Rapid topographic reorganization in adult human primary visual cortex (V1) during noninvasive and reversible deprivation

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Can the primary visual cortex (V1), once wired up in development, change in adulthood? Although numerous studies have demonstrated topographic reorganization in adult V1 following the loss of bottom-up input, others have challenged such findings, offering alternative explanations. Here we use a noninvasive and reversible deprivation paradigm and converging neural and behavioral approaches to address these alternatives in the experimental test case of short-term topographic reorganization in adult human V1. Specifically, we patched one eye in typical adults, thereby depriving the cortical representation of the other eye's blind spot (BS), and immediately tested for topographic reorganization using functional magnetic resonance imaging and psychophysics. Strikingly, within just minutes of eye-patching, the BS representation in V1 began responding to stimuli presented outside of the BS, and these same stimuli were perceived as elongated toward the BS. Thus, we provide converging neural and behavioral evidence of rapid topographic reorganization in adult human V1, and the strongest evidence yet that visual deprivation produces bona fide cortical change.

plasticity | remapping | reorganization | perceptual distortions | V1

When a region of the adult primary visual cortex (V1) is deprived of its typical visual input, neurons in the deprived region begin responding to stimuli that would otherwise activate adjacent cortex only, a process classically referred to as topographic reorganization, plasticity, or remapping (1, 2). This phenomenon has been extensively documented in adult macaques, cats, and mice during both long-term (months to years) (3–16) and short-term (minutes to hours) (4, 5, 17–19) deprivation due to retinal lesions. Furthermore, such topographic reorganization in adult nonhuman animals is initially mediated by the disinhibition of preexisting subthreshold connections and later by the growth of new connections (1, 2).

Topographic reorganization has also been observed in adult humans as a consequence of long-term deprivation due to macular degeneration (20–25) or stroke (26). However, no human studies have directly investigated short-term topographic reorganization—the hypothesis tested here—and the mechanisms driving topographic reorganization in adult humans remain unknown. Finally, while no nonhuman animal studies have ever investigated the perceptual consequences of such topographic reorganization, two human studies found systematic perceptual distortions (e.g., squares were perceived as rectangles) in adult humans during both long-term (26) and short-term (27) visual deprivation.

Still, despite these numerous findings, several other studies rejected claims of topographic reorganization, and instead offered alternative explanations for why the cortex might appear to reorganize when, in fact, no genuine changes actually occurred, thus generating significant controversy (24, 28–34). These alternative explanations include: 1) Retinal recovery from postlesion swelling, in which the deprived cortical area shrinks during retinal healing and mimics topographic reorganization; 2) measurement bias, in which neurons within the deprived cortex already responded to stimulation of adjacent, nondeprived cortex; 3) sampling bias, in which so-called changes actually reflect different populations of neurons sampled before and during deprivation; 4) outlier effects, in which only a few, sparsely distributed neurons drive the apparent topographic reorganization; or 5) task-specific feedback, in which general top-down signals alone produce activity in the deprived cortex due to the lack of competing feed-forward inputs to this region. Crucially, all of the above studies that report topographic reorganization in V1 have been susceptible to at least one of these pitfalls. Thus, the question remains: Can adult V1 topographically reorganize as a consequence of deprivation?

Here, we address this question using a noninvasive and reversible deprivation paradigm and converging neural and behavioral approaches to rule out all of the above alternative explanations in the test case of topographic reorganization in adult human V1 during short-term deprivation. Specifically, we patched one eye in typical adults, noninvasively and reversibly depriving the region in V1 corresponding to the other eye's blind spot (BS). Crucially, our method of deprivation rules out the first potential alternative explanation of adult V1 topographic reorganization (i.e., retinal recovery), since no retinal lesion was created. Following ∼10 min of deprivation, we then tested for rapid topographic reorganization in V1 using functional magnetic imaging (fMRI). We predicted that the cortical representation of the BS of one eye, which during binocular vison normally responds to stimuli

Significance

Topographic reorganization in adult V1 has been documented in multiple species (i.e., cats, rodents, nonhuman primates, humans), over a range of time scales (i.e., minutes to years), and with distinct methodologies (i.e., electrophysiology, fMRI, psychophysics), representing nearly 30 y of collective progress. However, the validity of this body of work has recently come into question due to a set of five alternative explanations. As a consequence, topographic reorganization in adult V1 remains the subject of an ongoing controversy. Here we rule out all five alternative explanations by taking advantage of a noninvasive and reversible deprivation paradigm and complementary fMRI and psychophysical methods. Consequently, we provide evidence of short-term topographic reorganization in adult human V1.

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presented inside the BS in the visual field via the opposite eye (Fig. 1*A*), would instead start responding to stimuli presented outside of the BS when the opposite eye is patched (i.e., when the BS cortical representation is deprived of its typical input) (Fig. 1*B*). Additionally, we also tested for the consequent perceptual elongation, replicating a previous study (27), and predicted that stimuli presented outside of the BS would be perceived as elongated toward the BS during deprivation.

Results

We presented stimuli (3° × 3° counter phasic checkerboards flickering at 8 Hz) in two locations in the right visual field, either centered inside the right eye's BS in the visual field (BS stimulus) or instead peripheral to (i.e., to the right of) the right eye's BS in the visual field (right stimulus). Participants viewed these stimuli when the left eye was patched (deprived condition) and also when no patch was worn (undeprived condition) (Fig. 1) (Exp. 1A). In each participant, we then functionally defined two regions of interest (ROIs) in V1, one corresponding to the representation of the right eye's BS in the visual field (BS ROI) and the other corresponding to the region peripheral to (i.e., to the right of) the right eye's BS in the visual field (right ROI), and subsequently measured the responses to the BS stimulus and the right stimulus in each ROI.

First, we verified the validity of the ROIs. In the BS ROI, using an independent set of data from those used to define the ROI, we found 1) a significantly greater response to the BS stimulus versus the right stimulus during the undeprived condition [$t_{(5)} = 3.61$, $P < 0.05$, $d = 1.47$], and 2) a significantly greater response to the BS stimulus during the undeprived versus deprived condition [$t_{(5)} = 4.42$, $P < 0.01$, $d = 1.82$], confirming that this region indeed corresponds to the BS in the visual field (Fig. 1). In contrast, again using an independent set of data from those used to define the ROI, the right ROI showed the exact opposite pattern of response during the undeprived condition, with a significantly greater response to the right stimulus versus the BS stimulus [$t_{(4)} = 7.17$, $P < 0.01$, $d = 3.21$], verifying the validity of the right ROI (Fig. 1*A*). Finally, directly comparing the two ROIs, a 2 (ROI: BS, right) × 2 (stimulus: BS, right) repeated-measures ANOVA revealed a double dissociation (i.e., the BS ROI responds significantly more to the BS stimulus compared to the Right stimulus, while the right ROI shows the complete opposite pattern) [$F_{(1,\ 4)} = 139.96$, $P < 0.0001$, $\eta_p^2 = 0.97$], confirming independent cortical representations for the BS and right stimulus positions in the undeprived condition.

