During vocal learning a bird forms an auditory memory or 'acquired template' of the tutor song. However, how the nervous system stores such a long-term auditory memory, and how this template guides subsequent vocal learning, has remained largely mysterious. Rose *et al.* now show that the template need not be a representation of the full song. Instead, based on their behavioural data, they propose that a population of phrase-pair detectors might be adequate. Evidence for neurons that might serve as such detectors already exists, so the behavioural results are certain to spur further research into the neural basis of vocal memory.

John Spiro, Senior Editor,
Nature

References and links

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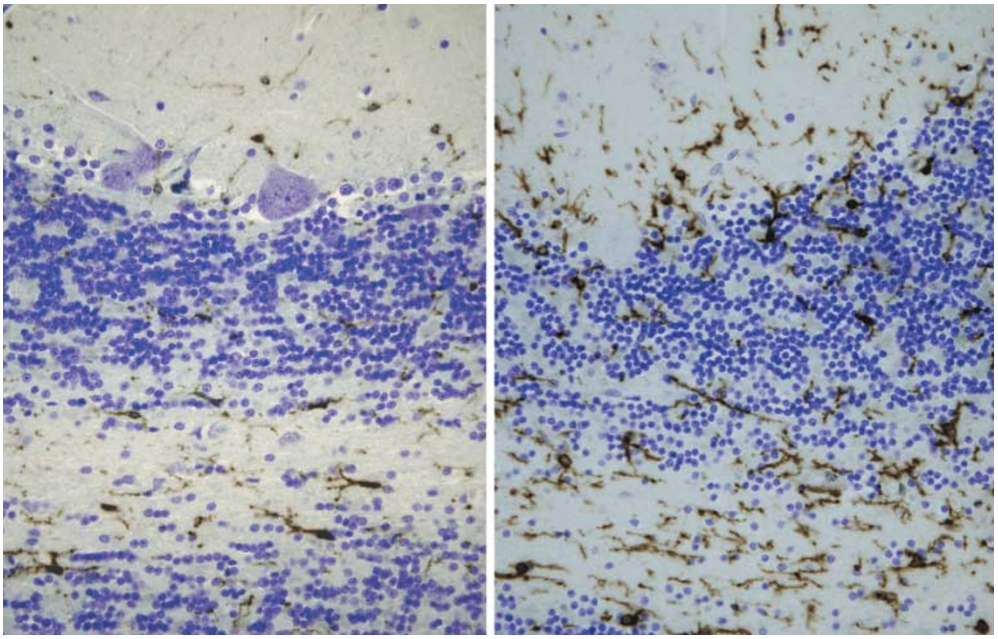

A marked increase in the number of activated microglia (stained brown) in the cerebellum from patients with autism (right) compared with healthy controls (left). Courtesy of C. A. Pardo, John Hopkins University.

NEUROLOGICAL DISORDERS

A new dimension of autism

Autism is regarded as a developmental disorder of the nervous system — an idea that is consistent with the gross abnormalities seen in the brains of patients with autism. The clinical manifestation of the disease is heterogeneous and the causes remain controversial. Reporting in the *Annals of Neurology*, Vargas and colleagues have added another layer of complexity by showing that immune cells are more active in the brains of patients with autism and cause increased inflammation.

Immune dysfunction has been implicated as a potential mechanism for the pathogenesis of autism, but previous research has focused on immunological measures made outside the brain. In this study, the authors analysed pathological changes in brain tissues from 7 healthy controls and 11 patients with autism. They found that, compared with brain tissues from the healthy controls, tissues from the patients with autism showed extensive neuroglial responses in the frontal cortex, cingulate gyrus and cerebellum. These responses are characterized by activation of microglia and astroglia, which are the only immune-competent cells in the nervous system and are important in both innate and adaptive immune responses.

As there was no indication of lymphocyte infiltration or deposits of immunoglobulin and complement in the brain tissues of patients with autism, the immune activity probably reflects the neuroinflammatory reaction associated with the central nervous system's innate immune system. Consistent with this view, there was an increase in the expression of inflammatory cytokines, such as macrophage chemoattractant protein 1 (MCP1) and transforming growth factor β1 (TGFβ1), in tissue samples from these regions of the brains of patients with autism. Astroglia and, to a lesser degree, microglia, seemed to be the main sources of cytokine production.

These are interesting findings, but immune activity in living patients cannot be detected in this way. The authors reasoned that if there is an ongoing inflammatory reaction in the brains of patients with autism, their cerebrospinal fluid (CSF) might also contain those cytokines. They investigated the immune system of six living patients with autism by measuring the levels of cytokines in their CSF. They found that there was a significant increase in the levels of MCP1 and other cytokines, such as interleukin-6 and interferon-γ, in the CSF of patients with autism, whereas the expression of TGFβ1 was comparable to that of controls.

Whether these cytokines serve as direct effectors of injury or as neuroprotectants to repair damage has still to be determined. However, these findings have important implications for understanding the pathogenesis of autism and might assist in the diagnosis of this condition.

Jane Qiu

References and links

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FURTHER READING Folstein, S. E. & Rosen-Sheidley, B. Genetics of autism: complex aetiology for a heterogeneous disorder. *Nature Rev. Genet.* **2**, 943–955 (2001)

WEB SITE

Pardo's laboratory: http://www.neuro.jhmi.edu/neuroimmunopath