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The Network Paradigm: New Niches for Psychosomatic Medicine

Imre Lázár

Abstract

Psychosomatic medicine, as a philosophical frame and practical approach of the diagnostic and therapeutical agency, had been undergone several renewals and reframing in the past. We overview the history of psychosomatics and map its branches. Psychoanalytic and psychodynamic frameworks, the Engelian biopsychosocial concept, the paradigm of behavioral medicine, the clinical psychophysiological research background, the clinical fields of PNI, psychocardiology, biobehavioral oncology, the so-called mind-body medicine, and stress medicine frameworks reflect a converging pluralism. Psychoneuroimmunology offers a comprehensive framework to analyze key issues of psychosomatics in a social neuroscience framework and to demonstrate the significance of the network approach in bridging the gap between psychosomatics and biomedicine. Network medicine creates a shared denominator for analyzing socioeconomic, interpersonal, life event-based narrative factors together with psychophysiological features of the clinical and health psychological problems and promotes convergence of psychosomatics, biomedicine, and lifestyle medicine, too. On the other side, psychosomatic medicine as a particular professional medical specialization is not universal at all. In Europe, one can find such specialization only in Germany, while psychotherapy applied by somatic experts is practiced in wider circles. Finally, we explore the new niches for psychosomatic orientation offered by integrative frameworks like lifestyle medicine and network medicine.

Keywords: names and frames of psychosomatics, psychoneuroimmunology, network medicine, institutionalization

1. The network paradigm: new niches for psychosomatic medicine

Man is not an indifferent hanger for carrying the disease. Man is the larger part of the disease. Temperament affects even skull fractures. It affects the coloration of acute diseases and especially certain chronic and maybe non-exogenous disease types, which cannot be properly understood or judged unless we follow the internal and typically more significant threads of their etiology into the unique tangle of individual characteristics (László Németh [1]).

1.1 Roots and branches, names and frames of psychosomatics: a historical analysis

Psychosomatic medicine, as a philosophical frame and practical approach of the diagnostic and therapeutical agency, had been undergone several renewals and reframing in the past. If we try to explore the archeology of psychosomatics, we can trace its orientation back to Galenus, Hippocrates, or the Chinese *The Yellow Emperor's Classic of Medicine*.

Galenus wrote about the connection between melancholy and mammary carcinoma following theories by Hippocrates, attributing the cause of breast cancer to an “excess of black bile,” implying more than a disbalance of humor, and pointing to the habitus, the emotional and behavioral character. Emotional disorders and mental illnesses also had been considered to constitute a significant part of diseases in Chinese medicine, where such illnesses were classified as Qing Zhi disorders. The so-called emotion-wills implied the Qi Qing:-seven emotion, namely happiness, anger, anxiety, pensiveness, sorrow, fear, and fright and the Wu Zhi five wills: happiness, anger, thinking, sorrow, and fear. According to the ancient Chinese approach, they play a primary role in the onset, progress, and prognosis of most of the diseases.

As emotions are deep *human ecological representations* of the environment depending on perceptions, evaluation, and interpretation of the outer and internal environment, we can realize that psychosomatics is also a human ecological approach immersed into external and internal networks of social, psychological, neuroendocrine-immune and molecular layers.

The emotional response to environmental challenges depends on personality (A, C, D type) as a result of personal history (early mother–child attachment, adverse childhood experiences); personal development; Pavlov's, Skinner's, and Bandura's learning processes and system-like social influences (family relationships in frame of Milano School, worksite mental health issues); competition and frustration; domination and submission; social rank; and self-evaluation (shame, feeling guilty).

In an overview of the history of psychosomatic concepts regarding human suffering, we find changing frames for the connection between mind and body in a multilayered human ecological setting. The psychoanalytic and psychodynamic frameworks, the hypnotic phenomena, stress medicine based on Cannon's fight-or-flight reaction, Selye's stress, Lipowski's consultation-liaison medicine, the Engelian biopsychosocial concept, and the paradigm of behavioral medicine have network features in common.

In the background, the clinical psychophysiological research emerges with the clinical fields of psychoneuroimmunology, psychocardiology, and biobehavioral oncology. This way, the so-called mind-body medicine and stress medicine frameworks reflect a converging pluralism. The frames are diverse, and the foci are common. Information flow through the social, cognitive-emotional, psychological, neural, endocrine, and immune interfaces and the molecular transcriptional interfaces and *backward*. These paths and regulative networks have shared evolutionary origins. These are the structural-functional, patterned heritage of ours, organizing biopsychosocial adaptation and the structural wisdom of the human body. Their adaptive/maladaptive potential depends on the changing environmental context.

Drawing a Venn diagram of different historical or competing schools of psychosomatic medical philosophy, we find many overlapping themes, which might also be considered as hubs of multilayered network organization of psychosomatic phenomena, working as a network of networks (**Figure 1**). The letters sign some of the evolutionary steps of psychosomatics without a claim for the whole picture (**Table 1**).

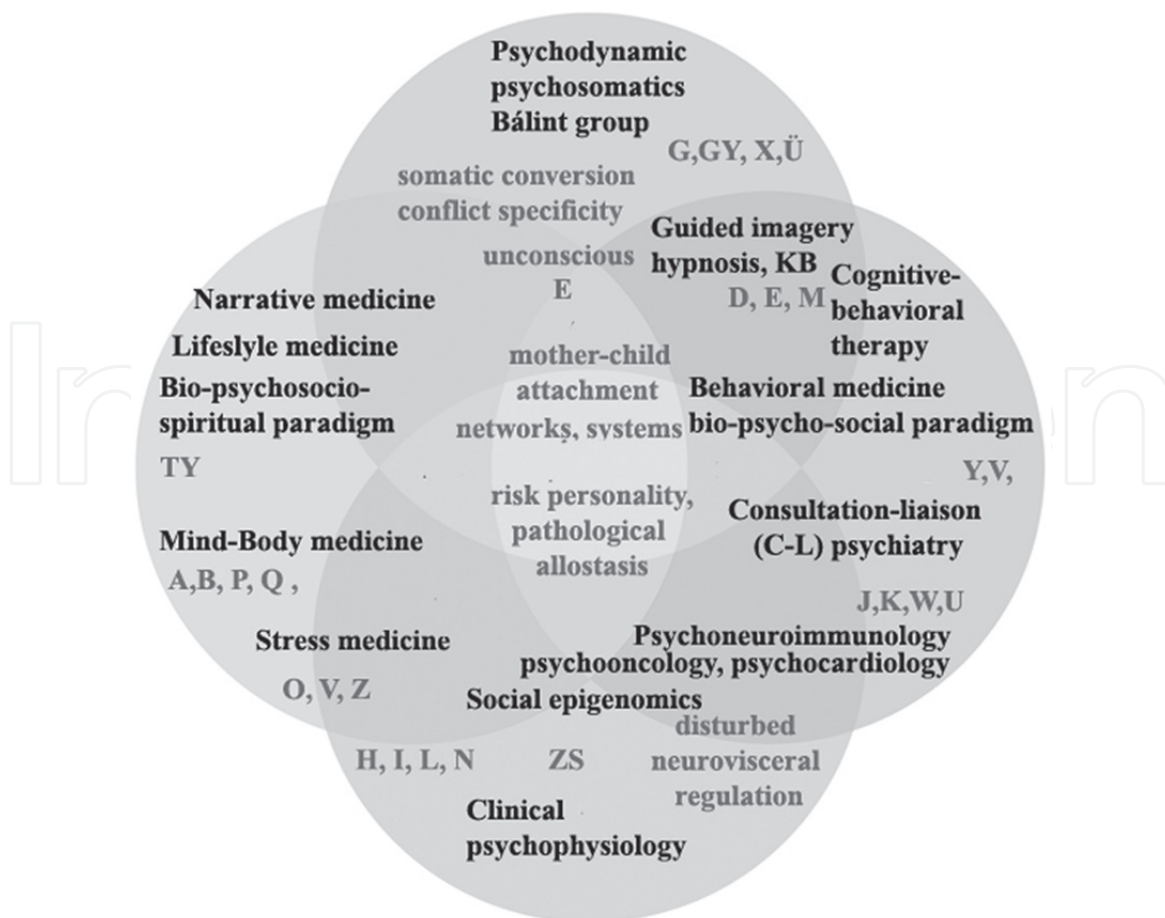


Figure 1.
 Venn diagram of different psychosomatic discourses.