Second, we tested our prediction that the cortical representation of the BS would start responding to stimuli presented outside of the BS (i.e., to the right of the BS), following just minutes of deprivation. Consistent with this prediction, we observed 1) a significantly greater response in the BS ROI to the right stimulus during the deprived compared to the undeprived condition [$t_{(5)} = 3.09$, $P < 0.05$, $d = 1.27$], and 2) a significantly greater response in the BS ROI to the right stimulus compared to the BS stimulus during the deprived condition [$t_{(5)} = 3.87$, $P < 0.05$, $d = 1.91$] (Fig. 1). Next, directly comparing the deprived and undeprived conditions in the BS ROI, a 2 (stimulus: BS, right) × 2 (condition: deprived, undeprived) repeated-measures ANOVA revealed a significant interaction [$F_{(1,\ 5)} = 72.24$, $P < 0.0001$, $\eta_p^2 = 0.94$], with the BS ROI responding significantly more to the right stimulus than to BS stimulus during the deprived condition, yet responding in the complete opposite way in the undeprived condition. Taken together, these results demonstrate a double dissociation within the BS ROI (i.e., the BS ROI responds significantly more to the BS stimulus compared to the right stimulus during the undeprived condition, but in the complete opposite way during the deprived condition), signifying

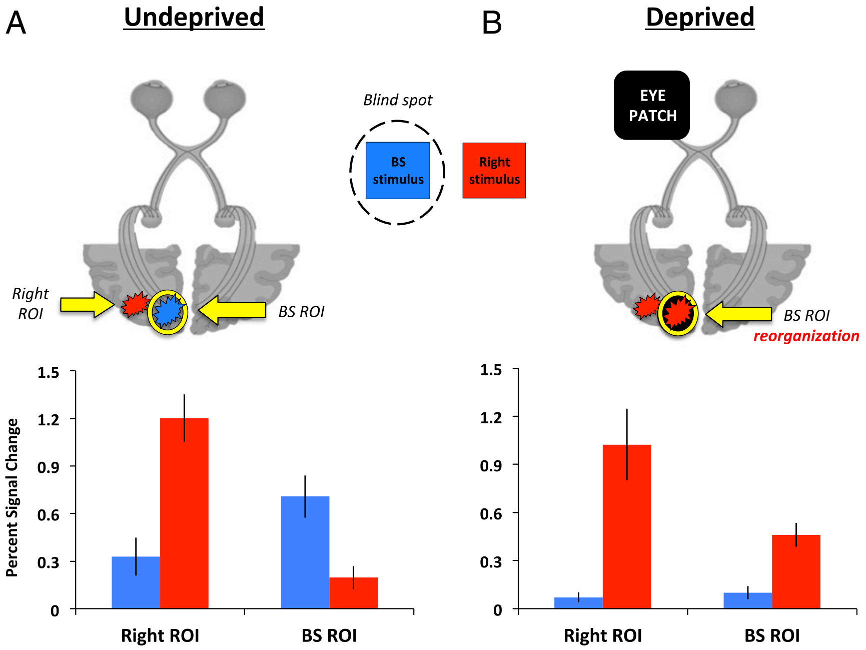

Fig. 1. Topographic reorganization of the BS representation in V1. (*A*) Schematic of the BS ROI and the right ROI in V1 (left hemisphere), corresponding to the BS and right stimulus positions, respectively, in the right visual field. The bar graph shows ROI responses during the undeprived condition (*y* axis: PSC, relative to fixation). The BS ROI (*x* axis) responds significantly more to the BS stimulus (blue) versus the right stimulus (red), whereas the right ROI (*x* axis) responds significantly more to the right stimulus versus the BS stimulus, demonstrating a double dissociation between the two ROIs and verifying independent cortical representations. (*B*) During the deprived condition, participants wore a patch on the left eye, depriving the BS ROI of its normal visual input. The bar graph shows ROI responses during the deprived condition. The BS ROI now responds significantly more to the right stimulus versus the BS stimulus, and also responds significantly more to the right stimulus during the deprived versus the undeprived condition, demonstrating rapid topographic reorganization in V1. In contrast, the right ROI shows no change compared to the undeprived condition, confirming that topographic reorganization is specific to deprived cortex only. Error bars show the SEM.

rapid topographic reorganization in V1 during deprivation. This rapid topographic reorganization was observed in all six participants tested in Exp. 1A.

Third, we predicted that this topographic reorganization would be restricted to the deprived cortex only (i.e., the BS ROI), and would not be observed in other parts of V1 that were never deprived (e.g., the right ROI). Consistent with this prediction, the response to the right stimulus in the right ROI was not significantly different between the deprived and undeprived conditions [$t_{(4)} = 1.21$, $P = 0.29$], and furthermore, a 2 (ROI: BS, right) × 2 (stimulus: BS, right) × 2 (condition: deprived, undeprived) repeated-measures ANOVA revealed a significant interaction [$F_{(1,\ 4)} = 18.58$, $P < 0.05$, $\eta_p^2 = 0.82$], with the BS ROI responding significantly more to the right stimulus versus the BS stimulus during the deprived condition relative to the undeprived condition, compared to the right ROI (Fig. 1).

But might this pattern of results simply be due to a difference between monocular stimulation in the deprived condition (i.e., left eye patched) and binocular stimulation in the undeprived condition (i.e., no patch worn)? To address this possibility, we repeated the above experiment with one exception: The right eye was now patched during the undeprived condition while the left eye was still patched in the deprived condition, thus providing monocular stimulation in both cases (Fig. 2) (Exp. 1B). Note that the right eye's BS representation, around which stimuli are presented, is deprived when the left eye is patched, and is undeprived when the right eye is patched. In this more tightly controlled manipulation, we replicated the results from Exp. 1A, and did so in all four participants tested in Exp. 1B. Specifically, we observed a significantly greater response to the BS stimulus in the BS ROI during the undeprived condition compared to the deprived condition [$t_{(5)} = 3.1$, $P < 0.05$, one-tail], and a significantly greater response to the BS stimulus compared to the right stimulus in the BS ROI during the undeprived condition [$t_{(5)} = 4.7$, $P < 0.05$, one-tail], confirming the validity of the BS ROI. We also observed a significantly greater response to the right stimulus compared to the BS stimulus in the right ROI during the undeprived condition [$t_{(5)} = 8.9$, $P < 0.05$, one-tail], confirming the validity of the right ROI (Fig. 2*A*).

Importantly, we again observed 1) a significantly greater response to the right stimulus compared to the BS stimulus in the BS ROI during the deprived condition [$t_{(5)} = 3.0$, $P < 0.05$, one-tail], and 2) a significantly greater response to the right stimulus in the BS ROI during the deprived versus the undeprived condition [$t_{(5)} = 2.4$, $P < 0.05$, one-tail], together signifying rapid topographic reorganization in the BS ROI during deprivation (Fig. 2). Directly comparing the deprived and undeprived conditions in the BS ROI, a 2 (stimulus: BS, right) × 2 (condition: deprived, undeprived) repeated-measures ANOVA revealed a significant interaction [$F_{(1,\ 3)} = 31.00$, $P < 0.05$, $\eta_p^2 = 0.91$], with the BS ROI responding significantly more to the right stimulus than to BS stimulus during the deprived condition, yet responding in the opposite way during the undeprived condition. Taken together, these results replicate the double dissociation within the BS ROI observed in the first experiment (i.e., the BS ROI preferentially responds to the BS stimulus during the undeprived condition and the right stimulus during the deprived condition), again demonstrating rapid topographic reorganization in adult V1 during deprivation. Finally, we also compared this BS ROI reorganization effect between our two experiments directly: A 2 (condition: deprived, undeprived) × 2 (Experiment: 1A, 1B) within-between repeated measures ANOVA failed to reveal a significant interaction in the response to the right stimulus in the BS ROI [$F_{(1,\ 8)} = 0.004$, $P = 0.95$, $\eta_p^2 < 0.001$], suggesting that the magnitude of reorganization in the BS ROI was similar between experiments.

