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Pathways Linking Affective Disturbances and Physical Disorders

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Comorbidity of psychological and physical disorders is substantial. This article presents a broad theoretical framework for identifying factors that contribute to and maintain comorbid conditions. The authors propose heuristic models of how co-occurrences of psychological and physical disorders are developed and maintained. The models specify biological, behavioral, cognitive, and social pathways that may account for comorbidity. Although the authors' discussion of psychological disorders is limited to the role of affective disturbances (subclinical negative moods as well as mood and affective disorders), the pathways they identify are thought to contribute to co-occurrences of other psychological disorders and physical disease as well. The authors emphasize that pathways linking comorbid states are bi-directional and that operative pathways differ depending on the specific affective response, illness behavior, disease, or disease stage.

Key words: affective disturbances, anxiety, comorbidity, depression, disease course, disorders, health, illness behavior

Comorbidity of psychological and physical disorders is substantial. Between 15% and 33% of medical inpatients suffer from mood and anxiety disorders compared with 2% to 4% of the general population (Katon & Sullivan, 1990). Similarly, 41% of patients with chronic medical illness have had a recent or concurrent psychiatric disorder (Katon & Sullivan, 1990). Although there is evidence for pathways linking a number of psychiatric and physical disorders (e.g., McNeil, 1987), the field lacks a broad framework for identifying factors that contribute to and maintain comorbid conditions.

What are the characteristics of psychological and physical disorders that promote comorbidity? What are the biological, behavioral, cognitive, and social pathways that promote and maintain the co-occurrence of psychological and physical disorders? The purpose of this article is to propose a conceptual framework in which interrelations between psychological and physical disorders can be addressed. Our hope is that this will provide a tool for organizing the existing literature and a source of hypotheses about factors that contribute to and maintain comorbid states. Specifically, we discuss key concepts and propose heuristic models of how the interrelations between psychological and physical disorders operate. The models specify biological, behavioral, cognitive, and social pathways that provide explanations for the development and maintenance of the co-occurrence of psychological and physical disorders. To make this task manageable within limited space, our discussion of psychological disorders is limited to anxiety and depression as both subclinical negative affective experiences and as clinical psychiatric disorders. We use the term *affective disturbance* to refer to both subclinical negative moods and to mood and affective disorders. Although the models focus on affective disturbances, the pathways we identify may contribute to the co-occurrence of other psychiatric disorders and physical illness as well.

Before presenting the heuristic models, we briefly discuss alternative characterizations of affective disturbances and of physical disorders. We begin with a discussion of the importance of determining the essential characteristics of affective disturbances that are associated with physical disorders. This includes distinguishing between shared and distinct components of affective disturbances, as well as between affective states, traits, and psychiatric disorders. We finish with a discussion of the importance of differentiating physical disease characteristics that are associated with affective disturbances. This includes distinguishing between stages of physical disease and between verifiable pathology and illness behaviors.

Shared Versus Distinct Components of Affective Disturbances

Mood and affective disorders can be described in terms of their physiological, cognitive, and affective constituents (cf. Leventhal & Patrick-Miller, 1993). Some components are shared by different disorders, whereas others occur in one emotion or disorder but not in another. For example, anxiety and depression share a common emotional distress component but also have distinct components that differentiate them: physiological hyperarousal for anxiety and lack of positive affect for depression (e.g., Clark & Watson, 1991; Watson, Clark, & Carey, 1988). To understand the causes of comorbid-

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ity, we need to determine whether some but not other components of affective disturbances are associated with physical disorder. The primary strategy for identifying essential constituents is to conduct studies that compare the relative roles of different affective disturbances in comorbidity. On the one hand, when different disturbances are equivalently associated with a specific physical disease process, it is likely that shared components of the disturbances are responsible for the relation. On the other hand, when different disturbances are independently associated (or some are and some are not associated) with a disease process, constituents specific to the disturbances are responsible. Unfortunately, too few studies in this literature compare affective disturbances. However, several articles in this special section contribute to our understanding of these issues by conducting such comparisons (Frasure-Smith, Lespérance, & Talajic, 1995; Gatchel, Polatin, & Kinney, 1995; Zautra et al., 1995).