Contemporary psychosomatic medicine broke away from the psychoanalytic foundations, and its research directions reflected a turn toward networking with other disciplines, as an interdisciplinary approach named behavioral medicine. The behavioral medicine and the concept of consultation-liaison psychosomatics bound to Lipowski [4] brought psychosomatics closer to mainstream biomedicine, enhancing their collaboration. The Engelian turn of the biopsychosocial paradigm explicitly expressed the importance of information flow through the network of networks that built up dynamically connected social, psychological, somatic, and molecular-genetic layers.

In 1977, the Yale Conference on Behavioral Medicine had a strong impact to the history of psychosomatic medicine. The participants, like Joseph Matarazzo, Redford Williams, David Shapiro, and Gary Schwartz, defined a new framework for the former psychosomatic medicine, as the study and treatment of diseases, disorders, or abnormal states in which psychological processes and reactions are believed to play a prominent role. There were several opinions regarding the identification of psychosomatics with behavioral medicine. Some considered it identical; others expressed the opinion that behavioral medicine was only a fraction of psychosomatics, while others viewed behavioral medicine implying psychosomatic medicine and additional areas of medical and psychological concern. The wider definition of behavioral medicine extended the former borders of psychosomatics, proposing *behavioral medicine* as “the field concerned with the development of behavioral-science knowledge and techniques relevant to the understanding of physical health and illness and the application of this knowledge and these techniques to prevention, diagnosis, treatment, and rehabilitation. Psychosis, neurosis, and substance use are included only insofar as they contribute to physical disorders as an endpoint” [5]. Further extension of former

A	1818	Heinroth	The name “psychosomatics”	Mind-body network
B	1843	Le Cabanis	Relationship between body and spirit	Mind-body network
C	1880	Fabre	A nervous system disorder can cause organ damage, and the abnormal functioning of an organ always affects the nervous system	Neurovisceral network
D	1886	Bernheim	Physical symptoms of hypnotic suggestions are results of ideosensory and motoric reflexes	Neurovisceral network
E	1889	Janet	The block, the dissociation, and reversible amnesia between the conscious and unconscious results in several psychopathological phenomena that can be treated by hypnosis	Neurovisceral network
F	1892	Male	Pathology of emotions, the organ symptoms that result from emotions, is similar to those caused by physical factors	Neurovisceral network
G	1896	Freud	Psychoanalysis based on the theory of dynamic psychiatry, libido theory, conversion neurosis, hysteria, symbolic organ speech	Mind-body network
Gy	1905	Ferenczi	Short dynamic psychotherapy	Mind-body network
H	1905	Pavlov	Paradigm of conditioned reflexes providing a framework for neurobiological learning theory	Neurovisceral network
I	1909	Eppinger and Hess	Description of sympathicotony and vagotony	Neurovisceral network
J	1928	Heileg and Hoff	Relationship between environmental pressure and infection incidence	Neuroimmune network
K	1926–1935	Metalnikov and Chorin 1926 Speransky 1935	The conditioned neutral stimulus might provoke inflammation “immune conditioning”	Neuroimmune network
L	1932	Cannon	The alarm reaction Fight-or-flight versus tend or mend	Neurovisceral network
M	1932	Erickson M.H.	Traumatic amnesia and psychosomatic symptoms are psychoneuro-physiological dissociations that can be resolved by “internal resynthesis” using hypnotherapy	Neurovisceral network
N	1935	Breur	Relationships between tuberculosis relapses and life events	Neuroimmune network
O	1936	Selye	Designates the information pathways of HPA axis as mechanism of stress-related psychosomatic problems	Neuroimmune network Neuroendocrine network

P	1936	Bergmann	Pathology of functional internal medicine	Neurovisceral network
Q	1937	Hetényi	Autonomous nervous system-based diseases of internal medicine	Neurovisceral network
R	1937	Papez	Mental experience is transformed into the psychophysiological pattern of emotions by the limbic-hypothalamic system	Neurovisceral network
S	1940	Scharrer	The central nervous system controls the hormone production of the endocrine system through the hypothalamus	Neuroendocrine network
T	1942	Bykow	Corticovisceral pathology	Neurovisceral network
TY	1943	Dunbar	Relationship between personality and psychosomatic disease	Mind-body network
X	1950	Alexander	Psychosomatic medicine	Neuroimmune network
Y	1955	Charva	The system model of neurohumoral integration	Neurovisceral network Neuroendocrine network
U	1955	LeShan	Specific pattern of cancer risk based on a biographical history and personality survey of cancer patients	Neuroimmune network
Ü	1957	Bálint	Doctor-patient relationship and communication as a factor in healing. Bálint groups	Mind-body network
V	1972	Weiner	Psychosomatic problems as disorders of information transmission between the limbic-hypothalamic-pituitary system	Neuroendocrine network
W	1974	Ader	Psychoneuroimmunology	Neuroimmune network
Sz	1977 1978	Matarazzo Schwartz/Weiss	Behavioral medicine	Mind-body network
Z	1984	Caccioppo	Development of social neuroscience	Mind-body network
ZS	1995	Meaney	Social epigenomics	Mind-body network

Table 1.
 Network features of psychosomatic models [2, 3].

psychosomatics included social and institutional spheres and deep biological system and network insights as well.

The disciplines contributing to the study of behavioral phenomena include psychology, sociology, anthropology, education, epidemiology, biostatistics, and psychiatry. These disciplines must be coupled with the biological and medical sciences relevant to understanding the disease processes under study. The networking position of behavioral medicine is apparent from epistemological perspective, too. The following matrix clarifies the deep connection with network medicine (**Figure 2**).

	Psychology	Internal Medicine	Sociology	Anthropology	Psychiatry	Epidemiology	Physiology	Cardiology	etc.
Prevention									
Etiology/Pathogenesis									
Diagnosis									
Treatment									
Rehabilitation									

Figure 2.
Matrix of problems with which behavioral medicine is concerned [5].

In this matrix, a disease is indexed at the sociological, epidemiological, anthropological, psychological, biomedical, and physiological levels of networks, and this is a multidimensional analysis with reference to different times (risks, pathophysiology, prognosis, treatment, and rehabilitation) and agency.

While behavioral medicine extended the core psychosomatic view to the broadest hermeneutical frame, the consultation-liaison psychosomatic medicine was connected to the mainstream psychiatry, with the following scope of interest:

1. The role of *psychosocial variables* in the development of illness (etiology)
2. The examination of the *causative connections between the changes of psychosocial variables and physiological parameters* (psycho-endocrinology, psychoimmunology, psychocardiology)
3. The fundamental *psychological changes accompanying illness* (illness behavior)
4. The *psychological and mental concomitants* of specific somatic processes
5. The effect of *therapeutic methods affecting behavior on somatic conditions* and somatic variables

Research into neuroimmunomodulation in immune laboratories had an explosion in the 1970s, in addition to research into the physiology of stress, creating the basis for a new “network” field of psychosomatics, the psychoneuroimmunology.

1.2 Psychoneuroimmunology: a “network discipline”

The rise of psychoneuroimmunology is a typical example of behavioral and medical interpretation of human disease. Its core explanatory model is based on insights of neuroimmune modulation, the bidirectional communication between neuroendocrine and immune system enabled by shared receptors and cross talk of messengers, and their integrated neuroendocrine-immune information pathways consisting of neurotransmitters, interleukins, neuropeptides, and hormone, including even myokines and adipokines [6]. These evolutionary patterned

communication networks create a *network of networks* throughout the whole body, including the brain and all the organs. In the social-psychological, cognitive-evaluative, emotional, neurovisceral associations, connections, and circles, regulative positive and negative feedback loops create unity of rational, emotive, visceral, molecular, receptorial, and transcriptomic-genetic levels. The prehistory of psychoimmunology is mostly shared with psychosomatics, and its hermeneutic and heuristic features are close to what network medicine offers [6].

