Triple Play

Donald Kennedy

This week's issue of *Science* finds us at an improbable but welcome convergence of events. We had planned all along to make this a special issue featuring Reports and Reviews in the neurosciences. Soon the rapidly growing Society for Neuroscience will hold its 30th annual meeting in New Orleans, beginning on 4 November. To be fair about it, this part is not exactly coincidental; we wanted the issue to emerge shortly before the meeting. But we had no idea that the 2000 Nobel Prize in Physiology or Medicine would go to three distinguished workers in this field. Three events, three awardees: Think of it as a triple witching hour for neurobiology, and all in the Millennial Year!

The work of the new laureates clusters around the signal transduction that takes place at "slow synapses." These junctions, instead of rapidly transferring episodic messages of excitation or inhibition, produce modifications in the excitability of postsynaptic cells that last for seconds, minutes, or even hours, and they may control the efficacy of other, "fast" synaptic pathways. More important, the work of these researchers began to elucidate the role of biochemistry in the central nervous system. Arvid Carlsson showed that dopamine was a transmitter in the brain—the first to be identified. He linked its presence in the basal ganglia to the control of movement and associated its depletion by reserpine with loss of motor function: discoveries that led to the use of L-dopa in the treatment of Parkinson's disease. Later he extended his work to findings that have become useful in the pharmacological treatment of depression and other mood disorders.

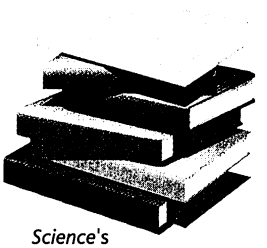
Paul Greengard then demonstrated that dopamine and other slow synaptic transmitters work through a cascade of cellular messengers, leading to the activation of a phosphorylating enzyme that affects other proteins, including ion channels in the membrane. In a series of beautiful investigations, Greengard worked out the choreography of these controls in particular neurons, implicating a key protein in the regulation of dopaminergic transmission. In a very recent paper in *Science* (11 February 2000, p. 1053), he links that mechanism directly to sexual behavior in rodents.

"...[A] triple witching hour for neurobiology..."

Such work had been done in mammals, for reasons that will surely be obvious. But now enter (drumroll!): *Aplysia*, an invertebrate with relatively small numbers of large readily identified neurons, first introduced to Eric Kandel by Ladislav Tauc. (Here I confess a personal delight in Eric's success; those of us working on such systems tired of hearing mammals called "real animals" as though ours were not). After working out the neural circuitry in elegant detail, he created a model for learning, using stimulus-dependent changes in the simple behavior of gill withdrawal. He was able to implicate Greengard's phosphorylation system in shorter term changes in synaptic efficacy. A much longer term kind of change required signals to reach the nucleus and then trigger new protein synthesis. Best of all, he subsequently showed that the same processes work in mice: real animals!

At *Science* we are happy to have had a relationship to these extraordinary experiments. Eric Kandel has published many of his papers with us; so has Paul Greengard, who is also a valued member of the editorial board of *Science*'s Signal Transduction Knowledge Environment—the Web-based forum for investigators in this exploding area.

The annual meeting of the Society for Neuroscience provides an invitation to reflect on the growth of excitement in this field. In 1970, when the society was brand new, it had 500 members. Membership is now almost 30,000—a compound growth rate of over 9% per year. My predecessor as editor-in-chief of *Science*, Floyd Bloom, played an important role in that explosion, as a founder and as president of the society in 1976–77. This November, about 25,000 neurobiologists will descend on New Orleans and register to hear papers, schmooze, and inspect (or ignore) posters: a total of 12,000 scientific communications! What a remarkable record of growth, and what a remarkable era of discovery. We have just finished the Decade of the Brain, which has brought us a harvest of new insights. Perhaps this will launch the Century of the Brain, in which we will explore and map the watershed between perception and behavior, learn about the organization of language, and perhaps even elucidate creative capacity. It is an exciting time to be in science, and at *Science*.



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