This Week in The Journal

Spatial Acuity of Mechanosensory Subfields in Fingers

Ewa Jarocka, J. Andrew Pruszynski, and Roland S. Johansson

(see pages 3622–3634)

Our ability to lift and manipulate objects depends greatly on our mechanosensory systems. Mechanosensory afferents that innervate our palms and fingerpads are divided into four subtypes based on receptive field size, response to sustained stimulation, and the type of mechanosensory organ innervated. Type I slowly adapting (SA-I) and fast-adapting (FA-I) fibers have the most compact receptive fields, and they innervate Merkel cells and Meissner corpuscles, respectively. Although compact, the receptive fields of these afferents are complex, having multiple areas of peak sensitivity, called subfields. Furthermore, the receptive subfields of multiple afferents are interdigitated. Jarocka et al. hypothesized that this arrangement increases the spatial resolution of tactile sensation.

To support this hypothesis, the authors estimated the spatial acuity of individual subfields of human SA-I and FA-I axons. They recorded from single axons in the upper arm while stimulating a fingertip with a series of tangentially moving, small, raised dots on a rotating drum. They mapped receptive fields by recording the position of dot stimuli when each action potential fired. And they estimated subfield acuity by using Gaussian convolution to add noise to the map and seeing how this manipulation affected the correlation between spike patterns produced during sequential presentations of the same stimulus. These analyses suggested that, regardless of fiber type, the spatial acuity of subfields was ~ 0.41 mm, similar to the width of a papillary ridge. Although subfield layouts were heterogeneous across neurons, subfield acuity and layout for a given neuron were similar across stimulus speeds and directions.

These results suggest that the spatial acuity of receptive subfields for both SA-I and FA-I fibers is in the submillimeter range, comparable to the spacing of the papillary ridges of the fingertips. This makes sense given that Meissner bodies

are localized to the sides of ridges, Merkel cells are centered on ridges, and ridges can be deflected individually by tactile stimuli. Nevertheless, how individual and populations of SA-I and FA-I fibers encode stimuli, given that each fiber has multiple subfields, remains to be elucidated.

Nine color-coded receptive field sensitivity maps of human tactile neurons projected onto a fingertip. Each receptive field has many subfields. The spatial acuity of these subfields is similar to the spacing of papillary ridges. See Jarocka et al. for details

A Transcription Factor that Protects Neurons from α -Synuclein

Brent J. Ryan, Nora Bengoa-Vergniory, Matthew Williamson, Ecem Kirkiz, Rosalind Roberts, et al.

(see pages 3731–3746)

Parkinson's disease (PD) is characterized by the degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNc) and by intracellular accumulation of α -synuclein, a protein thought to function in synaptic vesicle release. The pathological mechanisms underlying PD remain unclear, but several genetic mutations and environmental toxins have been linked to the disease. Notably, these genes and toxins affect neurons throughout the brain, yet SNc dopamine neurons are disproportionately prone to degeneration. This susceptibility may stem from the unusually high energy demands of SNc dopamine neurons

as a consequence of their tonic activity, large calcium fluctuations, and extensive axons with multitudinous release sites. The oxidative phosphorylation required to meet these energy demands generates high levels of reactive oxygen species (ROS), which can cause oxidative stress. Among other effects, oxidative stress promotes aggregation of α -synuclein, which is likely expressed at high levels in the large terminal arbors of SNc dopamine neurons. Aggregation of α -synuclein not only causes synaptic dysfunction, but also exacerbates mitochondrial stress, creating a positive feedback loop that may eventually lead to neurodegeneration (Gonzalez-Rodriguez et al., 2020, *Prog Brain Res* 252:61).

Ryan, Bengoa-Vergniory, et al. suggest that failure to upregulate RE1 silencing transcription factor (REST) also contributes to the vulnerability of SNc dopamine neurons in PD. In mice overexpressing human α -synuclein (which recapitulate features of PD), SNc dopamine neurons exhibit α -synuclein accumulation, mitochondrial fragmentation, and degeneration, but GABAergic neurons in the adjacent substantia nigra pars reticulata (SNr) do not. A proteomic screen prompted the authors to examine differential expression of REST. Whereas REST was prominent in the nuclei of SNr neurons, it was undetectable in the nuclei of SNc dopamine neurons. REST levels were also reduced in dopamine neurons derived from induced pluripotent stem cells from PD patients. Moreover, REST knockout led to increased mitochondrial fragmentation and increased ROS production in SH-SY5Y cells, whereas REST overexpression reduced the impact of a mitochondrial toxin on SH-SY5Y cell survival. Further work suggested that the protective effects of REST were mediated partly by upregulation of the oxidative response transcription factor PGC-1 α .

Overall, the results suggest that upregulation of REST protects neurons from mitochondrial dysfunction and fragmentation induced by α -synuclein overexpression. Why SNc dopamine neurons fail to upregulate REST is unclear. Nonetheless, targeting this pathway early in PD may help to slow progression.

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