Psychoneuroimmunology: How the brain and the immune system communicate with each other

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In 1929, Erich Wittkower published a paper in which he described his observations of pronounced increases in leucocyte numbers during different emotional states such as anxiety, rage, grief and joy. He postulated that this transient "Affektleukocytose" was due to a stimulation of the sympathetic nervous system which induced migration of leucocytes into the peripheral blood (Wittkower 1929).

This functional relationship between the sympathetic nervous system and the immune system was discussed as early as the beginning of this century. Different investigators observed pronounced increases in leucocyte and lymphocyte numbers in humans after injection of the neurotransmitter adrenaline, which had been discovered and produced synthetically a decade before (Hatigean 1917, Friedberg 1920). An adrenaline-induced vascular contraction in the spleen and a direct chemical contact between lymphocytes and adrenaline have been discussed as mechanisms of this neurotransmitter-induced lymphocytosis (Frey & Tonietti 1925, Patek & Daland 1935).

However, after the publication of studies conducted by Cannon and Selye, work on the interactions between the nervous- and immune system appeared to fall into oblivion and research focused instead on the effects of stress on endocrine variables, in particular adrenaline and cortisol secretion. It took more than 30 years until George F. Solomon published a paper entitled "Emotions, immunity, and disease: A speculative theoretical integration" in which he created the term "psychoimmunology" (Solomon & Moos 1964). Still, it took more than a decade since the first well-controlled studies were designed which showed impaired immune function in humans brought about by stressful situations such as bereavement (i.e. Bartrop et al. 1977). In 1981, the first volume was published by Ader & Cohen (1981) in which they, as protagonists of psychoneuroimmunology, summarized an impressive amount of data showing the functional relationship between the nervous-, endocrine- and immune systems.

At first glance, the CNS and the immune system have several characteristics in common. Both systems communicate at a distance (nerves vs. trafficking lymphocytes), are capable of developing memory (brain vs. long lived memory lymphocytes) and both systems use chemicals to transfer messages (neurotransmitters/neuropeptides vs. cytokines).

Today, we know that the interactions between the nervous-, endocrine and immune systems are complex and it is postulated that these systems communicate with each other as a biochemical network (Ader et al. 1991). Primary (thymus, bone marrow) and secondary (e.g. spleen) organs are innervated by noradrenergic nerve fibers (Felten et al. 1987). Hormones (ACTH, cortisol, prolactin, growth hormone etc.), neurotransmitters (adrenaline, noradrenaline) and neuropeptides (beta-endorphin, enkephalin, neuropeptide Y etc.) can alter cellular and humoral immune
functions via receptors expressed on immune competent cells (Reichlin 1993). Immune system functions also affect brain processes: Immune responses are associated with neurophysiological and neuroendocrine activities in the brain, and cytokines such as interleukin-1 affect central nervous activities (Besedovsky & Sorkin 1977, Bluthé et al. 1992). In addition, activated lymphocytes are capable to produce endocrine factors (Blalock 1989).

All these data provide evidence that psychological factors modulate functions of the immune system via neuroendocrine messengers, and underline the significance of psychology in promoting health and recovery from disease.

Psychoneuroimmunology in Germany is a new research field which became known predominantly by the work of Sybille and Wolfgang Klosterhalfen on conditioned immunosuppression in rats (Klosterhalfen & Klosterhalfen 1983, 1990) and by a review article published by Schulz & Raedler (1986). In 1989, the Volkswagen Foundation established a major new research area named "Neuroimmunologie, Verhalten und Befinden", funding research projects in Psychoneuroimmunology. In parallel to this new funding area, the VW-Foundation supported an international symposium on Psychoneuroimmunology which took place in September 1989 at the Hannover Medical School (Schmoll et al. 1992). Since 1990, a number of research groups all over Germany have been established which are active in this new and exciting field of research in order to analyze the complex interactions between the brain and the immune system.

Psychneuroimmunology in Germany is also strongly embedded in Medical and Biological Psychology along with disciplines such as immunology, endocrinology, pharmacology, physiology and psychiatry. The first symposium on psychoneuroimmunology was held with the participation of international colleagues from the UK and USA within the 9th Congress of the German Society of Medical Psychology (DGMP) in Mainz in 1992. Positive feedback from this meeting encouraged us to organize the second international symposium within the 10th Congress of the DGMP in Magdeburg, 20th May 1994 with colleagues from France, The Netherlands, Italy, USA and Australia who presented their work together with colleagues from different research groups in Germany.

In this issue the papers are grouped according to the topics of the symposium dealing with the impact of stress on immune functions (I. Session), with the functional relationship between the neuroendocrine- and the immune systems (II. Session) and with psychoneuroimmunology and disease (III. Session). The papers presented here show in an impressive way the variety of research strategies in order to analyze the interactions between psychological factors, neuroendocrine processes and immunological functions in animals and humans.

Keywords: interleukin-1, cytokines, neurotransmitters, neuropeptides, psychoimmunology, adrenaline, cortisol, stress, psychoneuroimmunology, immune system

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