

NEUROSCIENCE EXPLANATORY NOTES

THE HUMAN brain contains 100 billion neurons, each of which makes a thousand or more connections with other target cells. While each brain is unique, the basic neuronal circuitry that underlies the remarkable range of functions and behaviours of all brains emerges according to a common set of principles.

In making their award, the members of the Kavli Neuroscience Prize Committee recognized three scientists, Pasko Rakic, Thomas Jessell, and Sten Grillner, jointly: "for discoveries on the developmental and functional logic of neuronal circuits".

Neurosurgeon turned neuroscientist Pasko Rakic has profoundly changed our understanding of the development of the cerebral cortex, the seat of our cognitive functions.

In a pioneering series of anatomical studies carried out over the past three decades, Rakic has revealed how neurons in the developing cerebral cortex are generated and how they assemble themselves into highly ordered, distinctively layered, and densely interconnected circuits that direct higher order sensory and motor functions.

Early in his career he discovered that previously enigmatic support cells, known as radial glia, serve as guides for the migration of cortical neurons in the developing brain, and showed how this process is critical for the organisation of the multilayered structure of the cerebral cortex. His radial unit hypothesis set the stage for our current view of the evolutionary steps involved in constructing ever more complex and sophisticated vertebrate brains. Croatian-born Rakic, Professor of Neurobiology and Neurology at Yale University School of Medicine, New Haven, US, also introduced the influential idea that different regions of the cerebral cortex acquire many of their specialised anatomical and functional properties through genetic programmes intrinsic to the cortex itself. His early studies have, in large part, led to the current emphasis on and interest in mechanisms of cortical development.

British-born Thomas Jessell, Professor of Neuroscience and Howard Hughes Medical Institute Investigator at Columbia University in New York, US, has worked for more than two decades to understand how nerve cells in the developing spinal cord assemble into the circuits that control sensory perception and movement. He pioneered the molecular analysis of neural circuit assembly in the vertebrate central nervous system.

Using the spinal cord as a model, Jessell deciphered at the molecular level how different types of nerve cells are generated as well as the steps that drive their assembly into the circuits mediating motor coordination and reflexive behaviours.

Jessell's work has revealed how gradual changes in the concentration of secreted signalling factors induce and steer the molecular switches that turn genes on and off to determine the identity of specific neuronal subtypes, as well as the precise positions in which they are generated.

The principles of circuit construction that have emerged from Jessell's studies in the spinal cord are now known to apply throughout the brain, and in particular they have helped to explain, in molecular terms, how different parts of the cerebral cortex acquire their specialised character.

The work of Rakic and Jessell has provided, for the first time, a general framework for understanding the assembly of neural circuits within the mammalian brain.

Swedish-born Sten Griller has defined the principles that govern at the cellular level how nerve circuits that control vertebrate motor behaviours work. Early in his career Grillner showed how these circuits in the mammalian spinal cord generate periodic motor commands for the rhythmic movements involved in locomotion - a process that demands the coordination of dozens of different muscles.

Griller, a Professor of Neuroscience at The Karolinska Institute in Stockholm. Sweden, then used the lamprey, a jawless fish, as a simple experimental model in which to carry out a detailed analysis of the cellular mechanisms that underlie patterns of movement. Using a powerful combination of cellular physiology, pharmacology, behavioural analysis, and computer modelling, he defined the workings of different types of nerve cells that together constitute the pattern-generating circuits that control swimming. He discovered a new class of neuron and identified the receptors and ion channels that are critical for the working of these neural networks.

Grillner's experimental and theoretical analysis of motor coordination in the lamprey has served as a standard for other attempts to describe the circuits that encode vertebrate behaviours in precise The Norwegian Academy of Science and Letters Drammensveien 78, 0271 Oslo, Norway Phone +47 22 12 10 90 Fax +47 22 12 10 99 www.dnva.no

See also:

The Kavli Prize www.kavliprize.no

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cellular and anatomical terms. Together, the work of Grillner and Jessell on spinal circuits has bridged the gap between the developmental organisation of defined neural networks and the behavioural functions they encode.

Ultimately, the enhanced understanding of central nervous system organization that has derived from the research of these three scientists may lead to new and more effective ways to repair diseased or damaged circuits embedded in the human brain and spinal cord.

Jon Storm-Mathisen, Professor of Anatomy at the University of Oslo, and chairman of the Kavli Neuroscience Prize Committee, said: "Major questions in modern brain science are how the complex neuronal circuits of the brain and spinal cord are assembled during development and how they function in the adult.

"Together Rakic, Jessell and Grillner have managed to decipher the mechanisms that govern the formation and functioning of the complex networks of the neural system to a level of understanding never previously achieved. The insight spans from the level of signalling molecules to cell and network wiring and action, to behaviour. "The new knowledge carries promise for future treatments of brain disorders by repairing damaged circuits. The discovery of motor pattern generators, the neural networks underlying movements, in the spinal cord is already being used to reestablish locomotion in people paralysed after spinal cord injury."