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A general mechanism for perceptual decision-making in the human brain

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Findings from single-cell recording studies suggest that a comparison of the outputs of different pools of selectively tuned lower-level sensory neurons may be a general mechanism by which higher-level brain regions compute perceptual decisions. For example, when monkeys must decide whether a noisy field of dots is moving upward or downward, a decision can be formed by computing the difference in responses between lower-level neurons sensitive to upward motion and those sensitive to downward motion^{1–4}. Here we use functional magnetic resonance imaging and a categorization task in which subjects decide whether an image presented is a face or a house to test whether a similar mechanism is also at work for more complex decisions in the human brain and, if so, where in the brain this computation might be performed. Activity within the left dorsolateral prefrontal cortex is greater during easy decisions than during difficult decisions, covaries with the difference signal between face- and house-selective regions in the ventral temporal cortex, and predicts behavioural performance in the categorization task. These findings show that even for complex object categories, the comparison of the outputs of different pools of selectively tuned neurons could be a general mechanism by which the human brain computes perceptual decisions.

Consider driving home from work in clear weather. Stopping at a

light, you see pedestrians waiting to cross the street. Effortlessly, you decide whether one of them is your spouse, your boss or a stranger, and connect the percept with the appropriate action, so that you will either be waving frantically, greeting respectfully or taking another sip of coffee. During a rainstorm, however, the sensory input is noisier, and thus you have to look longer to gather more sensory data to make a decision about the person at the light and the appropriate behavioural response.

This type of decision-making has been studied in single-unit recording studies in monkeys performing sensory discriminations^{5–8}. Shadlen *et al.* proposed that perceptual decisions are made by integrating the difference in spike rates from pools of neurons selectively tuned to different perceptual choices⁹. For example, in a direction-of-motion task, in which the monkey must decide whether a noisy field of dots is moving upward or downward, a decision can be formed by computing the difference in responses between lower-level neurons that are sensitive to upward motion and those sensitive to downward motion^{1–4}. Similarly, in a somatosensory task, in which the monkey must decide which of two vibratory stimuli has a higher frequency, a decision can be formed by subtracting the activities of two populations of sensory neurons that prefer low and high frequencies, respectively^{8,10}. These findings suggest that a comparison of the outputs of different pools of selectively tuned lower-level sensory neurons could be a general mechanism by which higher-level cortical regions compute perceptual decisions^{1,2,11}. However, it is still unknown whether such a mechanism is at work for more complex cognitive operations in the human brain and, if so, where in the brain this computation might be performed.

We used functional magnetic resonance imaging (fMRI) while subjects decided whether an image presented on a screen was a face or a house (Fig. 1). Previous neuroimaging studies have identified regions in the human ventral temporal cortex that are activated more by faces than by houses, and vice versa^{12–16}. Increases in the blood-oxygen-level-dependent (BOLD) signal have been shown to be proportional to changes in neuronal activity in a given region^{17,18}. Therefore larger BOLD responses to faces than to houses and vice versa in specific voxels in the ventral temporal cortex reflect the change in activity in a population of neurons that are more responsive to faces than to houses, and vice versa. Our task thus enabled us to identify two brain regions, one more sensitive to faces and another to houses, and to test whether there are higher-level cortical regions whose output is proportional to the difference in activation in the face- and house-selective regions, respectively.

We based our hypotheses on results from single-unit recording studies in monkeys, which have shown that neuronal activity in areas involved in decision-making gradually increases and then remains elevated until a response is given, with the rate of increase being slower during more difficult trials^{1,2}. These studies have also shown that higher-level cortical regions, such as the dorsolateral prefrontal cortex (DLPFC), might form a decision by comparing the output of pools of selectively tuned lower-level sensory neurons^{4,9}. Therefore, we hypothesized that higher-level cortical regions computing a decision would have to fulfil two conditions. First, they should show the greatest activity on trials in which the evidence for a given perceptual category is greatest, for example, a greater fMRI response during decisions about suprathreshold images of faces and houses than during decisions about perithreshold images of these stimuli. Second, their activity should be correlated with the difference between the output signals of the two brain regions containing pools of selectively tuned lower-level sensory neurons involved; that is, those in face- and house-responsive regions.

To test the model of decision-making, we added noise to the face and house stimuli, which made the task arbitrarily more difficult by reducing the sensory evidence available to the subject (Fig. 1b). In the fMRI experiment, subjects viewed images that were either easy (suprathreshold, Fig. 1b top) or difficult (perithreshold, Fig. 1b bottom) to identify as faces or houses.