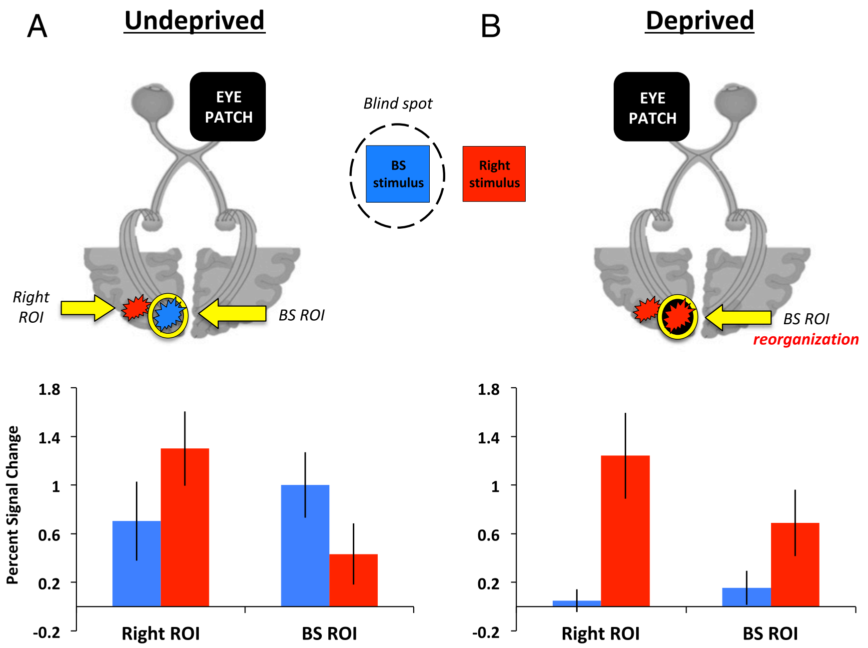

Fig. 2. Topographic reorganization of the BS representation in V1 in a monocular control experiment. Participants wore a patch on the right eye during the undeprived condition, and a patch on the left eye during the deprived condition, thus monocular stimulation was provided in both conditions. (*A*) The bar graph shows ROI responses during the undeprived condition (*y* axis: PSC, relative to fixation). The BS ROI (*x* axis) responds significantly more to the BS stimulus (blue) versus the right stimulus (red), whereas the right ROI (*x* axis) responds significantly more to the right stimulus versus the BS stimulus, thus verifying independent cortical representations. (*B*) The bar graph shows ROI responses during the deprived condition. The BS ROI now responds significantly more to the right stimulus versus the BS stimulus, and also responds significantly more to the right stimulus during the deprived versus the undeprived condition, demonstrating rapid topographic reorganization in V1. In contrast, the right ROI shows no change compared to the undeprived condition, confirming that topographic reorganization is specific to deprived cortex only. Altogether, these data replicate the results shown in Fig. 1, thereby ruling out the possibility that topographic reorganization in V1 is due to binocular versus monocular stimulation. Error bars show the SEM.

Again, we confirmed that such reorganization did not occur in a cortical region that was never deprived of its visual input (i.e., the right ROI). Indeed, we found no significant difference in the response to the right stimulus in the right ROI during the deprived versus the undeprived condition [$t_{(5)} = 0.24$, $P = 0.41$, one-tail], and in fact, we found the opposite numerical pattern in the right ROI compared to the BS ROI (i.e., there was a numerically greater response to the right stimulus during the undeprived versus the deprived condition in the right ROI, but the opposite pattern in the BS ROI) (Fig. 2*B*). Comparing the two ROIs directly, a 2 (ROI: BS, right) × 2 (stimulus: BS, right) × 2 (condition: deprived, undeprived) repeated-measures ANOVA revealed a marginally significant interaction with a large effect size [$F_{(1,\ 3)} = 3.92$, $P = 0.14$, $\eta_p^2 = 0.57$]. Here, the marginal significance is not surprising given the smaller sample size of this replication experiment, but the large effect size indeed suggests that reorganization is specific to the BS ROI only, and does not occur in the right ROI. Relatedly, we compared this specificity between the two experiments directly, and a 2 (ROI: BS, right) × 2 (stimulus: BS, right) × 2 (condition: deprived, undeprived) × 2 (Experiment: 1A, 1B) within-between repeated-measures ANOVA failed to detect a significant interaction [$F_{(1,\ 7)} = 0.74$, $P = 0.41$, $\eta_p^2 = 0.09$], suggesting that the specificity of the reorganization effect was similar between experiments. Crucially, however, a 2 (ROI: BS, right) × 2 (stimulus: BS, right) × 2 (condition: deprived, undeprived) within-between repeated-measures ANOVA still revealed a significant interaction $F_{(1,\ 7)} = 17.78$, $P < 0.01$, $\eta_p^2 = 0.72$], indicating that across both experiments, the BS ROI responded significantly more to the right stimulus versus the BS stimulus during the deprived condition versus the undeprived condition, relative to the right ROI. Altogether, these results confirm that binocular versus monocular stimulation cannot explain our pattern of results, and again demonstrate topographic reorganization in adult V1 during short-term deprivation.

Next, we tested our complementary behavioral prediction that within 10 min of depriving the cortical representation of the BS in V1, stimuli presented outside of the BS would be perceived as elongated (e.g., squares would be perceived as rectangles) toward the BS, as previously reported (27) (Fig. 3*A*). Consistent with our prediction, and closely replicating prior results in a new sample of typical adults, we observed significant perceptual elongation (nearly 10%) toward the BS in the deprived condition (left eye patched) relative to the undeprived condition (no patch) (Exp. 2A). Specifically, the point of subjective equality (PSE; that is, the 50% point on the psychometric function) for the undeprived condition was +3.0% (confidence interval [CI] = +2.5, +3.5; a positive PSE indicates truncation, revealing that these participants have a slight bias to perceive rectangles as slightly shorter when presented above or below the BS, or narrower when presented to the right or left). In contrast, the PSE for the deprived condition was −6.3% (CI = −7.1, −5.6; a negative PSE indicates elongation, indicating that these same participants now perceive rectangles as larger during deprivation), and the CIs for each PSE did not overlap, demonstrating a significant difference between the deprived and undeprived conditions. The magnitude of the difference between the deprived condition relative to the undeprived condition was −9.3% (i.e., −6.3 minus +3.0), indicating that rectangles were perceived as ∼9% elongated during deprivation (Fig. 3*B*). To again rule out the possibility that our results were driven by monocular (left eye patched) versus binocular (no patch) viewing, we conducted a follow-up experiment in which participants viewed stimuli with either the left eye patched (deprived condition) or the right eye patched (undeprived condition) (Exp. 2B). As described above, the right eye BS representation, around which stimuli are presented, is deprived when the left eye is patched, and is undeprived when the right eye is patched. This experiment again revealed significant elongation toward the blind spot in the deprived condition relative to the undeprived condition. The PSE for the undeprived condition was 0.9% (CI = −0.3%, +2.2), the PSE for the deprived condition was −6.4% (CI = −8.2%, −4.7), and the confidence intervals for each PSE did not overlap, demonstrating a significant difference. The magnitude of the difference between the deprived condition relative to the undeprived condition was −7.3%, indicating that rectangles were perceived as ∼7% elongated during deprivation. Furthermore, the CIs between the deprived PSEs in the first and second behavioral experiments overlapped, indicating no significant difference in the magnitude of elongation between these two experiments, and replicating a second previously reported finding (27).

