Digital versus analog control over cortical inhibition

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In the cerebral cortex, the balance between excitation (pyramidal neurons) and inhibition (interneurons) is thought to be mediated by the primary mode of neuronal communication: "all-or-none" action potentials, or spikes. However, Dr. Yousheng Shu's research group at the Institute of Neuroscience of Chinese Academy of Sciences has discovered a new strategy by which the cortex can maintain this balance, by showing that the amount of inhibition depends on the membrane potentials (Vm) in pyramidal cells, which represents an "analog" strategy. Their results will be published next week in the online, open access journal *PLoS Biology*.

The cortex consists of recurrent networks, where pyramidal cells send action potentials down their axons to excite interneurons, which in turn inhibit the pyramidal cells through disynaptic inhibitory postsynaptic potentials (IPSPs). This back-and-forth process serves to keep a stable excitation/inhibition ratio critical for proper cortical function. In the classic view, these action potentials are delivered if and only if the Vm crosses a certain threshold and are invariable in their shape, which is the all-or-none fashion of rapid neuron-to-neuron communication. But is there an analog component?

Using paired recording from two pyramidal cells within a recurrent circuit, Dr. Shu and colleagues discovered that a slight positive shift (depolarization) in Vm of the first pyramidal cell could increase the disynaptic IPSPs received by the second one. In other words, this study provides the first evidence demonstrating that an analog change of excitation can regulate feedback inhibition, with the information carriers no longer stereotyped.

"This type of regulation could be a key mechanism for the cortex to maintain a dynamic balance of excitation and inhibition, and generate appropriate cortical rhythms under different behavioral states," said Dr. Shu, "It may also play an important role in preventing abnormal cortical activities including epileptiform activity during seizures."

Therefore, future studies may focus on whether the Vm-dependent modulation of inhibition has an impact on information processing under both normal and pathological conditions, and whether the analog signaling influences the operation of other cortical circuits. Nevertheless, to what extent these findings may influence the conceptual framework of a "digital brain" is still open to further computational and theoretical investigation.

More information: Zhu J, Jiang M, Yang M, Hou H, Shu Y (2011) Membrane Potential-Dependent Modulation of Recurrent Inhibition in Rat Neocortex. PLoS Biol 9(3): e1001032. doi:10.1371/journal.pbio.1001032

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