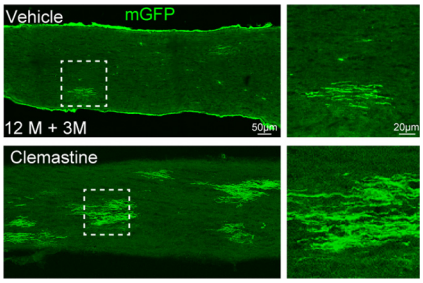
This Week in The Journal

To Preserve Vision in Advanced Age, Enhance Oligodendrogenesis

Jun-Jie Zhi, Shuang-Ling Wu, Hao-Qian Wu, Qi Ran, Xing Gao, et al.

(see pages 1859–1870)

Our eyesight falters as we age, and research has shown that axon degeneration in the optic nerve (ON) is to blame across species. These axons, extending from retinal ganglion cells (RGCs), are lost at a rate of up to 5,000 axons per year in humans. A better understanding of the process could yield strategies to slow age-related axon loss and thereby preserve vision in older age. This week, Zhi et al. home in on the role of myelination of the ON as a source of pathological change. Although the ON is myelinated by mature oligodendrocytes (OLs), they persistently turn over, continuously replenished by cells differentiating from oligodendrocyte precursor cells (OPCs). The authors measured electrical transmission in the ON in mice and found that processing speed was significantly slowed at advanced age (20 months) compared with mature (3 months) or middle-aged (13 months) mice, which is closely associated with demyelination of the ON. Accordingly, measures of OL myelin density also decreased with age, and unmyelinated axons and abnormal myelination were observed in aged mice. Transgenic experiments confirmed that OL turnover was actively contributing to newly generated myelin in adulthood. Interestingly, OPCs were plentiful in aged mice even as myelination declined, suggesting that oligodendrogenesis was diminished due to lower cell differentiation. To determine whether that could explain the age-related axon loss, the authors next induced conditional deletion of Olig2, a transcriptional factor essential for OPC differentiation, in young mice, which led to a decrease in newly formed myelin compared with control mice. Mice with knocked out Olig2 also demonstrated inhibited nerve processing and RGC axon survival, suggesting that oligodendrogenesis was required to maintain axon integrity and visual function. Conversely, enhancing oligodendrogenesis with conditional deletion of the muscarinic receptor 1 (M1R), a negative regulator of OPC differentiation, in 12-month-old mice led to increased myelination and axon density. Similarly, treatment with the Food and Drug Administration-approved, anticholinergic drug clemastine also promoted oligodendrogenesis and myelination as well as visual function, indicating that age-related functional deficits can be prevented or reversed by enhancing OL turnover.



Confocal images showing treatment of aged mice with clemastine resulted in increased myelination of the optic nerve. Boxes (left) contain magnified images on the right.

Brain Center Integrates Visual, Extraretinal Signals

Grace F. DiRisio, Yongsoo Ra, Yinghui Qiu, Akiyuki Anzai, and Gregory C. DeAngelis

(see pages 1888–1904)

In order to smoothly track the focus of our attention, we must rotate our eyes relative to our head, and the brain depends on information about eye velocity in order to perceive depth and other aspects of navigational vision. Extraretinal signals, such as copies of the motor commands that carry out rotational eye movements, were thought to be the source of that information, but recent studies have suggested that visual signals in the form of optic flow also contribute. Now, DiRisio et al. have investigated the neurons that process these signals and how they integrate them with extraretinal information to contribute to vision tracking. They focused on the dorsal region of the medial superior temporal area (MSTd), whose neurons have large receptive fields, respond to optic flow and project back to the medial temporal area (MT), a higher processing center. They trained two adult male rhesus macaque monkeys to maintain visual fixation on a target that was either stationary or smoothly moving while the head and body were fixed. They presented an eye-only (EO) condition, in which the animals had to make smooth pursuit eye movements to track a fixation point with no background visual cues, and dynamic perspective (DP) condition, in which a three-dimensional (3D) cloud of triangles moved and the eye remained stationary while visually simulating eye rotation. Multiunit and single-unit recordings of MSTd neurons showed similar neural tuning for real and simulated eye rotations. About half of MSTd neurons were selective for the direction of either real or simulated eye rotations, and about a third were selective for both, providing the first demonstration of such rotational selectivity in the MSTd. Neuronal responses to EO and DP conditions—real and simulated rotations—were remarkably similar in response magnitude, direction discriminability, rotation direction preference, and relationship to 2D motion preference, which suggests that the MSTd serves as an integral node representing both extraretinal and visual signals, and that MSTd neurons respond selectively to 3D rotational optic flow.

This Week in The Journal was written by Stephani Sutherland

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