

Current Biology

Recent Visual Experience Shapes Visual Processing in Rats through Stimulus-Specific Adaptation and Response Enhancement

Highlights

- Responses in the rat visual cortex are sensitive to stimulus frequency
- In primary visual cortex, this sensitivity was based on adaptation for regular input
- Latero-intermediate cortex also showed a response enhancement for irregular input
- The response enhancement could not be explained by adaptation

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In Brief

Rats rely on vision for timely detection of aerial predators and need a visual system specialized in change detection. Vinken et al. show an increased sensitivity for irregular stimuli from rat primary to latero-intermediate visual cortex. This effect is supported by a surprise-based response enhancement only observed in the latter.



Recent Visual Experience Shapes Visual Processing in Rats through Stimulus-Specific Adaptation and Response Enhancement

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SUMMARY

From an ecological point of view, it is generally suggested that the main goal of vision in rats and mice is navigation and (aerial) predator evasion [1–3]. The latter requires fast and accurate detection of a change in the visual environment. An outstanding question is whether there are mechanisms in the rodent visual system that would support and facilitate visual change detection. An experimental protocol frequently used to investigate change detection in humans is the oddball paradigm, in which a rare, unexpected stimulus is presented in a train of stimulus repetitions [4]. A popular “predictive coding” theory of cortical responses states that neural responses should decrease for expected sensory input and increase for unexpected input [5, 6]. Despite evidence for response suppression and enhancement in noninvasive scalp recordings in humans with this paradigm [7, 8], it has proven challenging to observe both phenomena in invasive action potential recordings in other animals [9–11]. During a visual oddball experiment, we recorded multi-unit spiking activity in rat primary visual cortex (V1) and latero-intermediate area (LI), which is a higher area of the rodent ventral visual stream. In rat V1, there was only evidence for response suppression related to stimulus-specific adaptation, and not for response enhancement. However, higher up in area LI, spiking activity showed clear surprise-based response enhancement in addition to stimulus-specific adaptation. These results show that neural responses along the rat ventral visual stream become increasingly sensitive to changes in the visual environment, suggesting a system specialized in the detection of unexpected events.

RESULTS

We recorded the action potential activity of multi-unit sites in V1 and extrastriate area LI of awake rats during a visual oddball

paradigm with an equiprobable control condition (see [Figure 1](#) and [Supplemental Experimental Procedures](#)). The standard, deviant, and control conditions allow us to identify two mechanisms: response suppression for highly probable stimuli (standard < control; standard < deviant) and response enhancement for unexpected stimuli (deviant > control).

Primary Visual Cortex: Identity Oddball Experiment

In V1, we recorded multi-unit spiking activity (MUA) in 55 responsive sites (28 in rat 1 and 27 in rat 2, in 13 and 14 sessions, respectively) to sequences in which two stimuli were presented with different probabilities: $p(\text{standard}) = 0.9$; $p(\text{deviant}) = 0.1$ ([Figure 1C](#); see [Supplemental Experimental Procedures](#)). In general, the V1 response to a stimulus was very transient, with a relatively low sustained response ([Figure 2A](#), first two rows). Because of the transient nature of the response, we focused the analysis on its first 100 ms. Using the average net firing rates per condition, we calculated adaptation indices (AI) that indicate response suppression ($AI < 0$) and enhancement ($AI > 0$) for the standard (S) and deviant (D) relative to the response to the same stimulus in the equiprobable control condition (C):

$$AI_{SC} = \frac{(S - C)}{(|S| + |C|)}, \quad AI_{DC} = \frac{(D - C)}{(|D| + |C|)}$$

The median AI demonstrated response suppression to the standard (AI_{SC} rat 1: median = -0.28 , $p < 0.0001$, sign test; AI_{SC} rat 2: median = -0.31 , $p < 0.0001$). However, we find no evidence for a change in response to the deviant, relative to the control (AI_{DC} rat 1: median = 0.01 , $p = 0.1849$; AI_{DC} rat 2: median = -0.03 , $p = 1.0000$; [Figure 2B](#)).

