Theories and Concepts in Psychoneuroimmunology: What is at Stake?

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**Psycho-neuro-immunology**

A Framework for Understanding the Pieces of Your Puzzle

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**Table 1. The early decades of research that shaped the field of neuroimmune interactions**

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<th>Early Neuroimmune Research</th>
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<td>1. The psychosomatic approach:&lt;br&gt;Psychological factors and emotions influence disease onset and progression (allergies, peptic ulcer, cancer, autoimmune diseases, infectious diseases)</td>
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<td>2. The biobehavioral approach:&lt;br&gt;Experimental stressors impact immune functions (1964: Solomon proposes the term <em>psychoimmunology</em>&lt;sup&gt;1&lt;/sup&gt;)&lt;br&gt;The immune system can be modulated by conditioned stimuli (Metalnikov and Chorine, 1926; Ader, 1974)</td>
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<td>3. The cellular communication approach:&lt;br&gt;Immune cells express neurotransmitter receptors (Szentivanyi, 1958; Hadden, 1970-5; Pert, 1985)&lt;br&gt;Immune cells produce brain and pituitary peptides (Blalock, 1980)</td>
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<td>4. The neuroanatomical approach:&lt;br&gt;Innervation of the spleen and other lymphoid organs by the autonomic nervous system (Felten, 1980)</td>
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<td>5. The effect of immune factors on the neuroendocrine system:&lt;br&gt;Interleukin-1 activates the hypothalamic-pituitary-adrenal axis by acting in the brain (Besedovsky and Del Rey, 1975)</td>
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*Dr. Dave*

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What I would like to discuss:

1. PNI and theories of cellular communication
2. PNI and the normal vs. the pathological
3. PNI and the opponent process theory
1/ Theories of cellular communication

- Cellular communication signals together with their signaling pathways can be found in most cells of the body and are not specific of a given organ.

- Specificity of cellular communication comes from the way organs are functionally structured.

- Organs that concur to the same function(s) must be able to coordinate their joint functions by reciprocal communication pathways.

- In addition to specific organ diseases, there are diseases that affect communication signals and communication pathways.
Schematic representation of neuroimmune interactions

Dantzer, Physiol Rev, 2018
An example of intricate communication pathways: inflammation-induced depression
2. The normal and the pathological

2.1 Health as a reversible condition
Canguilhem: “Ce qui caractérise la santé c’est la possiblité de tolérer des infractions à la norme habituelle et d’instituer des normes nouvelles dans des situations nouvelles. [...] 
La santé c’est une marge de tolérance des infidélités du milieu. [...] 
[...] Etre en bonne santé c’est pouvoir tomber malade et s’en relever, c’est un luxe biologique. Inversement, le propre de la maladie c’est d’être une réduction de la marge de tolérance des infidélités du milieu. [...]"
KE Sylvia, GE Demas, A return to wisdom: using sickness behaviors to integrate ecological and translational research, Integr Comp Biol, 2017, 57, 1204-13
Medical interpretation

Cytokines → Internal state (weakness) → Behavioral alterations

Motivational interpretation

Cytokines → Internal state → Environmental contingencies → Behavioral alterations

24°C

LPS

6°C
MOTIVATIONAL INTERPRETATION OF SICKNESS

- Threat ➔ Fear ➔
- Pathogenic micro-organisms ➔ Sickness ➔

- Fear feelings
- Fear behavior
- Visceral arousal
- Malaise
- Sickness behavior
- Visceral arousal
Major depressive disorder as a disease of immune-to-brain communication pathways?
2.2 What it means to be ill

Canguilhem: “Chercher la maladie au niveau de la cellule c’est confondre le plan de la vie concrète où la polarité biologique fait la différence de la santé et de la maladie et le plan de la science abstraite où le problème reçoit une solution. [...] nous voulons dire que la maladie d’un vivant ne loge pas dans des parties d’organisme. [...] Le même donné biologique peut être considéré comme partie ou comme tout. Nous proposons que c’est comme tout qu’il peut être dit ou non malade”
Ecoimmunology views sickness behavior as an integrated response to energetic, social, and environmental contexts.

KE Sylvia, GE Demas, A return to wisdom: using sickness behaviors to integrate ecological and translational research, Integr Comp Biol, 2017, 57, 1204-13
Some examples of the adaptive value of sickness behavior
Is immunopsychiatry a useful concept?

Compared to psychoneuroimmunology, “the recent use of the term immunopsychiatry represents a hierarchical shift: it suggests that our brain no longer governs the immune system, but, on the contrary, that our behaviours and emotions are governed by peripheral immune mechanisms…. The introduction of the term immunopsychiatry has created the opportunity of managing psychiatric disorders through novel treatment approaches targeting the immune system” (Pariante, Lancet Psychiatry, 2015)
From Immunoneurology to Immunopsychiatry: Neuromodulating Activity of Anti-Brain Antibodies

Branislav D. Janković

https://doi.org/10.1016/S0074-7742(08)60076-8
Is depression really maladaptive?

Possible adaptive functions of depression:
- Biasing cognition to avoid losses
- Conserving energy
- Disengaging from unobtainable goals
- Signaling submission
- Soliciting resources
- Promoting analytical thinking
Does conservation of energy play a role in inflammation-induced depression?

Metabolic features of inflammation:
- Increased glycolysis
- Reduced OXPHOS and generation of ATP

Ryan & O’Neill, Febs Lett, 2017
Does conservation of energy play a role in inflammation-induced depression?

**Metabolic features of inflammation:**

- **Increased glycolysis**
- **Reduced OXPHOS and generation of ATP**

*The brain represents only 2% of the body weight but demands 20% of our resting metabolic rate*

Ryan & O'Neill, Febs Lett, 2017
3/ Opponent process theory

(Cut because unpublished)