Although we view comparing the roles of different affective disturbances as central to understanding comorbidity, the models we present later do not reflect the question of the relative associations of different affective disturbances with physical disease. Instead, they are intended to be flexible so that they can be used to generate hypotheses about the role of any distinct disturbance or group of disturbances with common constituents.

Psychological Distress Versus Clinical Disorder

Similar issues of specificity arise when addressing the relative roles of state negative affect (NA), trait NA, and mood and anxiety disorders as primary variables in associations with physical disorder. Consider, for example, the differences between a depressive state, a depressive trait, and a clinical depressive disorder. States are transient fluctuations in mood; traits are stable individual differences in affective level that are often associated with cognitive and behavioral styles; clinical disorders are episodes of extreme affect that occur in conjunction with specified behavioral and cognitive dysfunctions. Do affective states, traits, and disorders have common or different pathways linking them with physical disorders? One possibility is that there is a shared property of affective disturbances that provides a common link between each of these classes of emotional response and physical disorder. This common property might be biological, psychological, or both. Assuming a common property, what we learn about one of these categories of response tells us something about the others. If this is the case, the chronicity and severity of the emotional response are what defines the important differences between states, traits, and disorders. For example, consistent with a common pathway approach is evidence indicating suppressed immunity for persons who experience state depression but even greater suppression of the same functions among clinically depressed persons (Herbert & Cohen, 1993).

Alternatively, it is possible that when considering physical outcomes there are important qualitative differences between states, traits, and disorders. For example, trait anxiety and depression are associated with cognitive dispositions such as self-consciousness and low self-esteem that are not necessarily associated with state depression and anxiety (Costa & McCrae, 1985). Consistent with the importance of qualitative differences between categories is evidence from studies of heart disease (Costa & McCrae, 1985) and upper respiratory infections (URI; Cohen et al., 1995), suggesting that trait but not state NA causes biases in symptom reporting. Moreover, state but not trait NA is associated with more severe URI pathology (Cohen et al., 1995). Again, our models avoid directly addressing classes of affective response by assuming that state NA, trait NA, and mood and anxiety disorders can all influence or be influenced by physical disorders but not specifying the relevant pathways for each affect category.

Verifiable Physical Disease Versus Illness Behaviors

The concept of "physical disorder" is also enormously complex and involves biologically verifiable disease onset and progression as well as illness behaviors. In some cases, disease onset and progression are measured in terms of the biological concomitants of disease pathophysiology. Examples include assessment of pulmonary function in asthmatic persons (e.g., Carr, Lehrer, & Hochron, 1995); elevations in enzymes such as creatine phosphokinase and lactate dehydrogenase, indicating the occurrence of a myocardial infarction (Braunwald, 1988); or viral isolation as an indication of infection (Cohen & Williamson, 1991). In others, nonverified illness behaviors are used such as self-reports of symptoms and pain, functional disability, or use of health care services (e.g., Gatchel et al., 1995; Zautra et al., 1995). We have argued elsewhere (Cohen & Williamson, 1991) that illness behaviors are often ambiguous outcomes. Although they may reflect underlying pathology, they may also reflect psychological biases in recognizing, interpreting, and acting on physical sensations. The effects of such biases can vary from reporting symptoms without any pathophysiologic basis, to increased sensitivity to disease-based physical sensations, to generalization from disease-based sensations to other related symptoms (Cohen et al., 1995). Even if primarily attributable to psychological rather than physiological processes, these outcomes are important in terms of both quality of life and appropriate policy for the effective and efficient use of the health care system. However, the influence of emotions on disease pathophysiology and the influence of emotions on biases in interpreting and acting on physical sensations probably occur for different reasons.

There are, of course, many different physical diseases with different etiologies and pathophysiologies. Moreover, disease processes include multiple stages such as onset, disease progression, event episodes, and flare-ups. Each disease and disease stage may be associated with different psychological causes and effects. The models we propose suggest a range of pathways that can contribute to interrelations between psychological and physical disorders, but we assume that the importance of any proposed pathway varies according to disease and disease stage.

