

SI Text

Behavioral Results. The mean success rate (\pm SD) of the subjects for the experimental trials was $81.1 \pm 10.0\%$, and the mean success rate for the control recognition trials was $98.9 \pm 1.3\%$. The subjects' mean reaction time in the experimental trials was 1.553 ± 0.191 s, and the mean reaction time in the control recognition trials was 1.097 ± 0.172 s. This difference in success rate and reaction times between the experimental and control trials was expected and reflects the additional requirement in executive control processing of the experimental trials. Note that error trials were excluded from the analysis and, therefore, the activity differences reported in this study were based only on trials in which the subjects answered correctly.

We also separated the experimental trials based on the dimension of the stimulus (duration or frequency) that was relevant for the memory decision. There was no difference in the activity pattern in the test period when retrieval of duration and retrieval of frequency were compared against each other. In addition, no significant difference in the subjects' mean success rate was obtained between the two types of experimental trial (78.8% and 82.4% , respectively). However, on average, the subjects took longer to respond during the trials that required a decision based on the duration of the stimuli [1.651 s for the duration cue and 1.455 s for the frequency cue; paired t test; $t(11) = 3.126$, $P < 0.05$].

Imaging Results. For the comparison of the encoding period against the last two seconds of the intertrial interval additional activity increases were seen in the cingulate motor areas, the supplementary motor area (SMA), the caudate nucleus, and the premotor cortex (SI Table 1). The motor areas seen in the comparison were probably due to the fact that subjects tensed their hand muscles when they received the vibrations. When we compared separately the trials where the subjects received vibrotactile stimulation on the right hand and left hand against the baseline period, there were stronger contralateral activity differences in the primary and secondary somatosensory areas for the right hand.

For that reason when we pooled the data from both hands together the activity differences were stronger on the left side.

All subjects received the vibrotactile stimulation on both hands. Half of the subjects received the vibrotactile stimulation on the right hand during the first three runs and then on the left hand for the last three runs. The other half of the subjects received the vibrotactile stimulation on the left hand during the first three runs and then on the right hand for the last three runs. When we separated the experimental trials on the basis of the hand that received the vibrotactile stimulation and compared separately the test period of these trials with the test period of the control trials, we found stronger contralateral midventrolateral prefrontal cortex activity for the right hand vibrotactile stimulation. The left hand vibrotactile stimulation yielded a bilateral midventrolateral prefrontal activity increase. No other differences were seen in the rest of the brain. In addition, the direct comparison between the right and left hand experimental trials did not yield any significant activity differences. Neither the order of presentation nor the hand that received the vibrotactile stimulation yielded any significant differences in the accuracy and reaction times of the subjects.

Supporting Methods. The vibrotactile stimulators (piezoelectric devices) were built in-house and were controlled by the computer that ran the software for the stimulus presentation and the recording of subjects' responses (E-prime 1.1; Psychology Software Tools Inc.). The subjects responded on an MR compatible optical computer mouse and visual stimuli were presented through a liquid crystal display (LCD) projector with a mirror system.

Images were realigned with the third frame of the first run as a reference using the AFNI image registration software (1) and then blurred using a 6 mm full-width half-maximum (FWHM) isotropic Gaussian kernel. Subsequently, all images were linearly registered in standardized stereotaxic space (2) based on the MNI model (ICMB152) using in-house dedicated software (3). As a second step, we performed a nonlinear registration that was estimated on MRI data blurred with an 8-mm FWHM Gaussian kernel and a 3D lattice

grid with 4-mm spacing between nodes. This transform corrects for overall brain shape and aligns major cortical structures (e.g., the central sulcus and the Sylvian fissure) but does not necessarily align secondary and tertiary sulci and gyri (4).

