NEUROLOGICAL DISORDERS

For emotion, size matters

Individuals with Williams syndrome, a genetic developmental condition that causes deficits in visuospatial processing but enhanced emotionality and face processing, have decreases and increases in relative cortical volume that parallel these abnormalities.

In a study published in *The Journal of Neuroscience*, Reiss and colleagues used a combination of volumetric analysis and voxel-based morphometry to compare the brains of people with Williams syndrome and those of control subjects. Williams syndrome causes various cognitive and behavioural abnormalities, including mild to moderate intellectual deficits, but visuospatial processing is disproportionately affected. The authors hypothesized that the parts of the cortex that make up the 'dorsal stream', which is responsible for visuospatial processing, might be abnormally small in affected individuals. They also looked for changes in parts of the brain that are involved in emotion and face processing, as people with the syndrome show increased emotional behaviour and are relatively good at face processing.

Overall, the study found that patients with Williams syndrome had an 11% reduction in cerebral volume. However, the thalamus, occipital cortex and other areas that are involved in visuospatial processing had greater decreases in grey matter volume, consistent with the pronounced deficits seen in these individuals. When the authors looked at areas involved with emotional processing and behaviour — including the amygdala, orbital and medial prefrontal cortex and anterior cingulate cortex — they found that these areas were relatively larger than normal.

VISUAL SYSTEM

Different shades of colour blindness

Despite the prevalence of colour blindness among men, and a good understanding of the genetics that underlies the condition, it has been unclear how the genetic abnormalities affect the cone receptors of the retina. Now, Carroll and colleagues use adaptive optics to show that there are two distinct phenotypes, caused by different types of genetic abnormality.

In individuals with X-linked red–green colour blindness, the function of either the long-wavelength (L) or middle-wavelength (M) photoreceptor pigment is lost. A central question in colour blindness research is whether these individuals have a normal complement of cone photoreceptors — but with the absent photopigment replaced by the remaining one — or a loss of the cones that would normally express the missing pigment.

Carroll *et al.* investigated this question in two red–green colour-blind men. Genetic analysis showed that in one individual (MM) the L-pigment gene on the X chromosome had been replaced by a second copy of the M-pigment gene. In the other (NC), by contrast, the M-pigment gene contained a mutation that caused it to encode a non-functional pigment.

The authors used a combination of two techniques — adaptive optics and retinal densitometry — to visualize the cone photoreceptors in the retinas of MM and NC, and to compare them with those in a normal trichromatic retina. In MM, they found a normal density of cones in the retina, which supports the idea that those cones that should contain the L pigment are still there, but contain the M pigment instead. However, NC's retina showed dark patches that appeared to correspond to missing M cones, scattered among a normal arrangement of L and S cones. In this case, it seems that the M cones had died, or at least become so abnormal that they did not reflect light as they should, and so could not be visualized. Surprisingly, the loss of about one-third of the cones in NC's retina did not significantly impair other aspects of his vision.

Until this study, the 'replacement' theory of colour blindness — the idea that dichromats had a normal number of cones, but only two instead of three pigments — had been more popular than the idea that cones were lost. These new findings show that both theories are apparently correct, depending on the genetic cause of the condition. They also demonstrate the usefulness of the high-resolution visualization of the retina that is allowed by adaptive optics — a technique that could prove invaluable for both research into and earlier diagnosis of retinal abnormalities.

Rachel Jones

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WEB SITE

Williams laboratory: http://www.cvs.rochester.edu/people/d_williams/d_williams.html

It is not unusual for damage or grey matter loss in a particular brain area to cause deficits in a specific aspect of cognition, perception or behaviour. But it is much rarer to find the opposite situation — a relative increase in volume in a part of the brain causing an enhancement in function. Now, the challenge for researchers is to discover how a deletion on one copy of chrom some 7 can produce such a striking and characteristic pattern of anatomical changes. If we can find the answer to this question, it must surely also shed new light on the normal development of the cortical networks that process visuospatial and emotional information.

Rachel Jones

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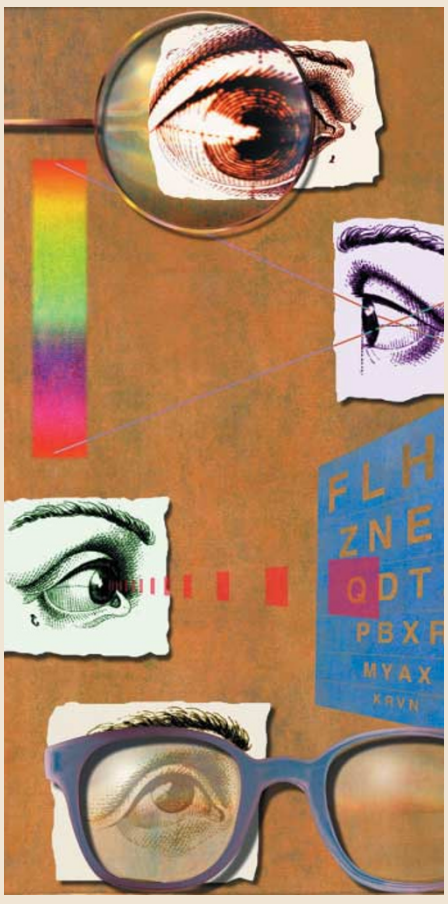


