure of similarity across conditions.



Fig. 52. Overall activity during encoding. Significant activation compared with the silent baseline is in red, whereas suppression is in blue. FDR-corrected values for multiple comparisons at P < 0.05. Note that frontal regions were not acquired in this study because of using a high-resolution EPI sequence that covered temporal and parietal cortex as well as sensormotor regions and parts of ventrolateral prefrontal cortex (including Broca's area) only.



Fig. S3. Graded contrasts (first and second columns) used in supplementary searchlight analysis to test for tonotopic frequency coding. (*A*) Contrast testing for a gradient, with tones closer in frequencies having a higher correlation. (*B–D*) Testing relationship between individual frequency ranges: (*B*) Δ f1 > (Δ f2 + Δ f3 + Δ f4)/3, (*C*) Δ f2 > (Δ f3 + Δ f4)/2, and (*D*) Δ f3 > Δ f4. The searchlight analysis revealed significant results (third and fourth columns; FDR-corrected at *P* < 0.05) in auditory regions for all four contrasts, indicating that the frequency-specific coding that we observe in auditory cortex during encoding (Figs. 5 and 6) reflects one or more tonotopic gradients and the sounds close in frequency were coded similarly.



Fig. S4. Encoding > probe contrast did not yield any significant activation (FDR-corrected at P < 0.05); instead, activity was higher during the probe phase than during the encoding phase of the task, suggesting that the frequency-specific suppression observed during maintenance is not caused by neural adaptation.



Fig. S5. MVPA ROI (*A*) and searchlight (*B*) results for the comparison of activity patterns during encoding and maintenance in the auditory cortex ROI. (*A*) Activity patterns during encoding were negatively correlated with activity patterns during maintenance. (*B*) Voxels marked in green showed significant frequency-specific suppression (peaks at 56, -16, 0 on the right and -50, -24, 0 on the left; FDR-corrected at P < 0.05).



Fig. S6. Positive correlation between degree of frequency-specific coding and memory capacity (K).



Fig. S7. Comparison between same and different trials during the probe phase of the task (uncorrected, P < 0.05).



Fig. S8. Spectrogram of the scanner noise with frequency ranges used in the experiment superimposed (red = 174 0.61–207.65 Hz, yellow = 415.30–493.88 Hz, green = 987.77–1,174.4 Hz, and blue = 2,349.3–2,793.8 Hz).