This Week in The Journal

Reduced Crowding at Peripheral Locus of Fixation

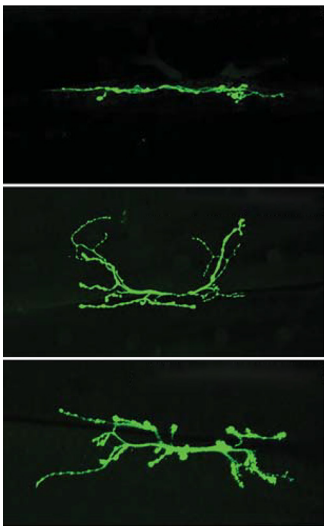
Nihong Chen, Kilho Shin, Rachel Millin, Yongqian Song, MiYoung Kwon, et al.

(see pages 3529–3536)

The ability to distinguish objects in the visual periphery is limited not only by visual acuity, but also by a phenomenon called crowding: an item that is recognizable when presented alone becomes difficult to distinguish if it appears among similar items. Although the neural mechanisms responsible for the crowding effect remain unclear, one model proposes that it is generated by inappropriate local connections in visual cortex that are strengthened whenever shifts in attention trigger saccades to peripheral locations (Nandy and Tjan 2012 Nat Neurosci 15:463). Crowding might contribute to visual impairment in people with central vision loss, but many of these people develop a new preferred retinal locus for fixation outside the fovea; if crowding is trained by saccades, then those originating from the new fixation locus might reshape cortical connections and reduce crowding at that site.

Chen et al. provide evidence that crowding is in fact reduced at new preferred fixation loci. They trained normally sighted people to track objects presented in a cluttered background on a screen. The subjects central vision was occluded by a gray patch that moved in conjunction with their eye movements, requiring them to position the tracked image at a peripheral retinal location. This training induced a new fixation locus. Before and after training, crowding was assessed by asking subjects to identify a target letter flanked by distractor letters. As predicted, crowding at the induced fixation locus was reduced after training. Moreover, the reduction in crowding was correlated with subjects ability to maintain fixation at the new position. Finally, functional MRI revealed that the training reduced crowding-related responses across visual cortical areas V1–V4, VO-1/2, and the intraparietal sulcus.

These results support the hypothesis that crowding depends on experience-dependent plasticity in the visual cortex. Notably, the reduction in crowding occurred selectively along the radial axis of the retina—the axis along which crowding is most pronounced—as predicted by the model. But because saccade variability also decreased during training, the results are also consistent with models linking crowding to saccadic precision. Regardless of underlying neural mechanisms, however, the results indicate that specific training might reduce crowding and thus improve visual discrimination in people with central vision loss.



After dSLC25A1 (middle) or dSLC25A4 (bottom) was knocked down in *Drosophila* larvae, terminal branching of motor neurons at the neuromuscular junction was greater than in control neurons (top). See Gokhale, Hartwig, Freeman, Bassell, et al. for details.

Mitochondrial Link between 22q11.2 Deletion and Psychosis

Avanti Gokhale, Cortnie Hartwig, Amanda A. H. Freeman, Julia L. Bassell, Stephanie A. Zlatic, et al.

(see pages 3561–3581)

Deletion of segment q11.2 of human chromosome 22 causes a highly heterogeneous syndrome affecting multiple organs, including the brain. The diverse phenotypes result from the hemizygous loss of genes encoding 46 proteins and 7 microRNAs, as well as other noncoding RNAs and pseudogenes. This hemizygosity not only reduces the expression of the products of the affected genes, but also alters the expression of hundreds of other proteins that are regulated by those gene products. Determining which of these changes contributes to specific phenotypes in 22q11.2 deletion syndrome is challenging.

Gokhale, Hartwig, Freeman, Bassell, et al. sought to identify proteins that might contribute to the greatly increased risk of schizophrenia found in people with 22q11.2 deletion. To home in on the likeliest candidates, they first quantified the proteomes of people that had both a 22q11.2 deletion and psychosis and the proteomes of unaffected relatives. They then compared these proteomes and used bioinformatics tools to identify cellular processes and organelles influenced by the proteins whose expression differed between the two groups. These analyses suggested that disruption of mitochondrial function is an important contributor to schizophrenia risk in people with 22q11.2 deletion. Analysis of interactions among the mitochondrial proteins that were most consistently altered by the deletion indicated that SLC25A1 and SLC25A4, two proteins involved in transport of molecules across the mitochondrial inner membrane, might be especially influential. Notably, expression of 45 of 106 proteins predicted to interact with SLC25A1 and SLC25A4 was altered in people with 22q11.2 deletion.

The authors next asked how reduced expression of SLC25A1 and SLC25A4 might affect neuronal function. Knocking out either SLC25A1 or SLC25A4 decreased calcium uptake by human mitochondria. In addition, partial knockdown of the *Drosophila* homologs altered the number of mitochondria and increased the number of synaptic boutons at neuromuscular junctions. Finally, partial knockdown of dSLC25A4 reduced ATP/ADP ratios in fly heads.

These results are consistent with those of previous studies linking alterations in mitochondrial function to schizophrenia and other neurologic and psychiatric conditions. Future work must assess whether deletion of the entire 22q11.2 segment similarly affects mitochondria in mammalian neurons and determine the relative contributions of disrupted mitochondrial transport, ATP synthesis, and calcium buffering to schizophrenia risk.

This Week in The Journal was written by Teresa Esch, Ph.D.
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