

## CHAPTER 8

### CONCLUSIONS

Psychoneuroimmunology is a developing interdisciplinary field that deals with the interactions between the psychological aspects, the interconnected neurological functions, and the related immunological processes. Unlike previous approaches to the mind-body paradox it introduces the immune system into the equation.

This thesis shows the central role of corticotropin-releasing hormone (CRH) and the pro-inflammatory cytokines in the psychoneuroimmunological approach to the mind-body interaction. It is concluded that psychoneuroimmunology in terms of the two major stress axes can largely be equated with psychoneuroimmunology in terms of CRH and that immunologically derived cytokines constitute the major interface between peripheral somatic events and the behavioural functions. It is clear that disturbances in the cytokine balance, a phenomenon previously associated mainly with physical disease, are of equal importance with regard to the development of abnormal behaviour and psychiatric symptomatology. In contrast to some previously published suggestions, particular patterns of cytokine activity should not summarily be considered as correlates of specific behavioural outcomes as the effects are largely determined by baseline neurohormonal activity and reactivity which, in turn, depends on predisposition by early psychosocial experiences and genetic disposition. Resilience and vulnerability factors at the time of the stressor onslaught may either decrease or increase the probability for the expression of the specific psychopathology as determined by the predisposition and precipitated by the stressor, in this case the immune dysregulation.

In addition, the thesis introduces the concept of sickness behaviour as precipitating factor for the development of mental disturbances in individuals so predisposed by previous life experience. It may be asked in what way this concept differs from the predisposition-stress model of mental disorders, i.e., whether the introduction of the concept of sickness behaviour as precipitating factor for the development of mental disorders makes any new contribution to our understanding of psychology or

psychiatry. The answer is contained in two facts. The first is that the coordinated set of behavioural changes that constitutes sickness behaviour represents a new homeostasis or state of adaptation intended to aid in coping with whatever stressor threatened the primary homeostasis. It is therefore the coping mechanism and not the initiating stressor that gives rise to the psychopathology. The second difference lies in the fact that sickness behaviour as syndrome of adaptation already consists of emotional, cognitive and physical changes that correspond to psychopathological states and that it is merely the prerequisite of non-termination of the adaptation process that determines the transition of sickness behaviour, as process of coping and adaptation, to a state of psychopathology with related symptoms. It is also important to note that it is the inappropriate continuation of a normal adaptive homeostasis which, in this thesis, is proposed as the cause of the mental disturbance and, in contrast to Darwinian approaches to the etiology of mental disorders, not a maladaptive variant of the adaptive response.

It can with confidence be said that psychoneuroimmunology provides the link between a number of previously unexplained associations between behaviour and disease. Many of these associations were made long before the existence of either psychiatry or immunology as independent disciplines, some dating as far back as Aristotle, Galen and Hippocrates. More recently, several hypotheses were described on viral or specific immunological activity as part of the etiology of mental disturbances such as depression, schizophrenia, chronic fatigue syndrome, multiple sclerosis and certain neurodegenerative disorders. Support for most of them waned as the presence of the suggested viral infection or immune alteration could very often not consistently be confirmed. The concept of cytokine involvement in the vulnerability to, and in the development of, mental disorders gives credence to these hypotheses if one remembers that it is most probably the non-specific cerebral inflammatory response and not any specific virus or other micro-organism, or even localized cerebral or other trauma, that constitutes the final pathway of most of these disturbances.

In addition, psychoneuroimmunology helps us to understand the cross-sensitisation between cognitive and non-cognitive stressors. It is, for instance, of great importance to realize that stress-induced activation of the CRH/HPA-axis, as well as the

production of pro-inflammatory cytokines, can be initiated through stressors as diverse as infections or negative emotions and perceptions, and that the effects of such stressors can be cumulative. It is more than likely that these biological aspects of the stress response can, at least partially, be reversed by positive emotions. This last aspect is a vastly under-researched area of psychoneuroimmunology and holds a wide range of research possibilities for mental health workers. Of equal importance is the fact that the relative non-specificity with regard to the initiating stressor is mirrored in the type of pathology which could develop from the same precipitating stressor which may vary from mild personality changes to overt psychopathology or even physical disease – depending on the nature of the predisposition. This apparent non-specificity with regard to the type of pathology that can develop carries the unfortunate implication that immune disturbances, as is the case for other biological markers, cannot in isolation be used as markers for specific mental disturbances. What it can do is to contribute to identification of the nature of the psychosocial factors that gave rise to the biological predisposition. It is tempting, and very feasible, to speculate that assessment of the pro-inflammatory/anti-inflammatory cytokine balance may find practical application as prognostic indicator in mental disorders. In this context reversal of immune disturbances may provide a convenient prognostic index of the success of psychotherapy and other interventions. This potential needs to be properly researched, as the possibility has, to the best of my knowledge, not yet been investigated

In view of the fact that the inflammatory reaction underlies a host of mental and physical disorders and that it may be a key factor in general physical deterioration, frailty and disability, coupled to the fact that negative emotional states and stressful experiences, high allostatic loads and cross-sensitisation between stressors can stimulate the production of pro-inflammatory cytokines, it is essential that the immune status be considered when investigating the psychophysiology of stress or health. There are, in fact, indications that stress-induced immune disturbances may be the fundamental mechanisms underlying the health risks imposed by negative emotions.

There can be no doubt that psychoneuroimmunology brings us one step closer to the understanding of the total interconnectiveness of body and mind. It is essential to

stress that the psychoneuroimmunological approach does not in any way detract from the value of existing biological or psychological approaches to health or disturbances thereof. In fact, the validity of opposing theories is in certain cases rather strengthened by the link psychoneuroimmunology provides between more reductionistic biological and environmental approaches. The pervasiveness of the psychoneuroimmunological interaction does indeed necessitate a paradigm shift in our approach to illness, be it primarily physical or mental in presentation.

Although psychoneuroimmunology can be seen as extension of the stress paradigm and helps to explain the mechanism underlying the interactions proposed by models such as the biopsychosocial and other approaches, much of the scientific evidence was initially derived from studies in neuroimmunomodulation. The majority of scientific studies are therefore from the biomedical field. While some relevant work has been published by psychiatrist abroad, there is a dire need in South Africa for the input of mental health workers, as well as for solid interdisciplinary cooperation between the behavioural and biomedical sciences, in the execution of psychoneuroimmunological studies with local relevance.