To account for the variability caused by differences among MUA sites across rats, we analyzed our data using a multi-level model [13–15]. We used a regression model in which average raw firing rates per condition and per unit are modeled with a log normal distribution. Responses of cortical neurons have been shown to follow a log normal distribution [16], and this was confirmed in the present data. From this model we report parameter δ , which expresses the ratio of the net responses for deviant (δ_{DC}) and standard (δ_{SC}) conditions relative to those for the control condition (see [Supplemental Experimental Procedures](#)). The results ([Figure 2C](#)) indicated that the response to the standard was 57% of the response to the control

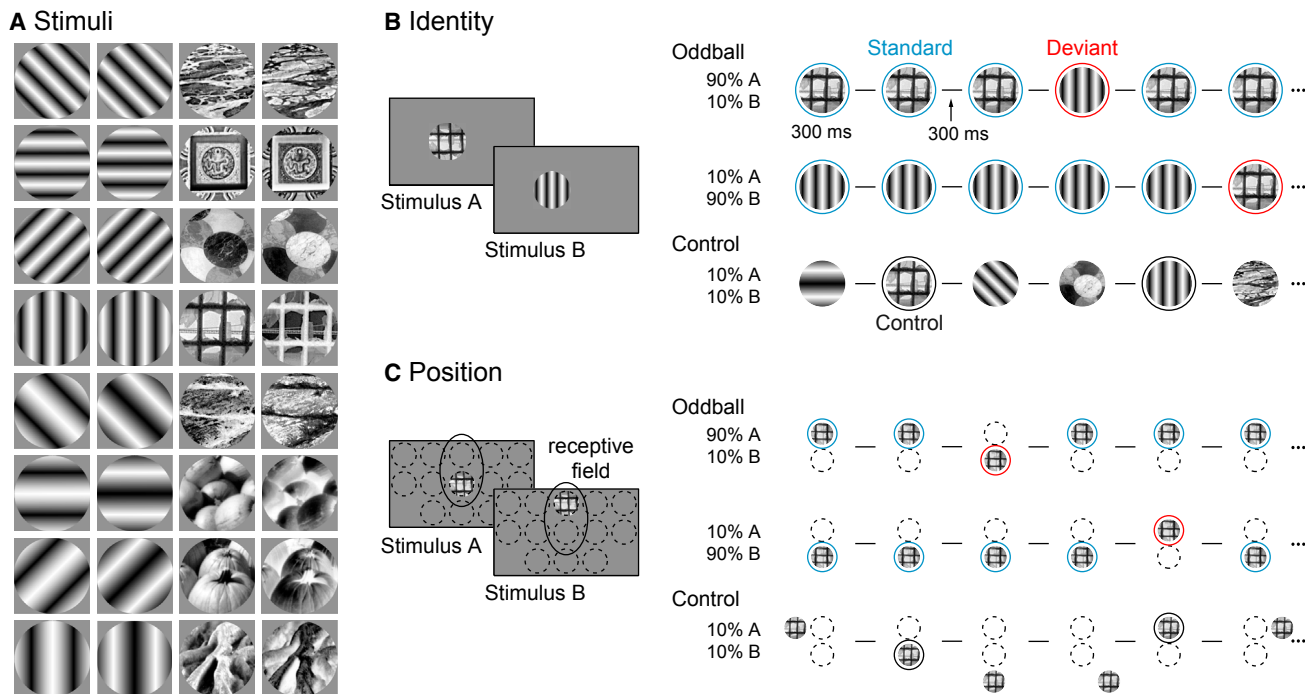


Figure 1. Stimulus Set and Visual Oddball Paradigm

(A) Stimuli included sine wave gratings (four orientations at two frequencies) and eight textures. For each sine wave we included the quadrature phase shift and for each texture the negative version. Sine wave gratings typically drive neural responses in V1 well, but extrastriate area LI might be more sensitive to complex stimuli like textures [12].

(B) In the identity oddball experiment, different stimuli were presented in different blocks of 100 randomized trials of 300 ms, separated by 300 ms. Oddball blocks consisted of two stimuli (A and B) shown at different probabilities: $p(\text{standard}) = 0.9$; $p(\text{deviant}) = 0.1$. Assignment of the probabilities to A and B was counterbalanced across blocks. In equiprobable control blocks, the probability of A, B, and eight additional stimuli is 0.1, so that none of them stand out as a deviant. Responses to the standard, deviant, and control conditions were averaged across A and B for sites that had a positive net response to both (see [Supplemental Experimental Procedures](#)).

(C) The position oddball experiment was identical, except that instead of presenting different stimuli, one stimulus was presented at different screen positions.

($\delta_{SC} = 0.57$; [Figure 3A](#)), and the response to the deviant was 101% of the control ($\delta_{DC} = 1.01$; [Figure 3A](#)). Both rats showed lower responses to the standard, compared with those to the deviant ($\delta_{DC} - \delta_{SC} = 0.44$; [Figure 3A](#)), and lower than those to the control, indicating stimulus-specific adaptation.

