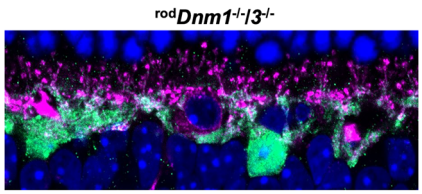
This Week in The Journal

Toward Interventions against Age-Related Cognitive Decline

Marta Garo-Pascual, Linda Zhang, Meritxell Valenti-Soler, and Bryan A. Strange

(see article e2059232024)

A gradual decline in memory as we get older is not abnormal, but some people do not experience significant cognitive decline as they age. Termed "superagers," these individuals have as good a memory as those 30 years younger. Scientists have begun to leverage this phenomenon as a tool to explore neuroprotective mechanisms for memory loss and dementia. In this issue, Garo-Pascual et al. present their findings from a 5 year longitudinal study in which the brain structure of superagers was compared with that of older adults experiencing typical memory loss. The authors observed smaller decreases in fractional anisotropy and lower increases in mean diffusivity over time, which altogether represent stronger and healthier brain white matter microstructure. In other words, they discovered that superagers have stronger preservation of the brain white matter, which could better support memory over time. Future work looking into the neural mechanisms underlying this structural difference may point to potential treatment targets for safeguarding memory in those of us who do not naturally have these neuroprotective mechanisms in place.



Retinal cross sections from a mouse with double *Dnm1*/*Dnm3* knockout in rod photoreceptors. Horizontal cells were labeled with an antibody for calbindin-1 (green), and their axon terminals were labeled with an antibody for Syt2/ZNP-1 (magenta). Hoechst staining (blue) was used to label photoreceptor nuclei. This technique was used to compare horizontal cell structure between knockout mice and controls. Knockout mice displayed degenerated horizontal cell axon terminals as early as P28 (shown). See Hanke-Gogokhia et al. for more details.

Dynamin Plays an Integral Role at Rod Ribbon Synapses

Christin Hanke-Gogokhia, Thomas E. Zapadka, Stella Finkelstein, Mikael Klingeborn, Timothy K. Maugel et al.

(see article e1379232024)

Rod and cone photoreceptors in the retina capture light in our external surroundings, which marks the start of the vision process. Following light's activation of photoreceptors, postsynaptic retinal neurons are activated at ribbon synapses, where glutamate vesicles are released and recycled. Typically, vesicle recycling at synapses depends on dynamins, which are GTPases encoded by three genes (*Dnm1–3*). But at ribbon synapses, the role of dynamins in glutamate vesicle recycling remains unclear. In this issue, Hanke-Gogokhia et al. address this knowledge gap. They used genetic lines of mice enabling cell-specific knockouts of *Dnm1* and *Dnm3* in rods. The authors examined synaptic protein expression, synapse ultrastructure, and retinal function and found that dynamins 1 and 3 redundantly support ribbon synapse structure and function in rods. Phenotypically, single *Dnm3* knockout had no effect, while single *Dnm1* slightly lowered vesicle density. Knocking out both *Dnm1* and *Dnm3* significantly affected vesicle recycling by reducing vesicle density, increasing vesicle size, reducing retinal responses, and degenerating synaptic terminals and postsynaptic processes. Cone function was unaffected by dual knockout of *Dnm1* and *Dnm3* in rods. This study provides the first evidence for dynamins 1 and 3 as being integral and functionally redundant for vesicle recycling at rod ribbon synapses.

This Week in The Journal was written by Paige McKeon
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