

## I Global Perspectives on Mental–Physical Comorbidity

MICHAEL R. VON KORFF

### I.1. INTRODUCTION

The picture of “Earth Rising” sent back by the first lunar expedition resulted in a global change in consciousness that humans are sustained by the environment of a small planet. The contributors to this book have made a similar, albeit less dramatic, contribution. They, and their many colleagues, carried out the first population surveys able to provide a portrait of the physical and mental health of human populations worldwide. The results of the World Mental Health Surveys afford an opportunity to consider and reflect on the health and well-being of populations in both developed and developing countries. Cultural relativists may be disappointed. While cross-national differences in the frequency of specific physical and mental disorders are evident, universal features in the relationships between physical disease and mental health are more prominent.

This book presents important new information from the World Mental Health Surveys on the extent of chronic illness in general and of the co-occurrence of mental and physical morbidity in particular. Rigorous population-based surveys in Asia, Africa, the Middle East, Europe, the Americas, and the South Pacific depict a global epidemic of chronic physical disorders, often co-occurring with psychological illness.

### I.2. AN EPIDEMIOLOGIC MAP

The growing burden of chronic disease, chronic pain, and mental disorders worldwide

is the result of what is arguably the greatest achievement of the twentieth century: the global extension of life expectancy as the physical and social conditions of life have improved worldwide, as infant mortality has been reduced, and as death rates from infectious diseases have been lowered via socioeconomic development and public health measures (Blum 1991; McMichael et al. 2004). In 1977, Ernie Gruenberg coined the phrase “the failures of success” to refer to the increase in the prevalence of chronic diseases when mortality rates are reduced to a greater extent among persons with chronic disease than the general decline in mortality (Gruenberg 1977). Over Gruenberg’s life span, from 1915 to 1991, life expectancy in the United States increased from 50 to greater than 75 years. Similar gains in life expectancy were achieved concurrently in Europe and Japan. It is less well known that most of the rest of the world was catching up during the second half of the twentieth century. In Latin America, life expectancy at birth increased from 51 years in 1950 to 70 years in 2000, while in Asia it increased from 41 to 66 years in the same time span. In Africa, gains have been less dramatic, but from 1950 to 2000 life expectancy increased from 38 to 54 years – an additional 16 years. These gains in life expectancy are resulting in older populations and increased chronic disease prevalence, both from the aging of the population and from comparatively greater reductions in mortality among those with chronic conditions.

While remarkable progress has been made in extending longevity worldwide, it is now imperative to address “the failures of success” on a global scale. The burdens of chronic disease, chronic pain, and co-occurring mental disorders experienced by growing numbers of people worldwide have an enormous impact on individuals and their families. The burdens of these disorders also have significant implications for the well-being of society at large, as larger numbers of persons depend on societal income maintenance programs due to old age or disability. With rapidly aging populations worldwide, both developed and developing countries need to maximize the ability of their adult citizens to be productive to support the growing costs of health care, old age, and disability insurance programs, as well as schools and universities to educate the next generation. These societal imperatives call attention to the need to control the major causes of chronic disease and disability in the population at large, to maximize the productivity of the adult population, and to minimize disability and dependency among the elderly.

In carrying out the World Mental Health Surveys in diverse cross-national settings, it was not possible to collect medical records data or to carry out standardized physical examinations and medical tests. For that reason, the ascertainment of physical disorders in the World Mental Health Surveys was based on self-report. In fact, the agreement of self-reported chronic physical diseases such as diabetes, heart disease, and arthritis with medical records data has generally been found to be good (Kriegsman et al. 1996; National Center for Health Statistics 1994). However, it is also likely that medically diagnosed physical diseases such as diabetes and heart disease may be under-ascertained or misclassified to some extent, particularly in developing countries where there is less adequate access to health care. Although the findings reported in this

volume are in general agreement with other studies that have used medical data to diagnose comorbid physical disorders, the limitations of self-report data need to be taken into account.

