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Analysis of the Neuronal Selectivity Underlying Low fMRI Signals

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Summary

Background: A prevailing assumption in neuroimaging studies is that relatively low fMRI signals are due to weak neuronal activation, and, therefore, they are commonly ignored. However, lower fMRI signals may also result from intense activation by highly selective, albeit small, subsets of neurons in the imaged voxel. We report on an approach that could form a basis for resolving this ambiguity imposed by the low (mm range) spatial resolution of fMRI. Our approach employs fMR-adaptation as an indicator for highly active neuronal populations even when the measured fMRI signal is low.

Results: In this study, we first showed that fMRI-adaptation is diminished when overall neuronal activity is lowered substantially by reducing image contrast. We then applied the same adaptation paradigm, but this time we lowered the fMRI signal by changing object shape. While the overall fMRI signal in category-related regions such as the face-related pFs was drastically reduced for non-face stimuli, the adaptation level obtained for these stimuli remained high. We hypothesize that the relatively greater adaptation level following exposure to "nonoptimal" object shapes is indicative of small subsets of neurons responding vigorously to these "nonoptimal" objects even when the overall fMRI activity is low.

Conclusions: Our results show that fMR-adaptation can be used to differentiate between neuronal activation patterns that appear similar in the overall fMRI signal. The results suggest that it may be possible to employ fMR-adaptation to reveal functionally heterogeneous islands of activity, which are too small to image using conventional imaging methods.

Introduction

An implicit and widely held assumption in functional magnetic resonance imaging (fMRI) research is that the strong magnetic resonance (MR) signals within a cortical area reflect the functional specialization of this region, so that weak activation is treated as "suboptimal" and is considered to be functionally irrelevant. However, a weak fMRI signal may not be a simple reflection of global, suboptimal, neuronal activation, but it may also result from a variety of heterogeneous neuronal activity patterns. An extreme example of such a case is a small set of intensely active neurons whose signal is averaged out by the vast majority of nonresponsive neurons within which they are embedded. An illustration of such a situation is depicted in Figure 1. As illustrated on the left, weak activation to a certain set of images (houses and words in this example) can reflect the activity of a uniform population of face-selective neurons, which are suboptimally activated by these object categories. However, as illustrated on the right, the same weak fMRI activation could reflect the presence of a few intensely active groups of neurons, which are not sensitive to faces at all but rather are preferentially activated by other object categories (e.g., houses or words). These neurons are embedded among a large number of face-selective neurons, and due to their relative low density, their activity is not sufficient to produce a strong fMRI signal in the measured voxel. Note that conventional MR imaging cannot differentiate between these two extreme alternatives. Here, we propose to use the fMR-adaptation phenomenon, in which repeated presentation of a stimulus leads to significant reduction in the fMRI signal, to differentiate between activity patterns that appear to be similar in conventional fMRI imaging (for a review, see [1]).

What are the factors that control the adaptation process? Previous studies have demonstrated that the level of adaptation was dependent on the similarity between the repeated stimuli and in fact could be used to probe the level of invariance and generalization of neuronal populations in the visual cortex [2, 3]. However, another parameter that was not considered so far in human fMRI studies is the activation level of the neuronal population; that is, it could be that the level of adaptation correlates to the level of activation produced by the adapting stimulus prior to the adaptation process. This issue is of crucial importance because if indeed the fMR-adaptation level is linked to neuronal activation, then the level of adaptation could be used as a measure for the level of activity of cortical neurons, thus bypassing the spatial resolution limits of the fMRI method.

We chose to study the relationship between the neuronal activation and adaptation level by creating suboptimal neuronal activation through drastic reduction of image contrast. Single-unit studies clearly indicate that lowering image contrast reduces neuronal activation and that this effect is not specific to a particular group

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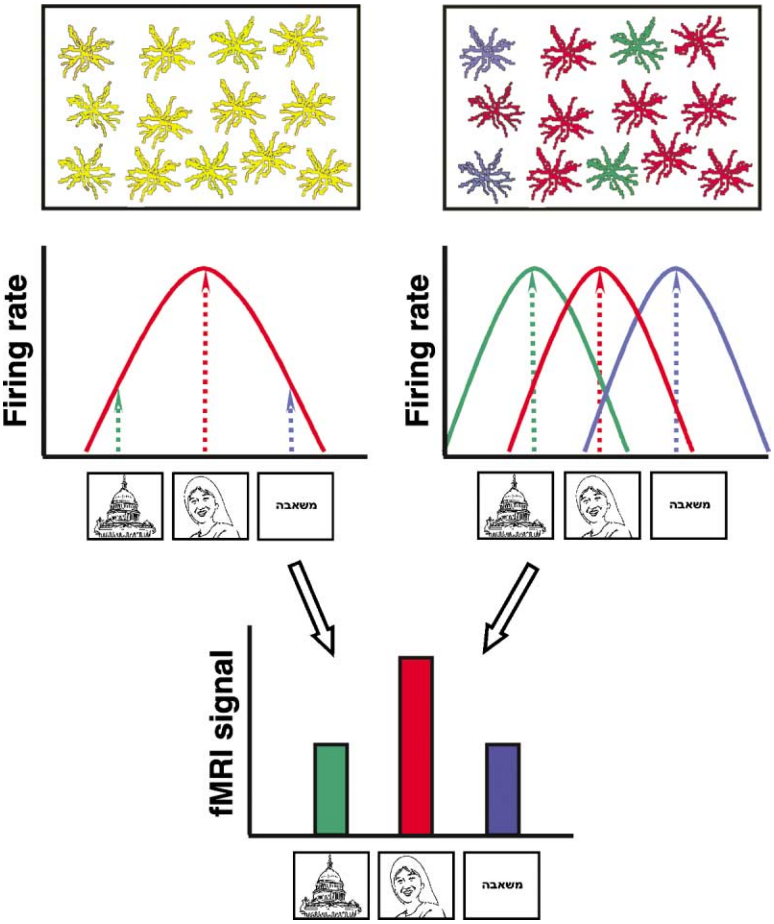