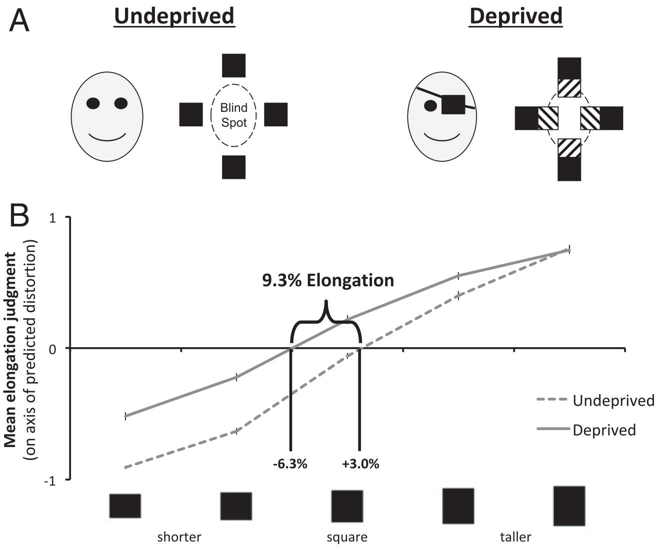

Fig. 3. Perceptual elongation of stimuli presented adjacent to the BS during deprivation. (*A*) All participants completed the square judgment task during undeprived (no patch) and deprived (left eye patched) conditions. Stimuli were presented in four positions, one at a time, around the right eye's BS, and were perceived as elongated (i.e., squares were perceived as rectangles), extending toward the BS during the deprived condition only. (*B*) Mean size judgments along the axis of predicted distortion (i.e., the horizontal axis for stimuli presented to the left and right of the BS; the vertical axis for stimuli presented above and below the BS) as a function of stimulus height (black rectangles). In the undeprived control condition (dashed black line), a square is perceived as shorter than a square (+3.0% PSE). In the deprived condition, this same stimulus is seen as elongated (−6.3% PSE) along the predicted axis of distortion (i.e., wider when presented to the left and right of the BS, and taller when presented to above and below the BS). More generally, the upward shift of the curve in the deprived condition (solid black line) indicates an elongation of all rectangles along the axis of predicted distortion following 10 min of deprivation. The PSE was significantly different between the deprived and undeprived conditions (i.e., the 95% CIs did not overlap), and the magnitude of difference was 9.3%, indicating that stimuli were perceived as ∼9% elongated during deprivation. Error bars show the SEM. These results replicate prior findings (27) in an independent sample of typical adults.

Together, the neural and perceptual changes described above demonstrate rapid topographic reorganization in adult human V1 following just 10 min of deprivation. However, could this topographic reorganization merely reflect the second potential alternative explanation (i.e., measurement bias)? Specifically, because each voxel represents the activity of thousands of neurons, it is possible that some of those neurons become silenced as a result of deprivation, but other neurons in the same voxel with receptive fields that were already outside of the deprived region still remain active. Thus, during deprivation, the average receptive field of that voxel would appear shifted, reflecting only the remaining active neurons and mimicking topographic reorganization even though no changes actually occurred (32). Accordingly, if in fact no changes have actually occurred in V1, and voxels within the BS were already responsive to stimuli outside of the BS, then the magnitude of that response would remain the same during deprivation. However, we observed the opposite pattern: The BS ROI responded significantly more to the right stimulus during deprivation, reflecting a bona fide change in the response to the stimulus outside of the deprived region, and ruling out measurement bias as an alternative explanation. In addition, note that the response in the BS ROI to the right stimulus during the undeprived condition is greater than zero, as is the response in the right ROI to the BS stimulus during the undeprived condition, which may indicate that neurons in these regions indeed have overlapping receptive fields (Fig. 1*A*). Regardless, the increased response in the BS ROI to the right stimulus during deprivation demonstrates a change in this baseline responsiveness, and thus rules out the possibility that these overlapping receptive fields alone are responsible for the observed topographic reorganization.

Our behavioral results also rule out the measurement bias described above as a potential confound. If, again, no changes actually occurred in the cortical representation of the BS during deprivation, and neurons inside the BS already responded to stimuli presented outside of the BS before deprivation, then stimuli would also be perceived as elongated during the undeprived condition. However, we found that stimuli are only perceived as elongated during deprivation, and even further, the measurement of this change in perception completely avoids the concerns associated with voxel-wise estimation of population receptive fields in V1. Even so, perhaps one might still imagine that stimuli are not perceived as elongated during the undeprived condition because of affirmative input from the BS that indicates no stimulus is present in that location. However, our stimuli were always presented 0.5° away from the BS border, so similar affirmative input is also received during the deprived condition, indicating that nothing is present between the BS and the stimulus, yet elongation toward the BS occurs across this gap regardless. Thus, stimuli are only perceived as elongated during the deprived condition, not because of affirmative input during the undeprived versus deprived condition, indicating that no stimulus is present, but rather, because neurons inside the BS topographically reorganize and start responding to stimuli outside of the BS during deprivation only. Therefore, the measurement bias described above cannot account for the neural and perceptual changes reported here.

Next, we rule out the third potential alternative explanation of topographic reorganization (i.e., sampling bias). Unlike prior electrophysiological studies that only measured single-unit activity and therefore may have misinterpreted differences between separate groups of neurons sampled before and during deprivation as evidence of actual change, an fMRI approach instead offers a more comprehensive assessment of cortical function by estimating the average activity of the same neural populations before and during deprivation, thus providing a more reliable measure of topographic reorganization (28). Interestingly, while Smirnakis et al. did not observe reorganization in V1 using fMRI, they did, in fact, show large phasic visual responses in their neuronal recordings within the deprived cortex, which might suggest that fMRI and single-unit recordings have different thresholds for detecting reorganized cortical activity (see also refs. 11 and 34). However, others have detected topographic reorganization in V1 using fMRI (20–26), confirming the measurement reliability of our approach.

Still, despite the advantages of fMRI in avoiding the sampling bias associated with single-unit electrophysiological experiments, the fourth potential alternative explanation of topographic reorganization (i.e., outlier effects) could apply to fMRI studies in which ROI results might be driven by a few (~5 to 7%) sparsely distributed voxels (29). To rule out this possibility, we used a volume-selectivity function approach to illuminate the full range of voxel-wise activity in the BS ROI from Exp. 1A (Fig. 4) (35, 36). We found that topographic reorganization is reliably observed in all 150 voxels of the BS ROI, with 42% (63 of 150) of voxels exhibiting a significantly greater response to the right stimulus during the deprived versus undeprived condition ($P < 0.05$, one-tail), thus confirming that our ROI results are not driven by outlier effects. Furthermore, our behavioral results rule out both sampling bias and outlier effects as potential confounds because such changes in perception are simply not susceptible to the sampling bias and outlier effects described above. Crucially, these behavioral results also demonstrate that the observed neural changes are not merely epiphenomenal, but indeed impact visual perception, thus directly addressing prior

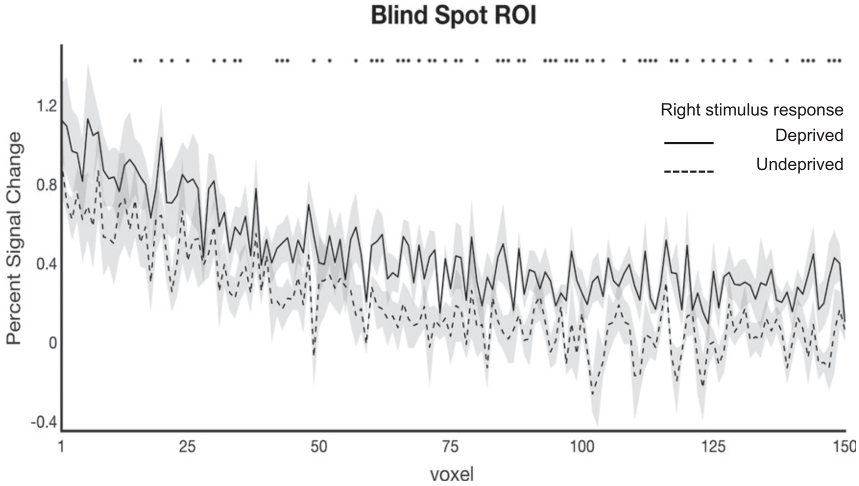

Fig. 4. Volume-selectivity function analysis. Voxels within the BS ROI from Exp. 1A were rank-ordered on selectivity for the BS stimulus relative to fixation, and PSC was calculated for each voxel. Topographic reorganization (i.e., a numerically greater response to the right stimulus during the deprived versus undeprived condition) is reliably observed in all voxels throughout the BS ROI, with a significantly greater response ($P < 0.05$, denoted by an asterisk) observed in 42% (63 of 150) of voxels. Shaded areas show the SEM.

concerns that reports of topographic reorganization in V1 largely reflect trivial or insignificant responses in the deprived cortex (28, 29).

