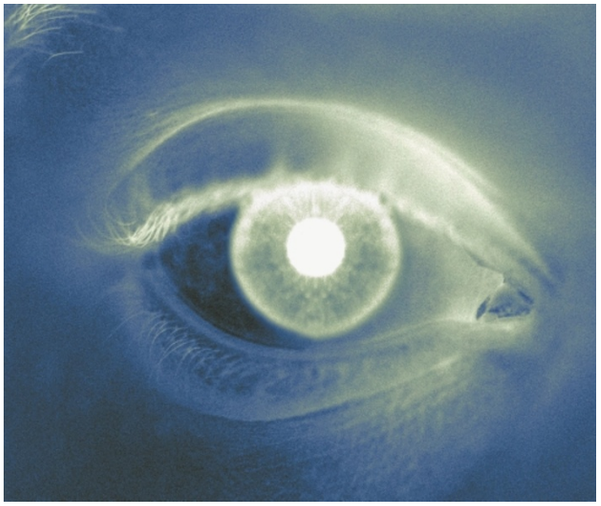

AGEING

Looking to the future

Human ageing is associated with a decline in visual function that is proposed to result from the degeneration and/or dysfunction of central visual pathways. But the precise nature of the changes in cortical function that accompany ageing remains obscure. In a paper published in *Science*, Leventhal *et al.* show that a shortage of GABA (γ-aminobutyric acid)-mediated inhibition in the visual cortex might underlie age-related visual deficits.

Senescent humans suffer from a number of disturbances of vision, including decreased visual acuity and motion sensitivity. The orientation- and direction-selective responses of cells in the primary visual cortex (area V1) participate in the perception of form and motion. Leventhal and co-workers have previously shown that V1 neurons in old monkeys lack orientation and direction selectivity. In their latest study, Leventhal *et al.* tested the hypothesis that a loss of GABA inhibition contributes to age-related changes in the responses of V1 cells.

In old monkeys, the electrophoretic application of GABA or muscimol, a $GABA_A$ receptor agonist, increased the proportion of cells that showed significant orientation or direction selectivity. GABA agonists were less effective in young monkeys, in which cells were already strongly selective. In young animals, the $GABA_A$ receptor antagonist bicuculline markedly diminished selectivity; however, this antagonist had little effect on the already low percentage of selective cells in old animals. GABA and muscimol both reduced the peak visual response and the spontaneous electrical activity of V1 cells, and increased the signal-to-noise ratio of these neurons; these effects were more pronounced in old monkeys. By contrast, bicuculline markedly impaired the ability of neurons to signal visual stimuli in young monkeys, but had relatively little effect on the neuronal responses of senescent animals.

These results indicate that GABA-mediated inhibition in the visual cortex degrades with age, possibly because GABA production is reduced in older animals. If reduced inhibition underlies age-related functional defects in widespread cortical regions, the GABA system could represent an important target for the treatment of sensory, motor and cognitive deficits that emerge as we grow old.

Rebecca Craven, Senior Subeditor, Nature

References and links

ORIGINAL RESEARCH PAPER Leventhal, A. G. *et al.* GABA and its agonists improved visual cortical function in senescent monkeys. *Science* **300**, 812–815 (2003)

FURTHER READING Schmolesky, M. T. *et al.* Degradation of stimulus selectivity of visual cortical cells in senescent rhesus monkeys. *Nature Neurosci.* **3**, 384–390 (2000)

SYNAPTIC PHYSIOLOGY

Means of transportation

Glutamate transporters are responsible for clearing the transmitter from the synaptic cleft after exocytotic release. But transporters also carry ions, and it has been shown that their activation can generate ionic currents in the postsynaptic membrane and in glial cells. Some glutamate transporters are also present in the presynaptic terminal, raising the possibility that they affect the presynaptic membrane potential, and thereby modify release probability through such an ionic current. Unfortunately, recording transporter-mediated currents from presynaptic terminals is a difficult task, owing to their small size. In a recent paper published in *The Journal of Neuroscience*, Palmer *et al.* get around this limitation by recording from two types of large presynaptic terminals, showing that glutamate transporters can indeed elicit presynaptic currents.

The authors recorded from the large terminals of the bipolar cells of the goldfish retina, and found that a presynaptic anionic current accompanied glutamate release from this synapse. This current had a large unitary conductance and was sensitive to glutamate transporter inhibitors with a pharmacological profile that pointed to the excitatory amino acid transporter 5 (EAAT5) as the molecular culprit. Importantly, this current was conspicuously absent from the second type of terminal from which Palmer *et al.* recorded — the calyx of Held — indicating that there is a degree of specificity to the putative function of presynaptic glutamate transporters and their associated current.

On the basis of the properties of this anionic conductance, the authors calculated that the activation of about 50 transporters after the fusion of about 600 synaptic vesicles would hyperpolarize the presynaptic membrane by about 7 mV, an amount that might affect the release properties of the synapse. Although future studies should probe the validity of this calculation, the data of Palmer *et al.* highlight the importance of a little-recognized mechanism to regulate presynaptic function.

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References and links

ORIGINAL RESEARCH PAPER Palmer, M. J. *et al.* Synaptic activation of presynaptic glutamate transporter currents in nerve terminals. *J. Neurosci.* 1 June 2003