As early as at the end of the nineteenth century, we see data about the effect of damaging the nervous system on the loss of protection against anthrax. At the beginning of the twentieth century, Salomondsen and Mandsen already connected vagotomy and the atopic and anaphylactic reactions, and Hatiegan first described the effect of adrenaline on increasing the amount of lymphocytes in 1925, which was confirmed by Frey and Tonietty in 1927.

In Metalnikov and Chorine's 1926 work, they already discussed the conditionability of immune phenomena. The general immunological influence of emotions was described by Erich Wittkower, when he detected an increase in the number of white blood cells in the states of anxiety, anger, grief, and heightened mood. He coined the term "Affektleukocytose" to describe this phenomenon, which he explained with the stimulation of the sympathetic nervous system. A group of physiologists from Cluj-Napoca, Csaba Hadnagy and the Romanian Baciú, also joined this trend when they examined the effects of emotions and the autonomous nervous system on the number of white blood cells at the beginning of the 1940s.

Locke had already prepared a bibliography of more than 1500 articles in 1983 under the title *Behavioral Immunology*. If we take into account the names given to the scientific field discussed in these articles, the first "christening" took place in 1974 and is connected to Robert Ader, who used the term psychoimmunology and in 1981 extended it as psychoneuroimmunology. The term of *neuroimmunomodulation* is connected to Herbert Spector, while Berczi and Szentiványi used the term *neuroimmune biology*. They all include the overlap of different networks thought to be autonomous.

Even in the comprehensive work of Franz Alexander, psychosomatic medicine includes also internal diseases which, some decades later, turned to be understood in psychoneuroimmune contexts, like IBD, bronchial asthma, rheumatoid arthritis, peptic ulcer, Graves disease, neurodermatitis, and, as recent data show, hypertension which is not an exception at all. Although Alexander did not realize the neuroimmune information pathways and the networked features behind these diseases, his "psychosomatic" internal medicine was strongly attached to psychosocial relationships and conflicts including clinical phenomena generated by neuro-immunobiological networks.

1.3 Hungarians' contributions to psychoneuroimmunology

Reviewing contributions to the prehistory of psychoimmunology, we can find the researchers' sensitivity toward the neuro-immunobiological network response to environmental challenges, as a shared feature in oeuvre of Hungarian scientists, like Selye, Berczi and Nagy, Bertók, Bohus, or Jancsó Jr. Selye presented the first neuroendocrine-immunological insight to human adaptation in 1936 when he proved the somatic triad of general adaptation syndrome, including peptic ulcer, adrenal hypertrophy (endocrine), and thymic and lymphoid atrophy. Selye confirmed the effect of the adrenocortical extract on inducing thymic atrophy in rats in 1943, and he called attention to the role of corticosteroids in regulating the inflammatory response in 1949. This research resulted in the development of

the medication that is so important for autoimmune or allergic patients. However, Selye's Hungarian students also achieved important results in the field of endocrine immunology. István Berczi became a colleague of Selye in the 1960s, and he was exploring the immunological effects of hypophysis hormones together with Éva Nagy. They were among the first to confirm that not only cortisol but other stress hormones, such as the growth hormone or prolactin, also participate in the regulation of the hemo-lymphopoietic system and the immune functions. Lóránd Bertók, a guest researcher of Selye in the 1960s, can also be considered one of the pioneers of natural immunity research. He examined the protective role of bile acids against bacterial lipopolysaccharides. The toxic effect of the lipopolysaccharide endotoxins released by bacteria is an essential promoter of inflammation since their membrane-disrupting, capillary-penetrating, shock-inducing, and fever-inducing effects provide dramatic components of the illness. During endotoxic shock, the levels of ACTH, corticoids, and beta-endorphin increase; however, the levels of prolactin, TSH, T3, and T4 are reduced. These effects are mediated by immune mediators such as IL-1, IL-6, and TNF, which are secreted by the macrophages activated by endotoxins and monocytes. Lóránd Bertók's research also confirmed that the radiotherapeutic treatment of the endotoxins reduces their toxic effect and this harmless product, the so-called Tolerin, can increase the natural immune reaction and mobilize stem cells.

Hungarian researchers played a pioneering role in the discovery of another system of connections, the "neuroimmune network." Besides István Berczi, Andor Szentiványi also played a role in discovering the nature of the connections between neuroendocrine-immune networks when he prevented the anaphylactic response by lesions created in the tubular area of the hypothalamus. The work of Miklós Jancsó Jr. was also important. He investigated the effect of histamine on the endothelial vascular cells and the reticuloendothelial system as early as in the 1940s and identified histamine as the physiological activator of the reticuloendothelial system. However, he also identified another neuroimmune network, which played a large role in the understanding of the neuroimmune processes taking place on the internal and external surface of the body. Through research sensory neurons in the 1950s, Miklós Jancsó Jr. concluded for the first time that *a neuroimmune network must exist*, in which the sensory fibers play an important role. The antidromic electric excitation of the sensory nerves triggered an inflammatory response, which the researcher was able to prevent with capsaicin treatment and the selective destruction of C fibers. On the internal surfaces of the gut or joints, sensory fibers and the increase of substance P play an essential role in inflammatory processes. The discovery of Miklós Jancsó Jr. still provides a *paradigmatic network interpretation* framework for psycho-immune research today. This network might play a role in trigger point and referred pain theory of Janet Travell and other reflextherapy theories, too.

Béla Bohus and his colleagues also brought a new slice of reality into the range of interpretation of PNI, examining the correlations between social interactions, dominance, subordination, behavioral traits, and physiological indicators. Social hierarchy is a network structure at ethological/social levels, which is transferred to neuroendocrine-immune networks through cognitive behavioral networks.

We should mention further Hungarian think tanks as well, such as the works of Elemér Endrőczy Csaba Nyakas and Lajos Korányi, or the research group led by Szilveszter Vízny, among which Ilia Elenkov's or Judit Szelényi can be mentioned as outstanding representatives of the field. In the field of applied psychoimmunology, we have to mention the pioneering role of György Németh and András Guseo.

The turning points and parallel evolutionary pathways of psychosomatics and psychoneuroimmunology, listed in **Table 1**, share covert network logic.

2. The neuroimmune networks

Networks are stand-alone factors in themselves, displayed by graphs depicting symmetrical or asymmetrical relations between cells, molecules, organs, and social relationships and life events. The network-type depiction is also warranted by the need to present regulatory cycles in block schematics, system theory modeling, and the communication and information paths and logical relationships. The neuroimmune networks are graphs, and the task is to identify the nodes (sometimes hubs) connecting them and the system of relations between them. However, under the socio-psychoimmunological approach, the limits of the graph's validity exceed the levels of the systems of molecules, organs, and organ systems and bypass the individual and personal as well. Under this approach, partnerships, social support, control, power, the territorial principle, dominance and submission, and social ranking are all presented in a set of relationships that can be outlined by graphs, edges, and hubs. However, connections over time are also aligned to the psychoimmunological interpretation of diseases as a graph and network, in the narrative framework of psychosomatics. Therefore, the particular "metagraph network" of socio-psychoimmunology lies across several layers of graphs.

The anamnesis and history disclosed by the patient, the writing or conversation therapy for exploring and disclosing traumas, the research for early traumas, and the investigation of infection chains, learning about the dramatic dynamics underlying socio-somatic relations, are all possible using the toolset of this expanded, narrative network analysis.

This is the anatomy of experience embodied in text, the crystallography of the petrified personal suffering. Identifying the persons and events included in the fate-text and exploring the system of their relations pose the same kind of challenge for network theory as the exploring the "small-world" networks of relevant mediators, and comparison of the neural, endocrine, and immune networks, and locating the hubs that connect them and drawing the graph lines of the relationships in them.