Why One Disorder and Not Another?

What determines the specific diseases involved in comorbidity? As we discuss later, some physical diseases alter biological systems that play a direct role in the development of specific

affective disturbances. Similarly, in limited cases, the alterations in biological systems that occur with affective disturbance can influence susceptibility to specific physical diseases. In many cases, however, there are no obvious biological links. Here, the comorbid condition that develops is presumed to be determined by the nature of the affected pathways, by biological predispositions that determine susceptibility to various physical and psychological pathologies, or both.

Models That Link Psychological and Physical Disorder

The models we propose are intended as heuristic tools to stimulate thought about these relations and not as formal or complete models. We recognize that there are other biological, psychological, social, cultural, and demographic factors that contribute to both physical and affective disturbances. However, the intent of this article is only to identify the pathways linking psychological and physical disorders, and therefore we do not consider these other factors here. We also focus on mechanisms that facilitate pathology without reference to potential positive or "buffering" responses such as social support or adaptive coping that provide some protection from comorbidity.

The relations between psychological and physical disorder are likely to be bi-directional and involve multiple feedback loops. However, each direction emphasizes different characteristics of the pathways we propose. As a result, we discuss these two directions separately. We start with the role of affective disturbances as contributors to physical disorder followed by the role of physical disorder as a contributor to affective disturbances.

How Affective Disturbances Can Influence Physical Disorder

Figure 1 provides a model of how affective disturbances can influence physical disorder. The paths identified in the model move in only the direction from affective disturbance to physical disorder. The absence of alternative paths is not intended to imply that they do not exist.

As apparent from Figure 1, we propose that affective disturbances can influence physical disorder through biological, behavioral, cognitive, and social pathways. In addressing affective disturbances as causal agents, we assume that subclinical as well as clinical disturbances can contribute to physical disorder (Melamed, 1995). We distinguish between physical disorder (biologically verifiable disease) and illness behaviors because we think that distinct mechanisms can contribute to each. In the case of physical disorder, the primary pathways

