Stroke symmetry

Throughout embryonic neurogenesis, neuronal precursors generate progenitor cells and migratory neurons; the ratio of these two cell types is determined by whether the precursor cell divides symmetrically or asymmetrically. Zhang and colleagues have investigated whether the same processes might operate in the adult brain, and they report in *The Journal of Neuroscience* that stroke not only increases neurogenesis in adult rats but also shifts the balance of dividing cells towards symmetric division and production of progenitor cells.

In early development, symmetric divisions predominate in the ventricular zone, producing progenitor cells that are proliferative throughout life. Symmetric division, therefore, has the potential to contribute exponentially to neuronal production. By contrast, half the daughter cells that are produced by asymmetric division remain progenitors, and the other half become young migratory neurons.

In the adult mammalian brain, the subventricular zone (SVZ) harbours neural stem cells that divide asymmetrically. Agreeing with previous reports that neurogenesis in the SVZ is induced by stroke, Zhang *et al.* report that the number of dividing cells in the rat SVZ increased after experimental stroke.

In addition, the authors assessed the orientation of mitotic cells as an indicator of whether the cells were dividing symmetrically or asymmetrically. Horizontal and vertical cleavage orientations produce asymmetric and symmetric divisions, respectively. Four and seven days after stroke, Zhang *et al.* found an increased percentage of vertically orientated dividing cells in fixed sections of brain; the same increase was not found in control animals or more than seven days after stroke.

A shift in neurogenesis was also evident from the frequency of cells that assumed neuronal identity, as shown by immunoreactivity to β -tubulin III. Four days after stroke, the frequency had increased to 47% in cells that divided symmetrically, compared with 33% in cells that divided asymmetrically.

The findings indicate that stroke reverses the usual preference of neuronal precursors in the SVZ to divide asymmetrically. As well as increasing total neurogenesis, stroke seems to shift the weighting towards the production of progenitor cells. This might reflect a strategy of coping with neuronal loss by expanding the pool of progenitor cells.

Finally, the authors looked at the possible involvement of the membrane-associated signalling protein Numb, which directs asymmetric cell division during development. However, they report that distribution of the protein was unchanged after stroke. So, identifying the signals that mediate these changes in neurogenesis remains a target for future studies.

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Nature Publishing Group

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NEURONAL PLASTICITY

PARP1 allows lasting memories

Activation of polyADP-ribose-polymerase-1 (PARP1) is normally a response to DNA damage, but new findings indicate that it also contributes to the formation of long-term memories — perhaps by facilitating gene transcription.

PARP1 is responsible for polyADP-ribosylation — a temporary modification that influences the binding of nuclear proteins to DNA. Although PARP1 is usually activated by DNA damage, it can also be activated in neurons by depolarization, so Cohen-Armon *et al.* investigated whether it is involved in the cellular processes that underlie memory formation in the sea slug *Aplysia californica*.

A. californica responds to an unpleasant stimulus by sensitizing its withdrawal reflexes. A single noxious stimulus produces short-term sensitization, but repeated stimulation produces long-term sensitization that can last weeks. This sensitization is due to facilitation of synapses between sensory neurons and motor neurons by the neuromodulator serotonin (5-HT, 5-hydroxytryptamine), and like other forms of long-term memory it requires gene expression.

The authors showed that repeated application of 5-HT to isolated pleural-pedal ganglia (which contain the facilitated neurons) caused activation of PARP1, although a single 5-HT application (which causes temporary facilitation) did not. In the

intact animal, repeated noxious stimulation also caused PARP1 activation, specifically in the pleural-pedal ganglion on the same side as the stimulus.

Another form of training can also produce long-term memory in *A. californica*. Feeding responses are reduced for several days after a training session in which the animals are given inedible food that cannot be swallowed. This training also activated PARP1, this time in the central and buccal ganglia that control feeding. Furthermore, blocking PARP1 activation by applying 3-amino-benzamide (3-AB) just before training prevented the development of long-term memory, although it did not affect short-term memory.

It is unclear how these types of stimulation cause PARP1 to be activated. Another important question is what function polyADP-ribosylation has in the development of long-term memory. Cohen-Armon and colleagues also show that PARP1 acts on the linker histone H1 in response to treatment with 5-HT. As polyADP-ribosylation of H1 causes relaxation of chromatin structure, this could allow rapid access to DNA for gene transcription, which is essential for long-term memory.

Rachel Jones

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