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We identified voxels in the ventral temporal cortex that responded more to faces than to houses, and vice versa, in each subject (Fig. 2a, 'Face' and 'House'). By analogy to the monkey studies, we then used only correct trials to calculate the mean fMRI responses to the four classes of stimuli relative to baseline (fixation) in face- and house-selective regions, respectively. For the preferred category, both face- and house-selective regions responded more to suprathreshold than to perithreshold images whereas the opposite was true for the non-preferred category, indicating that face- and house-selective regions represented the sensory evidence for the two respective categories (Fig. 2b).

Several brain regions typically associated with the attentional network showed a greater response to perithreshold than to suprathreshold stimuli of both faces and houses^{19,20}. These regions, which included the frontal eye field (FEF, Brodmann area (BA)6), the supplementary eye field (SEF) and parietal regions (intraparietal sulcus, IPS), gave a greater response when the task became more difficult, thereby requiring more attentional resources for correct performance (Fig. 3; Supplementary Information).

By contrast, higher-level decision-making areas should show a greater response when decisions are made about suprathreshold images as compared with when decisions are made about perithreshold images of both faces and houses. Several brain regions fulfilled this condition, including a region in the depth of the superior frontal sulcus (BA8/9) within the posterior portion of the DLPFC, the posterior cingulate cortex (BA31) and the superior frontal gyrus (BA9) (Fig. 3). To test the hypothesis that higher-level decision-making areas might use the output from lower-level sensory regions (namely face- and house-selective regions) to form a decision, we first averaged the BOLD signal across voxels in the lower-level face-selective and house-selective regions at each time point. For each participant we thereby derived two time series,

one for the face-selective region and another for the house-selective region (Face(*t*) and House(*t*)). We then computed the absolute difference between these two time series and determined which brain regions covaried with the resulting difference time course ($|Face(t) - House(t)|$). Finally, within these regions we searched for voxels that also showed a greater response during decisions about suprathreshold images relative to decisions about perithreshold images. The only region fulfilling both of the conditions was located in the depth of the left superior frontal sulcus in the posterior portion of the DLPFC (BA8/9, Fig. 4). This region is located just posterior to BA9/46 in the mid-DLPFC and just anterior to the FEF (Fig. 3). Task-related signal changes in the posterior portion of the DLPFC showed a positive correlation with task performance (Fig. 4b).

These results provide strong evidence that perceptual decisions are made by integrating evidence from sensory processing areas.

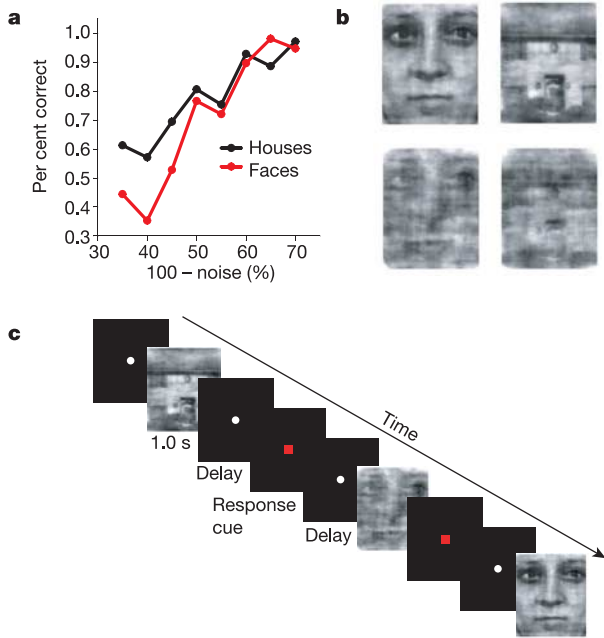


Figure 1 Experimental task. Subjects decided whether an image presented on a screen was a face or a house. By adding noise, the amount of sensory evidence in the stimuli was varied parametrically. **a**, Results of behavioural study to assess the amount of noise to add to the images. Thresholds (82% correct) were about 45% noise for both faces and houses. **b**, In the fMRI experiment, we used images of faces and houses that were either easy (95% correct, suprathreshold, **b** top) or difficult (82% correct, perithreshold, **b** bottom). **c**, Rapid event-related fMRI design. Stimuli were presented for 1 s, subjects responded with a button press after a forced delay (response cue shown for 300 ms, delay 1–5 s).

