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NEUROPHYSIOLOGY

Local tuning of spike shape

> the compartmentalized distribution of Kv3-mediated currents could account for the observed changes in action potential width

The width of an axon potential is governed by the rate of membrane repolarization. It is often assumed that the shape of an axon potential is unchanged as it propagates throughout an axonal arbour; however, this is at odds with evidence for heterogeneity in the axonal distribution of the ion channels that determine action potential dynamics. Rowan *et al.* now show that axon potential width varies within the arbour of a single cerebellar stellate cell (CSC) and is fine-tuned at individual synapses through the clustering of K^+ channels.

Like many local interneurons, CSCs exhibit numerous *en passant* synaptic boutons along their axons. The authors used subcellular recording and voltage imaging in slices of mouse cerebellum to analyse axon potential shape at multiple locations within an individual CSC axon. The results revealed striking variability in axon potential width, including differences in the width of action potentials at boutons present on the same or neighbouring axonal branches.

Many factors could contribute to differences in axon potential shape along the axon, including variable axon geometry and the heterogeneous distribution of ion channels. Here, compartmental modelling of the CSC axon, as well as measurements of the effects of experimentally induced changes in axon shape, showed that changes in its geometric properties could not account for the observed differences in action potential between compartments. However, using cell-attached patch-clamp recording, the authors found evidence for non-uniformity of K^+ currents along the axon: fast K^+ currents were clustered almost exclusively at boutons, and their density was highly variable between boutons.

Voltage-gated potassium channel 3 (Kv3)-family channels have an important role in spike repolarization at CSC boutons. The authors found that blocking Kv3 channels broadened action potentials at synaptic boutons but not in other parts of the axon, suggesting that these channels contribute to the local control of axon potential width. Indeed, compartmental modelling showed that the compartmentalized distribution of Kv3-mediated currents could account for the observed changes in action potential width as it propagated from the bouton into the axon shaft.

The authors hypothesized that, if Kv3-channel clustering enables synapse-specific tuning of action potential width, the influence of these channels must be restricted to their immediate locality. To determine whether this is the case, they used a two-photon laser to 'uncage' a photolysable version of the K^+ channel blocker 4-aminopyridine (4-AP) close to individual boutons. Broadening of action potential width in response to 4-AP uncaging was restricted to the bouton to which it was targeted. Local uncaging of 4-AP also altered the strength of GABAergic neurotransmission at the targeted bouton. These findings suggested that synapse-specific modulation of action potential width is possible and can influence neurotransmitter release.

This study provides evidence for the local regulation of action potential width and reveals some of the underlying mechanisms. Such synapse-specific control of action potential shape may contribute to the tuning of neurotransmission at individual synapses and thus to information processing.

Katherine Whalley

Nenov Brothers/Alamy

ORIGINAL ARTICLE Rowan, M. J. M. *et al.* Synapse-level determination of action potential duration by K^+ channel clustering in axons. *Neuron* http://dx.doi.org/10.1016/j.neuron.2016.05.035 (2016)