Latero-Intermediate Area: Identity Oddball Experiment

We performed the same experiment while recording MUA in 48 responsive sites in LI (29 in rat 2 and 19 in rat 3, in 11 and 8 sessions, respectively). The mean time course plots of firing rates ([Figure 2A](#)) indicate that a very small response was elicited to the standard compared to the control. The AIs ([Figure 2B](#)) showed strong reduction of the response to the standard (AI_{SC} rat 2: median = -0.53 , $p < 0.0001$; AI_{SC} rat 3: median = -0.58 , $p < 0.0001$). Contrary to V1, the response to the deviant was stronger compared to the control (AI_{DC} rat 2: median = 0.14 , $p = 0.0001$; AI_{DC} rat 3: median = 0.17 , $p < 0.0001$). The latter suggests LI response enhancement to the unexpected deviant stimulus in LI. This difference between V1 and LI could not be explained by a sampling bias in cortical layers (see [Figure S1](#)).

The multi-level model estimates ([Figure 2C](#)) indicated that the response to the standard was 32% of the response of the control ($\delta_{SC} = 0.32$; [Figure 3B](#)), while the response to the deviant was 135% of the control ($\delta_{DC} = 1.35$; [Figure 3B](#)). Logically, these re-

sults amounted to a strong difference in responses to standard and deviant ($\delta_{DC} - \delta_{SC} = 1.02$; [Figure 3B](#)).

Comparing LI with V1, the deviant-standard response difference was estimated to be stronger in LI ($[\delta_{DC}^{LI} - \delta_{SC}^{LI}] - [\delta_{DC}^{V1} - \delta_{SC}^{V1}] = 0.59$; [Figure 3D](#)). This difference between areas resulted from both an increase in stimulus-specific adaptation for the standard ($\delta_{SC}^{LI} - \delta_{SC}^{V1} = -0.25$; [Figure 3D](#)) and a change in effect of the deviant ($\delta_{DC}^{LI} - \delta_{DC}^{V1} = 0.34$; [Figure 3D](#)), with only the latter difference between the areas being significant.

We could compare the responses in V1 and LI within one animal (rat 2). Like on the population level, the deviant-standard response difference was estimated to be stronger in LI than in V1 ($[\delta_{DC}^{LI} - \delta_{SC}^{LI}] - [\delta_{DC}^{V1} - \delta_{SC}^{V1}] = 0.55$; [Figure 3D](#)). In addition, this animal showed in LI an increase in stimulus-specific adaptation for the standard ($\delta_{SC}^{LI} - \delta_{SC}^{V1} = -0.20$; [Figure 3D](#)), in addition to a change in effect for the deviant ($\delta_{DC}^{LI} - \delta_{DC}^{V1} = 0.35$; [Figure 3D](#)). Thus, the increase in the MUA difference between standard and deviant in rat 2 LI compared to V1 resulted from both a stronger repetition suppression and stronger response enhancement.

Latero-Intermediate Area: Position Oddball Experiment

A possible explanation for the deviant-control response difference in LI is that there was more cross-stimulus adaptation in