The identification of key players, dominant communities, groups, and the system of relationships between them, based on the personal narrative, and the understanding of tensions of social rank are an inevitable part of "decoding" the socio-psycho-immune network. This is how actual *dramatic hubs* connect patterns of vulnerable personality reactions, traumatic life events, social rank, and dominance relations and neuroimmune stress networks. As it is the person who explores and reveals it in the therapeutic process, psychoimmunotherapy includes a rearrangement of the representations of the external set of relations and the set of relations hidden by time generated in mind. This means a network analysis of social behavioral cognitive and clinical psychophysiological networks of relevance. This might offer revelatory rearrangements between the related set of life events, personality, and psychological network pattern and the narrative representation network, which may reach even the neuroimmune networks in the deep. This is why the social networks and their narrative reflection in life history should be analyzed together with biological networks of the socio-psychoimmunological network model.

Situation assessment, psychophysiological, and neuroendocrine networks make up such extended networks, and so do the neuroendocrine and neuropeptide patterns, cytokine networks, extracellular messengers, and intracellular molecular paths, genetic programs, and transcription processes. Overrepresented hubs and edges that determine the dynamics and types of physiological and pathological events, as well as possible therapies, are also outlined here.

2.1 Network features of Solomon postulates

George Freeman Solomon was one of those pioneers who established the scientific paradigm of psychoimmunology in the 1960s and 1970s, pointing to the connections between brain, behavior, and immunity. He gathered the psychoimmunological revelations in a corpus of postulates [7]. We can test these postulates from the network perspective.

Graph of neuroendocrine-immune networks might be seen as real *small-world networks* in which most nodes are not neighbors of one another, but the neighbors of any given node are likely to be neighbors of each other, and most nodes can be reached from every other node by a small number of hops or steps.

2.1.1 Neuroendocrine-immune chain

IL-1, paraventricular NA secretion- CRH-ACTH-adrenocortical cortisol/(sickness behavior, neuroendocrine-immune feedback, inflammation theory of depression based on depletion of dopamine, or diminishing serotonin secretion)

Immunological abnormalities may be accompanied by psychological or mental disorders.

Activation of the immune system can lead to changes in the activity of the central nervous system.

Immune signaling can also affect the central nervous system.

Cytokines of the immune system, as part of the neuroimmune endocrine axis, play a role in endocrine regulation, including stress-induced endocrine processes.

Cytokines influence psychological processes and cause psychiatric symptoms. Immunity influences behavior, and behavior can aid in immune regulatory functions.

2.1.2 Psychoneuro-endocrine-immune chain

Psychological states/traits-neural networks-stress hormones-immune system (C-type personality, right frontal hemispherical dominance, chronic stress, depression, shame, submissive status)

Adaptive coping styles and enduring characteristics can improve the prognosis of immune diseases and protect susceptible patients from the disease.

Stress coping and traits, including personality traits that influence stress management, may influence the immune response to exogenous antigenic stimuli.

Emotional changes and distress (state characteristics) can influence the onset, severity, and course of disorders controlled by immune processes or resulting from disturbed immune processes (allergies, autoimmune, diseases, AIDS).

Severe emotional and mental disorders can cause immunological disorders.

Immune functions may also be affected by altered states of consciousness.

Experimental behavioral effects may lead to immunological changes.

Damage to and stimulation of some regions of the central nervous system may lead to immunological changes.

Substances produced and regulated by the central nervous system (neurotransmitters, neuropeptides, other neuroendocrine factors) must influence immune processes.

2.1.3 Social-psychoneuroimmune network chains (social rank, social evaluative theory, shame, bereavement, social losses, social exclusion, voodoo, cultural nocebos)

In extensive prospective studies, specific patterns of psychological risk should be associated with a higher incidence of immune disease.

Genetic, gender, and behavioral factors influence the immunological effects of stress.

In addition to the influence on the adult psyche, early injury and the traumatic mother-child relationship can affect the adult immune system.

Therapeutic influencing behavior (psychotherapy, relaxation, biofeedback, and hypnosis) may also affect immune function.

Positive emotions stimulate immune function.

2.2. Bridges in the network

Immunocompetent cells have receptors for receiving neuropeptides, neurotransmitters, and endocrine signals.

Central nervous and hormonal factors may play a role in the regulation of feedback processes in the immune system.

Lymphocyte receptors are also affected by changes in transducer sensitivities that are characteristic of mental disorders and cells of the central nervous system.

2.3 Hubs in the network

Thymic hormones that regulate immune function may be under central nervous system influence.

CRH plays a role in the processes and symptoms of depression and immunosuppression associated with depression.

Certain cell groups of the nervous and immune systems occur together.

The prenatal hormonal environment has an effect on CNS and the development of the immune system, which can have lasting effects on both behavioral and immune functions.

Sleep affects both CNS and immune processes.

Immunological processes and specific personality characteristics (coping style, “hardiness”) may play a role in longevity.

Enzymes for the synthesis of brain neurotransmitters are found in immunocompetent cells and neurons.

Melatonin, a neuronal hormone involved in the regulation of circadian rhythmicity and affected by stress, affects immune function.

Mitogens, potent, non-specific immunostimulants, also act on the nervous system.

Immune cells influence the development and function of the surrounding nervous system.

Lymphokines may affect pituitary hormones directly and via the central nervous system.

Some cells of the central nervous system are capable of lymphokine production.

Cytokines of the immune system, as part of the neuroimmune endocrine axis, play a role in endocrine regulation, including stress-induced endocrine processes.

These psychoimmunological facts support the profound relevance of social and psychological network changes exerting deep visceral influence through psychophysiological networks. It also supports the connection between psychosomatics and broad areas of internal medicine.

The network-based interpretation of crucial issues of psychosomatics mapped in **Table 1** follows the above principles. Social networks and neuro-immunobiological networks are linked with psycho developmental hubs. Common, hub-like narrative foci are the early mother-child relationships and the adverse childhood experiences, just like the syndrome of post-traumatic stress. Distorted early mother-child attachment organizations have an impact on the so-called internal working model and

other personality features creating enhanced risks for some somatic diseases. A-type anxious avoidant secondary attachment organization might diminish empathy and hypothetically create a tendency toward A-type personality development, strive for dominance, competition, and hostility and tendencies for cardiovascular vulnerability. In contrast, C-type secondary anxious/ambivalent attachment organization creates lower self-esteem, behavioral inhibition of aggression, and expression of emotions, high anxiety, and psychophysiological arousal [8, 9].

Epigenetic consequences of distorted mother-child attachment, like down-regulation of hippocampal GR receptors via histone methylation, distorted HPA feedback, and distorted estrogen regulation with consequences on adult maternal behavior also prove the hub-like role of the mother-child relationship between socio-psychological and developmental personality networks, stress physiological networks, and neuroimmune network.

Relations between transactional events, traumas, feelings of submission, and loss of control, just as chronic psychosocial stressors, that carry psychological meaning are explored in the networks of the socio-psychological layer. Alexithymia or social inhibition and the psychological network patterns of the C-type personality convert all this into increased HPA activity, high arousal, and increased LC/NAerg activity, so that all this is eventually embodied in the disruptions of the immune cell network controlled by cytokines. Then, IL-1 and IL-6 as result of modified protein synthesis in the cell reach the central nervous system, and via modified dopaminergic and serotonergic molecular network changes is transcribed into psychological network patterns and depression. The disturbances of the rank position experienced in social networks (reduced motivation, lack of adequacy in the workplace, family conflicts, loss of socioeconomic status) are also embodied this way (via neural networks and proinflammatory cytokines).

3. The psychoimmunology of social stress in the network context

Human social relationships might be occasionally the source of severe conflicts. In the light of social exchange theory, it is apparent that the individual is often exposed to severe distress in the high-cost medium of the temporal, monetary, and emotional strain of social interactions. Plenty of evidence is available for presenting the social-psychoimmune consequences of distorted human relationships.

The negative or ambivalent social relationships and the resulting conflicts and associated negative emotions can influence immune processes. Hostility, which we primarily know as a cardiovascular risk factor of psychosomatics, promotes inflammatory processes as well, which is indicated by elevation of CRP and IL-6, according to the work of Suarez [10], and the increased level of the pro-inflammatory cytokines typical of depression as well.