### 1.3. MIND–BODY DUALITY RECONSIDERED

It is fitting that the first global initiative assessing physical and mental health is an opportunity to reconsider beliefs regarding the duality of physical disease and mental disorders. Plato believed that an immortal soul was imprisoned in the human body (Plato 1999). Aristotle held that the intellect was part of the soul lacking a bodily organ (Robinson 2003). Descartes viewed the body as a physical machine governed by natural laws. He believed that the mind interacted with the body, but that the mind did not exist in space and was not governed by physical laws (Descartes 1637/1968). The grand theories of the relationship between mind and body of these Western philosophers reflect a general human tendency to view mind and body as distinct and separable. Such attitudes and beliefs are manifested today in the thoughts and behaviors of physicians and patients in both developed and developing countries.

There is now a large body of research showing that beliefs in mind–body duality are neither empirically supported nor in the best interests of patients. Advances in neuroscience and medicine are inconsistent with traditional beliefs in mind–body duality (Baker, Kale, & Menken 2002; Bracken 2002; Goldberg & Goodyer 2005; Kendler 2001). Persons with mood and anxiety disorders are at increased risk of diverse physical disorders (e.g., diabetes, cardiovascular disease, arthritis, and back pain), and most physical disorders are associated with a heightened prevalence of psychological distress (Evans et al. 2005). Although it is hardly surprising

**Global Perspectives on Mental-Physical Comorbidity****3**

that demoralization and anxiety accompany chronic physical conditions, there is considerable evidence that the presence of significant physical disease *reduces* the likelihood that physicians recognize the presence of comorbid depression (Tylee 2006). A traditional view has been that “unexplained” physical symptoms are indicative of an underlying mental disorder (Escobar, Hoyos-Nervi, & Gara 2002; Kirmayer & Sartorius 2007). Whereas cross-national research has shown that diffuse physical symptoms are associated with mood and anxiety disorders (Simon et al. 1999), unexplained physical symptoms are not invariably or even typically due to an underlying mental disorder (Burton 2003).

The first section of this book shows that mood and anxiety disorders are associated with increased risks of both well-defined chronic physical diseases and medically unexplained chronic pain conditions. It also shows that although mental and physical morbidity are related, the large majority of persons affected by chronic pain or with a well-defined chronic physical disease do *not* have a comorbid mental disorder. The second section considers risk factors that may explain the co-occurrence of chronic physical conditions and common mental disorders. New results are offered, suggesting that both early-onset mood and anxiety disorders and significant childhood adversities may increase risks of a broad spectrum of chronic physical conditions in later life, including both well-defined physical diseases and chronic pain conditions. The third section concerns the consequences of mental-physical comorbidity for people's lives, including functional disability, labor force participation, health-related stigma, use of health care services, and mortality. The World Mental Health Surveys show that the consequences of comorbid mental disorders for the health and well-being of persons with chronic physical conditions are significant

in both developed and developing countries worldwide.

**I.4. PHYSICAL AND PSYCHOLOGICAL MORBIDITY AS INTEGRAL**

In considering the philosophical underpinnings of psychiatry, Kendler (2005) has argued that mental disorders are etiologically complex, that simple “spirochete-like” mechanisms are unlikely to be discovered, that explanatory pluralism is preferable to biological reductionism, and that we should strive for “piecemeal integration” to explain complex pathways to illness “bit by bit.” These perspectives are highly relevant to understanding the relationships between physical and mental disorders as well. Current thinking holds that physical and mental disorders are associated via “bidirectional” links, in which physical disorders increase risks of mental disorders on the one hand and mental disorders increase risks of physical disease on the other (Evans et al. 2005). The findings presented in this book suggest that a more nuanced and integrated conceptualization of the relationships between physical and mental morbidity is needed.