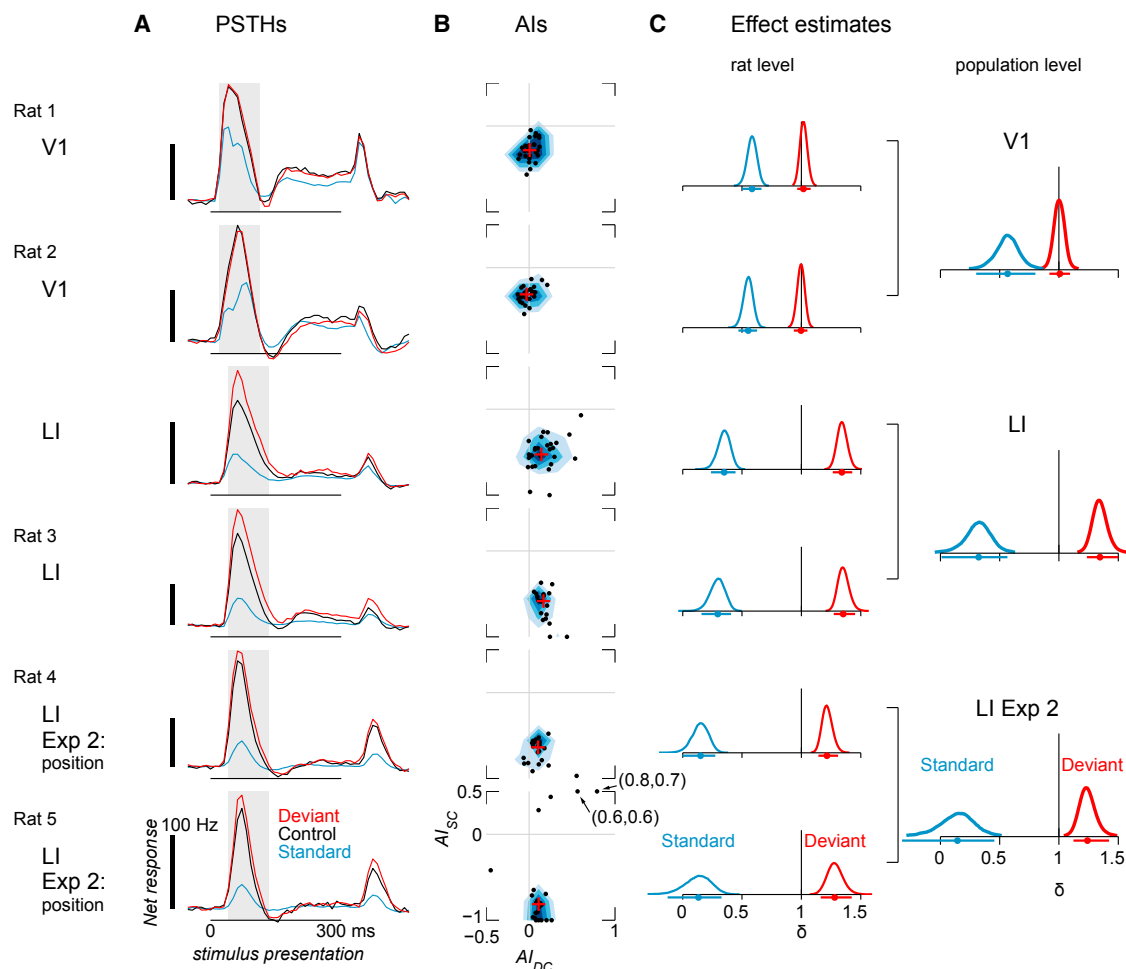


Figure 2. Multi-Unit Neural Responses for Deviant, Standard, and Control Condition

(A) The net (baseline subtracted) firing rate expressed in spikes per second is plotted across time (10 ms bins) averaged across deviant (red), standard (blue), or control (black) stimulus presentations. Vertical scale bars indicate a firing rate of 100 Hz. The horizontal line indicates the 300 ms stimulus presentation. The results are plotted separately for each rat x area combination. Further analyses were done on net spike counts of the first 100 ms onset of the response (area shaded in gray).

(B) Scatterplots of adaptation indices of multi-unit sites for deviant (abscissa; Al_{DC}) versus standard (ordinate; Al_{SC}) conditions, superimposed on a contour plot. Median values are indicated by a red cross. Points below the horizontal line ($Al_{SC} < 0$) indicate response suppression for the standard relative to the control condition. Points to the right of the vertical line ($Al_{DC} > 0$) indicate response enhancement for the deviant relative to the control condition.

(C) Multi-level model effect estimates (δ) for standard and deviant condition on rat x area level and on population level. Values of δ indicate net responses for standard or deviant conditions as a proportion of net responses for the control condition. Estimated posterior distributions are plotted, which indicate the estimated probability density for each parameter value δ given the data: the higher the density, the more probable the underlying values. The effects' point estimates (posterior median) and 95% intervals are indicated below each distribution by a dot and a horizontal line, respectively (see also Figure 3). The value of 1 is indicated by a black vertical line. Estimates close to 1 indicate similar responses in the control relative to the responses for a standard or deviant. See also Figures S1, S2, and S3.