Finally, we rule out the fifth potential alternative explanation of topographic reorganization (i.e., task-specific feedback). Specifically, one previous study in adults with macular degeneration found that a one-back task involving face or motion discrimination on stimuli presented adjacent to the scotoma produced increased activity in the deprived portion of V1, while a simple color-change detection task or passive viewing did not (24). This effect was shown in three of their four macular degeneration participants, with the opposite effect observed in the fourth. The authors then concluded that the mechanism underlying the increased activity in deprived cortex was due to "task-specific feedback," in which no genuine change actually occurred in the deprived cortex, but rather, general top-down signals broadly distributed throughout V1 disproportionately affected deprived cortex due to the mere absence of competing feed-forward inputs in this region. To rule out this possibility in our experiment, we eliminated the requisite one-back task involving face or motion discrimination, and instead used a simple color-change detection task similar to the one used by the study just described, yet we observed topographic reorganization regardless. Thus, the neural results we report cannot be driven by the task-specific feedback described above.

Furthermore, it is also critical to note that the conclusions Masuda et al. (24) assert regarding task-specific feedback warrant additional suspicion. For example, the task-specific effects they observed do not provide strong support for a general top-down mechanism. Such effects could alternatively suggest a top-down component in which feedback signals amplify existing horizontal signals, as shown in nonhuman animals (37, 38), but Masuda et al. (24) dismiss this possibility despite their own apparent supporting evidence. Specifically, if task demands did, in fact, amplify horizontal signals in the deprived cortex, then such task demands would also increase activity throughout V1 (i.e., in nondeprived cortex too), relative to passive viewing (39). Indeed, Masuda et al. (24) found increased activity throughout V1, in both deprived and nondeprived cortex, consistent with the idea that feedback signals amplify existing horizontal connections. Relatedly, if task-specific feedback alone were responsible for activity in the deprived cortex, then such activity should be observed during any task, regardless of stimulus. However, Masuda et al. found no difference in the deprived cortex between passive viewing and a color-change detection task, indicating that task-specific feedback alone is not sufficient to produce activity in the deprived cortex, again rejecting the possibility of a general top-down mechanism. Finally, the authors' claim that so-called reorganization is task-dependent has been directly challenged by three studies that demonstrated topographic reorganization in adult human V1 under passive viewing conditions (20, 23, 25), two other studies that found significant receptive field shifts in the deprived cortex during passive viewing, although they claimed topographic reorganization was absent nonetheless (29, 32), and numerous studies in adult nonhuman animals that demonstrated topographic reorganization under anesthetic conditions, which obviously cannot be explained by task-specific feedback. Therefore, we rule out task-specific feedback as an alternative explanation of neural evidence of topographic reorganization.

In our behavioral experiment, however, participants did perform a stimulus judgment task, which might allow the possibility that task-specific feedback drove these effects, but this seems unlikely for two reasons. First, there is no principled reason to expect that task-specific feedback would produce the perceptual elongations we report, and in fact, the predicted effect of such general top-down signals on perception of our stimuli is not obvious. Second, even if task-specific feedback alone led to perceived elongation of all stimuli when participants are eye-patched, then these same perceptual changes should occur when any bit of cortex is deprived. However, in our second behavioral experiment when the contralateral eye is patched (i.e., the contralateral BS is deprived), stimuli are not perceived as elongated, but rather, the reported perceptual elongations only occurred when stimuli were presented adjacent to the deprived BS. Thus, task-specific feedback cannot explain the perceptual elongations we report here either.

Discussion

Using a noninvasive and reversible method of visual cortical deprivation in healthy adult human participants, we found converging neural and behavioral evidence of rapid topographic reorganization in V1. Crucially, our results comprehensively rule out alternative interpretations of topographic reorganization in adult V1 more generally—namely, 1) recovery from retinal swelling, 2) measurement bias, 3) sampling bias, 4) outlier effects, and 5) task-specific feedback—and therefore represent the strongest evidence to date that topographic reorganization in V1 reflects genuine change.

The neural and behavioral changes reported here are too fast to be the result of the growth of new connections, and also cannot be inherited from changes in the lateral geniculate nucleus in the thalamus, given that the BS is represented in the lateral geniculate nucleus by literal gaps free of neurons (40). Rather, these changes must be mediated by the disinhibition of preexisting connections, consistent with findings from adult nonhuman animals (4, 5, 17–19). Intriguingly, our findings of rapid topographic reorganization dovetail with several prior fMRI studies demonstrating long-term topographic reorganization in adult human V1 during months to years of deprivation (20–25), raising the question of whether the mechanisms underlying rapid cortical change fully account for long-term topographic reorganization (32), or if there are additional changes that continue to occur during months to years of deprivation. Findings from adult nonhuman animals may offer a clue, suggesting that long-term deprivation involves an additional process beyond the initial disinhibition of preexisting connections: The growth of new connections (1, 2). Thus, we hypothesize that topographic reorganization in adult human V1 is driven by two mechanisms: 1) The disinhibition of preexisting connections during short-term deprivation, and 2) the growth of new connections during long-term deprivation, congruent with topographic reorganization in adult nonhuman V1 (2, 19). Crucially, however, further work is necessary to track the same deprived region of V1 over time to determine whether, and how topographic reorganization in adult humans continues to occur during the subsequent days, weeks, months, or even years of deprivation.

Relatedly, the rapid topographic reorganization we observed may be driven by horizontal connections within V1, top-down feedback connections from higher visual areas that contain cortical neurons with larger receptive fields than those in V1, or both. Indeed, in adult nonhuman animals, horizontal connections are responsible for driving topographic reorganization in V1 (1), and furthermore, such horizontal connections have been shown to interact with top-down feedback (37, 38), but whether a similar interaction also occurs in adult humans remains unknown. Regardless, it is crucial to recognize that such a feedback mechanism is distinct from the fifth alternative explanation ruled out in the present study (i.e., task-specific feedback). In the former, the deprived cortex, but not adjacent nondeprived cortex, receives new horizontal or top-down input as a result of disinhibition, representing genuine functional change. In the latter, the deprived cortex does not receive new input, and no genuine changes have actually occurred; instead, the same task-specific signals are broadly distributed throughout V1 before and during deprivation, but these signals appear disproportionately larger in the deprived cortex due to the lack of competing feed-forward inputs to this region (24). Although we believe only the former mechanism could contribute to the rapid topographic reorganization we report here, whether such top-down connections, horizontal connections, or both are actually responsible remains an open question.

To what extent must adult V1 be deprived of its typical input in order for topographic reorganization to occur? In adult nonhuman animals, some studies have observed topographic reorganization following homonymous binocular retinal lesions that completely abolish both visual and spontaneous retinal input (6), whereas other studies have found reorganization using only monocular retinal lesions, in which visual and spontaneous retinal input is only abolished in one eye (17, 41). Our noninvasive method of deprivation is analogous to the latter, because spontaneous retinal input into the cortical representation of the BS remains despite the loss of visual stimulation, but nonetheless, reorganization was still observed. It is also interesting to note here that because this region starts to respond to stimulation outside of the BS following the loss of feed-forward retinal inputs, both in our study and in prior studies (42–45), perhaps the BS representation was never perfectly deprived in these experiments, reflecting the highly flexible responsivity within V1. In fact, this possibility raises the yet unexplored question of what plasticity might look like if a region of adult V1 is additionally, or even alternatively, deprived of its typical horizontal or top-down inputs too.