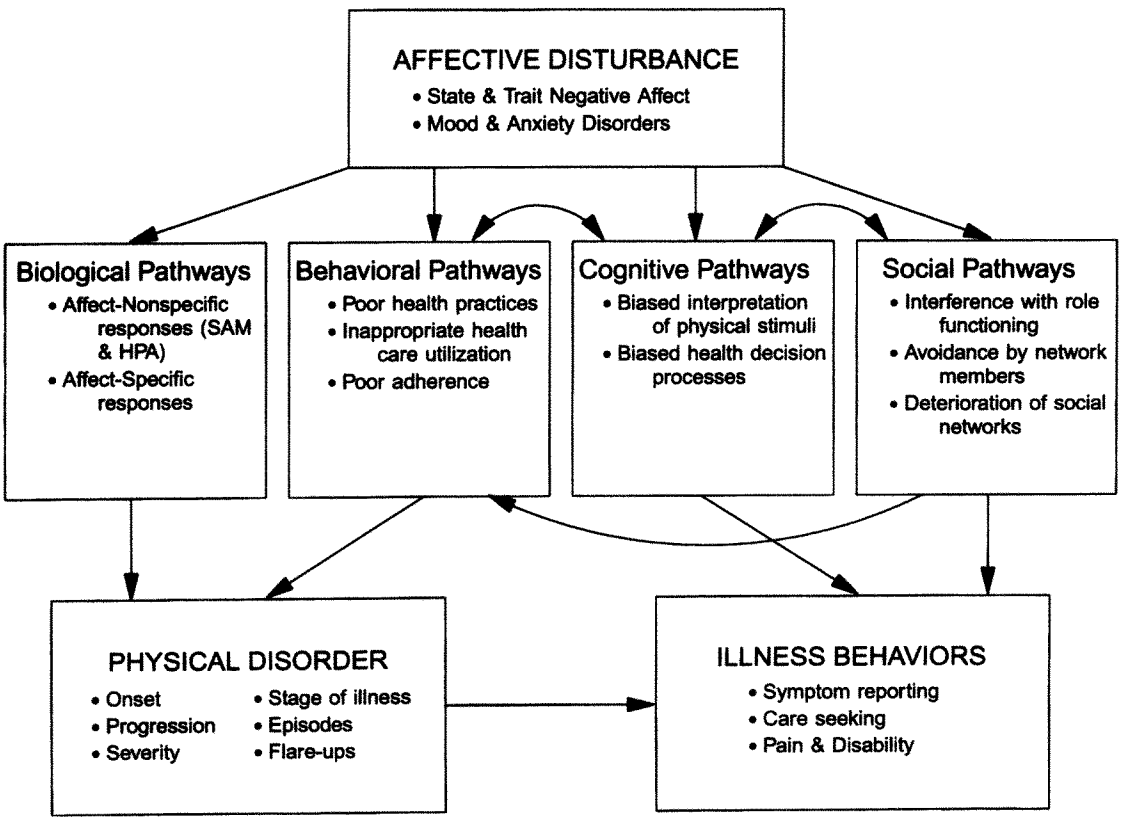

Figure 1. Pathways linking affective disturbances to physical disorders. The paths identified in the model move in only one direction from affective disturbance to physical disorder. The absence of alternative paths is not intended to imply that they do not exist. SAM = sympathetic–adrenal medullary system; HPA = hypothalamic–pituitary–adrenocortical axis.

are biological and behavioral. In the case of illness behaviors, the pathways include direct manifestations of disease pathology, cognitive biases in interpreting bodily sensations, and social pressures influencing care seeking.

Biological pathways. Biological pathways can include nonspecific responses that occur to most or all negative emotions and disorders, as well as affect-specific responses that occur in response to one affect or disorder but not others. Nonspecific responses include the activation of both the sympathetic–adrenal medullary (SAM) system and the hypothalamic–pituitary–adrenocortical (HPA) axis. These responses are associated with both clinical depression and anxiety as well as with anxious and depressed moods (e.g., Ritchie & Nemeroff, 1991; Stokes, 1987; Villacres, Hollifield, Katon, & Wilkinson, 1987). SAM activation is manifest in increased blood pressure, heart rate, circulating levels of the hormones epinephrine and norepinephrine, and constriction of peripheral blood vessels. It has been claimed that if SAM activation is excessive, is persistent over a period of time, or is repeated too often, it may result in a sequence of responses that culminate in disease. SAM activation has been implicated in the development of coronary heart disease (Manuck, Kaplan, Williams, & Marsland, in press), essential hypertension (Krantz & Manuck, 1984), and in susceptibility to infectious diseases (Cohen & Herbert, in press). HPA activation is manifest in increased circulating levels of three hormones: corticotropin-releasing hormone, adrenocorticotropic hormone, and cortisol. HPA activity has been implicated in the development of several diseases, including atherosclerosis (Troxler, Sprague, Albanese, Fuchs, & Thompson, 1977) and chronic inflammatory responses such as rheumatoid arthritis and increased hyperreactivity of the airways in asthmatic persons (McNeil, 1987).

There may also be biological responses associated with specific affective disturbances that place persons at risk for onset or progression of physical disorder. For example, there are cholinergically mediated disturbances resulting in increased rapid eye movement sleep (or loss of slow-wave sleep) in depression, but not anxiety (Akiskal, 1985; Kupfer et al., 1983), that potentially could influence physical disease pathology. Similarly, in an article reported in this special section, symptoms of anxiety are associated with the recurrence of thrombogenic cardiac events, whereas depressive symptoms have been associated with arrhythmic events (Frasure-Smith et al., 1995).

There are individual differences in biological response to affective disturbances. For example, people's cardiovascular (e.g., Kamarck, Jennings, & Manuck, 1993) and immune responses (Marsland, Manuck, Fazzari, Steward, & Rabin, 1995) to laboratory stressors are stable across tasks and time. These differences are thought to represent biologically based dispositions and may play an important role in susceptibility to affective disturbance-triggered onset or progression of physical disease.