the equiprobable blocks from the additional eight stimuli. For example, if the neural site responds very well to most stimuli in equiprobable blocks, neural fatigue [17] alone can cause reduced general responsiveness in these blocks. This can result in response suppression for the control condition, which might explain a difference in neural response between deviant and control. Such suppression can also be caused by feature-specific adaptation if the neural site responds to one or more features shared by the different stimuli in equiprobable blocks. We calculated a response equivalence index (EI ; see Supplemental Experimental Procedures) that indicates whether the

response to the additional stimuli is equivalent to ($EI = 0$) or lower ($EI > 0$) than the control. The EI was practically zero for the identity oddball recordings (rat 1 V1 EI : median = 0.03, $IQR = 0.11$; rat 2 V1 EI : median = 0.00, $IQR = 0.10$; rat 2 LI EI : median = 0.00, $IQR = 0.14$; rat 3 EI : median = 0.04, $IQR = 0.08$), indicating that cross-adaptation in the equiprobable blocks might indeed be present. This possibility was supported by a decrease of the responses with trial number in the control condition (see Figures S2C and S2D). We addressed this issue by performing an experiment in which we manipulated stimulus position instead of stimulus identity (Figure 1D; see Supplemental

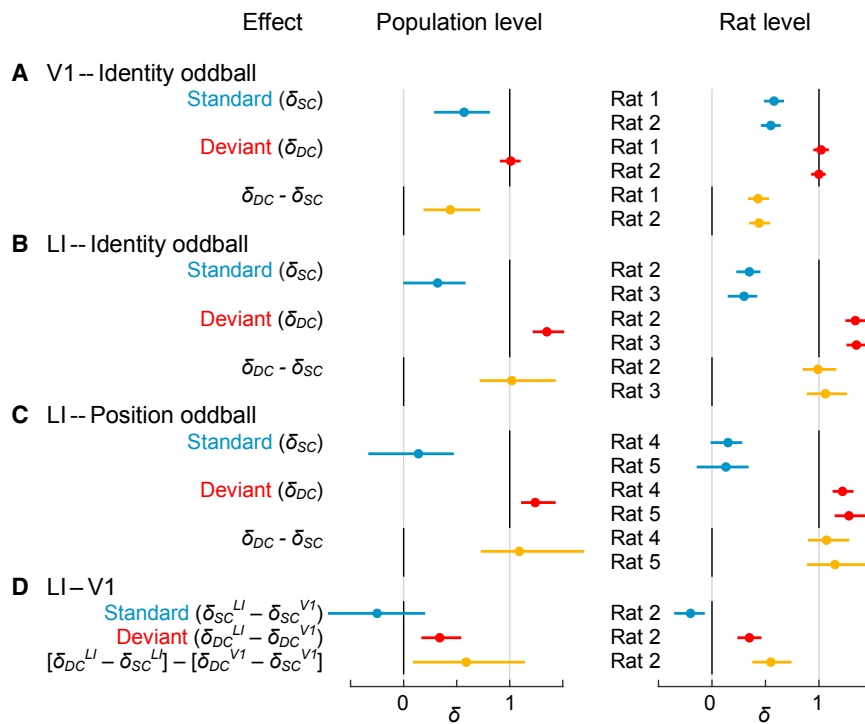


Figure 3. Multi-Level Model Effect Estimates on Rat \times Area Level and on Population Level

(A–D) Point estimates (posterior median) and 95% intervals (error bars) for each comparison. Relevant reference points (0 or 1) are indicated by black vertical lines. Note that effects for standard and deviant in panels (A)–(C) are the same as those presented in Figure 2.

combined result of a strong response reduction for the standard and an enhancement for the deviant. V1 did not show such an enhancement and might have weaker stimulus-specific adaptation.

Stimulus-specific adaptation has been documented to play an important role in modulating spiking activity in both auditory and visual cortices of rodent during modality-appropriate oddball sequences [9–11, 18], as well as recent sensory experience in general [19]. Our results confirm this in both V1 and LI. In addition, this adaptation might be stronger in LI compared to V1. This agrees with the

finding that stimulus-specific adaptation in auditory oddball sequences is stronger and faster outside primary auditory cortex [20]. In our data, the suppression for the standard was rapid and persistent and seemed only to be relieved by the occurrence of a deviant in the immediately preceding trial (see Figures S2G–S2L). Stimulus-specific adaptation also affected the response to the deviant/control, which was lower the more recent the previous deviant or the same stimulus was (see Figures S2G–S2L).

Spiking activity in rat V1 did not show an enhanced response to the deviant. Rather, a response reduction for trial numbers later in the sequence points toward cross-adaptation from the standard (see Figures S2A and S2B). The absence of a surprise response in rat V1 corroborates multi-unit recordings in primary auditory cortex of both rat [10] and monkey [9]. Recently, an increased response to a deviant was reported for neural responses in mouse V1 [21]. However, in that study the difference between standard and deviant stimuli (orthogonal orientations) was considerably greater than those between stimuli in their control condition. Thus, their effect can be explained by more cross-stimulus adaptation for the control than for the deviant [10].