Figure 1. Alternative Neuronal Organizations within a Face-Selective Voxel

Such a voxel may contain a homogenous population of neurons (left) optimally activated by faces and suboptimally activated by non-face stimuli. Alternatively (right), it may contain a heterogeneous mixture of neurons with small subsets of neurons ("hot spots") optimally tuned to non-face object categories. Both alternatives would produce an identical fMRI signal in a conventional experimental design.

of neurons [4, 5]. We have shown previously [6] that drastic contrast reduction leads to weak fMRI signals in both early and high-order visual areas. Here, we show that, in high-order, object-related areas, adaptation was significantly reduced when fMRI activation was reduced by lowering image contrast, thus demonstrating that adaptation was indeed correlated to the level of neuronal activation.

We then applied this method as an analysis tool to reveal that object shape changes produce markedly different neuronal activation patterns in category-specific cortex (e.g., face- and house-selective regions) compared to contrast changes, although their conventional fMRI signals are comparable. Similar to contrast reduction, shape changes in category-specific cortex lead to a drastically reduced signal for the nonselective stimuli (e.g., houses and words in the fusiform face area [FFA]). Crucially, unlike contrast changes, repetition of the same "nonoptimal" stimulus manifested a robust adaptation effect. Thus, adaptation effects can expose differential effects of contrast and shape changes. Such differences were pointed previously in single unit studies of mid-level visual areas [7]. We hypothesize that these high adaptation levels are due to the presence of small neuronal populations, which are strongly activated by the nonoptimal object stimuli.

Results

Dependency of Adaptation on Neuronal Activation

To explore the dependency of adaptation on neuronal activation, we conducted the experiment shown in Figure 2A. In this experiment, fMRI activation was measured for face images (see the Experimental Procedures, Experiment 1) and for non-face images (cars, Experiment 2; not shown) at different contrast levels. In both experiments, we measured the adaptation level by comparing the fMRI activation to "identical" versus "different" image presentations.

As reported previously using similar images [2], adaptation for high-contrast images was particularly evident at high-order object areas: a lateral-occipital focus (LO), which is situated ventrally and posteriorly to area MT and extends into the posterior inferotemporal sulcus, and a focus in the vicinity of the posterior fusiform gyrus (pFs), which is anterior and lateral to area V4/V8 and extends into the inferior temporal sulcus (see Table 1 for Talairach coordinates). The latter focus (pFs) may overlap the fusiform face area described previously [8]. Another focus that exhibited substantial adaptation was situated within the anterior portion of the collateral sulcus (CoS), and this focus may overlap the parahippocampal place area (PPA) reported previously [9] (see

