global regulator of motor neuron generation. Phox2b might first control the exit of the precursors from the cell cycle and favour their migration away from the proliferative zone and, later on, regulate the acquisition of the neuronal phenotype. It will be interesting to determine if other transcription factors have a similar role in other neuronal populations.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER Dubreuil, V. *et al.* The Phox2b transcription factor coordinately regulates neuronal cell cycle exit and identity. *Development* **127**, 5191–5201 (2000)
FURTHER READING Pattyn, A. *et al.* Control of hindbrain motor neuron differentiation by the homeobox gene *Phox2b*. *Development* **127**, 1349–1358 (2000) | Jessell, T. M. Neuronal specification in the spinal cord: inductive signals and transcriptional codes. *Nature Rev. Genet.* **1**, 20–29 (2000)
ENCYCLOPEDIA OF LIFE SCIENCES Neuronal subtype identity regulation
WEB SITE Developmental Biology Institute of Marseille

Greater priming during re-encoding in the scanner was associated with lower levels of subsequent explicit memory. Moreover, those subjects who showed the strongest priming during the re-encoding of the long-lag word list tended to demonstrate the least benefit during this re-encoding for subsequent explicit remembrance. These data indicate that priming for past experiences may disrupt new episodic encoding. The authors also provide an elegant possible explanation for these counter-intuitive findings that addresses the 'crosstalk' between memory systems. Further research that will shed new light on this neglected area is awaited with interest and will be facilitated by the decision to deposit these data in the newly formed National fMRI Data Center for public access (accession number 2-2000-11142).

Peter Collins

References and links

ORIGINAL RESEARCH PAPER Wagner, A. D. *et al.* Interaction between forms of memory: when priming hinders new episodic learning. *J. Cogn. Neurosci.* **12 Suppl. 2**, 52–60 (2000)
FURTHER READING Schacter, D. L. The cognitive neuroscience of memory: perspectives from neuroimaging research. *Phil. Trans. R. Soc. Lond. B* **352**, 1689–1695 (1997)
ENCYCLOPEDIA OF LIFE SCIENCES Learning and memory
WEB SITES National fMRI Data Center | Anthony Wagner | Daniel Schacter | *Journal of Cognitive Neuroscience*

NEURODEGENERATION

Birth of a supermodel?

The 'supermodel' concept that swept through the fashion world in recent years elevated a small group of catwalk stars to previously unknown celebrity status. Presumably Kate, Naomi and the rest had all the attributes required to succeed in the fashion shows of London, Paris, Milan and New York.

Models of a very different type have been important in our attempts to understand the aetiology of neurodegenerative disorders such as Parkinson's disease and to test the therapeutic potential of various natural and synthetic compounds. Analogous to the world of high fashion, every once in a while a supermodel is proclaimed in this arena — on the basis of a superior match between the characteristics of the disease in question and those of the new animal model. The most widely known supermodel in the field of Parkinson's disease is based on the use of the pro-toxin, *N*-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). This toxin induced an acute parkinsonian syndrome in humans that was virtually indistinguishable from the idiopathic disease. The use of MPTP and its metabolite 1-methyl-4-pyridium (MPP+) to create rodent and primate models of Parkinson's disease by inhibition of mitochondrial respiration at complex 1 of the electron transport chain have undoubtedly led to a greater understanding of the disease itself. But there are some aspects of the human disease that are not typically reproduced in animal models induced by these toxins, including the development of fibrillar cytoplasmic inclusions (Lewy bodies) containing ubiquitin and α-synuclein. So is there room for a new supermodel of Parkinson's disease?

Betarbet, Sherer and colleagues propose a possible candidate for supermodel status — administration of the pesticide rotenone (a complex 1 inhibitor) to rats. Continuous infusion of 2–3 mg per kg per day of rotenone via a jugular cannula for 1–5 weeks produced a highly selective degeneration of dopamine neurons of the nigrostriatal system and led to hypokinesia and rigidity. Moreover, the damaged nigral neurons accumulated fibrillar cytoplasmic inclusions that contained ubiquitin and α-synuclein, and may resemble those seen in Parkinson's disease.

For the authors, these results indicate that chronic exposure to a common pesticide may reproduce the anatomical, behavioural and neuropathological features of Parkinson's disease; for the field they may indicate even more — the birth of a new supermodel. Whereas the exact status of this model requires further research, epidemiological data indicating that pesticide exposure may be associated with an increased risk of developing Parkinson's disease will surely provide the impetus.

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References and links

ORIGINAL RESEARCH PAPER Betarbet, R. *et al*. Chronic systemic pesticide exposure reproduces features of Parkinson's disease. *Nature Neurosci.* **3**, 1301–1306 (2000)
FURTHER READING Jenner, P. & Olanow, C. W. Understanding cell death in Parkinson's disease. *Ann. Neurol.* **44**, S72–S84 (1998)
ENCYCLOPEDIA OF LIFE SCIENCES Parkinson's disease
WEB SITE J. Timothy Greenamyre

DEVELOPMENT

A smoother path to *LIS1*

Loss of one allele of the *LIS1* gene causes lissencephaly, a developmental disorder that affects cortical neuron migration, giving the brain surface a smooth appearance. LIS1 is a subunit of platelet-activating-factor acetyl hydrolase. However, this insight has not been sufficient to explain how LIS1 function is related in such an exquisite manner to cortical development. Now, three papers in *Nature Cell Biology* indicate that the link between LIS1 and lissencephaly may be related instead to the interaction of this protein with the microtubule motor dynein.

Dynein participates in cell division as well as in different forms of cellular trafficking, including axonal transport. These papers report a physical interaction between LIS1 and dynein and provide evidence for the regulation of microtubule transport by LIS1. Furthermore, changes in the levels of this protein interfere with mitosis and, in *Drosophila melanogaster* neurons, lead to shorter dendrites and abnormal axonal transport.

These findings raise the possibility that LIS1 affects neuronal migration by interfering directly with cytoskeletal dynamics or, alternatively, by reducing the number of migratory cells through its effect on mitosis. Although the exact mechanism has yet to be established, it is likely that these studies will provide a smoother path towards a fuller understanding of smooth brains.

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References and links

ORIGINAL RESEARCH PAPERS Smith, D. S. *et al*. Regulation of cytoplasmic dynein behaviour and microtubule organization by mammalian Lis1. *Nature Cell Biol.* **2**, 767–775 (2000) | Liu, Z. *et al*. *Drosophila Lis1* is required for neuroblast proliferation, dendritic elaboration and axonal transport. *Nature Cell Biol.* **2**, 776–783 (2000) | Faulkner, N. E. *et al*. A role for the lissencephaly gene *LIS1* in mitosis and cytoplasmic dynein function. *Nature Cell Biol.* **2**, 784–791 (2000)
FURTHER READING Morris, R. A rough guide to a smooth brain. *Nature Cell Biol.* **2**, E201–E202 (2000) | Walsh, C. A. Genetic malformations of the human cerebral cortex *Neuron* **23**, 19–29 (1999)
ENCYCLOPEDIA OF LIFE SCIENCES Cerebral cortex development

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