Depression highlights a distinct area of research within social-psychoimmunology, taking the correlations between depression and social integration into account, as well as the relationship conflicts and its negative effect on social perception. Depression is proven to be a mediating factor between socioeconomic patterns (personal income) and physical consequences (number of sick days) in behavioral and epidemiological research called Hungarostudy, verified by route analysis [11]. Depression is proven to be also an independent risk factor of myocardial infarction [12].

The attitudes and emotions increasing the stress of social interaction and interpersonal emotional relationships, such as anger or the hardships caused by depression, are also reflected in the differences in the immune response. Social conflict influences the course of rheumatoid arthritis, in which case catecholamine

plays an important role among the neurohormonal factors mediating psychosocial distress. In the social network of ambivalent individuals (those who exert positive and negative influence as well), the ambivalent persons cause increased adrenergic reactions based on the work of Uchino et al. [13], and the contact and conflict with ambivalent persons can provoke an increase in systolic blood pressure. Long-term tight ambivalent human relationships, rich in conflicts, are common in bad marriages, where worse health indicators are also often observed according to the findings of Kiecolt-Glaser and Newton [14]. The dissatisfaction indicator of marriage is accompanied by worse immune indicators, as seen in the case of the ratio of anti-EBV antibodies, CD4+, or CD8+ cells. The hostile behavior typical of bad marriage, impulsivity resulting in cutting each other off when speaking, as well as critical and judgmental impatience, can be indicators of physiological differences and increased blood pressure and endocrine values, based on the work of Malarkey et al. [15]. Among newlywed couples, those who are more prone to adverse, hostile reactions, and this is recalled during a short, 30-min discussion, suppressed immune function was shown in samples taken 24 h later. Kiecolt-Glaser et al. [16] stated that the discrepancy indicating dysfunction of the endocrine-immune regulation was true to older couples as well during discussions where they had to recall their conflicts. The amount of negativistic behavior was in direct correlation with the weakening of the immune response. Mayne et al. [17] confirmed that as much as 45 minutes of exploratory discussion of conflict was enough to reduce lymphocyte proliferation in the examined women. During prospective research, Levenstein et al. [18] found a connection between ulcerative inflammation of the oral cavity and marital stress, while Kiecolt-Glaser et al. observed significantly approximately 60% longer wound healing in the case of couples exhibiting hostile behavior.

Trait-like hostility, characterized by aggression, anger, and cynicism, causes an even more evident immune regulatory disorder in the event of family conflicts, according to Mayne et al. [17]. Miller et al. [19] found a distinct correlation between hostile and cynical attitudes and behavior during conflict management and the cardiovascular response, cortisol, and immune discrepancies. Social stressors induce a rise of pro-inflammatory mediators as well and cause systematic inflammation in the body, based on the work of Steptoe et al. [20]. Partnership conflicts, rejection, and exclusion have significant pro-inflammatory effects even compared to depression and various life events, according to the findings of Denson et al. [21].

4. Evolved network patterns in psychoimmunological risk situations

The neuroendocrine effects triggered in the brain by threatening environmental stimuli can create a preparatory pathogen-host defense effect on the native immune system, as a result of which the redistribution of the cells of the native immune system and their migration toward the exposed area are detected. All of this ensures the increased rate of healing after an injury. This response can be mobilized by both the presence of predators and the emergence of a significant conflict situation. In the opinion of Slavich and Cole [22], the mobilization of innate immunity is not only an evolutionary remnant but something that can be triggered by symbolic threats, social conflict, rejection, isolation, and exclusion as well. If we consider the genetic basis of the neuroendocrine and immune systems of mammals when investigating their immune system, we can identify a typical pro-inflammatory/anti-inflammatory response pattern by examining the transcriptome of the leukocytes circulated in the body that is the set of RNA typical of the cell.

Under normal circumstances, the activity of the sympathetic nervous system increases the conserved transcriptional response to adversity (CTRA) with the help of the adrenergic receptors, and the activity of the HPA axis reduces the CTRA-dependent inflammatory response as a result of the released cortisol.

However, in the case of chronic social isolation, the threat of grief, and post-traumatic stress, reduced activity of the anti-inflammatory glucocorticoid receptor (GR) can be detected. Therefore, the so-called conserved transcriptional response to adversity is triggered by threatening, stressful, or permanently uncertain adversity as well, as indicated in Antoni's report [23].

As mentioned above, the threat of grief, traumatic stress, social isolation, low socioeconomic status, or a cancer diagnosis all result in pro-inflammatory transcription disorders. In experimental animal models, social instability, low social rank, and repeated defeat also resulted in a CTRA. Such challenges increase the activity of the genes responsible for the inflammatory immune response to extracellular pathogens and bacterial infections and inhibit the genes responsible for the antiviral immune response to intracellular pathogens. The selective evolutionary advantage of all this is indicated by the fact that it increases the rate of CTRA, wound healing, and response to infection in the event of an actual physical threat. However, it is apparent from the observations that the CTRA is activated by several symbolic, social, anticipated, or imagined emergencies experienced in everyday life. In the event of prolonged perceived or real danger, social or physical threat, a glucocorticoid resistance might develop, which may lead to more severe inflammation or depression.

These phenomena had evolved as a result of the coevolution of hierarchic layers of social, cognitive, neural, immune, and transcriptomic, genetic layers of this hierarchical construction of different networks linked to each other. The highly conserved biological response to adversity, described above, is crucial to overcome the physical threats or injury. Modern-day social, symbolic, or perceived, even imagined, threats might also lead to a pro-inflammatory phenotype of (mal) adaptive answer. The elevation of pro-inflammatory cytokines, such as IL-1 and IL-6, may contribute to elicit depressive symptoms. The overlap of depression with several physical conditions, including asthma, rheumatoid arthritis, chronic pain, metabolic syndrome, cardiovascular disease, obesity, and neurodegeneration, shows the psychosomatic significance and network character of this civilizational paradox. It is a central issue of psychosomatics and roots in the nonadaptive linking of different, environmental, social, cognitive-emotional, neuroimmune, and genetic networks. Psychosomatics deals with this network of networks, where the informational pathways are the edges between nodes, hubs, and the more extensive network "patches." The so-called social signal transduction theory of depression is a proper example to track how social-environmental information activate biological processes that lead to depression.

The hypothesis that experiences of social threat and adversity upregulate components of the immune system involved in inflammation is central to the social signal transduction theory of depression. The key mediators or messengers, called *pro-inflammatory cytokines*, play a hub-like role in the network, which might induce profound changes in behavior like psychomotor retardation and social behavioral withdrawal, and influencing immune networks, and neural regulations of mood, anhedonia, and fatigue as symptoms of depression. Self-perceived/perceived lower social status is associated with higher pro-inflammatory cytokines (IL-6) in the dorsomedial prefrontal cortex (DMPFC) activity. The DMPFC plays a crucial role in the so-called mentalizing network, which is active in brain processes that model the thoughts and feelings of others, as well

as in evaluating the social status associated with this process. The ventromedial prefrontal cortex (VMPFC) plays an essential role in detecting and assessing signs of dominance. VMPFC damage leads to insensitivity to the social hierarchy and a lack of respect for age and gender. The amygdala plays an integrative role in the perception of dominance, learning processes are related to the social hierarchy, the perceived value of the individual within the group are linked to the amygdala, and its relationships with the hippocampus and striatum are productive. The lateral prefrontal cortex (LPFC) integrates social hierarchy information from the intraparietal sulcus and hippocampus, while VMPFC is responsible for organizing adaptive behavior. The network approach gives these centers a real social-psychoneuroimmune “hub” position.

On the other hand, diverse anatomical connections connect it to the amygdala, hypothalamus, and periaqueductal gray matter, thus reaching the stress pathways affecting the immune processes. Beyond its role in empathy and mentalization, it is also part of the so-called “aversive amplification” subnetwork, which activates the appropriate limbic areas in the event of threatening stress. In this regard, it plays a role in the processing of social impulses, perceiving others’ higher positions in social rank as a source of critical, negative, exclusionary, and punitive social impulses, as well as in their qualification of danger. The inferior social status presumption is associated with increased activity in this brain area.