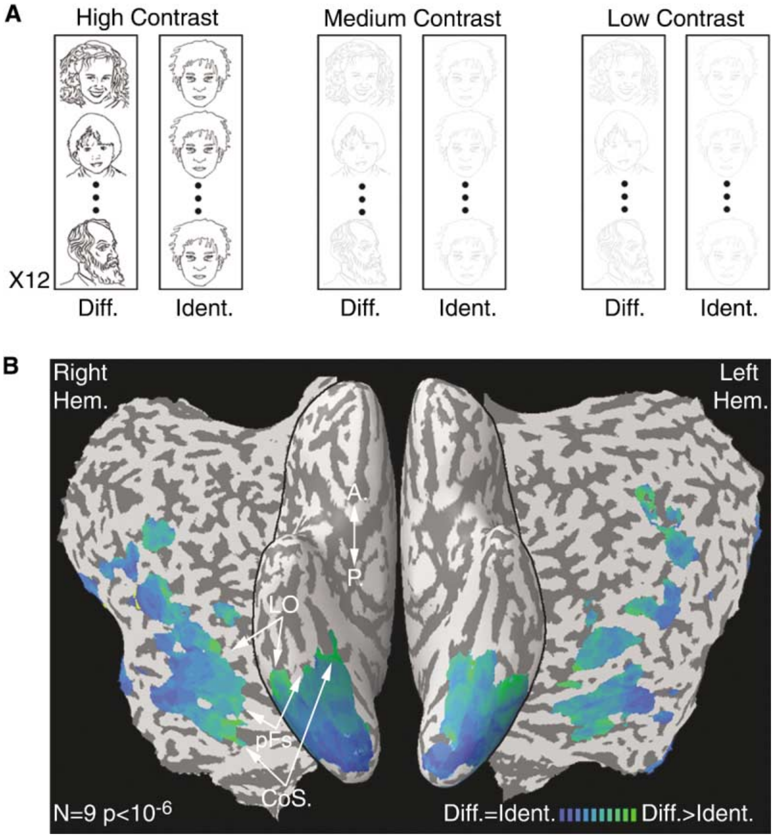

Figure 2. Experimental Design and Activation Maps of Experiments 1 and 2

(A) Experimental design: stimuli were presented in epochs containing either 12 different ("Diff.") or identical ("Ident.") images. Each stimulus was presented in three different contrast levels (low, medium, and high). Stimuli were either faces (Experiment 1) or cars (Experiment 2, not shown).

(B) Mapping the adaptation effect: an averaged activation map for the high-contrast car images (nine subjects, GLM statistics) presented on inflated (ventral views) and unfolded hemispheres. Green indicates highly adapted regions. Note the gradual increase of the adaptation level from early (posterior) visual areas to more anterior areas. Note also that the adaptation effect to high-contrast car images is distributed to essentially all object-related regions: LO, pFs, and CoS regions. Abbreviations: Diff., different; Ident., identical; LO, lateral occipital; pFs, posterior fusiform; CoS., collateral sulcus; A., anterior; P., posterior. The statistical criterion for the highlighted voxels was $p < 10^{-6}$ uncorrected.

Table 1 for Talairach coordinates). This is demonstrated in Figure 2B, which shows a functional map of the adaptation effect for high-contrast car images averaged across nine subjects.

Figure 3 shows the activation profiles in these anatomical regions. Note that, at low contrast, the averaged fMRI signal was reduced by a factor of 3 and the adaptation was concurrently reduced (Figure 3A: different faces, LO: high contrast: 1.28 ± 0.17% signal change, low contrast: 0.43 ± 0.12; pFs: 1.46 ± 0.24 versus 0.54 ± 0.14). The reduction of adaptation at low contrast was highly significant and did not depend on the object category used (faces or cars). (Three-way ANOVA: significant main effect of stimulus repetition: LO: $F = 37.8$, $p < 10^{-4}$; pFs: $F = 20.5$, $p < 10^{-4}$ and of stimulus contrast: LO: $F = 25.9$, $p < 10^{-4}$; pFs: $F = 20.2$, $p<10^{-4}$, and significant interaction of these effects: LO: $F = 13.1$, $p < 10^{-4}$; pFs: $F = 6.8$, $p < 0.002$. No significant effect of stimulus type, i.e., faces/cars: LO: $F = 0.6$, $p < 0.45$; pFs: $F = 0.9$, $p < 0.34$).

Similar results were obtained in the collateral sulcus for the car images used in Experiment 2 (Figure 2B: car images, two-way ANOVA: significant main effect of stimulus repetition: $F = 45.5$, $p < 10^{-8}$ and of stimulus contrast: $F = 45.5$, $p < 10^{-8}$, and significant interaction of these effects: $F = 19.4$, $p < 10^{-7}$).

This link between adaptation and fMRI activation suggests that the level of adaptation can now be used as an indirect measure of neuronal activity levels within the measured voxels.

Table 1. Talairach Coordinates

	Left			Right		
	X	Y	Z	X	Y	Z
Face Contrast Adaptation Experiment (Experiment 1)						
LO	−42 ± 5	−69 ± 8	−6 ± 5	42 ± 4	−60 ± 6	−7 ± 5
pFs	−36 ± 4	−48 ± 10	−19 ± 3	36 ± 5	−45 ± 10	−17 ± 5
Car Contrast Adaptation Experiment (Experiment 2)						
LO	−44 ± 2	−66 ± 4	−8 ± 5	43 ± 5	−63 ± 5	4 ± 5
pFs	−34 ± 4	−53 ± 11	−19 ± 4	35 ± 2	−51 ± 3	−17 ± 2
CoS	−27 ± 3	−44 ± 6	−10 ± 4	24 ± 3	−39 ± 7	−11 ± 2

Talairach coordinates [27] for LO and pFs, derived from all subjects in Experiments 1 and 2, and for the collateral sulcus (CoS), obtained from all subjects in Experiment 2. Values represent the mean ± SD in mm.