Statistical analysis of the BOLD data were based on a general linear model with correlated errors and was performed using fMRISTAT (5). The data were first converted to a percentage of the whole volume. In the design matrix we defined the onset time and duration of the test periods for the three trial types separately (i.e., the experimental active retrieval decision on frequency, the experimental active retrieval decision on duration, and the control recognition decision). The onset of these events was timed to coincide with the presentation of the cue and test stimuli in each trial, and the duration was different for every subject and every type of trial and was calculated based on the average reaction time of each subject for the different types of trial. We also defined the onset time and duration of the encoding period and a baseline period. For the encoding event, the onset time was timed to coincide with the presentation of the first stimulus, whereas for the baseline event the onset time was timed 2 s before the offset of the intertrial interval. The durations were 1 s for the encoding event and 2 s for the baseline event. The design matrix of the linear model was first convolved with a hemodynamic response function modeled as a difference of two gamma functions timed to coincide with the acquisition of each slice. (6). Temporal drift was removed by adding a cubic spline in the frame times to the design matrix (one covariate per 2 min of scan time), and spatial drift was removed by adding a covariate in the whole volume average. The correlation structure was modeled as an autoregressive process of degree 1 (7). At each voxel, the autocorrelation parameter was estimated from the least squares residuals using the Yule–Walker equations, after a bias correction for correlations induced by the linear model. The autocorrelation parameter was first regularized by spatial smoothing with a 15-mm FWHM Gaussian filter and then used to “whiten” the data and the design matrix. The linear model was then re-estimated using least squares on the whitened data to produce estimates of effects and their standard errors, as well as t statistics for each comparison of interest (5). The hypothesis-testing comparisons were the difference

between the coefficients of the encoding period with the baseline period of the intertrial interval and both experimental test periods with the control test period.

In a second step, we combined the runs within subjects using a fixed effects model and the results across subjects using a mixed effects linear model with fixed effects standard deviations taken from the previous analysis. This was fitted using residual error maximum likelihood implemented by the estimation maximization algorithm. A random effects analysis was performed by first estimating the ratio of the random effects variance to the fixed effects variance, then regularizing this ratio by spatial smoothing with a 15-mm FWHM Gaussian filter. The variance of the effect was then estimated by the smoothed ratio multiplied by the fixed effects variance. The amount of smoothing was chosen to achieve 100 effective degrees of freedom. More information is available at www.math.mcgill.ca/keith/fmristat.

The resulting t statistic images were thresholded using the minimum given by a Bonferroni correction, random field theory, and the discrete local maximum taking into account the non-isotropic spatial correlation of the errors. Significance was assessed on the basis of exploratory and directed search as well as on the basis of the spatial extent of consecutive voxels. A cluster volume extent $>697 \text{ mm}^3$ with a t value of >3 was significant ($P < 0.05$) corrected for multiple comparisons (8). For a single voxel in an exploratory search involving all peaks within an estimated gray matter of 600 cm^3 covered by the slices, the threshold for reporting a peak as significant ($P < 0.05$) was $t = 4.75$ (9), whereas for a single voxel in a directed search within predicted brain regions, the threshold for significance ($P < 0.05$) was set at $t = 4.18$. For these predicted brain regions, we also report peaks of activity difference that are below threshold in the contralateral hemisphere because they likely represent real effects rather than false positives.

We also used fMRISTAT to assess whether the functional connectivity between the mid-ventrolateral prefrontal cortex and posterior somatosensory regions would be modulated by our task, i.e., whether the functional connectivity would be different for the

experimental active retrieval compared to the control recognition trials. The interaction method in fMRISTAT is based on the method described by Friston *et al.* (10). Functional connectivity is computed as the correlation across time of the BOLD signal between a reference voxel that is chosen based on the previous comparison analyses and all voxels in the rest of the brain. The estimated drift and the estimated signal due to the paradigm was subtracted from the BOLD data before calculating the correlation, so that our correlations are not induced by common activation. In other words, we are looking at correlations of residual error on top of the BOLD activation. The correlation *per se* is not of primary interest; the more important scientific goal is to examine how this correlation is modulated by the task.

We identified reference voxels in both hemispheres in the mid-ventrolateral prefrontal cortex where we reported differences in activity in the experimental minus control comparison [i.e., the caudal and rostral parts of area 47/12 and area 45 (11)]. We used the general linear model where we added regressors for the task events and drift, so as to account for their effect, and then added a regressor for the time course at the reference voxel. Finally, we added as a regressor variable an interaction (product) between the task events and the reference voxel time course. The voxel values were extracted for each subject from native space after having applied slice time correction. Finally, we estimated the effect, standard error, and *t* statistic for the interaction in the same manner as described above. Increased functional connectivity for the test period of the experimental trials compared to the same period of the control trials between the reference voxels and other voxels in the brain is represented by positive *t* values. Given that we had an *a priori* hypothesis that the midventrolateral prefrontal cortex would demonstrate increased functional connectivity with the posterior somatosensory areas (namely the secondary somatosensory cortex, the rostral inferior parietal lobule, and the somatosensory part of the insula) during the experimental test period, we are reporting interaction results from there areas only ($P < 0.005$ uncorrected).

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