The hypothesis of social signal transduction theory of depression regarding experiences of psychoimmunological effects of social threat and adversity is central in our network theory of psychosomatics.

5. Network medicine as a psychosomatic metamodel

In the network medicine, identification of networks, hubs, and edges represents a true “big data” challenge, as the protein synthesis is determined by nearly 25,000 genes and the network hubs of “interactomes” are created by numerous proteins and functional RNS molecules as cell builders, on a scale of thousands. The number of network interactions with functional relevance is even higher. Learning about these interactions and identifying biological networks are the tasks for network medicine. However, the logic of network pathology is followed by research on the connections between the brain, hormone organs, and the immune system, on physiological networks, exploration of which is also a mapping task for interactomes of different levels. Such a map, comprising nearly 7000 interactions, is drawn by the protein-protein interaction network map of Rual et al. [24], the metabolic network summary by Duarte et al. [25], as well as the cytokine maps. However, the concept of meaningful narratives, life events, personality types susceptible to disease, or Berne’s transaction analysis also strives to draw up such maps. Exploring the connection between anamnesis and disease progression is also a similar effort at representation.

The task is to identify interactomes as networks, within which the network patterns and relevant connection paths associated with the disease should be identified. Probably, the analysis of the socio-psychoimmunology paths is necessary as well, given that the “interactomes” of this mappable system of network relations can be identified. It is possible to explore the relationships between these factors, causal relations, and multidirectional pathways of influence, the network characteristics of the personality and the body, and the dynamics of the evolution and progression of diseases. Low socioeconomic status, discrimination, and subordination are accompanied by an increased level of pro-inflammatory cytokines, with the

mediation of neurohumoral pathways, as demonstrated by Dickerson et al. [26], for instance. Anxiety, depression, and post-traumatic stress disease, along with the accompanying social and behavioral phenomena, are connected to neurohumoral and immune network anomalies, such as increased pro-inflammatory cytokines (e.g., IL-6) or the activation of the NF-kappa B path, which has central significance in the activity of inflammatory networks, according to Haroon et al. [27].

Identifying the degree of distribution and identifying the hubs characterized by several connections are needed to find the characteristics of these networks. At a molecular level, these can be TLR4, NF-kappa B, caspase, or, at the cellular level, macrophages or the cellular elements of the HPA axis representing nodes of the network. More abstract network modeling makes neurological structures participating in the assessment of controllability, the psychological processes of social perception and assessment, and neurophysiological structures that organize the personality also such as hubs. This way, the early mother-child relationship, which is vital for the development of personality, in the evolution of neurobiological structures, and carries permanent immunobiological consequences, becomes a network hub, as described above. Similarly, several neural networks as centers might create a greater network system responsible for translating social events.

The network itself is held together by a few hubs that have many connections. This is why socio-immunology explores lifetime hubs pointing in so many directions (mother-child relationship, separation, loss of object, loss of control), positive or negative traits (pessimism, C-type personality, active or passive coping) that are sensitive in immunological terms, pathologic network patterns (blunted HPA activity, deregulation of glucocorticoid receptors, TH1/TH2 shift), and allergic or autoimmune disease patterns in patient narratives at the social level. (**Figure 3**). These various key “hubs” may connect several types of networks of correlations. These small worlds are features of complex networks. The interconnected molecular networks are surrounded by relatively short path connections where a large portion of the component proteins are responsible for a low number of interactions, while they may be along main routes affecting the entire body, influencing the entire network.

Therefore, the hubs responsible for specific local cellular processes may be deemed to be “party” hubs, while they may also be “date” hubs interconnecting processes and associating relationships that organize the interactome. Further characteristics of the network are the “subgraphs” having motif power and in charge of biological functions such as negative or positive feedback or the oscillator function. These subgraphs are the totality of the interconnected hubs that make up a subnetwork within the network. Most networks may be described by a substantial creation of beams and are accompanied by the generation of topology modules characterized by the emergence of a high local region with mutual connections. Hubs are characterized by a high *betweenness centrality that describes the number of the shortest paths running through the hub*, otherwise referred to as “bottleneck.” This is the nature of regulatory networks with vector edges.

An essential part of network analysis is link analysis, which looks primarily at the relationships between factors, hubs, and objects. Immunology itself offers an excellent example for the analysis of key relationships and links between the various objects, as it identifies and maps relations between networks of different characters (wired neural, endocrine propagated by blood flow, immune cells and mediators moving through tissues). Socio-immunology allocates the anamnestic narrative network relations, life events, and the social and symbolic cultural hub networks, through personality patterns, social-neuroscientific insight to responsible neural circuits deep to the cellular transcriptomic level of neuro-endocrine-immune networks, exposing their mutual interactions. This network

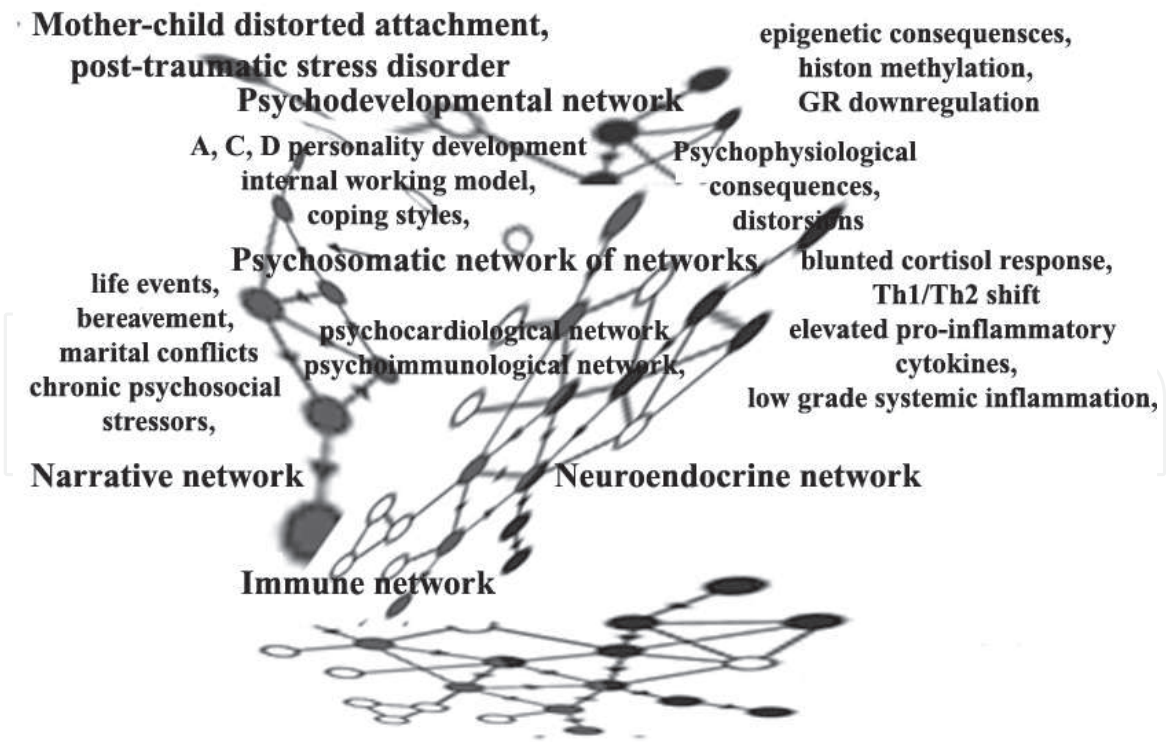


Figure 3.
Psychosomatic network of networks.

approach provides a new framework of cognitive mapping for anamnesis, diagnosis, and therapy. The result is a transversal metanetwork appearing through a series of information transcripts and translation mechanisms, which weaves a psychosomatic disease pattern through the network layers with its own heteronomous hubs.