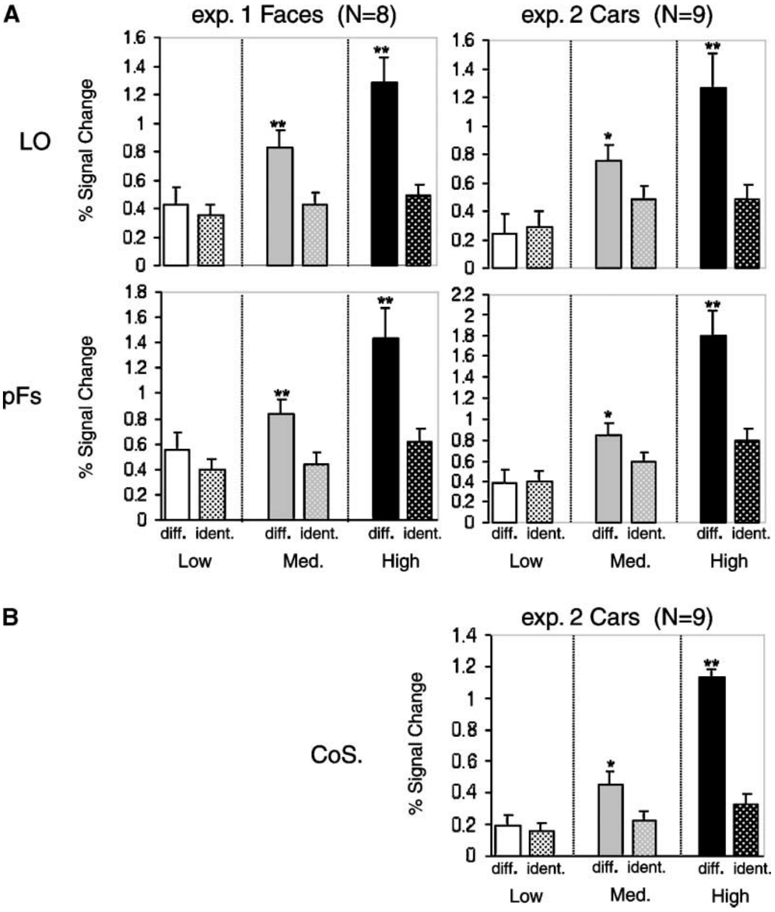

Figure 3. Activation Profiles from Experiments 1 and 2

(A) Activation profiles of areas LO (top) and pFs (bottom) obtained for the face stimuli (Experiment 1, left) and for the car stimuli (Experiment 2, right). White, gray, and black bars indicate low-, medium-, and high-contrast levels, respectively. Filled and dotted bars indicate different and identical conditions, respectively. Note the clear reduction in adaptation effect for both face and car stimuli as image contrast was reduced. Asterisks denote the significance level as calculated between "diff." and "ident." presentation of each condition (paired t test, an asterisk indicates $p < 0.05$, and a double asterisk indicates $p < 0.005$). The error bars indicate ± standard error of the mean (SEM). Abbreviations are as in Figure 2B.

(B) Activation profile of the collateral sulcus (CoS) for the car stimuli (Experiment 2), showing a similar trend of results. Same conventions as in Figure 3A.

Category-Adaptation Experiment: The Issue of Cortical Modularity

Having found that adaptation level could provide an indirect indication of the level of neuronal activation, we could now apply this method to study the activity patterns in ventral-stream, high-order areas. A fundamental issue, which appears particularly amenable for analysis using this approach, is the modular nature of high-order object representations, i.e., to what extent cortical regions are purely specialized for a single category of object images. Perhaps the best-studied example of such specialization is the fusiform face area [8, 10, 11] and the parahippocampal place area [9, 12]. The first was described as a cortical module specialized in processing faces, and the latter was associated with processing houses and scene images. The main feature of the FFA, which led to its characterization as an independent module, was the low level of its activation by non-face objects. The same characteristic was found for the PPA but for non-house or place stimuli. Is this weak activation a result of suboptimal neuronal activation throughout the FFA and PPA, similar to that produced by low-contrast images? Or is it the result of strong neuronal activation produced by a small set of highly selective neurons within those regions? To answer this question, we performed the category-adaptation experiment (Experiment 3), following the same experimental design as in the contrast-adaptation experiments but using three different object categories (faces, houses, and words). Figure 4A shows the activation level in face-selective voxels both in LO and in the pFs (corresponding to the FFA) for faces and the non-face images of houses and words. Note that, while the overall activation was drastically reduced for the non-face stimuli, the adaptation level remained robust and did not differ significantly for all stimulus types in both LO and pFs (two-way ANOVA: significant main effect of stimulus repetition: LO: $F = 4.5$, $p < 10^{-2}$; pFs: $F = 8.2$, $p < 10^{-3}$ and of stimulus type: LO: $F = 33.1$, $p < 10^{-6}$; pFs: $F = 21.8$, $p < 10^{-5}$, but no significant interaction between these factors: LO: $F = 0.7$, $p < 0.5$; pFs: $F = 0.4$, $p < 0.7$ and between hemispheres and stimulus repetition as calculated by a three-way ANOVA: pFs: $F = 1.5$, $p < 0.2$). Similar results were obtained in the collateral sulcus (corresponding to the PPA, Figure 4B), which was associated previously with specific house-related or place-related activity [9, 12]. This region was strongly activated by the house images, and its activity was drastically reduced for the face and word images. (Two-way ANOVA: significant main effect of stimulus repetition: $F = 8.0$, $p < 10^{-3}$ and of stimulus type: $F = 20.0$, $p < 10^{-4}$, but no significant interaction between these factors: $F = 0.6$, $p < 0.6$).

