performance actually worsened: they needed more contrast in the test gratings in order to successfully discriminate its orientation. However, discriminating test gratings presented at locations the observers had not been attending to was easier: participants needed less contrast to discriminate these test gratings. So, although attention 'turns up' the perceived contrast of a visual stimulus, prolonged adaptation to this enhanced signal can worsen performance. Further studies are needed to identify the loci of these effects.

Charvy Narain, Associate Editor,
Nature Neuroscience

ORIGINAL RESEARCH PAPER Ling, S. & Carrasco, M. When sustained attention impairs perception. *Nature Neurosci.* **9**, 1243–1245 (2006)

protein 70 (HSP70). They found that the protective function of TRiC depended on the presence of HSP70, and that TRiC could only act on HTT after it had been processed by HSP70. This fits with the well-known role of these proteins in normal protein regulation: HSP70 interacts first at the point of translation to prevent premature folding events, whereas TRiC functions downstream to regulate the correct folding and aggregation of proteins.

Previous work has shown that TRiC specifically prevents the aggregation of newly synthesized proteins by recognizing hydrophobic β-strands. Interestingly, toxic conformations of mutant HTT adopt a β-sheet structure, thereby providing a glimpse of how TRiC might recognize and regulate the conformation of HTT.

Tam *et al.* investigated the effect of overexpressing each of the eight subunits of TRiC. Whereas most subunits did not prevent the formation of cellular inclusions, subunit 1 strongly inhibited toxic HTT aggregation and increased neuron viability. This protective activity was found to reside in the apical domain of the protein, which has been recently shown to contain the protein's polypeptide binding site. However, RNA knockdown of just one of the other eight subunits was enough to stimulate HTT aggregation and neuronal toxicity, which, instead, indicates that only the fully assembled TRiC chaperonin complex can provide neuroprotection against mutant HTT.

So, it seems that mutant HTT can oligomerize by mechanisms that can lead to the formation of either toxic or benign aggregates. If the findings of Tam *et al.* — that part of subunit 1 is sufficient to promote a non-toxic HTT aggregation pathway — can be verified, then small peptide inhibitors, modelled on the TRiC binding site, might serve as effective therapies against Huntington's disease.

James Pickett, Associate Editor,
Nature Reviews Molecular Cell Biology

ORIGINAL RESEARCH PAPERS
Kitamura, A. *et al.* Cytosolic chaperonin prevents polyglutamine toxicity with altering the aggregation state. *Nature Cell Biol.* **8**, 1163–1169 (2006) | Behrends, C. *et al.* Chaperonin TRiC promotes the assembly of polyQ expansion proteins into nontoxic oligomers. *Mol. Cell* **23**, 887–897 (2006) | Tam, S. *et al.* The chaperonin TRiC controls polyglutamine aggregation and toxicity through subunit-specific interactions. *Nature Cell Biol.* **8**, 1155–1162 (2006)
FURTHER READING Young, J. C. *et al.* Pathways of chaperone-mediated protein folding in the cytosol. *Nature Rev. Mol. Cell Biol.* **5**, 781–791 (2004)

IN BRIEF

DEVELOPMENT

MicroRNA-9a ensures the precise specification of sensory organ precursors in *Drosophila*.

Li, Y., Wang, F. & Gao, F.-B. *Genes Dev.* 2 October 2006 (doi:10.1101/gad.1466306)

MicroRNAs (miRNAs) have important roles in several aspects of animal development, although their specific functions in the brain are less clear. New *in vivo* work in the *Drosophila* PNS shows that *miRNA-9a* is crucial for the generation of the correct number of sensory organ precursor (SOP) cells during development. Deletion of this miRNA led to the ectopic expression of SOPs, whereas overexpression resulted in a marked reduction in SOPs, suggesting that the role of *miRNA-9a* in non-SOP cells is to prevent precursor cells from becoming neurons.

NEUROTRANSMITTER RECEPTORS

Measurement of conformational changes accompanying desensitization in an ionotropic glutamate receptor.

Armstrong, N. *et al. Cell* **127**, 85–97 (2006)

Ligand-gated ion channels undergo conformational changes in response to ligand binding, leading to activation followed by deactivation or desensitization. Although much is known about the structural alterations underlying activation and deactivation, those leading to desensitization have proven elusive. Several techniques were used to explore structural rearrangments in the GluR2 receptor, showing that desensitization involves the rupture of the interface between two glutamate-binding core subunits, resulting in closure of the ion channel.

SYNAPTIC PHYSIOLOGY

Clathrin-mediated endocytosis is the dominant mechanism of vesicle retrieval at hippocampal synapses.

Granseth, B. *et al. Neuron* **51**, 773–786 (2006)

Following neurotransmitter release, synaptic vesicles must be recycled to prepare them for the next release event. Retrieval of the collapsed vesicle membrane has been proposed to occur through both slow and fast mechanisms of endocytosis. Using an enhanced fluorescent reporter that consisted of pHluorin fused to synaptophysin, these authors found evidence that, after physiologically relevant levels of activity, the slow mode of endocytosis provides the principal form of retrieval at hippocampal synapses and that this depends on clathrin.

COGNITIVE NEUROSCIENCE

Diminishing reciprocal fairness by disrupting the right prefrontal cortex.

Knoch, D. *et al. Science* 5 October 2006 (doi: 10.1126/science.1129156)

Ignoring self interest when responding to unfair actions in a manner consistent with moral and social values is apparently a uniquely human behaviour, yet the neural substrates underlying this behaviour are unknown. In the Ultimatum Game, subjects asked to choose between accepting an 'unfair' deal proposed by a stranger or rejecting it and gaining nothing for themselves often select the latter option. Disrupting dorsolateral prefrontal cortex (DLPFC) activity using transcranial magnetic stimulation showed that the right DLPFC has a role in overriding selfish impulses to promote fairness-related behaviour.