6. Network framework as the common denominator of psychosomatics and internal medicine

The integrated internal medicine/psychosomatic/lifestyle medicine method is beneficial in improving the treatment of the disease, including the psychosocial factors to be taken into account [28]. Such are loneliness, chronic stress, the role of life events, the loss of object, and the personal characteristics of coping. Psychosomatic diagnosis is supported by the Diagnostic Criteria for Psychosomatic Research (DCPR), which incorporates relevant psychological variables into the diagnostic system along the lines of the most important psychosomatic syndromes, like anxiety, functional physical and conversion symptoms, somatic symptom formation of psychiatric origin, somatic and hypochondriac perceptions and fears (disease phobia and fear of death), and suppression of the disease that refers to psychosomatically colored disease behavior. In contrast, alexithymia; risk patterns of A-, C-, and D-type personality; and behavior patterns include trait and state features of personality characteristics that affect the patient's condition, including psychophysiological risks [29, 30]. Patients may require appropriate anxiety-reducing therapeutic support or cognitive behavioral therapy for psychophysiological involvement of chronic diseases. Clinical psychoimmunology offers new explanatory model and therapeutic framework for bronchial asthma, inflammatory bowel diseases, rheumatoid arthritis, specific autoimmune endocrine pathologies, and psychosomatic skin diseases. It is crucial if 25% of cardiovascular patients suffer from untreated depression, and the chronic inflammatory process fed by

depression, or similar psychoimmunological processes might contribute to the atherosclerotic vascular processes. Oncological patients have similar problems with untreated depression and the immunosuppressive effects of depression (in the case of NK cells) on the disease process.

Significant evidence-based research has indicated the increasing importance of a psychosocial approach in the field of internal medicine diseases, such as the SPIRR-CAD study among depressed patients suffering from coronary arterial disease [31]; the PISO study, somatoform disorders [32]; or DAD study, diabetes [33]. Although the SPIRR-CAD study did not demonstrate the overall benefit of cascading interventional psychotherapy among depressed coronary artery patients, it showed the success of therapy in a “bond-damaged” group of patients and among adult bypass-linked ISB patients [34]. Katon et al. [35] integrated “behavioral medicine” and psychosomatic approach to primary care. Lower HbA1c, blood pressure, and serum cholesterol was demonstrated among diabetic patients in the TEAM-care program than the control group receiving average care. Psychosomatics is not an alternative but an extension of the perspective of internal medicine. Lipowski [4] emphasizes that “psychosomatics” is an expression of the inseparability and interdependence of psychosocial and biological (physiological, somatic) aspects of human existence. This extension includes the extension of networks, too.

7. Risk factors and lifestyle risks of internal medicine diseases

Independent risk factors that increase the risk of internal medical diseases are also objects of a separate discipline, lifestyle medicine, addressing the relationship between avoidable risk factors and lifestyle. However, lifestyle medicine links biomedicine and psychosomatics, also. Obesity; distorted coping that escalates into addictions (smoking, alcohol, drugs, sedatives, chemical comforters); sedentary lifestyle, or, on the contrary, overtraining due to a distorted body image; eating disorders; and high carbohydrate and fat intake may affect the risk of developing cardiovascular and metabolic disorders.

The Framingham study was one of the early follow-up studies that demonstrated the role of hypertension, smoking, and high blood fats among independent risk factors for coronary sclerosis. Today, depression and anxiety must also be considered an independent risk factor for coronary artery disease [12].

Life events can also affect the development and course of the disease. Bereavement, divorce with high values in the Holmes-Rahe scale, and common everyday stress experience called daily hassles all might play a role. For example, in respiratory diseases, a correlation is observed between stressful life events, perceived stress, and upper respiratory symptoms. The risk of provoking asthma is known for severe adverse life events. Rheumatoid arthritis often flares up after bereavement, divorce, and job loss. Serious conflict, divorce, bereavement, or love disappointment might induce or worsen course of ulcerative colitis.

Lifestyle medicine offers network-like interventions along with behavioral modification. One of these is regular exercise. In a plague of sedentarism, physical exercise might be a panacea for many lifestyle problems. The active muscles are part of the neuroendocrine-immune network of the human organism and exert significant influence on the metabolic system, the immune system, the brain, and the abdominal fat, which is also part of the complex informational network. Exercise induces endorphin secretion. Myokines exert their influence by the presence of their receptors on muscle, fat, liver, pancreatic, bone, heart, immune, and brain cells. Myokines like myostatin, IL-6, IL-8, IL-15, FGF21, follistatin-like 1, brain-derived neurotrophic factor (BDNF), hepatocyte growth factor,

fibroblast growth factor, and insulin-like growth factor play role in metabolism and tissue regeneration. IL-15 reduces abdominal adipose tissue, while in heavy physical exercise, the secreted IL-6 as myokine rises to 100-fold of resting level and increases IL-1 and IL-10 as an anti-inflammatory mediator. Brain-derived neurotrophic factor might be secreted as a myokine, and muscle-derived BDNF enhances fat oxidation.

8. Discourses and institutions: networks of psychosomatic agency

On the other side, psychosomatic medicine as a unique professional medical specialization is not universal at all. In Europe, one can find such psychosomatic professional specialization only in Germany, while psychotherapy applied by somatic experts is practiced in many other countries. The new niches for psychosomatic orientation offered by integrative frameworks of stress medicine, mind-body medicine, or lifestyle medicine and network medicine are based on the above insights of linked biopsychosocial networks. Is this a trans/interdisciplinary challenge or a constraint for networking of different disciplines? If we compare the definition of behavioral medicine by Schwartz and Weiss in 1978 [36] and the 2019 proposal for its renewal by the ISBM consensus boards, we find meaningful shifts. The “interdisciplinary field” was exchanged to “field characterized by the collaboration among multiple disciplines” with the meaning of networking of disciplines instead of filling the intermediary disciplinary gaps.

This way, network medicine means double challenge, to see the patient as socio-psycho-biological “network of networks” and organize his/her healing in networks of disciplines, discourses, and institutions.

Psychosomatic medicine has its permanent revival fed by new findings in social neuroscience, clinical psychophysiology, or the new public health; nevertheless, its institutional network shows a narrow picture. Mental disorders (depression, chronic stress) proved to be independent risk factors in the development of auto-immune, allergic and neoplastic diseases, and myocardial infarction. It has been confirmed by evidence-based basic research (social neuroscience, psychoneuroimmunology, psychocardiology) and epidemiological analyses.

However, the institutionalization of psychosomatic clinical discourse showed a rather marginal status in the shadow zone of the high-tech, evidence-based practical development of biomedicine in the frontline. The discourse dynamics reflects the power inequities of health economic, academic, educational, and clinical health service networks.

In some countries (e.g., Germany, Japan), psychosomatic medicine can be practiced as a specialist field, with specialized psychosomatic clinical departments, separate institutes, and somatic and psychotherapeutic care in a joint framework, in teamwork. In Germany, there are over 5000 specialist physicians with psychosomatic and psychotherapist certifications. Outpatient care employs 3058 psychosomatic professionals, while 10,269 physicians hold the title of the psychotherapist, and a total of 21,312 physicians with somatic background have the title of psychotherapist. There are 120 psychosomatic institutions in Germany with a total of approx. 20,000 beds (Statistik-Portal, 2014). Institutional care is also highly developed, and psychosomatic wards providing regional care in regional central hospitals provide patient care. Although the number of hospital beds is limited (9 to 36 beds), the units also provide consultation-liaison psychosomatic care for other clinical departments. The university and teaching hospitals (20–70 beds) have a higher supply capacity, where in addition to healing, there is research and education.

In March 2016, the Japanese Psychosomatic Society had 3300 members, 71.6% of whom were physicians (general practitioners, psychiatrists, pediatricians, obstetricians-gynecologists, dentists, and dermatologists). Psychosomatic internal therapists also formed a separate association with 1200 members (Japanese Society of Psychosomatic Internal Medicine) [37].

Although there are widespread organized discourse communities, academic associations of psychosomatic experts from gynecology and obstetrics, internal medicine, cardiology, and gastroenterology, just as numerous clinical departments all around the medical world, one can find significant disproportion between psychosomatic *medical specialization* and mainstream organized health care in most of the contemporary medical systems.

