This Week in The Journal

Transcranial Random Noise Stimulation Boosts Learning

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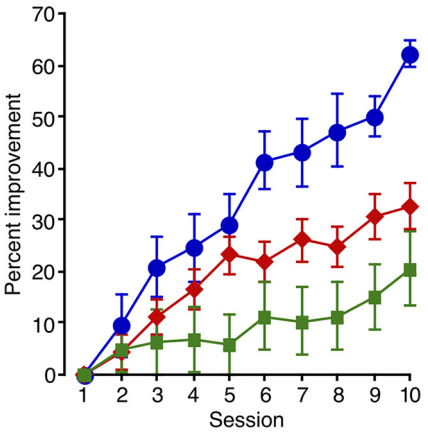
(see pages 5551–5561)

Strokes often damage primary visual cortex, resulting in partial vision loss (cortical blindness). Recent work has demonstrated that training on visual tasks can improve perception for a variety of visual features, including motion, orientation, luminance, and form, but these improvements require months of training and thus require strong motivation in patients. Moreover, after the visual cortex is damaged, afferents from the thalamus and retina begin to degenerate, reducing the potential for functional recovery. Therefore, speeding the effects of perceptual training would likely allow larger gains in cortically blind patients.

Noninvasive brain stimulation has been used to enhance recovery of motor and perceptual function after stroke, and it can speed visual perceptual learning. Yet more research is required to determine which types of stimulation are most beneficial and to assess the longevity of the effects, particularly in people with cortical blindness. Therefore, Herpich et al. compared the effects of two forms of direct current stimulation—transcranial random noise stimulation (tRNS) and anodal direct current stimulation (a-tDCS)—on perceptual training in a motion-direction discrimination task. In people with intact visual cortex, delivering tRNS over visual cortical areas during 10 daily training sessions greatly increased the rate and amount of improvement in motion-direction discrimination compared with that achieved through training alone. In contrast, neither tRNS over parietal cortex nor tDCS over visual areas significantly enhanced the effects of training. Notably, people who had received tRNS over visual cortical areas performed better than controls when tested without stimulation 6 months after the 10 d training period had ended. Perhaps more importantly, motion-direction discrimination improved over 10 d in all three cortically blind patients who received tRNS over visual cortex during training, whereas patients who did not receive stimulation showed no benefits of training.

These results provide preliminary evidence that tRNS can enhance the effects of visual training in cortically blind people. Additional work with more patients and additional tasks are required to confirm the effectiveness of the protocol, determine the longevity and generalizability of the benefits, and assess the extent to which the therapy improves patients' quality of life.



Perceptual training led to a greater improvement in performance when tRNS was delivered over primary visual cortex (blue) than when anodal tDCS (green) or no stimulation (red) was given. See Herpich et al. for details.

Ubiquitin Ligase in Myelinating Glia Helps Axons Survive

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(see pages 5606–5626)

Oligodendrocytes and Schwann cells do more than provide the insulating myelin that speeds action potential propagation: they also provide nutrients that maintain axonal health and integrity. For example, the transfer of lactate from myelinating glia to axons is thought to be necessary for axons to generate sufficient ATP to maintain spiking during periods of high activity. Hence, loss of glial lactate transporters or proteins that maintain channels that allow the transport of molecules through myelin leads to axon degeneration. Loss of proteins in myelinating glia can even result in axon degeneration when myelin remains largely intact.

Joseph et al. report that FBXO7, the substrate-recruiting subunit of a ubiquitin ligase complex, is required in myelinating glia to maintain axon health. Selectively knocking out FBXO7 in oligodendrocytes and Schwann cells of mice resulted in poor coordination and progressive hind-limb weakness. Myelination appeared normal in the CNS, but levels of several proteins—especially proteins involved in mitochondrial structure and metabolism—were lower in FBXO7-deficient white matter than in controls. In addition, axonal degeneration was present in optic nerves. Sciatic nerves in the PNS were more severely affected than optic nerves. Large areas of sciatic nerve were devoid of fibers and the number of large axons was significantly reduced. Remak bundles, in which axons are surrounded by non-myelinating Schwann cells, also degenerated in sciatic nerves. Nonetheless, where myelinated fibers were present, the myelin was of normal thickness, and there was no indication that Schwann cells underwent degeneration. Moreover, although compound muscle action potentials were greatly reduced, the nerve conduction velocity was only moderately slowed and the distal motor latency was unaffected, suggesting that axons were more strongly affected than myelin.

These results suggest that FBXO7 function in myelinating glia is more important for axonal survival than for the survival of the glia themselves. Notably, mutations in FBXO7 cause a juvenile form of Parkinson's disease (PD), and previous work has indicated that FBXO7 acts with other PD-associated proteins to rid cells of dysfunctional mitochondria. In addition, FBXO7 regulates the proteasomal system that degrades defective proteins. Future work should determine which of these functions is most important in myelinating glia for the maintenance of axonal integrity.

This Week in The Journal was written by Teresa Esch, Ph.D.
https://doi.org/10.1523/JNEUROSCI.twij.39.28.2019.