The V1a receptor is activated by vasopression, so the authors next set out to establish where this ligand might be produced. As expected, they found vasopressin immunolabelling in the paraventricular and supraoptic nuclei of the hypothalamus. However, these nuclei do not project to the PFC. Interestingly, vasopressin immunoreactivity was also found in the very cells in the PFC that showed increased dendritic spine density in response to fatherhood. It is therefore possible that locally produced vasopression activates V1a receptors in the PFC, which then stimulate the formation of new dendritic spines.

This study shows that fatherhood modifies the brains of marmosets in regions associated with parental behaviour. The intriguing findings raise some interesting questions about the mechanisms that might underlie such plasticity, and whether the quality of paternal care influences these changes.

Leonie Welberg

ORIGINAL RESEARCH PAPER Kozorovitskiy, Y. *et al.* Fatherhood affects dendritic spines and vasopressin V1a receptors in the primate prefrontal cortex. *Nature Neurosci.* **9**, 1094–1095 (2006)

initiate re-myelination. KROX20 has previously been suggested to suppress *Sox2*, indicating that, in addition to its established role in activating myelination, KROX20 might maintain myelin by repressing Schwann cell dedifferentiation.

This study shows that KROX20 is crucial for myelin maintenance, and introduces two models of delayed *Krox20* inactivation that might aid investigations into human myelinopathies. In particular, the inducible mutant replicates many features of late-onset myelinopathies such as Charcot-Marie-Tooth disease. Moving forward, it will be important to understand the mechanisms by which *Krox20* governs Schwann cell fate and to investigate the relationship to similar processes in the CNS.

Katherine Whalley

ORIGINAL RESEARCH PAPER Decker, L. *et al.* Peripheral myelin maintenance is a dynamic process requiring constant *Krox20* expression. *J. Neurosci.* **26**, 9771–9779 (2006)

PSYCHIATRIC DISORDERS

Depression gene in action

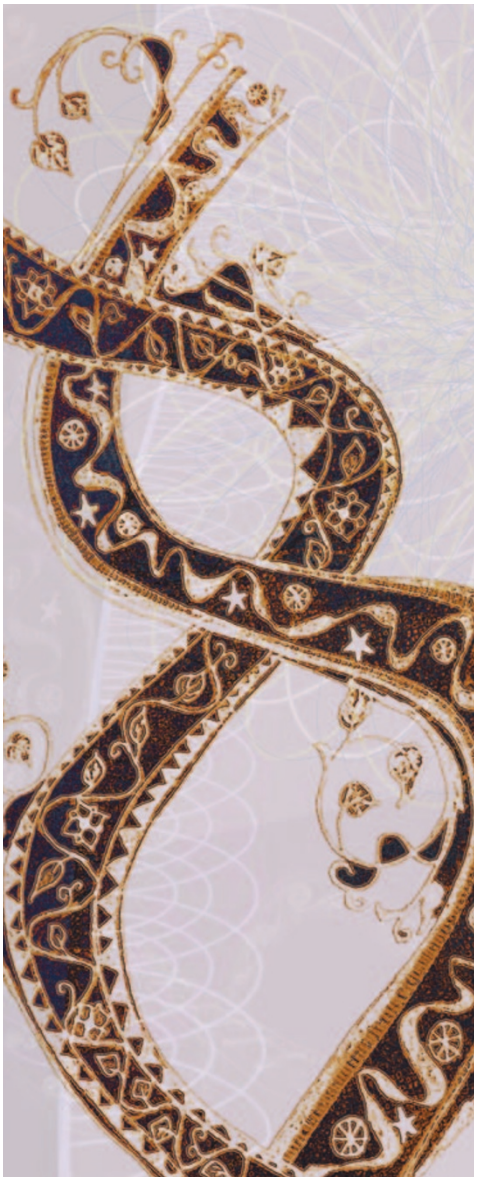
It is well established that interactions between genes and the environment contribute to psychiatric disorders. However, the way in which this is translated into changes in the brain has long been elusive. Now, a multimodal imaging study led by Turhan Canli, in collaboration with Klaus-Peter Lesch, shows that the variants of the serotonin transporter gene (*5-HTT*), which is involved in depression, have different effects on brain function depending on the level of stress that individuals have in their lives.

People carrying a short allele of *5-HTT* tend to have increased anxiety-related temperaments and are more vulnerable to depression compared with people who have two long alleles of the gene. Canli and colleagues set out to test whether this is due to heightened responses of the amygdala and hippocampus to negative emotional stimuli, as suggested by the phasic activation model. If this theory is correct, short-variant carriers with higher levels of stress in life should show more brain activity in response to stimuli such as fearful or sad faces. By contrast, the tonic activation model posits that the presence of the short allele and higher levels of stress increases the resting activity of the amygdala and hippocampus, rather than elevating brain reactivity to emotional stimuli or stress.

In support of the tonic activation model, the researchers found that in participants with a short allele of *5-HTT* there was a negative correlation between the reactivity of the amygdala and hippocampus — as measured by functional MRI — and the level of stress, regardless of the emotional nature of the stimuli. By contrast, a positive correlation was identified in people with two long alleles of the gene.

To further investigate the significance of these findings, Canli *et al.* used the perfusion scanning technique to measure the absolute cerebral blood flow — an indicator of the level of resting activity — in those brain regions. The resting activity of the amygdala and hippocampus was higher in subjects with a short *5-HTT* allele than in those with two long alleles. Interestingly, the more stress short-variant carriers have in their lives, the higher the resting activity. The opposite was observed in people with two long alleles.

The researchers also uncovered similar correlations between self-reported levels of rumination — a form of dysfunctional cognitive reappraisal of negative life events — and stress. So, short-allele carriers with high levels of stress tended to ruminate a lot, which might increase their risk for depression and anxiety disorders.



These intriguing findings lend support to the tonic activation model, and further suggest that short-variant carriers might be in a chronic state of vigilance, threat or rumination, which makes them more vulnerable to mental illnesses.

Jane Qiu

ORIGINAL RESEARCH PAPER Canli, T. *et al.* Neural correlates of epigenesis. *Proc. Natl Acad. Sci. USA.* 9 October 2006 (doi:10.1073/pnas.0601674103)
FURTHER READING Meyer-Lindenberg, A. & Weinberger, D. R. Intermediate phenotypes and genetic mechanisms of psychiatric disorders. *Nature Rev. Neurosci.* **7**, 818–827 (2006) | Caspi, A. & Moffitt, E. T. Gene–environment interactions in psychiatry: joining forces with neuroscience. *Nature Rev. Neurosci.* **7**, 583–590 (2006)