Psychosomatics might be absorbed by psychiatry, as C-L psychiatry might be seen as a branch of mainstream psychiatry. It shows the significant disciplinary distance from internal medicine and other disciplines, while issues of psychoimmunology and psychocardiology are deeply embedded in the health-care system of internal medicine. This way, the emerging network centered renewal of behavioral medicine remains only an ideology than everyday clinical practice.

If clinical practice incorporates psychosomatics as part of mainstream medical discourse, guaranteeing the possibility of specialist examinations and specialized care and creating such specialist care units and scenes, the institutional and economic “emancipation” of the field is assured. In 2004, the so-called DAK/AHG study weighed the cost/benefit of long-term institutional psychosomatic treatment burdened with costly hotel services in 338 insured persons treated in psychosomatic hospital wards between January 1999 and February 2000. The results supported its “raison d’être” and profitable values for *health economic* point of view [38].

One might see the reason of these contradictions even in nature of psychosomatic disease, as a patient complaining of somatic symptoms used to be reluctant to classify his or her complaints as psychiatric. One can overcome this situation by an invited consultation-liaison psychiatrist, as the patient is not seeking psychological treatment but a somatic care provider for his/her psychosomatic disorders. All of this requires collaboration, a psychosomatically informed professional organizational culture, and a genuinely competent psychosomatic therapeutic delivery environment for the other treatments offered. Psychosomatic patients travel through routes of somatic care with their symptoms because of their interpretation. Once treated in a somatic ward, they are strongly attached to the physical origin of their complaints based on their explanatory model. Psychological assessment of symptoms is often considered offensive. Therefore, psychosomatic care is highly dependent on patient choice. If the primary and specialist care systems do not offer this type of care, the patient will not make such a decision either. Few people turn to psychiatric care providers for physical complaints of psychological origin, and the fear of stigmatization is a barrier, too. It follows that the internal structural features of institutionalized discourse impede the proper care of a large group of patients. Whereas in general medical practice, about one-third of patients suffer from psychiatric symptoms, and 23% of patients in primary care experience depression, 22% with anxiety, and 20% with somatization, it may be relevant for primary care physicians to have additional psychosomatic licensure training. One-third of cardiological patients have mild depression without treatment; oncological patients have a similar situation, frequently. Beyond these institutional difficulties, there is a great need for integrating psychosomatic to biomedicine, as argued above.

Katon et al. [35] also demonstrated that the so-called TEAM-care program, integrating behavioral and psychosomatic approaches with the somatic practice of primary care, lowered HbA1c, blood pressure, and serum cholesterol levels. Psychosomatic patients also increase the costs of somatic care because of hotel costs

and ineffective, sometimes unnecessary diagnostics efforts. This costly, unnecessary “evidence-driven” defensive medical practice consumes energy, time, and space in patients requiring care. Specified psychosomatic care is mostly related/reduced to clinical “elite institutions” and does not form part of general public hospital and outpatient practice. A few psychosomatic centers are connected to the university education (e.g., like the Psychosomatic Outpatient Department at the Institute of Behavioral Sciences, Semmelweis University) or occasionally as a department of the psychiatry clinic or elements of hospital psychiatric wards.

The concept of networked medicine in medical systems can also create new theoretical “niches” for psychosomatic clinical thinking. All of this may be important to connect biomedicine with social neuroscience, clinical psychophysiology (e.g., psychoimmunology), stress medicine, or mind-body medicine. All these conceptual spaces, theoretical niches, also designate real institutional niches. There are vacant clinical spaces that can be filled with training, a new competent workforce, and purely organizational innovation. As the affected patient population is unaware of the psychological roots or modifiers of their complaints, and even this non-knowledge often forms the mechanics of symptom formation (suppression, complexation, alexithymia, traumatic learning,), therefore their care is closely linked to extension of somatic specialists’ competence toward the psychosomatic horizon (specialist exam, license exam). On the other hand, the involvement of highly trained psychologists with clinical psychology specialization might also have an essential part of this organizational change. Such psychosomatic development can also affect oncology, dermatology, rheumatology, cardiology, and gastroenterology networks.

The occupational health services offer a wide surface for preventive network medicine, too. Occupational health might have an important priority area for psychosomatic preventive work and early disease detection. Recognizing the increasing work-related stress in the industrial space of globalization and the consequent economic loss of nearly EUR 40 billion to European Member States’ budgets has prompted European Union decision-makers to do the management of work-related stress management and mental health support, as a Member State’s duty from 2007. Preventive stress management can be part of health promotion and may be of interest to both the employee and the employer in health psychological and psychosomatic practice, linked to screening and other public health preventive practices. The use of *de-medicalized* cognitive behavioral elements of mind-body preventive agency might be applied as worksite stress management training (like in case of Williams Life Skills training), new screening ways of psychophysiological risks, and available psychometric methods might help to implement worksite and community-based prevention and intervention.

Psychologists with such skills, and occupational health practitioners sensitized in this regard, would achieve economically demonstrable results. Occupational health is the apparent scene for preventive and early psychosomatic intervention, as such screening of employees is easy to do and suits to the personal and corporate interest.

Psychosomatic diagnostic and counseling work or psychosomatic “lifestyle medicine” might have their niches in spa health, wellness network. They are, like the occupational health or specialist network, empty niches to fill with psychosomatics. The map of diverse, nevertheless, coherent discourses of psychosomatics can be reframed by the network medicine concept, a common denominator. If clinical practice incorporates psychosomatics as part of mainstream medical discourse, guaranteeing the possibility of specialist examinations and specialized care and creating such specialist care units and scenes, the institutional and economic “emancipation” of the field is assured. The hermeneutic bridge, which had

been already established in the biopsychosocial framework, did not lead to closer hybridization. The neuroimmune biological network frame might help the social and psychological aspects join to the evidence-based biomedical disciplines including the molecular and genomic transcriptomic level.

9. Conclusion

Steps in the history of psychosomatics share common heuristics in connecting different levels of environmental, psychological, neural, and visceral phenomena. This “multilayer” approach reflects the scientific will to follow the information flow from the social through the psychoneural and the visceral down to the molecular and genetic sphere and back. The psychophysiological core of psychosomatics has a human ecological context and deals with regulative network patterns of evolutionary roots. Concept of behavioral medicine shifted psychosomatics from a comprehensive psychodynamic explanatory model toward an integrative, multidisciplinary framework including levels of social, psychological, and somatic networks. Specific subfields of behavioral medicine, like psychoneuroimmunology, offer insights to the multilayered network-based interpretation of diseases. Dysregulation of evolutionary-based adaptive network activities like *the conserved transcriptional response to adversity* or the *social signal transduction theory of depression* reflects the clinical significance of network approach.

Depression itself is proven to be a mediating element between SES and sick days, between social and somatic, just as between the immunological and the psychological networks. Network theory offers an inclusive metanarrative for the description of the different social, narrative, and psychosomatic network layers and their interconnections as well anamnestic, diagnostic, and therapeutic significance. Behavioral medicine has shifted from an “*interdisciplinary field*” to the promoter of the collaboration among multiple disciplines, so this collaboration might be reframed by the extended and comprehensive network approach. Network medicine [39] as shared conceptual explanatory frame might bring closer behavioral epidemiology, the preventive lifestyle medicine, behavioral medicine, and occupational health and biomedicine. The exploring and implementing efforts based on the above defined “networks of networks” includes medical sociology, medical ecology, behavioral epidemiology, new public health, health promotion on the social side, and clinical psychophysiological depth of psychosomatic therapies including several cognitive behavioral approaches, hypnosis, psychodynamic approaches, and narrative medicine on the psychological side. Internal medicine, behavioral medicine, and psychosomatics with related disciplines overlap in the different social and psychophysiological network layers; network medicine might be the common denominator and the widest inclusive conceptual framework for collaboration.

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Author details

Imre Lázár^{1,2}

1 Head of Medical Humanities Research Group, Institute of Behavioral Sciences, Semmelweis University, Budapest, Hungary

2 Faculty of Humanities and Social Sciences, Károli Gáspár University, Institution of Social and Communication Sciences, Budapest, Hungary

*Address all correspondence to: lazar.imre@med.semmelweis-univ.hu

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