Next, our behavioral findings bear some resemblance to perceptual filling-in, and it would be parsimonious to posit that topographic reorganization and filling-in share a common mechanism (46). Consistent with this prediction, one study in humans indicates that perceptual filling-in across the BS does occur for stimuli presented to only one side of the BS during deprivation (47), as was done in the present study, and several other studies reported neural responses in the deprived BS representation in V1 for stimuli presented across the BS that are then perceptually filled-in across the BS (42–45). However, it is also worth noting that when the BS is not deprived and stimuli are presented independently to each eye, filling-in still occurs, but stimuli presented to one side of the BS do not elicit activation in the V1 representation of the BS (48), nor are they perceived as elongated toward the BS (27). Furthermore, one other study in humans suggests that there are independent time courses for topographic reorganization and filling-in, where perceptual distortions near an artificial scotoma occurred within 2 s, whereas filling-in of that same scotoma occurred after 15 s in the same subjects (49). Thus, there might still be key differences that distinguish traditional filling-in from the perceptual elongations reported here.

Finally, we wish to highlight a key point of tension regarding the terminology at stake. Classically, the terms "plasticity" and "reorganization" have remained neutral with respect to mechanism, referring to changes in the topography of primary somatosensory (S1) (50), visual (V1) (3), and auditory (A1) (51) cortices. In contrast, a small group has, in recent years, claimed these terms in a more restricted sense, defining them by structural change only (24, 30–32). We adhere to the more traditional usage, in line with the vast majority of studies that have investigated this phenomenon, but also wish to emphasize the importance of substance over semantics for future research.

In conclusion, we present evidence of bona fide topographic reorganization in adult human V1 during short-term deprivation. Still, many questions remain regarding the nature and extent of such topographic reorganization, pointing to exciting avenues for future research. For example, what are the neurotransmitters that mediate the rapid changes reported here? How does topographic reorganization in adulthood relate to developmental cortical plasticity? How do the perceptual and neural changes that occur during deprivation compare to those changes that occur during learning? Whatever the ultimate answers to these questions are, our results highlight the remarkable capacity for V1 to rapidly change in adulthood.

Materials and Methods

Participants. All participants gave informed consent and had normal or corrected-to-normal vision. All procedures were approved by the Emory University Institutional Review Board.

For Exp. 1A (fMRI), eight participants were recruited from Emory University (four females; ages 21 to 39), but two were excluded from due to excessive motion or lack of steady gaze fixation during the scan session. For Exp. 1B (fMRI), four participants were recruited from Emory University (two females; ages 27 to 37), one of whom also completed Exp. 1A.

For Exp. 2A (psychophysics), 34 participants were recruited from Emory University (20 females; ages 18 to 39), 11 of whom also completed the fMRI experiment. For Exp. 2B (psychophysics), 10 participants were recruited from Emory University (8 females; ages 18 to 21). One participant was excluded due to lack of steady gaze fixation during the experiment.

fMRI Procedure. Before entering the scanner, each participant was patched with an opaque 5.7 × 7.9-cm adhesive occlusor over the left eye, an opaque 10 × 10-cm felt cloth placed on top of the occlusor, and a solid black elastic eye patch over the cloth. Inside the scanner, participants again localized the borders of their right eye's BS, as previously described (27), and custom stimuli were generated for each subject immediately upon completion of the BS localization procedure. On average, the size of the BS was 5.1° (width) × 6.0° (height) and was centered 12.8° away from the vertical meridian and 1.1° below the horizontal meridian. Stimuli were 3° × 3° counter phasic checkerboards (spatial frequency = 0.15 cycles per degree; temporal frequency = 8 Hz) and centered either inside the BS or with the closest edge 0.5° peripheral to (i.e., to the right of) the BS in the visual field. Stimuli were presented to the right of the BS because of prior evidence that the greatest magnitude of perceptual change during deprivation occurs in this position (27). All stimuli were generated and presented using custom Matlab code (The MathWorks) and the Psychophysics Toolbox software package (52).

Immediately after BS localization (about 10 min), all participants completed eight runs (i.e., fMRI acquisitions). In Exp. 1A, participants completed four runs while still wearing the eye patch (deprived condition), and four additional runs after patch removal (undeprived condition), with a 10-min rest period between the deprived and undeprived conditions. Participants—without moving their heads—removed the eye patch at the beginning of the rest period while still inside the scanner. Similarly, in Exp. 1B, participants completed four runs while still wearing the eye patch (deprived condition), but then exited the scanner, switched the eye patch to the opposite (i.e., right) eye, and subsequently reentered the scanner to complete four additional runs (undeprived condition), again with a 10-min rest period between the deprived and undeprived conditions.

Each run consisted of 12 16-s blocks of either fixation or stimulus presentation, and block order was counter-balanced within and across all subjects. All eight runs were completed in a single scan session. During all runs, participants completed a target detection task in which they responded via button press each time they saw the flickering checkerboard stimulus become solid green (zero to three times per block). Each participant correctly responded to greater than 95% of all targets during the undeprived condition and responded to greater than 95% of targets to the right of the BS during the deprived condition, confirming that participants were vigilant and attentive to the visible stimuli throughout the scan session. In contrast, participants correctly responded to less than 1% of BS targets during the deprived condition, confirming that the BS was indeed deprived of its normal input. Gaze position was also recorded throughout each run using the in-scanner EyeLink 1000 eye-tracker (SR Research) and runs with less than 80% of collected gaze samples within 2° of the fixation cross were not included in the analysis (4 of 48 runs).

fMRI Scanning and Analysis. All scanning was performed on a 3T Siemens Trio scanner in the Facility for Education and Research in Neuroscience at Emory University (Atlanta, GA). Functional images were acquired using a 32-channel head matrix coil and a gradient-echo single-shot echoplanar imaging sequence (28 slices, TR = 2 s, TE = 30 ms, voxel size = 1.5 × 1.5 × 2 mm, 0.5-mm interslice gap). For all scans, slices were oriented approximately between perpendicular and parallel to the calcarine sulcus, covering all of the occipital and temporal lobes, as well as the lower portion of the parietal lobe. For each participant, whole-brain T1 weighted images (voxel size = 1 × 1 × 1 mm) were also acquired for each participant for registration and anatomical localization. fMRI data analysis was conducted using FSL software (FMRIB's Software Library; https://www.fmrib.ox.ac.uk/fsl) (53) and the FreeSurfer ROI toolbox (FS-FAST; http://surfer.nmr.mgh.harvard.edu). Before statistical analysis, images were motion-corrected using FSL-MCFLIRT (54). Data were then detrended and fit using a double-γ function. Data were not spatially smoothed.

ROI Analysis. Two custom ROIs were defined for each subject: One corresponding to the cortical representation of the BS (BS ROI) and the other corresponding to the area of the visual field immediately peripheral to (i.e., to the right of) the BS (right ROI). Previously, the BS ROI has been defined using a handpicked approach with a constant statistical threshold across subjects (48, 55). However, we observed substantial variability of the BS ROI volume across subjects at any given threshold (56), such that certain subjects' BS ROIs were either absent at conservative thresholds or unreasonably large at liberal thresholds. Thus, to ensure that our results would not be confounded by such variability, especially because overestimating the size of the BS by including areas of cortex that were never deprived of visual input would limit experimental validity, we developed a volume-selectivity function method (35, 36) that allowed us to functionally define ROIs in all subjects and maintain a constant, conservative ROI volume across subjects. Crucially, separate sets of data were always used to define ROIs and test hypotheses.