Physical disease can occur through integrated action of the psychological and physical processes implicated in adaptation to chronic physical and psychosocial stressors. The concept of “allostasis,” or the maintenance of stability through change, was initially developed to describe how the cardiovascular system adjusts to changes between arousal and resting states (Sterling & Eyer 1988). Allostasis is now viewed as having broader relevance to diverse, interrelated homeostatic systems. “Allostatic load” refers to the burdens placed on homeostatic systems repeatedly activated and deactivated in response to chronic psychosocial, psychological, and physical stressors (McEwen 1998a, 1998b). Chronic effects of allostatic load on neural,

endocrine, and immune stress mediators are believed to have adverse effects on diverse organ systems. These adverse effects increase risks of physical disease as effects of allostatic load accumulate over time (McEwen & Stellar 1993). Individual differences in genetics, development, and prior experience modify effects of such stressors on allostatic load and downstream effects on physical disease and psychological illness risks (Goldberg & Goodyer 2005; Korte et al. 2005). The integrated action of the central nervous system, the neuroendocrine system, and the immune system influences risks of both physical disease (Kopps & Rethelyi 2004) and psychological illness (Goldberg & Goodyer 2005). From this perspective, the effects of psychological processes on physical health and of physiological processes on psychological health are integral and concurrent, rather than mental disorders acting on physical health status and physical disorders acting on mental health status as if mind and body were distinct entities.

Chronic pain mechanisms exemplify the integrated action of physical and psychological processes in producing both physical and psychological morbidity. Pain is a sensory and emotional experience that results from the integrated action of peripheral and central nervous systems (Schaible 2007). The peripheral nervous system is activated by mechanical, chemical, thermal, or electrical stimulation. The central nervous system transmits and regulates transmission of pain signals from the peripheral nerves to the central projection neurons and then to those parts of the brain responsible for perception and evaluation of painful stimuli. Tissue damage, degenerative disease (e.g., arthritis), and life stress inducing allostatic load can each cause inflammatory changes that produce substances such as bradykinins, prostaglandins, cytokines, and chemokines (Millan 1999). These substances mediate tissue repair and healing, but they are also irritants that result in peripheral sensitization of sensory neurons

(Rittner, Brack & Stein 2003). Sustained stimulation of peripheral and central pain pathways, accompanied by inflammatory changes, can result in sensitization. Thresholds for transmission of pain signals are temporarily or permanently lowered and the area of peripheral sensitization expands beyond the original site of injury (Melzack et al. 2001). In effect, pain pathways and neurotransmitters are modified so that the neurons develop a “memory” that facilitates responding to pain signals. In the development of persistent pain states, psychological factors are implicated in many ways. Depression and anxiety amplify physical sensations so that noxious stimuli are perceived as more severe (Barsky et al. 1988). This may occur via interrelated psychological processes such as hypervigilance, and neurophysiological processes, such as centrally mediated neurotransmitter changes that facilitate transmission of pain signals (Ren & Dubner 1999). At the same time, pain itself is a significant physical and psychological stressor that may induce or increase psychological distress (Von Korff & Simon 1996). Depression and anxiety may, in turn, alter the meaning attached to pain so that the same pain inputs are regarded as more severe and more threatening when the person is psychologically distressed (Edwards et al. 2006). Depression and anxiety also influence behavioral responses to painful stimuli, resulting in a person being more likely to rest and limit activities, more fearful and vigilant about actions that may cause pain, and less likely to engage in pleasant or productive activities that distract attention from pain (Grotle et al. 2004; Pincus et al. 2002). Physical and psychological processes act in concert in producing chronic pain and associated activity limitations in a highly integrated fashion.

### 1.5. A LIFE-SPAN PERSPECTIVE

Relationships between physical and mental disorders are multifaceted and develop over

**Global Perspectives on Mental-Physical Comorbidity****5**

the life span. For example, emotional distress and sleep disturbance are integral features of physical pain, whether the physical pain is medically explained or not (deBock et al. 1995; Von Korff & Simon 1996). Persons who are depressed or anxious are more likely to amplify physical symptoms and develop catastrophic ideas about the causes and consequences of their symptoms, whether the physical symptoms are medically explained or not (Barsky 1979; Edwards et al. 2006). Childhood adversities may increase risks of early-onset mental disorders (Goldberg & Goodyer 2005), while both childhood adversities and early-onset mental disorders may increase risks of a range of physical diseases in later life (Felitti et al. 1998; Gluckman & Hanson 2004). Mood and anxiety disorders present in adolescence may increase risks of tobacco use, obesity, and sedentary lifestyle; the presence of both affective disorder and behavioral risk factors may have independent effects on risks of cardiovascular disease and diabetes in later life (Lett et al. 2004). Among persons with medically diagnosed chronic disease, both disease severity and emotional distress contribute to functional disability (Ormel et al. 1993; Von Korff et al. 1992, 2005). Mood and anxiety disorders increase the likelihood of poor self-management of physical disease, less positive disease control, and less favorable physical disease outcomes (DiMatteo, Lepper, & Croghan 2000; Katon et al. 2004; Lin et al. 2004). These observations suggest that we need to think about the relationships between mental and physical factors in illness as multifaceted and developmental rather than as distinct. Rather than trying to identify causal pathways from mental to physical disorder and from physical to mental disorder, the empirical results of the World Mental Health Surveys suggest that “piecemeal integration” of multifaceted, life-span developmental pathways, in which boundaries between physical disease and mental disorder are inherently blurred, is more likely to be productive.