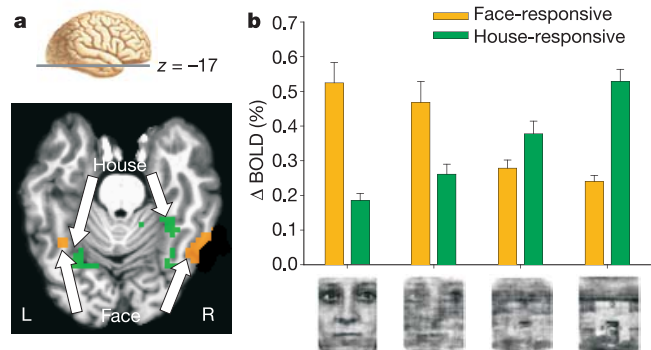


Figure 2 fMRI data illustrating representation of sensory evidence in maximally face- and house-responsive voxels. **a**, Maximally face- (Face, orange) and house-responsive (House, green) voxels in one subject. **b**, BOLD change corresponds to perceptual evidence for respective classes of stimuli. Mean responses ($n = 12$, error bars represent standard error of the mean) in face- and house-selective voxels to the four different conditions (from left to right: suprathreshold face (~10% noise), perithreshold face (~45%), perithreshold house (~53%), suprathreshold house (~10%). For the respective preferred category, both face- and house-selective regions responded more to suprathreshold than to perithreshold images (face-selective: $P < 0.041$, paired *t*-test one-tailed; house-selective: $P < 0.001$) while the opposite was true for the non-preferred category (face-selective: $P < 0.013$; house-selective: $P < 0.002$). For face-responsive: suprathreshold face > perithreshold face > perithreshold house > suprathreshold house (analysis of variance, linear contrast, $P < 0.001$); for house-responsive: opposite pattern ($P < 0.001$).

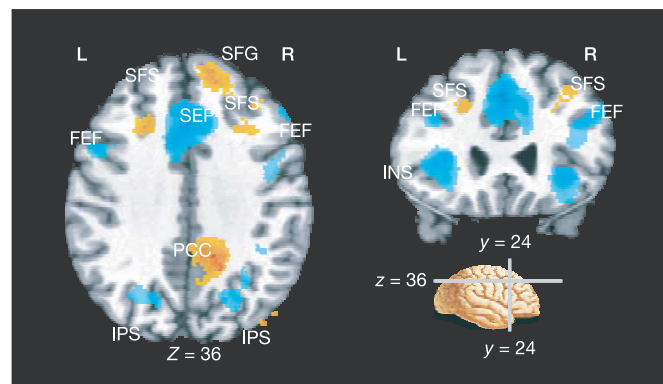


Figure 3 Brain regions showing a main effect of task difficulty: orange: easier (low noise proportion) > harder (high noise proportion); blue: harder > easier. FEF, frontal eye field; INS, insula; IPS, intraparietal sulcus; PCC, posterior cingulate cortex; SEF, supplementary eye field; SFG, superior frontal gyrus; SFS, superior frontal sulcus.

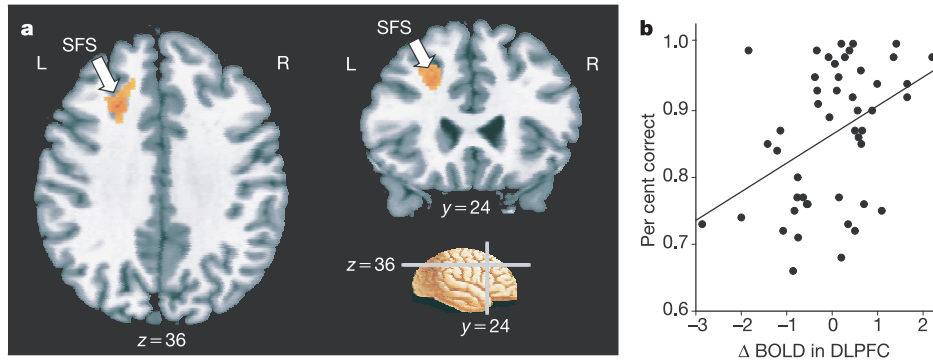


Figure 4 Perceptual decision-making in posterior DLPFC. **a**, Region in the depth of the left SFS, showing both a higher response to suprathreshold images of faces and houses relative to perithreshold images, and a correlation with $|Face(t) - House(t)|$, suggesting that this brain region integrates sensory evidence from sensory processing areas to make a perceptual decision (BA8/9, easier > harder: $x = -24/y = 24/z = 36$, $z_{max} = 4.20$; correlation with $|Face(t) - House(t)|$: $x = -22/y = 26/z = 36$,

$z_{max} = 3.66$, coordinates in MNI system refer to local cluster maxima, and z_{max} to the corresponding z-value). **b**, Signal changes in the posterior portion of the DLPFC predicted task performance ($r = 0.413$, $P = 0.004$). Points represent average BOLD change and performance for each condition (suprathreshold face, perithreshold face, perithreshold house and suprathreshold house) and subject.