To define the BS ROI for each participant, we first identified the peak BS voxel (contrast: BS stimulus > fixation) in V1 using two of the four undeprived runs. Second, we centered a 5-mm sphere around the peak voxel, constrained by a probabilistic V1 mask in the subject's native space [FSL Juelich Histological Atlas) (57)]. Third, all voxels in this search sphere were rank-ordered by statistical significance on the same contrast that defined the peak voxel, and then grouped into bins of 50 voxels each. Fourth, we extracted the responses to the BS stimulus in each bin, again using the same pair of undeprived runs that defined the peak BS voxel, as well as the corresponding pair of deprived runs. This entire process was repeated for all possible pairs of runs (i.e., six permutations) for each participant, and responses in each bin were averaged together. Finally, we averaged the responses in each bin across participants, and ultimately determined the BS ROI volume by the final bin in which the group response to the BS stimulus was significantly greater during the undeprived versus deprived condition ($P < 0.01$, Bonferroni-corrected). Accordingly, in all subjects, the BS ROI was defined as the first three bins, corresponding to a constant volume of 150 mm^3 (Fig. 1). Importantly, the anatomic location and volume of this ROI closely matches prior histological and fMRI estimates (48, 55, 56).

To define the right ROI for each participant, the same procedure was used except the search sphere was instead centered around the peak voxel in V1 that corresponded to the right position (contrast: right stimulus > fixation), and the constant volume of the right ROI was instead defined by the final bin in which the average response was significantly greater for the right stimulus versus the BS stimulus during the undeprived condition ($P < 0.01$, Bonferroni-corrected). Consequently, the right ROI was reliably defined in 10 of 11 subjects as the first bin in each right search sphere, corresponding to a volume of 50 mm^3. The right ROI was located adjacent to the BS ROI in V1 (Fig. 1), and is expected to be smaller than the BS ROI because of the relative sizes of these regions in the visual field (right: 3° × 3°; BS: 4° × 6°) and because of cortical magnification in V1.

To test our hypotheses, we calculated the responses to the deprived and undeprived conditions in each ROI as percent signal change (PSC) relative to fixation. As stated above, PSC values were always calculated using an independent set of data from those used to define the ROI.

Psychophysical Experiments. All participants completed an abbreviated version of a previously reported square judgment task (27). First, all participants localized the right eye's BS. On average, the size of the BS was 4.7° (width) × 5.3° (height) and was centered 14.3° away from the vertical meridian and 1.1° below the horizontal meridian. In Exp. 2A, participants then completed one run while still wearing the patch on the left eye (deprived condition), followed by another run without the patch (undeprived condition), with a 10-min rest period between the deprived and undeprived runs. In Exp. 2B, participants completed one run with a patch on the left eye (deprived condition), followed by one run with a patch on the right eye (undeprived condition). While maintaining gaze on a fixation cross at the left edge of the screen, participants judged the height (shorter than a square, square, taller than a square) of solid white rectangle stimuli (2° width × 1.5°, 1.75°, 2°, 2.25°, or 2.5° height) presented for 150 ms against a solid black background in each of four locations (left, right, top, bottom) around the BS with 0.5° spacing between the closest edge of the rectangle and the calculated border of the BS (to ensure visibility of this edge) in the visual field. Each run consisted of 320 trials. Gaze position was recorded using the EyeLink 1000 eyetracker (SR Research) and the analysis only included trials in which gaze position was within 2° of the fixation cross. Each participant successfully maintained fixation for more than 90% of all trials. Finally, the method of probits was used to identify the point of subjective equality (PSE)—that is, the 50% point on the psychometric function—for both the undeprived and deprived conditions separately, collapsing across all four locations around the BS, as previously described (27). A negative PSE indicates elongation, whereas a positive PSE indicates truncation. This analysis also identified the 95% CI around each PSE, and the two PSEs were considered significantly different if the confidence intervals did not overlap.

Data Availability Statement. All datasets generated in this study are available to readers at https://osf.io/2qdkf.

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1. C. D. Gilbert, W. Li, Adult visual cortical plasticity. *Neuron* **75**, 250–264 (2012).
2. R. P. Sammons, T. Keck, Adult plasticity and cortical reorganization after peripheral lesions. *Curr. Opin. Neurobiol.* **35**, 136–141 (2015).
3. J. H. Kaas *et al*., Reorganization of retinotopic cortical maps in adult mammals after lesions of the retina. *Science* **248**, 229–231 (1990).
4. C. D. Gilbert, T. N. Wiesel, Receptive field dynamics in adult primary visual cortex. *Nature* **356**, 150–152 (1992).
5. C. Darian-Smith, C. D. Gilbert, Topographic reorganization in the striate cortex of the adult cat and monkey is cortically mediated. *J. Neurosci.* **15**, 1631–1647 (1995).
6. C. Darian-Smith, C. D. Gilbert, Axonal sprouting accompanies functional reorganization in adult cat striate cortex. *Nature* **368**, 737–740 (1994).
7. Y. M. Chino, E. L. Smith 3rd, J. H. Kaas, Y. Sasaki, H. Cheng, Receptive-field properties of deafferentated visual cortical neurons after topographic map reorganization in adult cats. *J. Neurosci.* **15**, 2417–2433 (1995).
8. A. Das, C. D. Gilbert, Receptive field expansion in adult visual cortex is linked to dynamic changes in strength of cortical connections. *J. Neurophysiol.* **74**, 779–792 (1995).
9. L. M. Schmid, M. G. Rosa, M. B. Calford, J. S. Ambler, Visuotopic reorganization in the primary visual cortex of adult cats following monocular and binocular retinal lesions. *Cereb. Cortex* **6**, 388–405 (1996).
10. M. B. Calford, L. L. Wright, A. B. Metha, V. Taglianetti, Topographic plasticity in primary visual cortex is mediated by local corticocortical connections. *J. Neurosci.* **23**, 6434–6442 (2003).
11. D. V. Giannikopoulos, U. T. Eysel, Dynamics and specificity of cortical map reorganization after retinal lesions. *Proc. Natl. Acad. Sci. U.S.A.* **103**, 10805–10810 (2006).
12. T. Keck *et al*., Massive restructuring of neuronal circuits during functional reorganization of adult visual cortex. *Nat. Neurosci.* **11**, 1162–1167 (2008).
13. G. Palagina, U. T. Eysel, D. Jancke, Strengthening of lateral activation in adult rat visual cortex after retinal lesions captured with voltage-sensitive dye imaging in vivo. *Proc. Natl. Acad. Sci. U.S.A.* **106**, 8743–8747 (2009).
14. E. P. Botelho, C. Ceriatte, J. G. Soares, R. Gattass, M. Fiorani, Quantification of early stages of cortical reorganization of the topographic map of V1 following retinal lesions in monkeys. *Cereb. Cortex* **24**, 1–16 (2014).
15. S. A. Marik, H. Yamahachi, S. Meyer zum Alten Borgloh, C. D. Gilbert, Large-scale axonal reorganization of inhibitory neurons following retinal lesions. *J. Neurosci.* **34**, 1625–1632 (2014).
16. H. Abe *et al*., Adult cortical plasticity studied with chronically implanted electrode arrays. *J. Neurosci.* **35**, 2778–2790 (2015).
17. L. M. Schmid, M. G. Rosa, M. B. Calford, Retinal detachment induces massive immediate reorganization in visual cortex. *Neuroreport* **6**, 1349–1353 (1995).
18. Y. M. Chino, J. H. Kaas, E. L. Smith 3rd, A. L. Langston, H. Cheng, Rapid reorganization of cortical maps in adult cats following restricted deafferentation in retina. *Vision Res.* **32**, 789–796 (1992).
19. T. Keck *et al*., Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex. *Neuron* **71**, 869–882 (2011).
20. C. I. Baker, D. D. Dilks, E. Peli, N. Kanwisher, Reorganization of visual processing in macular degeneration: Replication and clues about the role of foveal loss. *Vision Res.* **48**, 1910–1919 (2008).
21. D. D. Dilks, C. I. Baker, E. Peli, N. Kanwisher, Reorganization of visual processing in macular degeneration is not specific to the "preferred retinal locus". *J. Neurosci.* **29**, 2768–2773 (2009).
22. D. D. Dilks, J. B. Julian, E. Peli, N. Kanwisher, Reorganization of visual processing in age-related macular degeneration depends on foveal loss. *Optom. Vis. Sci.* **91**, e199–e206 (2014).