**1.6. ECOLOGICAL AND POPULATION PERSPECTIVES**

In the nineteenth century, explanations of disease focused on the role of microorganisms. Koch’s famous postulates (e.g., that a cultured microorganism should reliably cause disease when introduced into a healthy organism) are now recognized as overly simplistic (Evans 1976). In the wake of the Darwinian revolution, ecological and systems models of disease espoused by Rene Dubos (1959/1987) and others came to the fore, in which host, agent, and environmental factors were viewed as interacting to cause disease. The ecological perspective and the host–agent–environment model served as the foundations for revolutionary advances in public health that increased longevity. These included more sanitary and healthful water and food supplies, mass immunization to prevent infectious diseases, compulsory public education for boys and girls, and improved prenatal and postnatal care. Ecological approaches, and the host–agent–environment model, are equally applicable to the control of chronic physical disease and mental disorders, but new approaches are needed. In developing new approaches to control the burden of chronic physical and mental disorders, population-based data on the extent and distribution of physical and mental disorders are critically important.

**1.7. INTEGRATION OF LIFE-SPAN, ECOLOGICAL, AND POPULATION PERSPECTIVES**

In applying epidemiologic methods to study comorbidity of chronic physical disease, chronic pain, and mental disorders, the ecological (host–agent–environment) model goes hand in hand with population and life-span (developmental) perspectives (Von Korff 1999). The population perspective implies that efforts to control chronic conditions must be grounded in an understanding of the

distribution and determinants of illness on a population basis, not only among cases seen in clinical settings. The life-span or developmental perspective views the development and course of disease as changing and dynamic rather than fixed and static (Goldberg & Goodyer 2005). In combination with the ecological model, the life-span perspective calls attention to the potential for diverse factors to influence the development and expression of disease in human populations. There is a natural affinity between the ecological model of epidemiology and the biopsychosocial model (Engel 1960) of the behavioral sciences. Both models are multifactorial systems perspectives that view disease as occurring within a complex web of factors operating both within and external to the affected individual (Dworkin, Von Korff, & Le Resche 1992).

Chronic conditions develop and run their course over time spans measured in decades. The ecological, life-span, and population perspectives suggest very different approaches to controlling disease than when a single disease is considered in isolation. For chronic recurrent conditions, the prevalence of the disease in a population is the product of its incidence rate, the average episode duration, and the average number of recurrences of the condition over a life span (Von Korff & Parker 1980). This means that from a life-span perspective, a chronic condition can be controlled by preventing onset, by shortening episode duration, and by reducing the likelihood of recurrence. Even though this volume reports data from cross-sectional surveys, the interpretation of results is informed by a life-span perspective that may offer clues to new strategies for reducing the burden of chronic physical disease and of mental disorders on a population basis, by preventing onset, by shortening episode duration, or by preventing recurrence. In addition, the burden of disease can be reduced on a population basis by improving adaptation to disease, by reducing

disability, by enhancing self-management of disease, and by increasing participation in life activities among persons affected by mental or physical disorder.

