Streamlining brain signals for speed and efficacy

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Life exists at the edge of chaos, where small changes can have striking and unanticipated effects, and major stimuli may go unheard. But there is no space for ambiguity when the brain needs to transform head motion into precise eye, head, and body movements that rapidly stabilize our posture and gaze; otherwise, we would stumble helplessly through the world, and our vision would resemble an undecipherable blur.

In their latest study, published in the current issue of the journal *Neuron*, researchers at the Salk Institute for Biological Studies explain how the vestibular-ocular reflex, which keeps us and the world around us stable, achieves the accuracy it is famous for. Unlike most signals in the brain, whose transmission is frequency-dependent, signals from the vestibular system of the inner ear, which detects motion, are relayed in a linear fashion no matter how fast the neurons are firing.

"Most of what we know about signal transmission between neurons comes from studying special cortical or hippocampal neurons, but many vital functions, such as balance and breathing, are controlled by neurons in the brain stem, which, as we discovered, work very differently," says Howard Hughes Medical Institute investigator Sascha du Lac, Ph.D., an associate professor in the Systems Neurobiology Laboratory. "Pursuing the mechanisms that control neurons in the brain stem is important for developing new classes of biotherapeutic agents."

Du Lac and her team focus on a simple type of learning: How does the brain learn to stabilize an image on the retina and use eye movement to compensate for a moving head? This so-called vestibular-ocular reflex, or VOR, needs to be fast; for clear vision, head movements must be compensated for almost immediately. To achieve the necessary speed, the VOR-circuit involves only three types of neurons: sensory neurons, which detect head movement; motor neurons, directing eye muscles to relax or contract; and so-called vestibular nucleus neurons in the brainstem that link the two.

While the brevity of this circuit keeps reflex times short, it was less clear what qualities of the circuit ensure that eye velocity is precisely matched to head velocity. Since the VOR operates accurately no matter how fast we move our head, scientists long expected that the signal transmission at the synapses—specialized points of contact between nerve cells—that connect the sensory onto the vestibular nucleus neurons would be linear.

However, transmission at most synapses is non-linear. Brain cells signal by sending electrical impulses along axons, long, hair-like extensions that reach out to neighboring nerve cells. When an electrical signal reaches the end of an axon, the voltage change triggers release of neurotransmitters, the brain's chemical messengers. These neurotransmitter molecules then travel across the space between neurons at a synapse and trigger an electrical signal in the adjacent cell—or not.

"Most known synapses act as information filters, and both the probability and the extent of neurotransmitter release as well as the efficacy of the postsynaptic response depend heavily on the recent history of the synapse," says first author Martha W. Bagnall, Ph.D., a former graduate student in du Lac's lab and now a postdoctoral researcher at the University of California, San Diego. "But no matter whether you go jogging or watch TV on your couch, the VOR needs to accurately match sensory input with motor output," she adds.

When Bagnall and her colleagues took a closer look at the first synapse in the VOR circuit, they found that no matter how fast the sensory neuron was firing, the same amount of neurotransmitter was released. And instead of vacillating, the post-synaptic neuron took the information and transmitted it faithfully.

Source: Salk Institute