This Week in The Journal

Motion Integration Is Enhanced in Autism

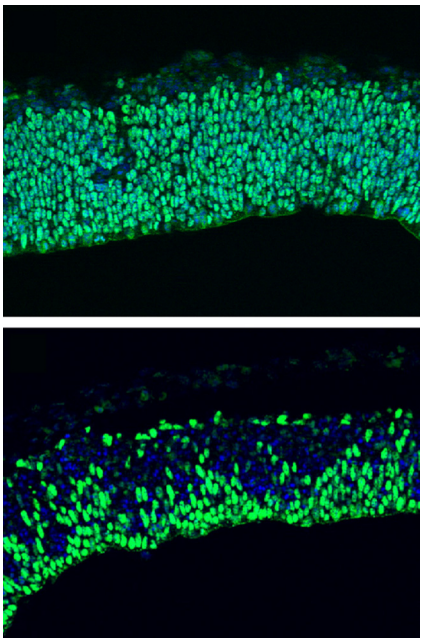
Catherine Manning, Marc S. Tibber, Tony Charman, Steven C. Dakin, and Elizabeth Pellicano

(see pages 6979 – 6986)

Autism is a neurodevelopmental disorder defined by impaired social interactions and an unusually narrow scope of interests. In addition to high-level behavioral and cognitive symptoms, low-level sensory processing is altered in autism. In some tasks, people with autism have enhanced perceptual abilities. For example, they are unusually adept at visual tasks that require attending to fine detail and ignoring context, such as finding hidden shapes in a drawing. Conversely, people with autism are impaired on tasks requiring integration of motion information. For example, when presented with a field of dots in which some move in the same direction while the remainder move in random directions, people with autism require a greater proportion of coherently moving dots to accurately report the movement direction.

Three hypotheses have been proposed to explain increased coherent motion thresholds in autism. First, the deficit may result from inaccuracy in estimating the direction of individual dots. Alternatively, it could reflect impaired integration of motion information gathered from different points in the visual field. Finally, it may stem from difficulty in ignoring the irrelevant dots. To test these alternatives, Manning et al. used a motion-detection task in which all dots contained signal: the movement directions were normally distributed around a mean, and participants were asked to discern the mean movement direction. When all dots were moving in the same direction (i.e., there was no variability), children with autism were able to discern motion direction as accurately as controls, arguing against the first hypothesis. Unexpectedly, when the direction variability was high, those with autism were more accurate than controls in discerning the mean direction. This suggests, contrary to the second hypothesis, that autism enhances the ability to integrate information from many dots. The authors thus conclude that deficits in coherent motion tasks arise because people with autism do not effectively discount information from randomly moving dots.

One can imagine that a failure to ignore irrelevant information could underlie some of the behavioral manifestations of autism, such as a failure to preferentially attend to faces and hypersensitivity to lights and sounds. However, definitively linking the neural bases of perceptual and behavioral deficits in autism will require much more work.



Mice happloinsufficient for Rbm8a (bottom) had fewer radial glia cells (green) in the developing neocortex at embryonic day 12.5 than control brains (top). See the article by Mao et al. for details.

Loss of Exon Junction Complex Protein Causes Microcephaly

Hanqian Mao, Louis-Jan Pilaz, John J. McMahon, Christelle Golzio, Danwei Wu, et al.

(see pages 7003–7018)

Deletions of portions of the 1q21.1 locus on human chromosome 1 result in various phenotypes, which may include intellectual disability, schizophrenia, and microcephaly. *Rbm8a*, one of several genes present at this locus, encodes a component of the exon junction complex (EJC). This protein complex, which attaches to mRNA sites where two exons are joined during splicing, facilitates nuclear export and promotes assembly of translation machinery on mRNAs. Because EJCs are removed during the first round of translation, they selectively enhance translation of newly synthesized mRNAs. Thus, EJCs can speed the production of proteins in response to extracellular signals. In addition, the EJC helps prevent the production of truncated proteins by signaling the presence of a premature stop codon: if an mRNA contains a stop codon upstream of a splice junction, the presence of an EJC at that junction triggers a decay process that eliminates the transcript.

In forming EJCs, Rbm8a heterodimerizes with another protein, Magoh. Because previous studies reported that haploinsufficiency of Magoh causes microcephaly in mice, Mao et al. reasoned that loss of *Rbm8a* may underlie microcephaly in 1q21.1 deletion syndromes. Indeed, deleting one copy of *Rbm8a* in mouse neural progenitors starting at embryonic day 9.5 decreased Rbm8a protein levels by 70% and caused cortical thinning. This thinning appeared to stem from premature exit of radial glia cells from the cell cycle, resulting in excess neuron production at a stage when cell divisions should have been expanding the progenitor pool. Consistent with this hypothesis, more than twice as many neurons were present in *Rbm8a*-haploinsufficient neocortex than in controls. Many excess neurons were subsequently eliminated by apoptosis, and the vast majority of neurons present at birth expressed markers of early-born, lower-layer neurons; few later-born, upper-layer neurons were present.

These results support the hypothesis that *Rbm8a* haploinsufficiency contributes to phenotypes observed in 1q21.1 deletion syndromes. Although Rbm8a has some EJC-independent functions, given that the effects of *Rbm8a* haploinsufficiency were similar to those reported for *Magoh* haploinsufficiency (Silver et al., 2010, Nat Neurosci 13:551), it is likely that loss of EJC function caused the premature generation of neurons and their subsequent loss by apoptosis.

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