Behavioral pathways. Affective disturbances are also associated with changes in behavior that place persons at risk for disease onset, progression, or increased severity. For example, NA and mood and anxiety disorders are associated with loss of sleep, less exercise, poor diets, increased smoking, alcohol consumption, drug use (Conway, Vickers, Ward, & Rahe, 1981; Gregory & Smeltzer, 1983), and poor adherence to medical regimens (LaPorte, 1990). Persons high in state or trait NA also report more symptoms when ill (Cohen et al., 1995), report more pain (e.g., Gaskin, Greene, Robinson, & Geisser, 1992), and tend to either over- or underuse health care services (e.g., Cameron, Leventhal, & Leventhal, 1995). Examples of studies that investigated mediating roles of such behavioral pathways include those by Martin et al. (1995) and Goldston, Kovacs, Obrosky, and Iyengar (1995).

Cognitive pathways. Increased symptom reporting and health care use among persons with affective disturbances might occur because negative moods result in negative biases in the evaluation and categorization of stimuli; for example, facilitating the labeling of physical sensations as representing negative consequences (symptoms and pain) and defining symptom constellations as disease states (Cohen & Williamson, 1991; Mechanic, 1972; Pennebaker, 1982). Negative construals of potential implications of symptoms may also influence decisions about seeking care (Cohen & Williamson, 1991). Examples of medical procedures in which such construals may influence important care-seeking behavior include breast mammography (e.g., Rimer, 1994) or HIV-1 antibody testing (e.g., Lyter, Valdiserri, Kingsley, Amoroso, & Rinaldo, 1987).

Social pathways. Affective disturbances interfere with the enactment of normative social roles such as parent, marital partner, and workmate. Social network members often avoid interaction with persons in bad moods, especially those suffering from clinical mood and anxiety disorders (e.g., Coyne, 1976). Moreover, when persons who are psychologically distressed require continued support, it may fatigue and deteriorate their network. Social networks support physical health by promoting positive health practices, positive views of the world, and providing resources for facing and avoiding stressful life events (Cohen, 1988). Hence, interference with these network functions can increase risk for physical disorder. Social pressures from network members may also influence the use of health services either promoting or discouraging care seeking in the face of symptom reports.

How Physical Disorders Can Influence Affective Disturbances

We now turn our attention to the pathways linking physical disorders to affective disturbances, as depicted in Figure 2. In our first model, we distinguished between verifiable disease and illness behaviors. Here we do not differentiate these two because both are potential contributors to all of the causal pathways indicated in the model. In describing physical disorders in this model, we focus on characteristics that differentiate physical disorders in regard to their relative risk for affective disturbances. We propose that more severe and chronic disorders, and those associated with pain, disability, and disfigurement, place persons at greater risk for affective disturbances (cf. Kokkonen & Kokkonen, 1993). Pathologies that alter biological processes associated with affective response are also proposed as increasing risk. In addressing affective disturbances as an outcome, we assume that whether the disturbance is subclinical or clinical is a function of characteristics of the physical disorder, specific operating

