Multimodal synaptic integration in the mouse posterior parietal cortex is modality- and cell type-specific

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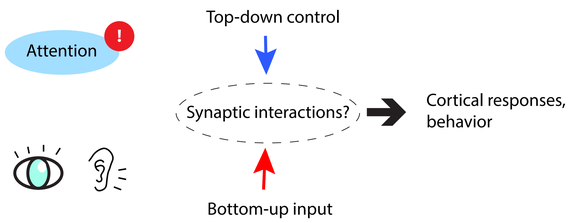
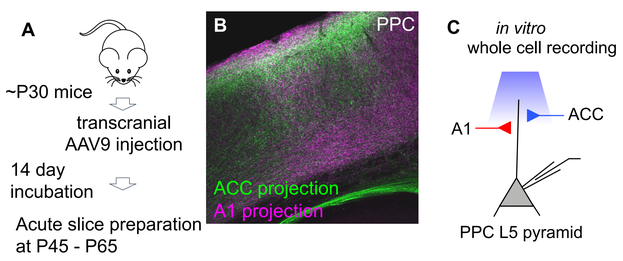
Background

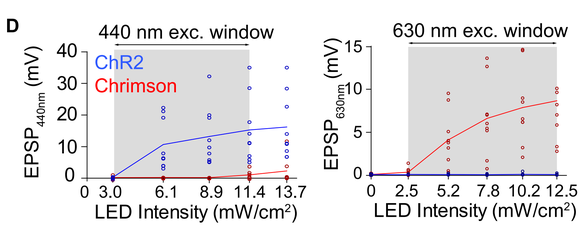
Cognitive control of sensory processing has important consequences for animal behavior.

Top-down input can enhance both cortical and behavioral responses, yet any description of a synaptic interaction of cognitive and sensory information streams remains undescribed.



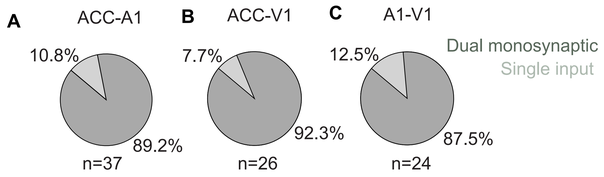
Independent control of long-range PPC inputs by dual-color optogenetics in acute slices





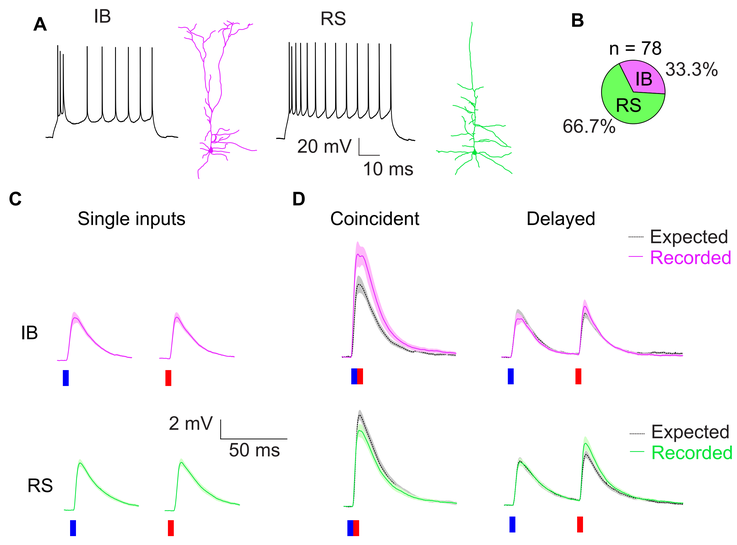
A. Timeline of injections for acute slice experiments. **B.** Anterior cingulate cortex (ACC) and primary auditory cortex (A1) afferents to PPC. **C.** Diagram of acute slice recording. PPC afferents express either a blue-sensitive channelrhodopsin ChR2 or a red-sensitive channelrhodopsin Chrimson. **D.** LED stimulation of PPC afferents expressing either ChR2 or Chrimson by 440 nm (left) or 630 nm (right). Shaded grey areas represent excitation windows with minimal cross-activation of opsins.

Majority of deep layer PPC neurons recieve dual monosynaptic input from frontal, visual, and auditory cortices



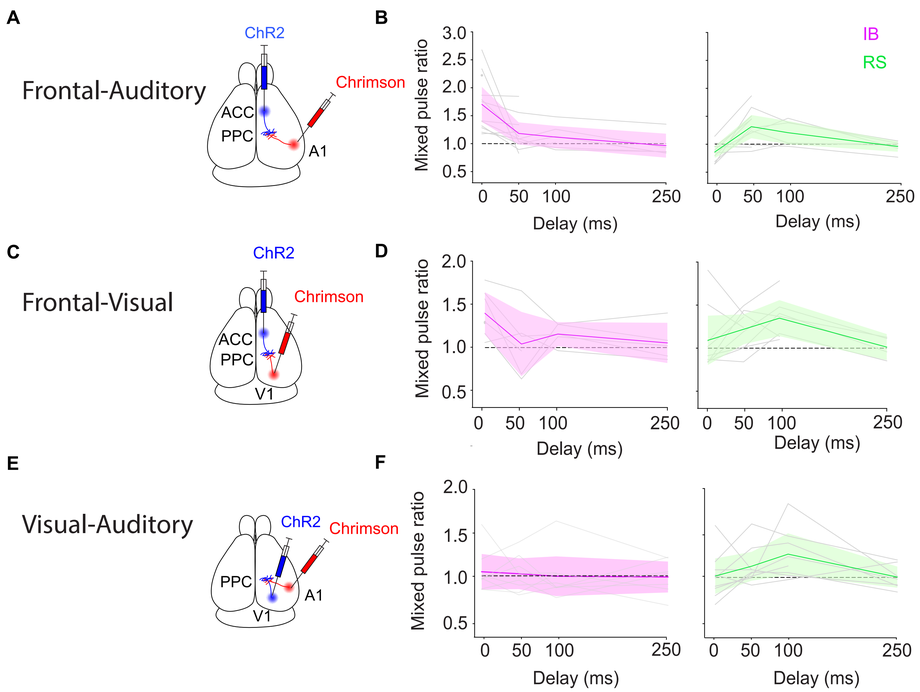
Percent of layer 5 pyramidal cells receiving dual monosynaptic input from ACC and A1 (A), ACC and V1 (B), or A1 and ACC (C). Monosynapticity was determined by TTX/4-AP recovery and EPSP latency. If the after-stimulus latency to EPSP was greater than 4ms cells were judged to be disynaptically connected.

