feature was that they seemed to be 'high-threshold' interneurons — many pyramidal neurons are needed to recruit each NBC. The authors conclude, however, that once recruited, NBCs provide most of the perisomatic inhibition in these layers.

It is clear that such a precise and thorough classification of neurons is vital if we are to approach a full understanding of neural circuitry and interactions in any area of the brain. This kind of multidisciplinary approach will be important in future studies of neuronal classification. In particular, it will be interesting to see whether the properties of basket cells in the cerebellum and hippocampus reflect those found in the cortex.

Rachel Jones

References and links

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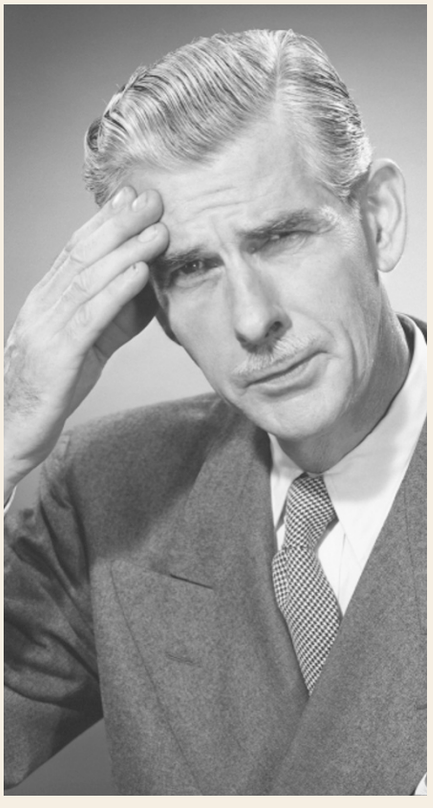
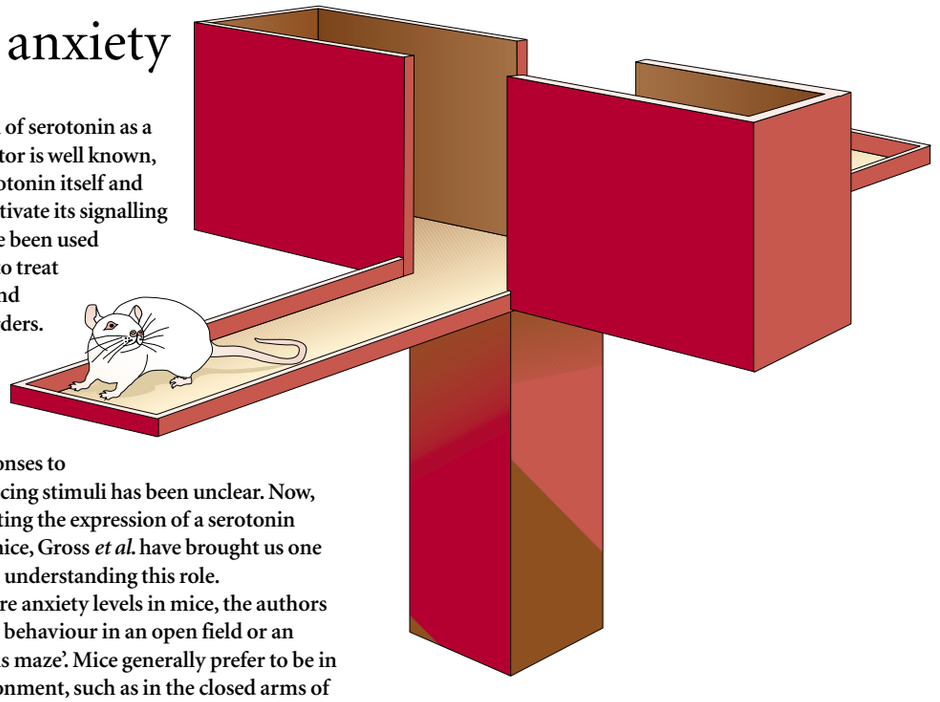
WEB SITES

Markram's lab: http://www.weizmann.ac.il/neurobiology/labs/markram/markram.html



BEHAVIOURAL GENETICS

High anxiety



The function of serotonin as a mood regulator is well known, and both serotonin itself and drugs that activate its signalling pathway have been used successfully to treat depression and anxiety disorders. However, the role of serotonin in establishing normal responses to anxiety-inducing stimuli has been unclear. Now, by manipulating the expression of a serotonin receptor in mice, Gross *et al.* have brought us one step closer to understanding this role.

To measure anxiety levels in mice, the authors studied their behaviour in an open field or an 'elevated-plus maze'. Mice generally prefer to be in a 'safe' environment, such as in the closed arms of the maze or at the sides of the open-field box, but their natural curiosity causes them to explore more aversive environments, such as the open arms of the maze or the centre of the open field. Their level of anxiety is determined by the amount of time that they spend exploring the aversive compartment of the apparatus; the more adventurous the mouse, the less anxious it is perceived to be.

It was previously shown that a global knockout of the serotonin$_{1A}$ receptor (5-HT1AR) causes an increase in anxiety-like behaviour in adult mice. By engineering a conditional knockout line in which the receptor gene could be selectively reactivated in the forebrain, Gross *et al.* were able to rescue this phenotype, allowing the mice to behave normally in response to anxiety-inducing situations. This result indicated that 5-HT1AR activity at its other main site of expression, the raphe nuclei of the brainstem, is not needed to reverse the anxiety phenotype in the knockout mice.

Another property of this 'rescued' mouse line was that 5-HT1AR expression could be switched off again by treating the mice with the antibiotic doxycycline. Gross *et al.* compared the effects of inactivating the receptor during late embryonic/early postnatal development and during adulthood. If the receptor was inactivated in adult mice, their responses to anxiety-inducing stimuli were indistinguishable from those of wild-type mice. By contrast, if the receptor was inactivated during development, the adult mice behaved like knockout mice, even when 5-HT1AR expression was restored at postnatal day 21. This result, combined with the observation that 5-HT1AR expression begins at postnatal day 5 in the rescued mice, indicates that there is a critical period between 5 and 21 days after birth when 5-HT1AR is required in the forebrain to establish normal anxiety responses. Failure to express the receptor during this period causes the mice to become excessively anxious in later life, but sustained expression in the adult mouse is not necessary to maintain a normal anxiety response.

The mechanism underlying this effect is as yet unknown, although 5-HT1AR has previously been implicated in synaptogenesis in the hippocampus and cortex, so it could be involved in establishing the neuronal circuits that are required for normal anxiety responses. Interestingly, in adults, chronic treatment with 5-HT1AR agonists can decrease anxiety, raising the possibility that similar mechanisms can be triggered in adulthood. Understanding these mechanisms should help in the design of more sophisticated therapies to treat anxiety disorders. It will also be interesting to look at factors that are believed to influence emotional well-being, such as maternal nurturing, and examine whether they affect 5-HT1AR activity during early life.

Heather Wood

References and links

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Encyclopedia of Life Sciences: http://www.els.net/serotonin receptors