The similar level of adaptation for "optimal" and non-optimal stimuli in these regions exhibits a marked discrepancy from contrast-related effects. Furthermore, it

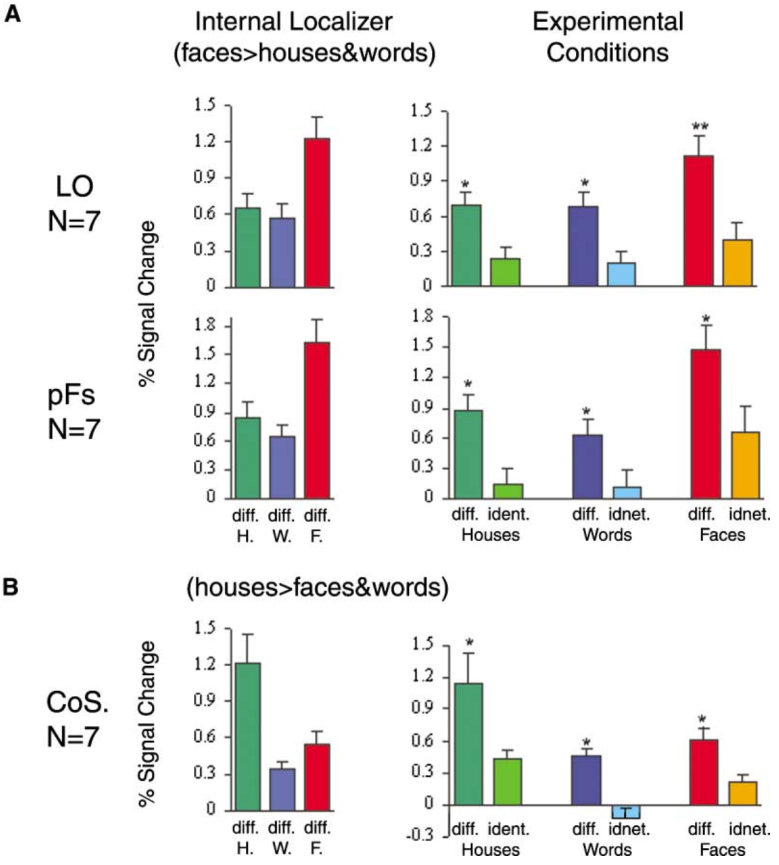

Figure 4. Category Adaptation

(A) Activation profiles in face-related areas during the category-adaptation experiment: LO (top), pFs (bottom). Internal localizer data (see the Experimental Procedures) is shown in the left graphs, and the measured activation is shown in the right graphs. Note the significant adaptation effect evident for all stimulus categories, although the overall signal was clearly face-selective in these regions. Dark and light colors indicate different and identical conditions, respectively. Green, blue, and red indicate house, word, and face stimuli, respectively. Asterisks denote the significance level as in Figure 3, but it is calculated for each stimulus category. Error bars indicate ± SEM. Abbreviations are as in Figure 2; H., houses; W., words; F., faces.

(B) Activation profiles in the house-related area (CoS); again, note the significant adaptation for all stimulus categories despite the drastic reduction in activation for the face and word images. Conventions are as in Figure 4A.

strongly suggests that, despite the weak overall signals, there was robust functional activation by the nonoptimal stimuli in all these regions.

Direct Comparison between Contrast and Category Adaptation

In the two sets of experiments described above (Experiments 1 and 2 and Experiment 3), the fMRI-activation level was manipulated in two different ways: image contrast changes in one case, and shape changes in the other. While adaptation was reduced when lowering the image contrast, it remained robust for both optimal and nonoptimal object categories despite the drastic reduction in the overall activation level for the nonoptimal categories. However, it could be argued that the lack of adaptation in the low-contrast conditions in the contrast-adaptation experiments is a result of a floor effect, i.e., a nonlinear effect that precluded the fMRI signal from being reduced further below the low-contrast nonadapted state. Furthermore, the results were obtained in two separate experiments, thus enabling only indirect comparisons.

In order to address these issues, we conducted another experiment, which combined the critical conditions from both the contrast-adaptation and the category-adaptation experiments. In this experiment, we measured the adaptation level in face-related regions for two stimulus types: face images presented in medium-contrast level (optimal category presented in a suboptimal fashion), and house images presented in high-contrast level (nonoptimal category presented in an optimal fashion). Face-related regions were independently localized by including localizer conditions (high-contrast faces and houses).