Furthermore, our data suggest that in the human brain such a computation might be performed in the left posterior DLPFC. This region fulfilled the two conditions implicit in the Shadlen model of perceptual decision-making^{1,2}. First, the region showed greater activity during those trials in which more sensory evidence for one of the alternative categories was available (suprathreshold versus perithreshold stimuli), and second, the activity in this region was correlated with the absolute difference between the signals of face- and house-selective regions. Finally, signal changes in this region predicted task performance.

Our results using fMRI in humans parallel those using single-unit recordings in monkeys. Recording from a similar region in the posterior DLPFC in monkeys performing a motion discrimination task, Kim and Shadlen² found that neural activity increased proportionally to the strength of the motion signal in the stimulus. Similarly, in our study, the fMRI response was greater when easier decisions were made than when more difficult ones were made. In both monkeys and humans, the outputs of visual processing areas provide the sensory evidence for a decision. In the motion discrimination task, the activity of neurons in cortical area MT, selectively tuned to opposite directions of motion, represent the sensory evidence⁵. Similarly, in our task, the neurons in the ventral temporal cortex tuned to faces and houses, respectively, represent the sensory evidence. Recently, it has been shown in electrical stimulation experiments that the sensory evidence for competing motion directions is compared during the formation of a decision⁴. Similarly, we were able to demonstrate that the sensory evidence for competing categories in maximally face- and house-responsive voxels, respectively, is compared during a decision.

As noted, brain regions in an attentional network played a part in task performance (such as bringing to bear attentional resources), but they did not show the pattern of responses predicted by the model derived from single-unit monkey data. Additionally, control analyses (see Supplementary Information) confirmed that the correlation between BOLD activity in the DLPFC and the difference signal could not be explained either by changes in face- and house-responsive regions alone or by task difficulty, indicating that we have succeeded in localizing the subtraction operation to the left posterior DLPFC.

There is evidence that the involvement of the DLPFC in decision-making processes is not specific to our task but that it generalizes across different tasks. For example, the same area in the left posterior DLPFC that we observed in our study was activated in a positron-emission tomography (PET) study when subjects per-

formed a visual conditional task, such as ‘if you see a red cue, point to the pattern with stripes, but if you see a blue cue point to the pattern with red circles’²¹ (see also ref. 22). Moreover, we found that when subjects performed the same direction-of-motion discrimination task that was used in the single-unit recording studies, the identical left posterior DLPFC showed a greater fMRI response to stronger motion signals, whether the subjects responded with a button press or an eye movement³¹. These studies thus indicate that this prefrontal region has general decision-making functions, independent of stimulus and response modalities. Our results are also consistent with reports that lesions in the posterior DLPFC impair conditional discrimination tasks in both monkeys and humans^{21,23}. Others have suggested that the main function of the prefrontal cortex is to guide activity along task-relevant pathways from lower-level sensory regions to areas that plan and execute responses²⁴. Here, we have demonstrated a mechanism for how perceptual decision-making processes might be instantiated in the human brain, using a relatively simple subtraction mechanism. What remains to be shown is how this model can account for additional variables that affect the decision-making process, such as the expected value of different options²⁵, the prior probability of the appearance of different options²⁶ and their internal valuation²⁷. Ideally, this model and the mechanisms described here will also help to explain the much more complicated decisions we confront in everyday life. □

Methods

Subjects

Twelve healthy volunteers participated in the imaging experiment (6 females, mean age 31.1) and 12 healthy volunteers in the behavioural experiment (7 females, mean age 26.8). All were right-handed, had normal or corrected vision, no past neurological or psychiatric history and no structural brain abnormality. Informed consent was obtained according to procedures approved by the NIMH-IRP Internal Review Board.

Visual stimuli

A set of 38 images of faces (face database, MPI for Biological Cybernetics, Germany) and houses were used. Fast fourier transforms (FFT) of these images were computed, producing 38 magnitude and 38 phase matrices. The average magnitude matrix of this set was stored, then stimulus images were produced by calculating the inverse FFT (IFFT) of the average magnitude matrix and individual phase matrices. The phase matrix used for the IFFT was a linear combination of the original phase matrix computed during the forward fourier transform and a random noise matrix. The resulting images all had an identical frequency power spectrum²⁸ (corresponding to the average magnitude matrix) with graded amounts of noise.