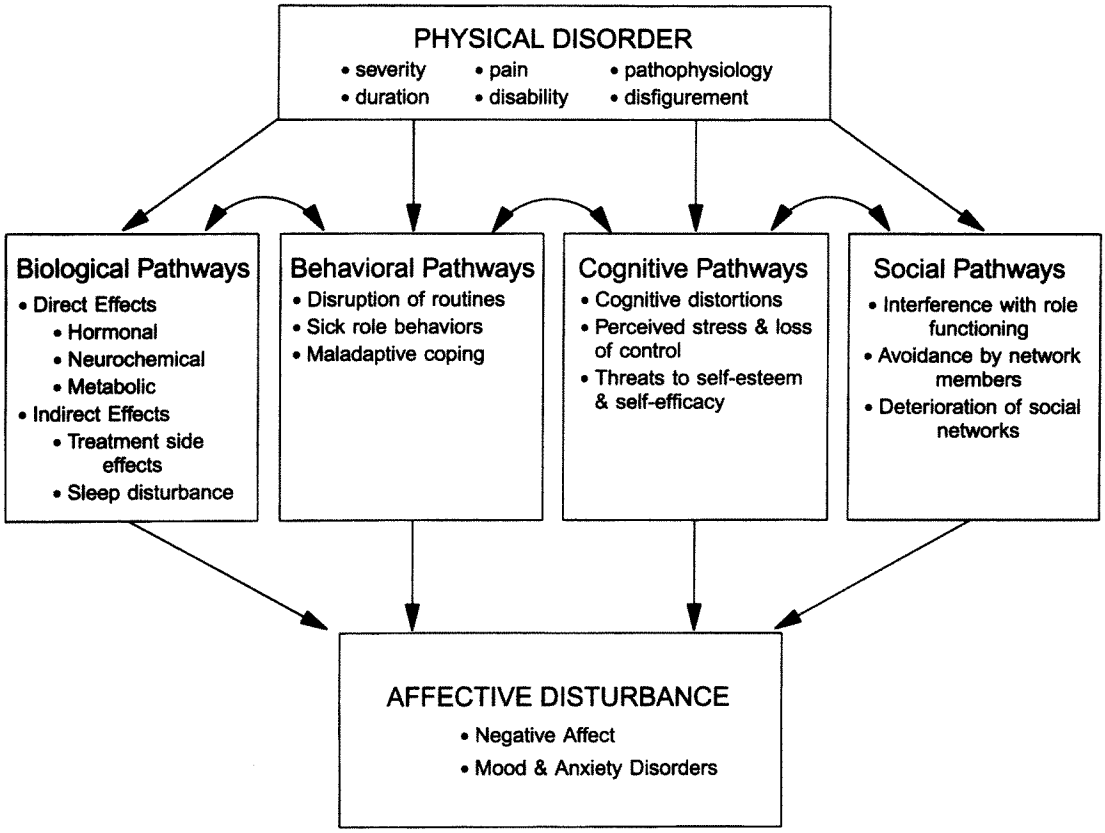

Figure 2. Pathways linking physical disorders to affective disturbances. The paths identified in the model move in only one direction from physical disorder to affective disturbance. The absence of alternative paths is not intended to imply that they do not exist.

pathways, and biological predispositions that place persons at risk for psychiatric disorders.

Biological pathways. Biological factors associated with a variety of physical disorders can have both direct and indirect effects on emotional state. Direct biological influences on affect reflect the specific pathophysiology of a disease and can include hormonal, neurochemical, and metabolic disturbances. Examples of hormonal concomitants of primary endocrine disorders that result in symptoms of anxiety and depression include abnormal levels of thyroid hormones in hypo- and hyperthyroidism, cortisol in Addison's disease and Cushing's syndrome, and aldosterone in Conn's disease (McNeil, 1987). Neurochemical abnormalities, as seen in diseases of the central nervous system, can also have significant effects on patients' emotional states. For example, Parkinson's disease and primary depression are thought to share a common pathogenesis, namely decreased levels of dopamine and serotonin in the brain (Ehmann, Beninger, Gawel, & Riopelle, 1990; McNeil, 1987). Metabolic disturbances, such as uremia and hyperkalemia in patients with decreased renal function or hypoxia and hypercalcemia in patients with some forms of cancer, can also result in significant emotional disturbances (McNeil, 1987).

Indirect biological pathways linking physical disorder and affective disturbances include patients' responses to medications and radiation therapy. Many medications have been shown to cause affective disturbances. For example, depression is associated with antihypertensives and chemotherapeutic agents such as vinca alkaloids. Anxiety is associated with sympathomimetics and xanthine derivatives used in the treatment of asthma, and an array of disturbances including depression, anxiety, and mood swings are associated with corticosteroids used in the treatment of chronic inflammatory diseases (McNeil, 1987). Although radiation therapy per se may or may not be a cause of mood disturbance, cranial irradiation is associated with clinical depression (Forester, Kornfeld, & Fleiss, 1978; Proctor, Kernahan, & Taylor, 1981). Lastly, sleep disturbances associated with medical disorders can also lead to depression and irritability (Soreff, 1987). These sleep disturbances include sleep apnea and both insomnia and hypersomnolence due to physical symptoms, pain, and medication side effects.