Behavioral data were collected during the experiment. Since adaptation levels may depend on the perceived similarity between presented images, we quantified the ability of subjects to discriminate between the different images during the different conditions. To that end, we calculated a response alteration measure for each subject (see the Experimental Procedures). Statistical analysis revealed that the response alteration measure differed significantly between the different and identical image presentations (stimulus repetition effect). Importantly, this measure was not significantly different for the two contrast levels that were used in the experiment (i.e., high-contrast houses compared to medium-contrast faces). Furthermore, no significant interaction was found between these factors. (Two-way ANOVA: a significant main effect of stimulus repetition: $F = 116$, $p < 10^{-9}$, but not of stimulus contrast: $F = 0.3$, $p < 0.6$, and no significant interaction between these factors: $F = 10^{-4}$, $p < 1.0$). Thus, any differences between the high-contrast houses and the medium-contrast faces in terms of the adaptation level could not be ascribed to the subjects' inability to discriminate between the different stimuli in these two conditions.

Figure 5A shows the activation profile obtained in face-related voxels defined by the independent localizer (faces > houses) in LO and the pFs for the medium-

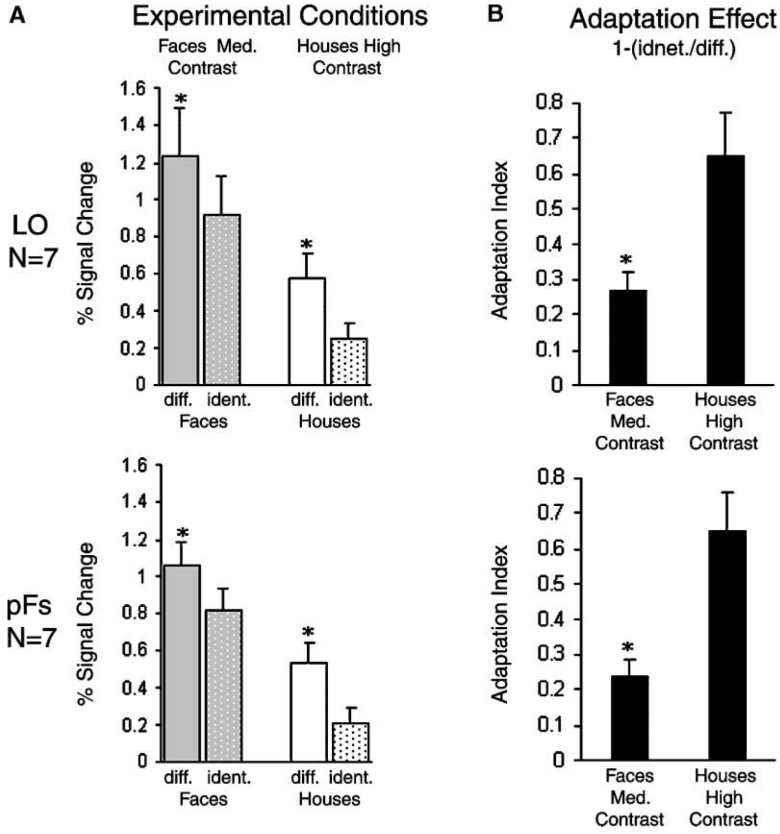

Figure 5. Direct Comparison of Contrast and Category Adaptation

(A) Activation profiles of face-related regions in LO (top) and pFs (bottom) obtained for the medium-contrast face stimuli and for the high-contrast house stimuli used in Experiment 4. Gray and white bars indicate activation to faces and houses, respectively. Filled and dotted bars indicate activation to different and identical conditions, respectively. Note that, while significant adaptation was obtained for both stimulus categories, the adaptation level was stronger for the house stimuli than for the face stimuli. This occurred despite the higher signal for the face compared to the house stimuli. Asterisks denote the significance level as calculated between "diff." and "ident." presentation of each condition (paired t test, an asterisk indicates $p < 0.01$). The error bars indicate ± SEM.

(B) The graphs show the adaptation index for the medium-contrast faces and the high-contrast houses obtained in LO and pFs. An index of zero indicates no adaptation, while larger values indicate stronger adaptation. Note that the adaptation index for the house stimuli was significantly larger (stronger adaptation) than the adaptation index obtained for the medium-contrast face stimuli, further stressing that the overall level of fMRI activation was not the limiting factor in determining the level of adaptation. Asterisks denote the significance level as calculated between the adaptation index for houses and faces (paired t test, a double asterisk indicates $p < 0.01$). The error bars indicate ± SEM.

contrast faces and the high-contrast houses. The adaptation index (Figure 5B) for the medium-contrast faces was significantly weaker (paired t test, $p < 0.01$) than the adaptation index for the high-contrast houses despite the fact that the fMRI-signal level for the face stimuli was actually higher. This trend is in agreement with the results of the previous experiments.

These results demonstrate that strong adaptation can be obtained in face-related regions (LO, pFs) for nonoptimal images yielding a low fMRI signal (high-contrast houses), while much weaker adaptation is obtained for stimuli eliciting a stronger fMRI signal due to contrast reduction. This indicates that the level of adaptation is not a consequence of the level of the overall fMRI signal, but rather is determined by the underlying neuronal activity.