### **1.8. THE SEARCH FOR BROAD-SPECTRUM RISK FACTORS**

The findings of the World Mental Health Surveys reported in this volume are consistent with three significant generalizations: (1) diverse chronic physical diseases, chronic pain conditions, and mental disorders frequently occur together; (2) these diverse conditions may have common risk factors that influence onset, duration, recurrence, and adaptation to illness; and (3) risk factors for disease expression may also be important determinants of adaptation to disease (disability and chronic disease self-management). These findings, when viewed from ecological, life-span, and population perspectives, suggest that it may be productive to search for broad-spectrum risk factors. Broad-spectrum risk factors refer to (1) common causes of multiple disorders and (2) risk factors whose effects are realized over different developmental stages of those disorders, including onset, duration, and recurrence, as well as adaptation to disease. Examples of broad-spectrum risk factors include educational attainment, childhood adversities that result in chronic stress and less-than-optimal development, socioeconomic adversities that induce physical and psychological hardships, and health behaviors such as tobacco use, sedentary lifestyle, and poor diet that result in malnutrition or obesity.

The value of identifying broad-spectrum risk factors is that they are at play across conditions and at different phases in the natural history of specific conditions and comorbidities. Control of broad-spectrum risk factors may yield benefits across diverse conditions and over the full developmental cycle of those



**Global Perspectives on Mental-Physical Comorbidity****7**

disorders. While the results of cross-sectional population surveys, such as the World Mental Health Surveys, are limited in their ability to identify causal pathways, the results reported in this volume provide intriguing observations regarding possible broad-spectrum risk factors relevant to strategies for preventing and controlling mental-physical comorbidity and associated disability. In particular, the findings regarding the association of childhood adversities and early-onset mood and anxiety disorders with a broad range of chronic physical conditions merit further investigation. This research may suggest avenues for controlling chronic disease in human populations with potential for larger population benefit than do traditional efforts to recognize and treat prevalent cases. Case finding and treatment programs in health care settings are only one tool for controlling physical disease and psychological illness on a population basis, a tool that has significant limitations and considerable costs. The findings reported in this volume may provide a launching pad for consideration of broader and ultimately more cost-effective strategies to control chronic physical disease and psychological illness, such as programs to enhance the developmental circumstances of children and adolescents (Goldberg & Goodyer 2005).

**I.9. HEALTH CARE IMPLICATIONS**

Even casual perusal of the findings reported in this volume suggests that the co-occurrence of physical disease and mental disorders is a common phenomenon in both developed and developing countries. An obvious implication of these findings, often commented on by mental health professionals, is that physicians and other health care providers treating persons with physical conditions need to be adequately trained to recognize and treat common mental disorders. An equally important implication, less often noted, is

that mental health professionals now need to be adequately trained to treat mental disorders in patients who are afflicted by co-occurring physical diseases and chronic pain conditions. In fact, many primary care physicians are now well trained in the recognition and management of major depression, and most treatment of depression worldwide occurs in general medical settings. In contrast, the mental health professional adequately trained to treat patients with comorbid diabetes, heart disease, respiratory disease, neurological disorders, or chronic pain is the exception rather than the rule. If mental health professionals aspire to offer holistic treatment of their patients, not treatment of mental disorder in isolation from the broader health status of their patients, then they will need to pay increased attention to addressing co-occurring physical diseases and chronic pain conditions as part of adequate treatment of mental disorders.

A second implication is that health care may need to develop new strategies of protecting population health beyond traditional efforts to identify and treat prevalent cases of chronic physical and psychological disorders, including efforts that address broad-spectrum risk factors.

**I.10. POLICY IMPLICATIONS**

Countries spending far less on health care now have mortality rates approaching those of Europe and the United States. For example, Costa Rica, whose annual per capita health care expenditures at the turn of the millennium were around \$500 per year, had achieved life expectancy among its citizens equal to that of the United States, whose per capita health care expenditures exceeded \$5,000 per year. On the one hand, this means that developing countries face significant health care challenges with limited resources currently allocated to health care, as the extent of

chronic disease in their populations grows. On the other hand, these countries have unique opportunities to devise more innovative and less costly approaches to managing the growing burden of chronic physical diseases and mental disorders. They have opportunities to develop more effective and efficient health care systems than the legacy systems of developed countries now staggering under the burden of rapidly inflating health care costs.