Cell type-specific coincidence detection and temporal integration of frontal-sensory synaptic inputs



A. Representative firing pattern and morphology of intrinsically bursting (IB) and regular spiking (RS) cells. **B.** Percent distribution of IB vs. RS cells in PPC. **C.** Average IB and RS cell postsynaptic EPSP responses ± SEM to ACC (blue) and A1 (red) optogenetic stimulation. **D.** Supralinear enhancement of coincident inputs in IB cells. Coincident inputs are sublinear in RS cells, with supralinear integration of delayed inputs.

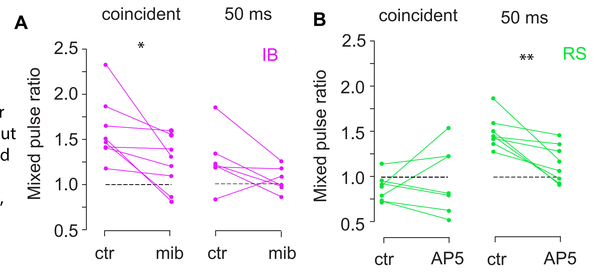
Coincident enhancement is restricted to frontal-sensory input combinations and absent in sensory-sensory integration



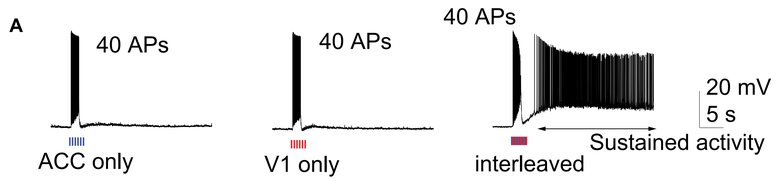
A. Schematic of injections into ACC and A1. **B.** Temporal dynamics of integration. Mixed pulse ratio is calculated as the recorded mixed pulse / expected single pulse response. A mixed pulse ratio of 1.0 represents linear integration of inputs. Grey lines represent individual mice. Colored lines represent cell-type averages ± SEM to frontal-auditory synaptic input. **C.** Schematic of injections into ACC and V1. **D.** Same as (C) but for frontal-visual synaptic input. **E.** Schematic of injections into V1and A1. **D.** Same as (C) but for visual-auditory synaptic input.

Coincidence detection in IB cells mediated by R,T,L-type Ca^{2+} channels while temporal integration in RS cells mediated by NMDA receptors

A. Coincident enhancement in IB cells is largely abolished by the R,T,L-type calcium channel blocker mibefradil (20 uM). **B.** Delayed input enhancement of RS cells is reduced by the NMDA receptor antagonist AP5 (50 uM). Paired t test, *p<0.05, **p<0.01.

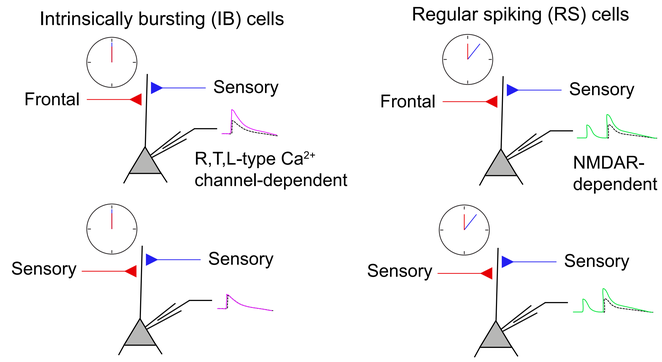


Persistent firing in PPC initiated by combination of frontal-sensory synaptic input



A. Repetitive 20 Hz optogenetic stimulation of ACC or V1 fibers in PPC slices in carbachol-cointaining ACSF is insufficient to induce sustained activity. Interleaved stimulation of ACC and V1 fibers initiates a robust period of persistent firing for several seconds.

Graphic Summary



- Dual-color optogenetics allows independent control of input afferents
- Intrinsically bursting neurons act as coincidence detectors and enhance simulatenous frontal-sensory inputs
- Coincidence detection in IB cells is mediated by an R,T,L-type calcium conductance
- Regular spiking neurons act as temporal integrators and enhance delayed frontal-sensory inputs
- Temporal integration in RS cells is mediated by an NMDA receptor conductance
- Multimodal synaptic interactions of intrinsically bursting neurons is restricted to frontal-sensory input combinations
- Sustained activity in PPC is initiated only by a combination of frontal and sensory synaptic inputs

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