Discussion

Problems Inherent in the Spatial Resolution of fMRI

While substantial attention is given to the relatively low temporal resolution of the BOLD signal [13–15], major difficulties are also inherent in the limited spatial resolution of fMRI and indeed in any functional neuroimaging method that records the averaged activity of neuronal populations. We have previously discussed this difficulty with respect to the assessment of the invariant properties of cortical neurons (for a review, see [1]). Here, we address the issue of putative small populations of functionally distinct neurons, which are at a subvoxel resolution. Our results show that, although the existence of such populations can not be revealed by direct measurement of the BOLD signal, it may be possible to use adaptation effects to highlight their existence.

Relationship between Adaptation and Cortical Activity

Our suggestion that the existence of fMRI-adaptation can be taken as a measure of high neuronal activity level is based on the results of the contrast-adaptation experiments (Experiments 1 and 2), which showed that the adaptation level was significantly correlated to the activation level. Thus, substantial reduction in fMRI activation practically abolished the adaptation (low-contrast condition, Figure 2). We attribute this reduced adaptation to an overall reduction in the neuronal activation.

Of the single neuron studies of adaptation in the inferior-temporal (IT) cortex, the only report that is somewhat relevant is that of Li et al. [16], which indeed found an association between optimal activation and familiarity effects in a small subset of IT neurons. However, the adaptation procedure was substantially different than the one used here, so it is difficult to make direct comparisons.

The Issue of Cortical Modularity

An influential concept of cortical organization, delineated most forcefully by Fodor [17], has been the existence of highly specialized and relatively isolated cortical modules for specific cognitive tasks. As mentioned above, the most documented example of such a putative module has been the fusiform face area [8, 10, 11, 18], but other areas of cortical specialization have been suggested as well [9, 12]. However, it is not clear to what extent these regions are purely specialized for one stimulus category and to what extent other object representations may coexist within them. The fact that we observed similar adaptation levels to optimal and nonoptimal stimuli illustrates that the strength of fMRI signals might not reveal the full functional profile of these regions. The most straightforward interpretation of our results is that, within the category-selective object areas, there are functionally distinct "hot spots" of neuronal activation that are strongly activated by the nonoptimal stimuli.

Thus, our results point to the possibility that, although a clear functional specialization within ventral stream areas does exist [8], it is not absolute, and representations of various object categories coexist within these regions. Such mixing might occur on a columnar level, so that shape-selective columns [19] of various object categories interdigitate within the same cortical region. The source of such a heterogeneous mosaic is not clear, but it might be related to complex acuity demands [20, 21], differential expertise effects [22], or distributed object representation [23, 24].

However, lacking direct evidence for such hot spots, it should be emphasized that alternative, albeit more complex, schemes might account for the present results. For example, it could be the case that the low fMRI activation to house images found in the face-related FFA is due to a uniformly distributed, weak input from the neighboring, house-related PPA. If this is the case, then the adaptation found for house images in the FFA is a reflection of the neuronal adaptation that occurs in the PPA and is transmitted to the FFA through lateral cortico-cortical connections. Since we found adaptation effects throughout the object-selective cortex, such a model implies extremely exuberant intracortical connections. However, until more direct studies using techniques such as single-unit recordings or optical imaging of adaptation effects in primate IT are performed, this issue can not be fully resolved.

Conclusions

In conclusion, we propose a method based on fMR-adaptation that allows better differentiation of neuronal activation patterns, which appear ambiguous using conventional fMRI. Using this approach, we demonstrated a qualitative difference in the impact of contrast and shape changes in high-order human object areas. Finally, we hypothesize that our results point to the presence of highly active neuronal islands that are selective for nonoptimal stimuli in category-selective human object areas.

Experimental Procedures

Subjects

Fourteen healthy subjects (eight women, ages 24–50) participated in one or more of the experiments. All subjects had normal or corrected-to-normal vision and provided written informed consent. The Tel Aviv Sourasky Medical Center approved the experimental protocol.

MRI Setup

Subjects were scanned in a 1.5 Signa Horizon LX 8.25 GE scanner equipped with a standard birdcage head coil. Blood oxygenation level-dependent (BOLD) contrast was obtained with gradient echo echo-planar imaging (EPI) sequence (TR $=$ 3000, TE $=$ 55, flip angle $= 90^\circ$, field of view 24×24 cm^2, matrix size 80×80). The scanned volume included 17 nearly axial slices of 4-mm thickness and 1-mm gap. Three subjects who participated in Experiment 1, one subject who participated in Experiment 3, and the seven subjects who participated in Experiment 4 were run with a quadrature surface coil (Nova Medical), which covered the posterior brain regions. T1-weighted, high-resolution ($1 \times 1 \times 1$ mm) anatomical images and 3D spoiled gradient echo sequences were acquired on each subject to allow accurate cortical segmentation, reconstruction, and volume-based statistical analysis.