Task

Images of faces and houses with low (per cent correct above 95%) and high (corresponding to the 82%-threshold) proportions of noise, respectively (see Fig. 1b) were

presented using the Psychophysics Toolbox (www.psychtoolbox.org) under Matlab (Mathworks). Stimuli were projected for 1 s onto a back-projection screen using an LCD projector (Sharp). Subjects decided whether an image was a face or a house and responded with a button press after a forced delay, which was included to make the task as analogous to the studies in monkeys as possible (those experiments typically include a forced delay¹) (compare Fig. 1c). The sequence of events was optimized using rsfgen (AFNI, <http://afni.nimh.nih.gov>).

Data acquisition and analysis

Whole-brain MRI data were collected on a 3T GE Signa (GE Medical Systems). Echoplanar data were acquired using standard parameters (Field of view, 200 mm; matrix, 64 × 64; 25 axial slices, 5 mm thick; in-plane resolution, 3.125 mm; repetition time, TR, 2.0 s; error time, TE, 30 ms; flip angle, 90°). Five to eight runs of 162 volumes each were acquired. The first four volumes were discarded to allow for magnetization equilibration. To minimize head motion, we used both a bite bar and a vacuum head pad. AT1 weighted volume (MP-RAGE) was acquired for anatomical comparison.

MRI data were analysed using a mixed effects approach within the framework of the general linear model (GLM as implemented in FSL 5.0, <http://www.fmrib.ox.ac.uk/fsl>). Pre-processing was applied: slice-time correction, motion correction, non-brain removal, spatial smoothing using a kernel of 8 mm full-width at half-maximum, mean-based intensity normalization of all volumes by the same factor; highpass temporal filtering (gaussian-weighted least-squares straight line fitting, with $\sigma = 50.0$ s). Time-series statistical analysis was carried out using FSL with local autocorrelation correction²⁹. Trials in which subjects gave no response or an incorrect response were pooled together and modelled as a regressor of no interest (error trials). Hence, similar to the studies in monkeys, only correct trials were used to model regressors for the four conditions (suprathreshold face, perithreshold face, perithreshold house and suprathreshold house). The average number of trials was 215.5 ± 29.7 (mean \pm s.d.) for suprathreshold face, 190.17 ± 31.6 for perithreshold face, 194.7 ± 30.8 for perithreshold house and 202.8 ± 26.8 for suprathreshold house, respectively. Time series were modelled using event-related regressors for each of the four conditions as well as error trials, and convolved with the haemodynamic response function (gamma variate). Contrast images for each condition and the contrasts of interest for each subject were computed and transformed, after spatial normalization, into standard (MNI152) space. Group effects were computed using the transformed contrast images in a mixed effects model treating subjects as random. The resulting Z statistic images were thresholded at $Z > 3.1$, corresponding to $P < 0.001$, uncorrected. For display purposes, statistic images are shown with $Z > 2.6$, corresponding to $P < 0.005$. In each subject we determined voxels in the temporal cortex that were more responsive to faces than to houses, and vice versa. The region analysed included the lingual, parahippocampal, fusiform and inferior temporal gyri 70 to 20 mm posterior to the anterior commissure in Talairach brain atlas coordinates (see ref. 30). To test in which voxels the BOLD signal significantly covaried with $|\text{Face}(t) - \text{House}(t)|$, we set up an additional model using the following three regressors: (1) the difference between the regressors for the suprathreshold and the perithreshold conditions used in the GLM analysis described above ($(\text{suprathreshold face} + \text{suprathreshold house}) - (\text{perithreshold face} + \text{perithreshold house})$); (2) the absolute difference between the time series in face- and house-responsive voxels in each subject ($|\text{Face}(t) - \text{House}(t)|$); and (3) the product of the first and second regressors, representing the interaction between $(|\text{Face}(t) - \text{House}(t)|)$ (physiological signal) and task-related parameters (psychological factor, hence psychophysiological interaction). Contrast images and group effects were computed as described above. We did not find any voxels in which changes in activity significantly covaried with the psychophysiological interaction term.

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Coupled oscillators control morning and evening locomotor behaviour of *Drosophila*

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Daily rhythms of physiology and behaviour are precisely timed by an endogenous circadian clock^{1,2}. These include separate bouts of morning and evening activity, characteristic of *Drosophila melanogaster* and many other taxa, including mammals^{3–5}. Whereas multiple oscillators have long been proposed to orchestrate such complex behavioural programmes⁶, their nature and interplay have remained elusive. By using cell-specific ablation, we show that the timing of morning and evening activity in