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**Parvalbumin neurons and gamma rhythms enhance cortical circuit performance.**

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**Public Summary:**

Synchronized oscillations and inhibitory interneurons have important and interconnected roles within cortical microcircuits. In particular, interneurons defined by the fast-spiking phenotype and expression of the calcium-binding protein parvalbumin have been suggested to be involved in gamma (30-80 Hz) oscillations, which are hypothesized to enhance information processing. However, because parvalbumin interneurons cannot be selectively controlled, definitive tests of their functional significance in gamma oscillations, and quantitative assessment of the impact of parvalbumin interneurons and gamma oscillations on cortical circuits, have been lacking despite potentially enormous significance (for example, abnormalities in parvalbumin interneurons may underlie altered gamma-frequency synchronization and cognition in schizophrenia and autism). Here we use a panel of optogenetic technologies in mice to selectively modulate multiple distinct circuit elements in neocortex, alone or in combination. We find that inhibiting parvalbumin interneurons suppresses gamma oscillations in vivo, whereas driving these interneurons (even by means of non-rhythmic principal cell activity) is sufficient to generate emergent gamma-frequency rhythmicity. Moreover, gamma-frequency modulation of excitatory input in turn was found to enhance signal transmission in neocortex by reducing circuit noise and amplifying circuit signals, including inputs to parvalbumin interneurons. As demonstrated here, optogenetics opens the door to a new kind of informational analysis of brain function, permitting quantitative delineation of the functional significance of individual elements in the emergent operation and function of intact neural circuitry.

**Scientific Abstract:**

Synchronized oscillations and inhibitory interneurons have important and interconnected roles within cortical microcircuits. In particular, interneurons defined by the fast-spiking phenotype and expression of the calcium-binding protein parvalbumin have been suggested to be involved in gamma (30-80 Hz) oscillations, which are hypothesized to enhance information processing. However, because parvalbumin interneurons cannot be selectively controlled, definitive tests of their functional significance in gamma oscillations, and quantitative assessment of the impact of parvalbumin interneurons and gamma oscillations on cortical circuits, have been lacking despite potentially enormous significance (for example, abnormalities in parvalbumin interneurons may underlie altered gamma-frequency synchronization and cognition in schizophrenia and autism). Here we use a panel of optogenetic technologies in mice to selectively modulate multiple distinct circuit elements in neocortex, alone or in combination. We find that inhibiting parvalbumin interneurons suppresses gamma oscillations in vivo, whereas driving these interneurons (even by means of non-rhythmic principal cell activity) is sufficient to generate emergent gamma-frequency rhythmicity. Moreover, gamma-frequency modulation of excitatory input in turn was found to enhance signal transmission in neocortex by reducing circuit noise and amplifying circuit signals, including inputs to parvalbumin interneurons. As demonstrated here, optogenetics opens the door to a new kind of informational analysis of brain function, permitting quantitative delineation of the functional significance of individual elements in the emergent operation and function of intact neural circuitry.