

The review of the Italian association of psycho-neuro-endocrine-immunology

Edited by Francesco Bottaccioli

PNEI NEWS

The new knowledge of science and health

A TRIBUTE TO RITA LEVI-MONTALCINI

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Editorial

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A tribute to Rita Levi Montalcini

Francesco Bottaccioli

Page 3. Interview. Inside the brain

“I look ahead”.

Calissano remembers his Teacher, Rita Levi-Montalcini.

Memories of Rita Levi-Montalcini from Pietro Calissano, the neurobiologist who shared half a century of studies with her. He remembers her strong determination in wanting the International Research Institute to be located in Italy, a mission almost impossible.

Paola Emilia Cicerone

INSIDE THE BRAIN

Page 6. Rita Levi-Montalcini's molecule

Since its discovery sixty years ago, pharmacological research has suggested several times that the Nerve Growth Factor could be used as a therapeutic treatment for Alzheimer's disease and peripheral neuropathies although no significative results were yet available. Now the latest developments in scientific studies put this molecule at the centre of medical attention.

Luigi Manni

CRF

Page 10. At the core of stress

In 1981 the hypothalamic peptide was identified. A decade before, Hans Seyle had hypothesized that it could activate the stress neuroendocrine axis. Nowadays we know that CRF has plenty of other functions such. The modulation of anxious and depressive states is one of them.

EXCITATORY AMINO ACIDS

Page 13. Glutamate, the stress neurotransmitter

Glutamate - the main stress neurotransmitter – is an amino acid which is found abundantly in food. It is also produced through the metabolism of glutamine and

glucose. Together with cortisol, stress strongly stimulates the release of glutamate in nervous synapses

Francesco Bottaccioli

THE OPIOID SYSTEM

Page 16. Endogenous opioids – powerful substances with a multiple action

The opioids produced by the nervous system are known for their action in pain modulation. They also have other functions such as regulating gastro-intestinal activities (both endocrine and vegetative) to the processes of satisfaction, addiction as well as learning and memory.

Elisa Carlino and Fabrizio Benedetti

THE CANNABINOID SYSTEM

Page 19. More than marijuana: the multiple roles played by the endogenous cannabinoid substances

The endocannabinoid system is just amazing. In the last twenty years discoveries, there is no other system in the modulation of the nervous signal which has ever generated so many expectations for the development of new drugs treating the most different pathologies.

Vincenzo Micale

SIPNEI NEWS

Page 22. Courses and study days

Page 23. PNEI Review, a new review for a new scientific and healthcare model.

EDITORIAL

INSIDE THE BRAIN

A TRIBUTE TO RITA LEVI-MONTALCINI

Francesco Bottaccioli – Sipnei Honorary President.

This issue is in honour of the late great scientist and it is entirely focused on the partial recognition of the knowledge of a few fundamental neurochemical systems.

In his interview Pietro Calissano recalls the main steps in Rita Levi-Montalcini's life-long research activity. A path which is deeply interwoven with the discoveries that lead to our discipline's birth. Psychoneuroendocrineimmunology was in fact born in the 80s as a field of study on the relationships between the central and peripheral nervous system and among these compartments and the immune system. During her Nobel lecture in 1986, the Italian scientist described the evolution of the knowledge of NGF. At the beginning it was considered as a factor occurring in the early stages of embryonic development. In the middle of the eighties it was found that it also played a role in the communication between brain, sympathetic and immune system. Ten years later, in a remarkable article (*Trends in Neurosciences* 1996; 19: 514-520) Levi-Montalcini described thoroughly the communication among the nervous, the endocrine and the immune system. The most important quoted works in that article belonged to David Felten, a neuroanatomist who signed the first Psychoneuroimmunology textbook together with the experimental psychologist Robert Ader and the immunologist Nicholas Cohen.

Levi-Montalcini study is characterized by a constant opening to pathophysiology. For instance, after having identified the NGF – mast cells connection and the role of stress in the inflammatory response mediated by mast cells which are sensitive to the NGF activating stimuli, she proposes a pathological mechanism. A mechanism that starting from stress and other imbalanced conditions can result in the appearance of neurodegenerative disorders such as Multiple Sclerosis and Alzheimer.

Pietro Calissano's interview and Luigi Manni's article (pages 6-9) remind us how the pharmacological applications of NGF discoveries have been below the expectations. In my opinion the reason for this lies on the fact that a reductionist approach can not comprehend the NGF complexity . The articles about opioids, cannabinoids, CRF and glutamate explain clearly that the intertwinement with systems and their signals is quite the norm.

Thinking to produce drugs able to fit such complexity just by focusing on a single molecule and on one of its receptors seems therefore to be the top epistemological mistake which is currently slowing down therapeutic innovation. Finally a last observation. During her Senator activity at the Parliament Rita Levi-Montalcini was insulted due to her support to Prodi's government. I see that the same riffraff are now sitting again at the Parliament and they are more

aggressive than ever. I feel very ashamed for these electors and elected people. This sad feeling can not spoil the fortune to have had such an extraordinary person as a role model.