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Your genes decide what you are listening to

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Ion channels, in particular low-voltage activated potassium channels (K_{LVA}) guard neuronal excitability and shape individual neurons' frequency-firing patterns. The article by Lu et al.,[1] published in the current issue demonstrates how differential expression of K_{LVA} channels generates unique filtering properties that tune neurons to their stimulus-specific inputs.

In the auditory system, phase-locking to a specific phase of the stimulus waveform is an effective way to encode the temporal pattern of a periodic stimulus like a soundwave. However, generating ideally one spike for each stimulus cycle poses 2 difficulties for this computation: First, low stimulus frequencies have longer stimulus cycles which would accommodate more than one spike per cycle and thus leading to a reduced temporal representation of the stimulus. Second, for higher stimulus frequencies a single stimulus cycle approaches the neuron's refractory period – jeopardizing its ability to generate even one spike for each cycle. Obviously, the brain overcomes this difficulty, but the question of which particular intrinsic and/or synaptic properties destine auditory neurons to phase-lock to either low- or higher stimulus frequencies has been addressed in 2 recent studies. Lu[1] and Oline[2] both took advantage of the chick cochlear nucleus (nucleus magnocellularis; NM) where gradients of synaptic convergence and differential expression of K_{LVA} are superimposed onto the tonotopic map of the nucleus. Neurons tuned to low-frequency input overcome the "problem" of generating more than one spike per cycle by integrating over multiple coinciding subthreshold inputs.[2] This is only possible because K_{LVA} expression is low in these low-frequency neurons, as the slow slope of low-frequency stimuli would activate K_{LVA} and prevent temporal summation.[2] Indeed, NM neurons processing mid-to-high stimulus frequencies show a much higher expression of K_{LVA} resulting in faster membrane time constants and limitation of temporal summation. Injecting sinusoidal currents of different frequencies into mid-to-high frequency neurons nicely demonstrated their filtering properties which result in rejection of low-frequency inputs and foster single spike responses to higher stimulus frequencies.[1,2]

The high expression of K_{LVA} in mid-to-high frequency neurons significantly hyperpolarizes their resting membrane potential. Besides removing inactivation from voltage-activated sodium channels, this hyperpolarization caused by K_{LVA} also engages hyperpolarization-activated cyclic nucleotide modulated (HCN) channels, which together further reduce the input resistance of the neurons membrane and speed up their membrane time constant. The expression of K_{LVA} and HCN is co-regulated in neurons of the mammalian cochlear nucleus.[3] Here this would suggest a higher expression of HCN channels in mid-to-high frequency neurons compared with low-frequency NM neurons. Together K_{LVA} and HCN provide an ideal composition to encode fast, high-frequency inputs.

Given such differences in input convergence, ion channel expression, output filtering properties or even

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the presence or absence of dendrites between NM neurons processing low-frequencies compared with those processing mid-to-high frequencies it is actually interesting that these neurons have not yet been categorized into 2 distinct populations. At least in the future, scientists should be aware of the properties specific to each frequency-specific population, when reporting data on NM neurons. This principle very likely extends to other neurons that have previously been thought of as more or less homogeneous populations, but where there is increasing evidence for neuronal subpopulations based on gradients that are superimposed on the tonotopic axis. A prominent example in the mammalian auditory pathway would be the medial nucleus of the trapezoid body where there are gradients for voltage-gated potassium channels,[4,5,6] HCN channels,[6] encoding of input timing[7] and even neuronal soma size.[8] In summary, the expression of specific sets of genes encoding for membrane proteins and their regulation are impressive predictors of what inputs neurons are tuned to.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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