



**Figure 4. Effects of VIP activation are strongest in layer 4.**

**A.** Mean sound modulation index during laser-on and laser-off trials, across cortical layers. VIP activation significantly suppressed modulation of neural activity by sound in layer 4, but not other layers. L2/3 laser-off  $0.51 \pm 0.04$ , laser-on  $0.47 \pm 0.05$ ,  $n = 22$ ; L4 laser-off  $0.45 \pm 0.04$ , laser-on  $0.28 \pm 0.07$ ,  $n = 34$ ; L5 laser-off  $0.44 \pm 0.02$ , laser-on  $0.44 \pm 0.02$ ,  $n = 122$ ; L6 laser-off  $0.67 \pm 0.03$ , laser-on  $0.64 \pm 0.03$ ,  $n = 45$ ;  $\chi^2 = 14.47$ ,  $p = 0.0023$ , post-hoc signed-rank for L4 (MI laser-on vs laser-off)  $p = 0.001$ ;  $r = 0.40$ ).

**B.** The effect of VIP activation on sound modulation in layer 4 was driven by evoked activity in narrow-spiking neurons. Laser effect is the difference in evoked activity between laser-on and laser-off trials, normalized to each cell's peak laser-off firing rate. Evoked activity in layer 4 narrow-spiking cells was significantly suppressed by VIP activation (NS:  $\chi^2 = 11.75$ ,  $p = 0.008$ ,  $n = 73$ ).

**C.** Laser effect for spontaneous activity was similar across all cortical layers (NS:  $\chi^2 = 4.12$ ,  $p = 0.24$ ,  $n = 73$ ).

**D.** Depth distribution of cells that were either suppressed or disinhibited by VIP activation, for evoked activity. Peak density of disinhibited cells was in layer 5; suppressed cells showed an additional peak in layer 4 (arrow).

**E.** Depth distributions of suppressed and disinhibited cells for spontaneous activity were similar to each other. Peak densities were in layer 5.