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► **COVER:** 'Exercising the mind' by Kirsten Lee, inspired by the review on p697.

The world around us can have profound effects on our brain development and function: interactions between the environment and molecular, cellular and behavioural processes contribute to the plasticity and refinement of neural circuitry.

A growing body of evidence now indicates that environmental modulation has important influences on numerous disorders of the nervous system, including neurodegenerative diseases with Mendelian inheritance patterns such as Huntington's disease. On page 697, Hannan and Nithianantharajah provide an insightful and informative overview of the striking and beneficial effects of enriched environments on brain plasticity in several disorders of the nervous system and their potential therapeutic implications.

One neurodegenerative disorder for which effective therapeutic approaches have remained elusive is amyotrophic lateral sclerosis (ALS). On page 710, Pasinelli and Brown present a comprehensive and articulate review of the state of knowledge of the molecular and cellular mechanisms of motor neuron death in this fatal condition, focusing on the impressive insights provided by studies of genetic mutations found in humans.

Finally, two Research Highlights in this issue (pages 682 and 684) describe findings that could lead to advances in the treatment of Parkinson's disease. One reports a previously unidentified therapeutic target — a ubiquitylation pathway — that contributes to the pathogenesis of the disorder. The other describes a new approach to stimulating endogenous progenitor cells to promote the restoration of the nigrostriatal pathway and improve motor function. Ultimately, it is likely that combinations of different therapeutic strategies that involve the modulation of molecular, cellular and environmental processes will be key to combating debilitating neurodegenerative disorders.



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