SENSORY SYSTEMS

The importance of staying active

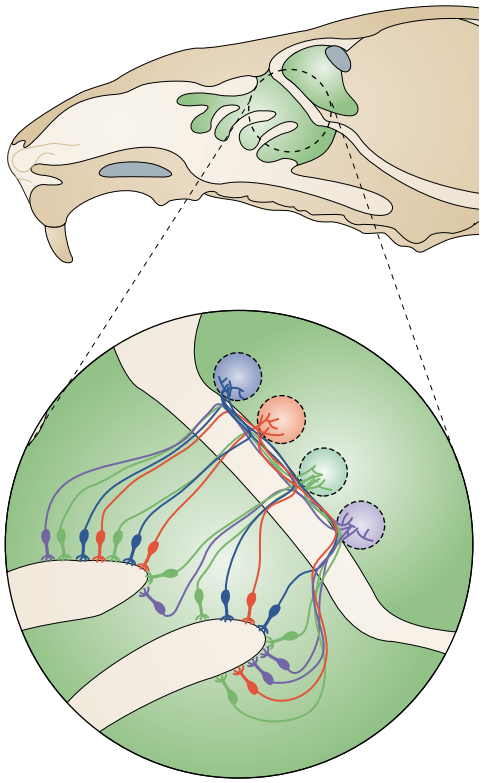
The mammalian olfactory system is organized so that projections from olfactory sensory neurons (OSNs) that express the same odorant receptor converge on structures called glomeruli in the olfactory bulb. Two recent reports highlight the roles of spontaneous and odorant-evoked neuronal activity in the establishment and maintenance of this glomerular map.

In a study reported in *Neuron*, Yu and colleagues inhibited neuronal activity in the developing mouse olfactory system, using constructs that expressed the tetanus toxin light chain or the inwardly rectifying potassium channel Kir2.1. They found that development of the glomerular map seemed to be largely normal if all OSNs were inactivated. However, if activity was blocked only in selected neurons, the phenotype was more severe — although the inactive neurons could initially establish normally targeted synaptic contacts in glomeruli, the contacts were unstable and broke down after around three weeks.

Therefore, spontaneous activity seems to give OSNs an advantage that is manifested only in a competitive environment. Yu *et al.* favour the interpretation that the active neurons have a survival advantage. However, as they used odorant receptor expression to track the fate of the neurons, the possibility remains that the inactive neurons simply switch to expressing a different odorant receptor gene.

Reporting in *Science*, Zou and colleagues show that odorant-evoked activity is required for the refinement of the olfactory map during postnatal development. They tracked the development of glomeruli that are innervated by neurons that express the odorant receptors M71 and M72. The olfactory bulbs of normal young animals (postnatal day (P) 10) contained multiple M71 and M72 glomeruli, whereas in the adult (P60), approximately one glomerulus for each receptor was found in each half-bulb. In addition, in the young mice, the 'M71' and 'M72' glomeruli were often also innervated by neurons that expressed different odorant receptors. These heterogeneous glomeruli usually disappeared by adulthood.

The authors examined the effects of sensory deprivation on glomerulus development by surgically closing one of the nares (nostrils) at birth. They found that the multiple and heterogenous glomeruli that characterize the immature glomerular map persisted into adulthood in the olfactory bulb that was ipsilateral to the closed naris. By varying the time of naris closure, they showed that the M71 and



M72 glomeruli develop with distinct time courses and have different periods of sensitivity to sensory deprivation.

What mechanisms might underlie these observations? The role of spontaneous activity in normal map development remains unclear, and Yu *et al.* suggest that it is likely to be permissive rather than instructive. It could also help to weed out weak synaptic connections, thereby contributing to map refinement and plasticity. Zou *et al.* offer a possible explanation for the effects of sensory deprivation on map refinement — closure of the nares was previously shown to reduce OSN turnover, so the persistence of the immature map might be attributable to an increase in neuronal survival. Clearly, more work will be needed to test these ideas, but these studies undoubtedly provide some important leads.

Heather Wood

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