The results reported in this volume suggest that both developed and developing countries face tremendous burdens in caring for rapidly growing populations with chronic conditions, including those with multiple physical conditions and mental health problems. However, leaving aside mortality rate differences that may be largely due to factors other than health services, it is not evident from the results of the World Mental Health Surveys that countries spending far more on health care have consistently achieved notably better population health than those countries spending less. An important question, one not addressed by the World Mental Health Surveys, is the relative health benefit of investment in educational programs and socioeconomic development versus traditional health care services in terms of benefits for health outcomes of common chronic physical and psychological disorders. Perhaps the developed world will have an opportunity to learn from the developing world in finding better ways of addressing population health in the coming decades.

### 1.11. RESEARCH IMPLICATIONS

This volume provides an epidemiologic map of the occurrence of common chronic physical diseases, common chronic pain conditions, and common mental disorders on a global basis. The focus of this volume is on the universals of the occurrence and co-occurrence of physical and mental morbidity, not on

cross-national or cross-cultural differences. The many authors who have contributed to this volume share a common perspective that it is time to reconsider traditional and deeply ingrained beliefs in the duality of physical disease and mental disorders. Although the work presented in this volume is empirical and descriptive, the view that physical and mental morbidity are integral permeates the work reported here. In particular, the results of the World Mental Health Surveys invite future researchers to investigate the role of early-onset mental disorders and childhood adversities as broad-spectrum risk factors for a wide range of adverse health outcomes. The results reported in this volume also suggest the need for future research that seeks to understand the role of mood and anxiety disorders in increasing risks of physical disease and in impairing the abilities of persons affected by chronic disease to adapt to their health conditions, thus minimizing disability and optimizing self-management. In reporting data from cross-national population surveys, ecological, life-span, and population-based perspectives can be brought to bear on the vexing and complex problems of understanding whether and why specific physical and mental disorders tend to co-occur in human populations.

The collective efforts of the research teams that carried out the World Mental Health Surveys provide an unprecedented view of the health and mental health status of the world population at the dawn of a new millennium. The results presented in this volume provide a basis for new ideas and fresh perspectives concerning how the growing burden of chronic physical and psychological disorders in aging populations can be effectively addressed so that the worldwide gains in life expectancy achieved in the twentieth century can be matched by comparable gains in health and quality of life of the world population in the twenty-first century.



