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The complexion of fear

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HENRY GEE

An anxious mouse could provide a useful tool for testing drugs against stress disorders in humans. Because the researchers know exactly why the mouse is anxious, right down to the molecular level, the path is now clear to alleviate a range of distressing disorders in people who may be genetically predisposed to anxiety following some traumatic experience.

Anxiety disorders belong on the borders between genetics and experience. Although people vary enormously in their responses to traumatic experiences such as combat, rape or seeing a disturbing horror film, there are clear signs that genes are involved. For example, the shared incidence of post-traumatic stress disorder (PTSD) among combat veterans is higher in identical than in fraternal twins.

But what are the genes involved? A clue comes from the action of drugs commonly used to treat anxiety in the clinical setting. Valium, for example, works by binding to a receptor in the brain that normally responds to a chemical called gamma-aminobutyric acid (GABA, for short). From this, it seems clear that defective binding of GABA to its receptor might lie at the root of anxiety disorders. Given that the GABA receptor is made of proteins that are encoded by genes, it could be that the genes for the GABA receptor are as prone to disabling mutations as any other.

This seems likely, given the results of work on a strain of mouse genetically engineered to have defective GABA receptors, as reported in the September issue of Nature Neuroscience[1] by Florence Crestani of the Swiss Federal Institute of Technology and the University of Zurich, Switzerland and colleagues. In maze tests used to assess behaviour, mutant mice (that is, ones with defective GABA receptors) avoided new and potentially threatening situations, such as having to walk across narrow bridges without sides. The mice also tended to overreact to potential threats, compared with normal mice. All in all, the mice exhibited a range of behaviour seen in stressed humans, such as the tendency to see threats in ambiguous, novel situations, regardless of the actual degree of threat posed. As if to underline the conclusions, the mutant mice responded positively to small doses of Valium-like drugs that had no effect on normal mice.

With such a happy ending, it seems clear that we should have nothing to fear except fear itself.

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References

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