Behavioral pathways. Behavioral changes necessitated by the presence of disease and recommended by health care providers can also lead to affective disturbances. Recommended changes in health behaviors, such as use of prescribed medications, regular medical follow-ups, dietary and alcohol restrictions, aerobic exercise programs, and smoking cessation, frequently represent substantial deviations from routine lifestyles. Similarly, physical limitations due to pain and sick role

behaviors can alter routines. Examples include the inability to participate in recreational activities, drive an automobile, and carry out work-related tasks. The extent to which these changes constitute a disruption of routine patterns of behavior may contribute to the overall perception of the illness as a significant stressor and result in emotional distress (e.g., Mandler, 1984). Maladaptive coping responses to the stress elicited by physical disorder, such as increased alcohol consumption, elicit drug use, and behavioral disengagement, can also exacerbate stressor-induced NA responses.

Cognitive pathways. Physical diseases can be viewed as psychological stressors that place demands on persons and tax their abilities to cope (Moos & Tsu, 1977). Moreover, loss of control over one's activities and increased dependence on others associated with chronic and disabling physical disorders can contribute to feelings of hopelessness, helplessness, and loss of self-esteem (Taylor, 1983). Both psychological stress and loss of control are associated with increases in NA and risk for affective disturbance (Lazarus & Folkman, 1984).

Perceptions of symptoms and self-conceptions of vulnerability to disease contribute to the production of emotional reactions to illness (Leventhal & Patrick-Miller, 1993). These can include irrational thought patterns such as catastrophizing, perfectionism, dichotomous thinking, and blaming self and others. Such patterns can result in a variety of inaccurate appraisals and distorted beliefs about the significance of physical symptoms, efficacy of medical treatment, likelihood of potential disease outcomes, and the meaning of illness. They also can result in a cascade of negative psychological responses including increased perceptions of stress, decreased perceptions of control, self-esteem and self-efficacy, and associated affective disturbances (e.g., Beck, Rush, Shaw, & Emery, 1979). These cognitive distortions can also indirectly alter affect and mood and anxiety disorders through their influence on behavioral and social pathways. For example, they may alter behavioral coping choices or interpersonal transactions. The preeminence and efficacy of cognitive–behavioral interventions in the treatment of mood and anxiety disorders in medical populations by clinical health psychologists attests to the importance of cognitive processes as mediational pathways linking physical disorder with affective states (e.g., Levenson, 1992).

Social pathways. Diseases that are life threatening, stigmatized, and result in disfigurement or disability often result in network members avoiding patients (e.g., Bloom & Kessler, 1994). Patients with a chronic disease who require continued support may fatigue and deteriorate their social network (e.g., Schulz & Williamson, 1991). Moreover, physical disorders that interfere with patients' role function make it difficult to participate in the social contacts and interactions necessary to maintain social networks (e.g., Burman & Margolin, 1992). Interpersonal relationships support mental health by helping maintain regular routines, allowing expression and consequent regulation of emotion, and providing opportunities for interactions that support positive mood states and positive ways of thinking (Cohen, 1988). Hence, disruption of social networks increases the risk for affective disturbance.

Conclusion

The articles in this special section contribute to our understanding of appropriate categorization of affective disturbances, conceptualization of physical outcomes, and identification of pathways responsible for links between psychological and physical disorders. We hope that future work in this area will adopt a broader conceptual view of the relations between psychological and physical disorders. This should include specifying the nature (illness behaviors, disease, and stage) of the physical disorder, the affective disturbance, and the potential pathways that might link them. Questions about how affective disturbances and physical disorders should be classified and how psychological and physical disorders influence one another can only be answered when their interrelations are viewed in the context of psychologically and biologically plausible models of these processes. They are also best addressed in multivariate studies considering multiple pathways and their interrelations.

These models also suggest proximal causes of comorbidity of psychological and physical disease that are subject to psychological intervention. Intervention research comparing the potential importance of alternative pathways would help us understand the causal contribution of each pathway as well as further advance our ability to successfully intervene in the prevention of comorbidity.

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