## Global Perspectives on Mental-Physical Comorbidity

9

## REFERENCES

- Baker, M. G., Kale, R., & Menken, M. (2002). The wall between neurology and psychiatry: Advances in neuroscience indicate it's time to tear it down. *British Medical Journal*, **324**, 1468–9.
- Barsky, A. J. (1979). Patients who amplify bodily sensations. *Annals of Internal Medicine*, **91**, 63–70.
- Barsky, A. J., Goodson, J. D., Lane, R. S., & Cleary, P. D. (1988). The amplification of somatic symptoms. *Psychosomatic Medicine*, **5**, 510–19.
- Blum, R. W. (1991). Global trends in adolescent health. *The Journal of the American Medical Association*, **265**, 2711–19.
- Bracken, P. (2002). Time to move beyond the mind-body split. *British Medical Journal*, **325**, 1433–4.
- Burton, C. (2003). Beyond somatization: A review of the understanding and treatment of medically unexplained physical symptoms (MUPS). *The British Journal of General Practice*, **53**, 231–9.
- deBock, G. H., Kaptein, A. A., Touw-Otten, F., & Mulder, J. D. (1995). Health-related quality of life in patients with osteoarthritis in a family practice setting. *Arthritis Care and Research*, **8**, 88–93.
- Descartes, R. (1637/1968). *Discourse on Method and the Meditations*, trans. (with introduction) F. E. Sutcliffe. London: Penguin Books Ltd.
- DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk-factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of Internal Medicine*, **160**, 2101–7.
- Dubos, R. (1959/1987). *Mirage of Health: Utopias, Progress & Biological Change*. Reprint, New Jersey: Rutgers University Press.
- Dworkin, S. F., Von Korff, M., & Le Resche, L. (1992). Epidemiologic studies of chronic pain: A dynamic-ecologic perspective. *Annals of Behavioral Medicine*, **14**, 3–11.
- Edwards, R. R., Bingham, C. O., III, Bathon, J., & Haythornewaite, J. A. (2006). Catastrophizing and pain in arthritis, fibromyalgia and other rheumatic diseases. *Arthritis and Rheumatism*, **55**, 325–32.
- Engel, G. L. (1960). A unified concept of health and disease. *Perspectives in Biology and Medicine*, **3**, 459–85.
- Escobar, J. I., Hoyos-Nervi, C., & Gara, M. (2002). Medically unexplained physical symptoms in medical practice: A psychiatric perspective. *Environmental Health Perspectives*, **110**, 631–6.
- Evans, A. S. (1976). Causation and disease: The Henle-Koch postulates revisited. *The Yale Journal of Biology and Medicine*, **49**, 175–95.
- Evans, D. L., Charney, D. S., Lewis, L., Golden, R. N., Gorman, J. M., Krishnan, K. R., Nemeroff, C. B., Bremner, J. D., Carney, R. M., Coyne, J. C., Delong, M. R., Frasure-Smith, N., Glassman, A. H., Gold, P. W., Grant, I., Gwyther, L., Ironson, G., Johnson, R. L., Kanner, A. M., Katon, W. J., Kaufmann, P. G., Keefe, F. J., Ketter, T., Laughren, T. P., Leserman, J., Lyketsos, C. G., McDonald, W. M., McEwen, B. S., Miller, A. H., Musselman, D., O'Connor, C., Petitto, J. M., Pollock, B. G., Robinson, R. G., Roose, S. P., Rowland, J., Sheline, Y., Sheps, D. S., Simon, G., Spiegel, D., Stunkard, A., Sunderland, T., Tibbits, P., Jr., & Valvo, W. J. (2005). Mood disorders in the medically ill: Scientific review and recommendations. *Biological Psychiatry*, **58**, 175–89.
- Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., & Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. *American Journal of Preventive Medicine*, **14**, 245–58.
- Gluckman, P. D., & Hanson, M. A. (2004). Living with the past: Evolution, development, and patterns of disease. *Science*, **305**, 1733–6.
- Goldberg, D., & Goodyer, I. (2005). *The Origins and Course of Common Mental Disorders*. London: Routledge.
- Grotle, M., Vollestad, N. K., Veierod, M. B., & Brox, J. I. (2004). Fear-avoidance beliefs and distress in relation to disability and chronic low back pain. *Pain*, **112**, 343–52.
- Gruenberg, E. M. (1977). The failures of success. *Milbank Memorial Fund Quarterly. Health and Society*, **55**, 3–24.
- Katon, W., Von Korff, M., Ciechanowski, P., Russo, J., Lin, E. H. B., Simon, G., Ludman, E., Walker, E., Bush, T., & Young, B. (2004). Behavioral and clinical factors associated with depression among individuals with diabetes. *Diabetes Care*, **27**, 914–20.
- Kendler, K. S. (2001). A psychiatric dialogue on the mind-body problem. *The American Journal of Psychiatry*, **158**, 989–1000.
- Kendler, K. S. (2005). Toward a philosophical structure for psychiatry. *The American Journal of Psychiatry*, **162**, 433–40.

