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NEUROIMMUNE INTERACTIONS: A BIDRECTIONAL *FLOW THAT LEADS TO HEALTH AND DISEASE*

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Abstract: The Vedic philosophy deals with harmony and balance between the mind and the body as well as interactions with nature. This ancient approach to health and well-being is being more and more appreciated in part as we understand the intimate relationship between the immune system, our major defense mechanism and the nervous system. Like other organ systems, the immune system is dependent on the central nervous system (CNS) and the endocrine system in its role for effective defense against foreign and domestic invaders.

The influence of the CNS on the immune system is demonstrated by strong physical and biochemical associations between the two systems (1). Accordingly, the immune system can exert a powerful influence on the CNS. For example, the thymus, spleen, and lymph nodes of the immune system is innervated strongly by the sympathetic nervous system (SNS) (1) . Moreover, the sensory nervous system, a sentinel transducer of pain in the skin and organs also influences the immune response (2). This physical association extends from the brain to central and peripheral lymphoid organs and also the liver that also exerts a strong influence on the immune response (Fig 1,2).

The major, anatomic/biochemical relationship between the central nervous system and the immune system is the hypothalamic, pituitary, adrenal (HPA) axis. Different areas of the brain selectively affect diverse immune responses (1). Here one can visualize this influence by the stimulus of an immune response by an antigen derived from any foreign material, bacteria, virus, parasite, or altered cell. If the brain "perceives' this invader a signal may be sent to the immune system. To induce an adaptive immune response, the antigen is taken up and processed by antigen presenting cells (mostly dendritic cells) in the circulation and/or the spleen and lymph nodes. This " processed" antigen is "presented" to thymus-derived T lymphocytes that proliferate and differentiate into cells that (i) interact with B lymphocytes that produce antibody to the antigen, (ii) cells that respond to the antigen by eliciting a destructive hypersensitivity reaction or (iii) cytotoxic T cells that interact with and kill the invader. In addition to these effecter T cells, T cells that regulate other T or B cells and protect against an immune system response to self antigens causing autoimmune disease are also amplified during an immune response. In addition to an adaptive immune response, inflammatory cells are stimulated by some antigens and these cells may provide a (destructive) inflammatory response. The net effect of these responses may be the destruction and elimination of the invader and subsequent healing if damage has been caused by the invader and/or collateral damage by the Immune response that is not directed towards tissue.

CNS IMMUNE SYSTEM

- **REGULATION**
- **ENHANCED RESPONSE**
- **INFLAMMATION**
- **FEVER**
- **BEHAVIOR**

IMMUNE RESPONSE CNS

- **BEHAVIOR**
- **FEVER**
- **AUTOIMMUNITY:**
  - **MULTIPLE SCLEROSIS (EAE)**
  - **MYASTHENIA GRAVIS**
  - **RETINITIS**
  - **PARANEOPLASTIC SYNDOME**
  - **ALSHEIMER'S DISEASE**

Figure 1

The CNS can impact all of the various stages of an immune response from the uptake of antigen by antigen presenting cells or macrophages, to the proliferation, differentiation and activity of T cells or B cells. The sympathetic nervous system (SNS) influences the nature of an immune response such that experimental ablation of the SNS results in a loss in cell-mediated hypersensitivity, a loss the generation of regulatory T cells that likely impact the generation of autoimmune disease or an enhancement of antibody production (1-4) probably through a loss of the neuropeptides norepinephrine and NPY and a loss in tissue plasminogen activator, critical in the dissolution of clots[5] . Relationships between the SNS and stress-induced corticotrophin-releasing hormone (CRH) provide more indicators of the effects of the CNS on the immune system (1,2). Clearly, stress can impact both immune defense and autoimmune disease.