23. C. I. Baker, E. Peli, N. Knouf, N. G. Kanwisher, Reorganization of visual processing in macular degeneration. *J. Neurosci.* **25**, 614–618 (2005).
24. Y. Masuda, S. O. Dumoulin, S. Nakadomari, B. A. Wandell, V1 projection zone signals in human macular degeneration depend on task, not stimulus. *Cereb. Cortex* **18**, 2483–2493 (2008).
25. E. H. Schumacher *et al*., Reorganization of visual processing is related to eccentric viewing in patients with macular degeneration. *Restor. Neurol. Neurosci.* **26**, 391–402 (2008).
26. D. D. Dilks, J. T. Serences, B. J. Rosenau, S. Yantis, M. McCloskey, Human adult cortical reorganization and consequent visual distortion. *J. Neurosci.* **27**, 9585–9594 (2007).
27. D. D. Dilks, C. I. Baker, Y. Liu, N. Kanwisher, "Referred visual sensations": Rapid perceptual elonvgation after visual cortical deprivation. *J. Neurosci.* **29**, 8960–8964 (2009).
28. S. M. Smirnakis *et al*., Lack of long-term cortical reorganization after macaque retinal lesions. *Nature* **435**, 300–307 (2005).
29. H. A. Baseler *et al*., Large-scale remapping of visual cortex is absent in adult humans with macular degeneration. *Nat. Neurosci.* **14**, 649–655 (2011).
30. B. A. Wandell, S. M. Smirnakis, Plasticity and stability of visual field maps in adult primary visual cortex. *Nat. Rev. Neurosci.* **10**, 873–884 (2009).
31. K. V. Haak, A. B. Morland, S. A. Engel, Plasticity, and its limits, in adult human primary visual cortex. *Multisens. Res.* **28**, 297–307 (2015).
32. B. Barton, A. A. Brewer, fMRI of the rod scotoma elucidates cortical rod pathways and implications for lesion measurements. *Proc. Natl. Acad. Sci. U.S.A.* **112**, 5201–5206 (2015).
33. J. C. Horton, D. R. Hocking, Monocular core zones and binocular border strips in primate striate cortex revealed by the contrasting effects of enucleation, eyelid suture, and retinal laser lesions on cytochrome oxidase activity. *J. Neurosci.* **18**, 5433–5455 (1998).
34. M. B. Calford *et al*., Neuroscience: Rewiring the adult brain. *Nature* **438**, E3, discussion E3–E4 (2005).
35. F. S. Kamps, E. J. Morris, D. D. Dilks, A face is more than just the eyes, nose, and mouth: fMRI evidence that face-selective cortex represents external features. *Neuroimage* **184**, 90–100 (2019).
36. S. V. Norman-Haignere *et al*., Pitch-responsive cortical regions in congenital amusia. *J. Neurosci.* **36**, 2986–2994 (2016).
37. C. D. Gilbert, M. Sigman, Brain states: Top-down influences in sensory processing. *Neuron* **54**, 677–696 (2007).
38. H. Liang *et al*., Interactions between feedback and lateral connections in the primary visual cortex. *Proc. Natl. Acad. Sci. U.S.A.* **114**, 8637–8642 (2017).
39. A. C. Huk, D. J. Heeger, Task-related modulation of visual cortex. *J. Neurophysiol.* **83**, 3525–3536 (2000).
40. J. H. Kaas, R. W. Guillery, J. M. Allman, Discontinuities in the dorsal lateral geniculate nucleus corresponding to the optic disc: A comparative study. *J. Comp. Neurol.* **147**, 163–179 (1973).
41. M. B. Calford, L. M. Schmid, M. G. Rosa, Monocular focal retinal lesions induce short-term topographic plasticity in adult cat visual cortex. *Proc. Biol. Sci.* **266**, 499–507 (1999).
42. M. Fiorani Júnior, M. G. Rosa, R. Gattass, C. E. Rocha-Miranda, Dynamic surrounds of receptive fields in primate striate cortex: A physiological basis for perceptual completion? *Proc. Natl. Acad. Sci. U.S.A.* **89**, 8547–8551 (1992).
43. M. Matsumoto, H. Komatsu, Neural responses in the macaque v1 to bar stimuli with various lengths presented on the blind spot. *J. Neurophysiol.* **93**, 2374–2387 (2005).
44. H. Komatsu, M. Kinoshita, I. Murakami, Neural responses in the retinotopic representation of the blind spot in the macaque V1 to stimuli for perceptual filling-in. *J. Neurosci.* **20**, 9310–9319 (2000).
45. H. Komatsu, I. Murakami, M. Kinoshita, Surface representation in the visual system. *Brain Res. Cogn. Brain Res.* **5**, 97–104 (1996).
46. V. S. Ramachandran, Filling in the blind spot. *Nature* **356**, 115 (1992).
47. Y. Araragi, H. Ito, S. Sunaga, Perceptual filling-in of a line segment presented on only one side of the blind spot. *Spat. Vis.* **22**, 339–353 (2009).
48. H. Awater, J. R. Kerlin, K. K. Evans, F. Tong, Cortical representation of space around the blind spot. *J. Neurophysiol.* **94**, 3314–3324 (2005).
49. M. K. Kapadia, C. D. Gilbert, G. Westheimer, A quantitative measure for short-term cortical plasticity in human vision. *J. Neurosci.* **14**, 451–457 (1994).
50. M. M. Merzenich *et al*., Topographic reorganization of somatosensory cortical areas 3b and 1 in adult monkeys following restricted deafferentation. *Neuroscience* **8**, 33–55 (1983).
51. W. Mühlnickel, T. Elbert, E. Taub, H. Flor, Reorganization of auditory cortex in tinnitus. *Proc. Natl. Acad. Sci. U.S.A.* **95**, 10340–10343 (1998).
52. D. H. Brainard, The psychophysics toolbox. *Spat. Vis.* **10**, 433–436 (1997).
53. M. Jenkinson, C. F. Beckmann, T. E. Behrens, M. W. Woolrich, S. M. Smith, FSL. *Neuroimage* **62**, 782–790 (2012).
54. M. Jenkinson, P. Bannister, M. Brady, S. Smith, Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage* **17**, 825–841 (2002).
55. F. Tong, S. A. Engel, Interocular rivalry revealed in the human cortical blind-spot representation. *Nature* **411**, 195–199 (2001).
56. R. B. Tootell *et al*., Functional analysis of primary visual cortex (V1) in humans. *Proc. Natl. Acad. Sci. U.S.A.* **95**, 811–817 (1998).
57. K. Amunts, A. Malikovic, H. Mohlberg, T. Schormann, K. Zilles, Brodmann's areas 17 and 18 brought into stereotaxic space-where and how variable? *Neuroimage* **11**, 66–84 (2000).