- Kirmayer, L. J., & Sartorius, N. (2007). Cultural models and somatic syndromes. *Psychosomatic Medicine*, **69**, 832–40.
- Kopps, M. S., & Rethelyi, J. (2004). Where psychology meets physiology: Chronic stress and premature mortality – The Central-Eastern European health paradox. *Brain Research Bulletin*, **62**, 351–67.
- Korte, S. M., Koolhaas, J. M., Wingfield, J. C., & McEwen, B. S. (2005). The Darwinian concept of stress: Benefits of allostasis and costs of allostatic load and the trade-offs in health and disease. *Neuroscience and Biobehavioral Reviews*, **29**, 3–38.
- Kriegsman, D. M., Penninx, B. W., van Eijk, J. T., Boeke, A. J., & Deeg, D. J. (1996). Self-reports and general practitioner information on the presence of chronic diseases in community dwelling elderly. A study on the accuracy of patients' self-reports and on determinants of inaccuracy. *Journal of Clinical Epidemiology*, **49**, 1407–17.
- Lett, H. S., Blumenthal, J. A., Babyak, M. A., Sherwood, A., Strauman, T., Robins, C., & Newman, M. F. (2004). Depression as a risk factor for coronary artery disease: Evidence, mechanisms and treatment. *Psychosomatic Medicine*, **66**, 305–15.
- Lin, E. H. B., Katon, W., Von Korff, M., Rutter, C., Simon, G. E., Oliver, M., Ciechanowski, P., Ludman, E., Bush, T., & Young, B. (2004). Relationship of depression and diabetes self-care, medication adherence and preventive care. *Diabetes Care*, **27**, 2154–60.
- McEwen, B. S. (1998a). Stress, adaptation, and disease: Allostasis and allostatic load. *Annals of the New York Academy of Sciences*, **840**, 33–44.
- McEwen, B. S. (1998b). Protective and damaging effects of stress mediators. *The New England Journal of Medicine*, **338**, 171–9.
- McEwen, B. S., & Stellar, E. (1993). Stress and the individual: Mechanisms leading to disease. *Archives of Internal Medicine*, **153**, 2093–101.
- McMichael, A. J., McKee, M., Shkolnikov, V., & Valkonen, T. (2004). Mortality trends and setbacks: Global convergence or divergence. *Lancet*, **363**, 1155–9.
- Melzack, R.,Coderre, T. J., Katz, J., & Vaccarino, A. L. (2001). Central neuroplasticity and pathological pain. *Annals of the New York Academy of Sciences*, **933**, 157–74.
- Millan, M. J. (1999). The induction of pain: An integrative review. *Progress in Neurobiology*, **57**, 1–164.
- National Center for Health Statistics. (1994). Evaluation of National Health Interview Survey diagnostic reporting. *Vital and Health Statistics* **2**, **120**, 1–116.
- Ormel, J., Von Korff, M., Van Den Brink, W., Katon, W., Brilman, E., & Oldehinkel, T. (1993). Depression, anxiety and social disability show synchrony of change in primary care patients. *American Journal of Public Health*, **83**, 385–90.
- Pincus, T., Burton, A. K., Vogel, S., & Field, A. P. (2002). A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. *Spine*, **27**, 109–20.
- Plato. (1999). *Pheado*, trans. & ed. D. Gallop. Oxford: Oxford University Press.
- Ren, K., & Dubner, R. (1999). Central nervous system plasticity and persistent pain. *Journal of Orofacial Pain*, **13**, 155–63.
- Rittner, H. L., Brack, A., & Stein, C. (2003). Proalgesic and analgesic actions of immune cells. *Current Opinion in Anaesthesiology*, **16**, 527–33.
- Robinson, H. (2003). Dualism. In *The Blackwell Guide to Philosophy of Mind*, ed. S. Stich & T. Warfield, pp. 85–101. Oxford: Blackwell.
- Schaible, H. G. (2007). Peripheral and central mechanisms of pain generation. *Handbook of Experimental Pharmacology*, **177**, 3–28.
- Simon, G. E., Von Korff, M., Piccinelli, M., Fullerton, C., & Ormel, J. (1999). An international study of the relation between somatic symptoms and depression. *The New England Journal of Medicine*, **341**, 1329–35.
- Sterling, P., & Eyer, J. (1988). Allostasis: A new paradigm to explain arousal and pathology. In *Handbook of Life Stress, Cognition and Health*, ed. S. Fisher & J. Reason, pp. 629–49. New York: John Wiley & Sons.
- Tylee, A. (2006). Identifying and managing depression in primary care in the United Kingdom. *The Journal of Clinical Psychiatry*, **67**, 41–45.
- Von Korff, M. (1999). Epidemiologic methods. In *Epidemiology of Pain*, ed. I. K. Crombie, P. R. Croft, S. J. Linton, L. Le Resche & M. Von Korff, pp. 7–15. Seattle, WA: IASP Press.
- Von Korff, M., Katon, W., Lin, E. H. B., Simon, G., Ludman, E., Oliver, M., Ciechanowski, P., Rutter, C., & Bush, T. (2005). Potentially modifiable factors associated with disability among