Visual Stimulation

Stimuli were generated on a PC, were projected via an LCD projector (Epson MP 7200) onto a tangent screen positioned over the subject's forehead, and were viewed through a tilted mirror located above the subjects' eyes.

Experiments

Experiment 1: Face Contrast Adaptation

Experiment 1 (Figure 2A, 8 subjects), lasted 480 s, included 6 different stimulus conditions, and had 51 epochs that were presented in a counterbalanced block design paradigm; stimulus and blank epochs were interleaved. A stimulus epoch consisted of either 12 different stimuli (different condition) or 12 repetitions of the same stimulus (identical condition) all presented in the same contrast level. Stimuli were presented in 4.4%, 6.1%, or 95.6% contrast level (low, medium, and high contrast, respectively, in the following text). Stimuli were $12^\circ \times 12^\circ$ black on white line drawings of faces. The illumination level of the white background was 97 cd/m^2, and that of the black line drawings at 95.6% contrast was 2 cd/m^2, as measured directly from the tangent screen. Stimulus contrast was defined as follows, where L is luminance:

$$\text{Stimulus Contrast} = \frac{\text{Lmax} - \text{Lmin}}{\text{Lmax} + \text{Lmin}}$$

Contrast levels were verified by direct measurement from the tangent screen. The contrast of stimuli was varied by changing the gray level of the line drawing while keeping the background (white) constant. Each experimental condition was repeated 4 times; in addition, there were 26 interleaving blank epochs, and the experiment started with an epoch of pattern stimuli, which was excluded from all the statistical analysis. Each stimulus epoch lasted 12 s, and each blank epoch lasted 6 s, with the exception of the first and last blanks, which lasted 21 s and 15 s, respectively.

Within an epoch, each of the 12 images was presented for 800 ms followed by 200 ms of fixation point on a blank screen. Subjects were instructed to fixate on the fixation point located in the middle of each stimulus and to covertly categorize each stimulus as a man, woman, or child. To enable subjects to differentiate between low-contrast epochs and blank epochs, stimulus epochs had a gray fixation point, while blank epochs had a red fixation point.

Experiment 2: Car Contrast Adaptation

This experiment was identical in its design to Experiment 1, but the stimuli that were used were car images. Nine subjects were run on the experiment. Subjects had to covertly categorize each stimulus as a private car, a bus, or a truck.

Experiment 3: Category Adaptation

This experiment was identical in its design to Experiment 1, but instead of using three different contrast levels, we used three different stimulus categories: faces, houses, and words all presented in a high-contrast level. Eight subjects were run on this experiment, and their task was to covertly name each stimulus.

Experiment 4: Category and Contrast Adaptation

Seven subjects were run in this experiment, which was similar in its design to Experiment 1. The experiment included 4 conditions, which consisted of either 12 different stimuli (different condition) or 12 repetitions of the same stimulus (identical condition). Two conditions included medium-contrast faces, and two conditions included high-contrast houses. In order to independently localize face-related regions, we included two additional localizer conditions of high-contrast faces and houses. Each stimulus condition was repeated four times. Within an epoch, each of the 12 images was presented for 800 ms, followed by 200 ms of a blank screen. Subjects were instructed to fixate on the fixation point located in the middle of each stimulus and to perform a two-alternative forced choice recognition task. Each face had to be categorized as a man or a woman, and each house image had to be categorized as a public or a private facility. Subjects provided their responses via a "Neuroscan Co." response box, and data were collected by in-house software. Due to a technical failure, behavioral data were collected for five out of the seven subjects who participated in the experiment.

Data Analysis

Details of the analysis are provided in [6]. Briefly, fMRI data were analyzed with the BrainVoyager software package (Brain Innovation). The cortical surface was reconstructed and unfolded into the flattened format. Statistical analysis was based on the General Linear Model [25]. Statistical maps (Figure 2) were colored according to the relative contribution of selected predictors [6]. The percent signal change (PSC) for each subject in each experiment was calculated as the percent activation from a blank baseline:

$$\text{Percent Signal} = \frac{\text{signal} - \text{mean[signal (blanks)]}}{\text{mean[signal (blanks)]}} \times 100$$

"Internal Localizer" Test

Details of this analysis are given in [26]. Briefly, we used one set of epochs to define anatomical regions of interest, while another set was used to estimate the PSC, providing an independent measure of activation.

Regions of interest in Experiment 4 were defined using the localizer conditions, applying a statistical test that searched for all face-related voxels (faces $>$ houses) while ignoring all the experimental conditions. The adaptation index was defined as: $1-$ (activation [PSC] in the identical condition/activation in the different condition) for each stimulus type.

Analysis of Behavioral Data from Experiment 4

We calculated a response alteration measure as follows: a binary value ("0" or "1") was assigned to each of the two possible key presses in each epoch; the standard deviation across these values was calculated separately for each epoch and was then averaged across all the repetitions of the same experimental condition for each subject. A two-way ANOVA was then calculated across all subjects in order to evaluate whether the response alteration measure differed significantly across the four experimental conditions.

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