DISCUSSION

Multi-unit responses we recorded in area LI did demonstrate a higher response to the deviant compared to the control. This enhancement was also present in an additional experiment that decreased cross-stimulus adaptation in the equiprobable sequences (i.e., the position oddball experiment). The absence of a decreased response to the control stimuli as a function of trial number (see Figures S2E and S2F) indicates that cross-adaptation was eliminated. Thus, we provide the first demonstration of a surprise response in spiking activity in an oddball paradigm when controlling for adaptation, which is an important prediction of the predictive coding framework [5]. The timing of this effect is in the earliest phase of the response and thus may

To summarize, we observed a clear difference between multi-unit responses to the deviant and standard stimuli in an oddball paradigm consistently across all rats and areas. This response difference was bigger in LI compared to V1. In LI, it was the

finding that stimulus-specific adaptation in auditory oddball sequences is stronger and faster outside primary auditory cortex [20]. In our data, the suppression for the standard was rapid and persistent and seemed only to be relieved by the occurrence of a deviant in the immediately preceding trial (see Figures S2G–S2L). Stimulus-specific adaptation also affected the response to the deviant/control, which was lower the more recent the previous deviant or the same stimulus was (see Figures S2G–S2L).

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originate in LI itself. The high frequency of the standard stimulus could affect the processing of stimuli in the local LI circuit, giving rise to surprise responses. Perhaps NMDA receptor neurotransmission might be involved in deviant responses [4] as opposed to stimulus-specific adaptation [10]. The relative contribution of local versus top-down processes [22] requires further investigation. In addition to multi-unit responses, we analyzed single-unit data and local field potentials. A trend for an enhanced response to the deviant was also present in single LI neurons, and this was significant when responses were not individually normalized for firing rate (see [Supplemental Experimental Procedures](#)). Furthermore, the results of simultaneously recorded local field potentials correspond to those of the MU activity (see [Figure S3](#)).

The results of our recordings in LI differ noticeably from those of monkey IT neurons. Various observations in monkeys show a sensitivity for statistical structure of visual information after weeks of exposure [23, 24]. Nevertheless, surprise-related enhancements in an oddball paradigm were not observed in primate visual cortical areas [11]. We have to be careful when engaging in such species comparisons for various reasons, such as difficulties to know which areas and pathways correspond and differences in the details of experiments (stimulus size, behavioral tasks, reward schedules, etc.). Still, we stayed as close as possible to the experiment by Kaliukhovich and Vogels [11], and both rat and monkey were not actively engaged in a task with the stimuli. In addition, rodent LI belongs to a processing stream that has been suggested to be homologous to the primate ventral stream that culminates in IT [25]. However, it remains an open question whether and to what extent they might be functionally similar. Other studies have reported unexpected properties of the proposed rat ventral pathway before, namely an increased response to moving stimuli [26], as well as a lack of a categorical representation and lack of higher responses to natural stimuli [12]. Nevertheless, the same studies also reported commonalities with the primate ventral pathway, namely an increased tolerance for stimulus position [26] and clustering of natural versus scrambled movie representations [12].

A clear difference in neural response between regular and irregular stimuli is a necessary prerequisite for a system specialized in change detection. We observed this difference in all of our recordings, and it increased between V1 and higher visual area LI. The fact that we see this transition might indicate that change detection is an important functional specialization of the processing stream that both areas belong to. This claim is compatible with previous reports emphasizing predator detection as one of the major ecologically valid functions of vision in rats and mice [1, 3]. Previous research has indeed shown that sensory adaptation facilitates perceptual detection of deviant stimuli by increasing the difference in neural responses [27]. A response enhancement for the unexpected stimulus will only further increase this difference. Future studies are needed to study the behavioral relevance of this surprise-based response enhancement.

SUPPLEMENTAL INFORMATION

Supplemental Information includes Supplemental Experimental Procedures and three figures and can be found with this article online at <http://dx.doi.org/10.1016/j.cub.2017.02.024>.

AUTHOR CONTRIBUTIONS

Conceptualization: K.V., R.V., and H.O.d.B.; Investigation: K.V.; Formal Analysis: K.V.; Visualization: K.V.; Writing – Original Draft: K.V., R.V., and H.O.d.B.; Supervision: H.O.d.B.

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