

# FIFTY YEARS OF NEUROPSYCHOPHARMACOLOGY

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In the fifty years since the first Pula congress a lot has changed in neuropsychopharmacology. Granted, the major groups of psychoactive drugs had already been discovered: neuroleptics, antidepressants, benzodiazepine anxiolytics, psychostimulants... Neurology was using the basic antiepileptics while, for example, the treatments for vascular and immunological diseases were more expectative. At the time of the first Pula congress in 1960 we had only just discovered that myasthenia gravis is an autoimmune disease. It is also the year when dopamine deficiency in the brain of Parkinsonian patients was discovered, a finding which was to revolutionize understanding and treatment of this disease. The last fifty years have also seen a proliferation of approaches to therapy and the success of these medical fields has grown considerably. During this time, more than twenty researchers have been awarded the Nobel Prize for research related to functioning of the nervous system and have or will have a significant influence on the development of new drugs. The greatest breakthroughs still waiting for clinical implementation have been in the field of basic research. Discoveries of excitotoxicity mediated by glutamate receptors as well as neurogenesis in adults are creating brand new hypotheses on the pathophysiology of different psychiatric and neurological diseases ranging from schizophrenia and drug abuse to ALS. However, speaking subjectively, there are two developments that had the deepest and strongest impact on pharmacology. First was the discovery of endogenous opioids based on the inquiry into real function of different pharmacological receptors in our organism. This discovery has shown that the so-called pharmacological receptors did not evolve solely for the purpose of drug-deliverance but that they also have a physiological purpose in the functioning of an organism. The second important event was the discovery

of methodology of reverse pharmacology – instead of a classic approach, nowadays receptors are more and more often synthesized from the human genome followed by search for their endogenous ligands and possibilities of their pharmacological manipulation. Through this, we now have orexines (hypocretins) as key neurotransmitters of wakefulness. By reverse pharmacology we have discovered such receptors as the new opioid receptor ORL1 and its endogenous ligand, nociceptin and finally, after several decades of different assumptions, the prolactin-stimulating factor. What is especially intriguing and motivating is the fact that there are still hundreds of G-protein receptors, nuclear receptors and synaptic receptors waiting for researchers to discover their function and useful implementation through pharmacology.

## Pharmacology in 60'

### Nobel prizes in Pharmacology

Fundamental change in concepts: coexistence of neurotransmitters, the question what really pharmacological receptors Endogenous opioids, endocannabinoids

Fundamentally new research strategy: „Reverse pharmacology. Orexins, Prolactin stimulating factor

- 2009 - Elizabeth H. Blackburn, Carol W. Greider, Jack W. Szostak
- 2008 - Harald zur Hausen, Françoise Barré-Sinoussi, Luc Montagnier
- 2007 - Mario R. Capecchi, Sir Martin J. Evans, Oliver Smithies
- 2006 - Andrew Z. Fire, Craig C. Mello
- 2005 - Barry J. Marshall, J. Robin Warren
- 2004 - Richard Axel, Linda B. Buck
- 2003 - Paul C. Lauterbur, Sir Peter Mansfield
- 2002 - Sydney Brenner, H. Robert Horvitz, John E. Sulston
- 2001 - Leland H. Hartwell, Tim Hunt, Sir Paul Nurse

- 2000 - Arvid Carlsson, Paul Greengard, Eric R. Kandel
- 1999 - Günter Blobel
- 1998 - Robert F. Furchgott, Louis J. Ignarro, Ferid Murad
- 1997 - Stanley B. Prusiner
- 1996 - Peter C. Doherty, Rolf M. Zinkernagel
- 1995 - Edward B. Lewis, Christiane Nüsslein-Volhard, Eric F. Wieschaus
- 1994 - Alfred G. Gilman, Martin Rodbell
- 1993 - Richard J. Roberts, Phillip A. Sharp
- 1992 - Edmond H. Fischer, Edwin G. Krebs
- 1991 - Erwin Neher, Bert Sakmann
- 1990 - Joseph E. Murray, E. Donnall Thomas
- 1989 - J. Michael Bishop, Harold E. Varmus
- 1988 - Sir James W. Black, Gertrude B. Elion, George H. Hitchings
- 1987 - Susumu Tonegawa
- 1986 - Stanley Cohen, Rita Levi-Montalcini
- 1985 - Michael S. Brown, Joseph L. Goldstein
- 1984 - Niels K. Jerne, Georges J.F. Köhler, César Milstein
- 1983 - Barbara McClintock
- 1982 - Sune K. Bergström, Bengt I. Samuelsson, John R. Vane
- 1981 - Roger W. Sperry, David H. Hubel, Torsten N. Wiesel
- 1980 - Baruj Benacerraf, Jean Dausset, George D. Snell
- 1979 - Allan M. Cormack, Godfrey N. Hounsfield
- 1978 - Werner Arber, Daniel Nathans, Hamilton O. Smith
- 1977 - Roger Guillemin, Andrew V. Schally, Rosalyn Yalow
- 1976 - Baruch S. Blumberg, D. Carleton Gajdusek
- 1975 - David Baltimore, Renato Dulbecco, Howard M. Temin
- 1974 - Albert Claude, Christian de Duve, George E. Palade
- 1973 - Karl von Frisch, Konrad Lorenz, Nikolaas Tinbergen
- 1972 - Gerald M. Edelman, Rodney R. Porter
- 1971 - Earl W. Sutherland, Jr.
- 1970 - Sir Bernard Katz, Ulf von Euler, Julius Axelrod
- 1969 - Max Delbrück, Alfred D. Hershey, Salvador E. Luria
- 1968 - Robert W. Holley, H. Gobind Khorana, Marshall W. Nirenberg
- 1967 - Ragnar Granit, Haldan K. Hartline, George Wald
- 1966 - Peyton Rous, Charles B. Huggins
- 1965 - François Jacob, André Lwoff, Jacques Monod
- 1964 - Konrad Bloch, Feodor Lynen
- 1963 - Sir John Eccles, Alan L. Hodgkin, Andrew F. Huxley
- 1962 - Francis Crick, James Watson, Maurice Wilkins
- 1961 - Georg von Békésy
- 1960 - Sir Frank Macfarlane Burnet, Peter Medawar