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PSYCHONEUROIMMUNOLOGY

IN TERMS OF THE TWO MAIN STRESS AXES

**Sickness Behaviour as Trigger for the Development of Mental
Disorders**

by

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SUMMARY

The thesis deals with the mind-body paradox in psychoneuroimmunological context. Psychoneuroimmunology is defined as a post-modern approach to the mind-body connection. It is an extension of the stress paradigm. The thesis therefore concentrates on psychoneuroimmunology in terms of the two major stress axes, i.e., the central noradrenergic/sympatho-adrenomedullary-axis (CNA/SAM-axis) and corticotropin-releasing hormone/hypothalamo-pituitary-adrenocortical-axis (CRH/HPA-axis). The psychoimmunological link is investigated and a pervasive connection is shown between behaviour and immunology, as well as immune disturbances in mental disorders of most categories of the DSM-IV. The psychoneuroimmunological interaction in terms of the two main stress axes is demonstrated by consecutively examining the psychoneurological and neuroimmunological interactions of the CNA/SAM-axis and CRH/HPA-axis. A total interdependence between the psychological, neuroendocrine and immunological functions is shown to exist, not only in adult life, but also during the developmental perinatal period. It is seen that corticotropin-releasing hormone (CRH) constitutes the principle neuropeptide in the regulation of the neurobehavioural stress response and that psychoneuroimmunology in terms of the two main stress axes can be equated to psychoneuroimmunology in terms of CRH. CRH is, in fact, shown to act as central coordinator and integrator of neuroendocrine, immunological, autonomic nervous system, motor and behavioural functions through the pervasive distribution of its cell bodies and projections throughout the central nervous system. The mechanisms through which peripheral events such as infectious, inflammatory and traumatic complications can influence behaviour are subsequently examined and it is seen how peripherally derived cytokines can transfer information to the central nervous system and in this way alter neuroendocrine function and behaviour. The CRH/HPA-axis, and CRH *per se* is, in line with its central regulatory and coordinating role, shown to be a major target for the modulatory actions of cytokines. The thesis is concluded by presenting sickness behaviour as practical example of the psychoneuroimmunological interaction. A hypothesis is presented describing sickness behaviour as adaptational new homeostasis with the potential to develop into mental disorders in those individuals so predispose by genetics and adverse early life experiences. Cross-sensitisation between

cognitive and non-cognitive stressors is seen to exacerbate the potential threat to mental as well as physical health. Once again the CRH/HPA-axis is shown to fulfill a central role in the development and expression of sickness behaviour and in the transition to mental disorders.

Psychoneuroimmunology provides the link between many previously inexplicable connections between mind and body. It explains how negative emotions can induce immune dysregulations with considerable health risks, and how peripheral events such as infections and physical trauma can predispose to short- and long-term behavioural disturbances. Psychoneuroimmunology, in fact, demands a paradigm shift in our approach to the mind-body paradox.

Key words: Psychoneuroimmunology; psychoimmunology; immunology; behaviour; mind-body; central noradrenergic/sympatho-adrenomedullary-axis; corticotropin-releasing hormone/hypothalamic-pituitary-adrenocortical-axis; stress; cytokines; cortisol; pro-inflammatory; sickness behaviour; mental disturbance.

OPSOMMING

Die tesis handel oor die gees-liggaamsparadoks in psigoneuroimmunologiese konteks. Psigoneuroimmunologie word gedefinieer as 'n postmoderne benadering tot die gees-liggaamverwantskap. Dit is 'n uitbreiding op die stresparadigma. Om hierdie rede word daar dus gekonsentreer op psigoneuroimmunologie in terme van die hoof stresasse, dws, die sentrale noradrenerge/simpato-adrenomedullêre-as (SNA/SAM-as) en die kortikotropien-vrystellingshormoon/hipotalamo-adrenokortikale-as (KVH/HPA-as). Die psigoimmunologiese verband word ondersoek en 'n deurlopende verwantskap tussen gedrag en immunologiese veranderinge gevind. Immunologiese versteurings word ook in feitlik al die kategorië van die DSM-IV aangetoon. Die psigoneuroimmunologiese interaksies word bevestig deur agtereenvolgens die psigoneurologiese en die neuroimmunologiese wisselwerkings in terme van die SNA/SAM-as en die KVH/HPA-as te ondersoek. Daar word aangetoon dat 'n totale interafhanklikheid tussen die psigologiese, die neuroendokriene en die immunologiese funksies bestaan - tydens volwassenheid, sowel as gedurende die perinatale ontwikkelingsfases. Daar word gewys dat kortikotropien-vrystellingshormoon (KVH) die belangrikste neuropeptied vir die regulering van die stresresponse is en dat psigoneuroimmunologie in terme van die twee hoof stresasse gesien kan word as psigoneuroimmunologie in terme van KVH. Daar word inderwaarheid bewys dat KVH, as gevolg van die wye verspreiding van KVH selliggame en projeksies in die senuweestelsel, die sentrale koördineerder en integreerder van neuroendokriene, immunologiese, outonome, motor en psigologiese funksies is. Verder word aangetoon hoe perifere sitokien-induserende aktiwiteite, soos infeksies en trauma, die neuroendokriene funksies en gedrag kan beïnvloed. Dit word gesien dat die KVH/HPA-as, en in besonder KVH, 'n belangrike sitokienteiken is. Die tesis word saamgevat deur siektegedrag as praktiese voorbeeld van die psigoneuroimmunologiese interaksie uit te beeld. 'n Hipotese van siektegedrag as 'n aanpassingshomeostase met die potensiaal om oorsprong te gee aan psigologiese versteurings, word geformuleer en verdedig. Daar word verder aangetoon dat genetiese disposisie en vroeë lewenservarings die individu kan predisponer tot die omskakelling van siektegedrag na gedragsversteurings. Dit word ook duidelik dat die potensiaal van siektegedrag om aanleiding te gee tot psigologiese versteurings nie

slegs beïnvloed word deur genetika en vroeë lewenservarings nie, maar ook deur kruis-sensitiserings tussen kognitiewe en nie-kognitiewe stressors. Die KVVH/HPA-as word weereens waargeneem as sentrale determinant in die ontwikkeling en ekspressie van siektegedrag en in die oorskakeling na psigologiese versteurings.

Psigoneuroimmunologie verklaar die verband tussen talle voorheen onverklaarbare assosiasies van liggaam en gees. Dit verduidelik ook hoe negatiewe emosies kan lei tot immuunwanregulering met gevolglike gesondheidsrisiko's, en hoe perifere gebeurtenisse soos infeksies en beserings die individu kan presensitiseer vir die ontwikkeling van kort- sowel as langtermyn gedragsversteurings. Psigoneuroimmunologie vereis inderdaad 'n paradigmaterskuiwing in ons benadering tot die gees-liggaamsparadoks.

Sleutelwoorde: Psigoneuroimmunologie; psigoimmunologie; immunologie; gedrag; gees-liggaam; sentrale noradrenerge/simpatoadrenomedullere-as; kortikotropien-vrystellings hormoon/hipotalamo-pituitere-adrenokortikale-as; stres; sitokiene; kortisol; pro-inflammatories; siektegedrag; gedragsversteuring.

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