Neurons work like a chain of dominos to control action sequences (w/ Video)

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(PhysOrg.com) -- As anyone who as ever picked up a guitar or a tennis racket knows, precise timing is often an essential part of performing complex tasks. Now, by studying the brain circuits that control bird song, MIT researchers have identified a "chain reaction" of brain activity that appears to control the timing of song.

The song of the zebra finch is very stereotypic; each song lasts about 1 second, and consists of multiple syllables whose timing is almost precisely the same from one performance to the next. "It's a great model system for studying how the brain controls actions", says Michale Fee, senior author of the study and a member of the McGovern Institute for Brain Research.

The brain structures involved in bird song production have been identified, and Fee and colleagues had previously shown that the tempo of the song is controlled by a brain area known as HVC. During the 1-second song, individual neurons in HVC fire just one short burst of activity at a precise time point within the song. Different neurons fire at different times, so the activity of these neurons represents a 'time stamp' that causes the correct instructions to be sent to the vocal organs at each instant within the song.

But how does each HVC neuron know when to fire with such perfect timing? Several different ideas have been proposed, but one especially appealing idea is the "synfire chain" model, in which neurons fire in a chain reaction – each one triggering the next in the sequence, like a cascade of falling dominos.

In a new study, which appears in the October 24 online issue of *Nature,* Fee and colleagues have now tested this idea using intracellular recordings, an approach that can record tiny voltage fluctuations in individual HVC neurons. In a technical tour-de-force, they developed a method in which these recordings could be made while the bird was freely moving around his cage and engage in natural behaviors such as singing.

Their results support the chain of dominoes model. When individual HVC neurons fire, they do so suddenly, as if hit by the preceding domino. There was no prior build-up of activity; instead, each neuron remained silent until its turn came to fire, at which point it showed a sudden burst of activity, presumably caused by excitatory input from the previous neuron in the chain. In further experiments, the authors showed that this burst of activity is triggered suddenly by an all-or-none influx of calcium through specialized membrane channels that open in response to this excitatory input.

The MIT researchers also showed that the timing of neural bursts in HVC neurons is not easily disturbed by small electrical perturbations. That's important, explains first author Michael Long, who is now at New York University's Langone Medical Center. "If one neuron made a mistake in its timing, every subsequent neuron down the chain would also be off. It would be like a musician with no sense of rhythm."

"This is the first time we've been able to understand the generation of a learned behavioral sequence", says Fee. "We predict that similar mechanisms probably exist in other brains, including our own."

More information: "Support for a synaptic chain model of neuronal sequence generation," Long MA, Jin DZ, Fee MS. *Nature*. 24 Oct 2010.

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