response across orientations. OSI was extremely low for PV cells (0.1 ± 0.1; n = 63), significantly lower than in Pyr cells (0.4 ± 0.2; n = 60; $p < 1 \times 10^{-11}$ Wilcoxon rank-sum test; Figure 1). Only 3% of PV cells, as compared to 65% of Pyr cells, had an OSI > 0.25 (Figure 1D). Furthermore PV cells were more broadly tuned than Pyr cells. To estimate the tuning sharpness we calculated the half width at half height (HWHH) of a double Gaussian fit to the tuning curve of each cell; PV cells: 52 ± 24 degrees; n = 63; Pyr cells: 42 ± 23 degrees; n = 60; $p < 0.05$). Finally, the contrast response function of PV cells differed in two clear ways from that of Pyr cells (Figure 1D). First, the maximal firing rate was two times higher for PV cells than for Pyr cells (9.1 ± 5.6 spikes/s; n = 43; versus 4.5 ± 3.0 spikes/s; n = 30). Second, the increase in firing rate of PV cells with increasing contrast, captured by the exponent of the curve fitted to contrast responses, for PV cells was significantly shallower than for Pyr cells (2 ± 2; n = 43; versus 3.0 ± 2.5; n = 30; $p < 0.005$). Thus, in contrast to a previous report (Runyan et al., 2010) the response properties to visual stimuli of PV cells differ markedly from those of Pyr cells.

Bidirection Control of PV Cell Activity

Next, we assessed the impact of optogenetic manipulation on the visual responses of PV cells. We recorded from Arch- or ChR2-expressing layer 2/3 PV cells at least two weeks after viral injection and illuminated the exposed cortex with a fiber-coupled LED (470 nm, Figure 2). Since strong suppression of inhibition can result in runaway activity (Prince, 1978) and strong activation of PV cells can completely silence cortical activity (not shown), we perturbed PV cell firing over a moderate range chosen to fall within the reported firing rates of these neurons in active awake mice (Niell and Stryker, 2010). Control measurements in uninjected animals established that illumination by itself did not affect visual responses (Figure S5).

Photo stimulation of Arch significantly reduced the firing rate of targeted PV cells, both spontaneous (from 3.0 ± 3.5 to 1.9 ± 3.4 spikes/s; n = 31; $p < 0.02$ paired Wilcoxon sign-rank test) and visually evoked (from 9.2 ± 7.3 to 6.6 ± 7.0 spikes/s; n = 31; $p < 0.0001$; Figure S2A). PV cell firing rate decreased at all contrasts tested (Figure 2D) and was well described by a linear fit (0.6 × control rate − 0.4 spikes/s). Thus, PV cell firing rates decreased by approximately the same factor, 0.6, minus an offset, 0.4 spikes/s, regardless of stimulus contrast (Figure 2D).

Photo stimulation of ChR2-expressing PV cells had the diametrically opposite effect, increasing both their spontaneous firing (from 3.0 ± 3.8 to 5.8 ± 6.1 spikes/s; n = 16; $p < 0.01$) and their visually evoked firing (from 13.6 ± 13.2 to 18.0 ± 15.1 spikes/s; n = 16; $p < 0.01$; Figure S2B). As for Arch-mediated suppression of PV cells, the fractional increase in PV cell firing rate with ChR2 was similar for all presented contrasts (linear fit: 1.2 × control rate + 2.0 spikes/s; Figure 2E).

Thus, we could bidirectionally modulate visually evoked activity of PV cells by approximately the same factor, plus a small offset, independently of how strongly these neurons were driven by the visual stimulus.

PV Cells Tightly Control Visual Responses of Pyr Cells

To assess how PV cell activity impacts cortical responses to visual stimuli, we asked how their suppression or activation changes the visual responses of layer 2/3 Pyr cells. We concentrated on three response attributes: response to contrast, overall selectivity for orientation and direction, and sharpness of tuning.

Optogenetic modulation of PV cell activity strongly affected the response of Pyr cells to visual stimuli. Suppressing PV cell activity by photo stimulating Arch led to an increase in the spike rate of Pyr cells (change in firing rate: 0.8 ± 1.5 spikes/s; 73% ± 85%; n = 43 cells; $p < 0.005$; Figure S2C). This increase was again well described as a linear transformation (1.4 × control rate + 0.3 spikes/s) independently of the contrast tested (Figure 2F). Complementarily, activating PV cells by photo stimulating ChR2 resulted in decreased Pyr cell spike rates (change in firing rate: −3.7 ± 2.2 spikes/s; −38% ± 30%; n = 19 cells, $p < 0.005$; Figure S2D), again at all contrasts tested (0.7 × control rate − 0.3 spikes/s; Figure 2G).

These results indicate that PV cells tightly control the response of Pyr cells, and they do so in a manner that is independent of stimulus contrast. Indeed, manipulation of PV cell activity scaled the response of Pyr cells, with little effect on the shape of their contrast responses curves. PV cells, therefore, control the response but not the contrast sensitivity of Pyr cells.

PV Cells Only Modestly Impact Pyr Cell Orientation Tuning

Despite the strong influence of PV cells on the firing rate of Pyr cells, bidirectional modulation of PV cell activity only modestly impacted the tuning of Pyr cells for stimulus orientation. Suppression of PV cells with Arch increased Pyr responses to all stimulus orientations (Figure 3A), and activation of PV cells with ChR2 suppressed Pyr responses to all orientations (Figure 3B). Neither manipulation, however, had much of an effect on the shape of Pyr cell tuning curves (see e.g., normalized tuning curves in Figures 3A and 3B). Indeed, the changes in PV activity had hardly had any impact on the relative responses of Pyr cells to each grating direction (Pearson's correlation = 0.8 ± 0.2; n = 45).

Accordingly, PV cell suppression or activation caused only modest changes in the overall selectivity of Pyr cells. Suppression of PV cells with Arch stimulation caused an increase in Pyr firing rate at all orientations. In relative terms, however, it increased responses less at the preferred orientation than at the orthogonal orientation. This resulted in a small but significant decrease of the OSI by −0.06 ± 0.08 (n = 31 Pyr cells; $p < 0.001$; Figure 3C; 13/31 individual cells showed significant changes in OSI). Activation of PV cells with ChR2 led to the opposite effect: a modest (but significant) increase in the OSI of Pyr cells (mean change in OSI: 0.07 ± 0.07; n = 14 cells; $p < 0.003$; 7/14 individual cells showed significant changes; Figure 3B).

These small changes in overall selectivity depended systematically on the change in Pyr cell firing rate caused by PV cell perturbation. A linear regression of the percentage change in spiking response at the preferred orientation versus OSI revealed a highly significant correlation ($r = -0.6$; n = 45 cells; $p < 0.0001$; Figure 3C). In other words, the Pyr cells that displayed the greatest increase in response also experienced the largest decrease in OSI. Conversely, the Pyr cells that displayed the greatest decrease in response experienced the largest increase in OSI. This said, the changes in OSI were minor even