NEUROIMMUNE INTERACTIONS

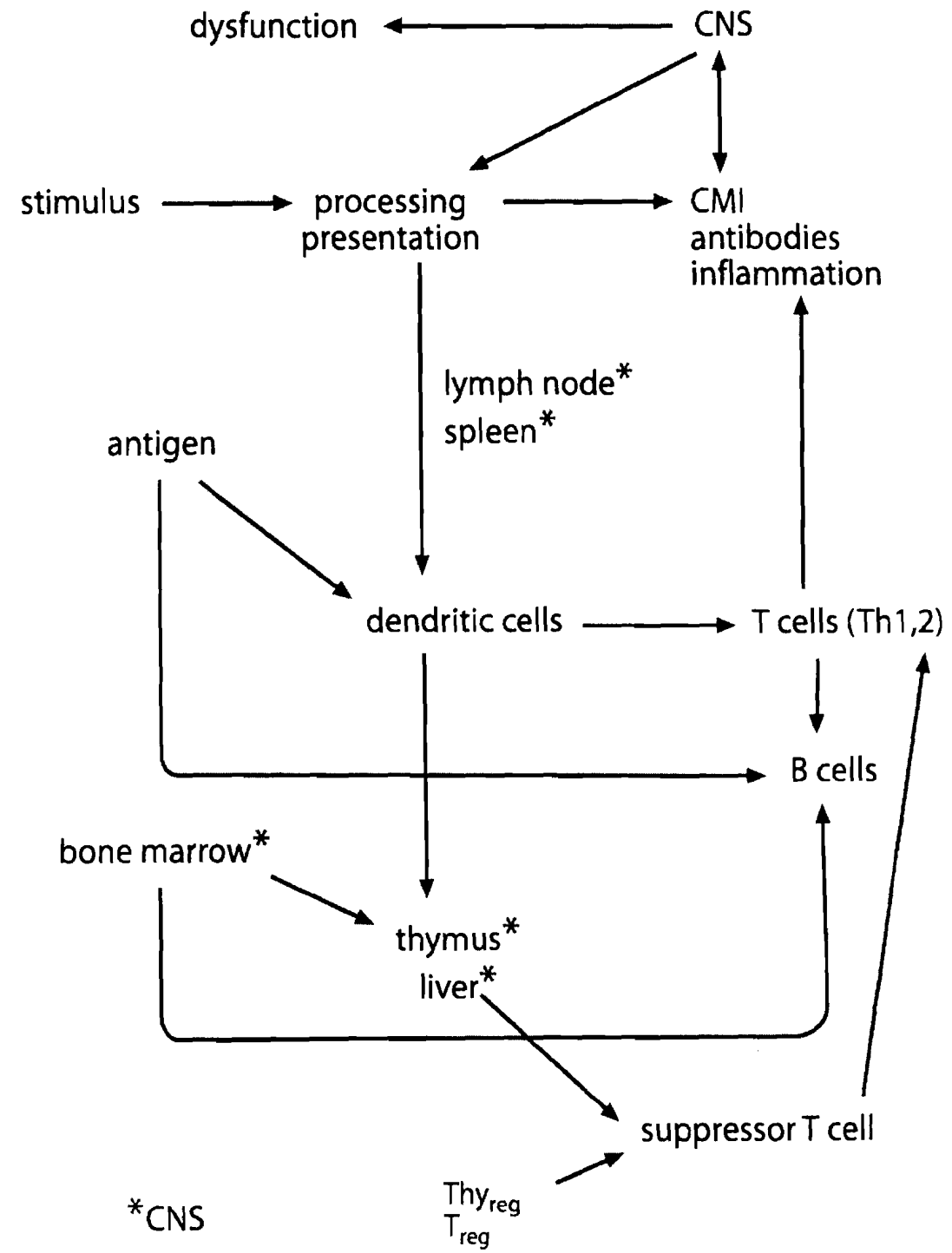

Figure: 2

In addition to a close physical relationship, the CNS and the immune system "communicate" biochemically. On the other side of the neuro-immune axis, T lymphocytes, macrophages and/or dendritic cells (antigen presenting cells) may produce neuropeptides and other cytokines that influence the CNS. For example, although the immune response may not be optimal in Depression, the immune response itself produces cytokines that may induce depressive symptoms (6)

In aggregate, there is considerable evidence that the CNS, including the mind itself can exert a strong influence on the immune system, primarily a down regulation of immune defenses under stressful conditions. Moreover, the immune response itself impacts on behavior. As I've often told my students, your physical and mental feelings during illness are often your (own) immune system reactions. A balanced approach could potentiate and in some cases regulate this critical defense mechanism.

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