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Pain in Depression — Depression in Pain

Historical Background

Nearly two millennia ago, the Roman emperor and philosopher Marcus Aurelius wrote: "when unbearable, pain destroys us. ... Recollect this, too, that many of our everyday discomforts are really pain in disguise, such as drowsiness or want of appetite."[1] Also for millennia, the mutual interaction between physical pain and one's world view has been observed by philosophers and religious figures. Yet with few exceptions (e.g., Burton's *The Anatomy of Melancholy*[2]), the systematic analysis of the relationship between these two experiences from the perspective of medical science is a relatively recent occurrence.

In the 19th century, medical authors commented explicitly upon pain, insomnia, weight loss, sweating, dizziness, and cardiac and respiratory complaints in depressive disorders. Griesinger[3] regarded depression as a spectrum of disorders with mental and somatic aspects whose relative proportions reflect individual predisposition, concurrent somatic disease, and psychosocial influences. Schneider's[4] triad of organic, reactive, and endogenous depression seemed to some researchers to be an insufficient scheme. Wernicke, Kleist, and Leonhard[5] differentiated several forms according to heredity, symptoms, course, and prognosis.

In recent decades, in an effort to clarify semantic confusion and end rancorous academic debate, the American Psychiatric Association and the World Health Organization introduced formal diagnostic taxonomies into the field of mental health. These classifications, the *Diagnostic and Statistical Manual* (DSM) and the *International Classification of Diseases* (ICD), are now in their 4th and 10th revisions, respectively. Both systems abandoned the more explicit term "endogenous depression" in favor of the etiologically vague term "major depression." The DSM-III (1980) introduced the category "psychogenic pain disorder," which was renamed "somatoform pain disorder" in subsequent versions. Because neither system attempts to address the root biological cause of the syndrome described, diagnosis focuses on complaints, symptoms, and signs. Rational therapy that links etiopathogenesis and targeted pharmacotherapy is still in its infancy. Clinical investigations have disclosed that selective serotonin reuptake inhibitors, while efficacious for depression, are much less useful for neuropathic pain than are the older antidepressants of the tricyclic category. The lack of selectivity of the latter agents (e.g., amitriptyline) allows them to modulate noradrenergic as well as serotonergic pathways and thereby achieve greater analgesic benefit.

Pain in Depression

The importance of pain within the symptom complex called depression was recognized incrementally (Table 1). Over 70 years ago, Pletnew[6] indicated that physical complaints are an integral part of the depressive syndrome. Montassut[7] used the terms *dépression larvée* (masked depression) and *cénestopathie* (cenestopathy) for aberrant bodily sensations in mental illness. Cenesthesias may

Table 1
Depression and pain: history of ideas

Author	Year	Topic
Pletnew[6]	1928	On the question of "somatic" cyclothymia
Montassut[7]	1936	Minor forms of periodic melancholy
Hempel[8]	1937	Vegetative dystonic depression
Schick[9]	1947	On a physical form of periodic depression
Lemke[10]	1949	On vegetative depression
Kral[11]	1958	Masked depression in middle-aged men
Da Fonecsca[12]	1963	Affective equivalents
Diamond[13]	1964	Depressive headaches
Lesse[14]	1968	The multivariant masks of depression
Lopez-Ibor[15]	1973	Depressive equivalents
Walcher[16]	1969	The masked depression
Wörz[17]	1980	Chronic pain as expression of endogenous depressions
Blumer and Heilbronn[18]	1982	Chronic pain as a variant of depressive disease; the pain-prone disorder

occur in affective, schizophrenic, and schizoaffective disorders.[19] They are now considered to be centrally produced erroneous or bizarre sensory interpretations, in other words, functional variants of central pain.[20]

Among the vegetative and somatic symptoms of depressive disorders, pain ranks second only to insomnia.[13,21] Pain, including headache, facial pain, neck and back pain, thoracic, abdominal, and pelvic pain, and extremity pain, occurs in over 50% of depressive disorders.[22-24] In some cases, pain-related suffering so dominates the clinical picture that the underlying depressive disease is not recognized for months or even years.[17]

In older papers, the term "masked depression" was applied in a broad sense to many physical complaints and disorders,[25] some of which were later elaborated as separate clinical entities, for example anorexia nervosa, restless leg syndrome, and meralgia paresthetica. Modern international classifications no longer use this term.

Depression in Pain

International recognition of chronic pain as a syndrome—even a disease in its own right[26,27]—led to the founding of the International Association for the Study of Pain in 1973. In the generation since, the systematic evaluation of patients with acute, recurrent, and chronic pain states has uncovered comorbidity of pain with depression, anxiety, anger, cognitive impairment, and abnormal personality traits, and has revealed various psychosocial and socioeconomic influences. Depression is more common among patients with chronic pain than in healthy controls.[28,29] A study based on interviews by skilled clinicians determined that according to standardized criteria, depression afflicted 87% of 300 patients with chronic pain.[23] Depending upon the setting, population, diagnosis, and diagnostic instruments used, estimates of major depression and dysthymic disorder can vary greatly (Table 2). Equally wide variations in prevalence estimates according to the survey methods and diagnostic criteria applied are found for chronic pain itself.[30]

In these diverse surveys, the prevalence of major depression according to the DSM-III criteria ranges from 1.5% to 57%. This figure must be augmented by estimates (when available) of dysthymic disorder, a milder condition. The high percentage of depressive symptoms in many clinical investigations of chronic pain might appear to confirm the essential role of depressive disorders in such patients. However, the populations sampled are often from specialized institutions or clinics; as a rule such patients are more impaired than those seen in primary care. Using the Research Diagnostic Criteria (RDC), Kramlinger and associates[47] reported that of 100 consecutive patients admitted to a

Table 2
Major depression and dysthymic disorder in patients with chronic pain

Author	Year	Setting	Population (*N*)	M (%)	D (%)
Reich et al.[31]	1983	Pain board	Chronic pain (43)	23.2	7.0
Remick et al.[32]	1983	Psychiatric consultation	Atypical facial pain (68)	13.2	
Katon et al.[33]	1984	Psychiatric consultation	Chronic pain (49)	57.1	8.2
Turner, Romano[34]	1984	Pain clinic	Pain >6 mo (40)	30.0	
Hudson et al.[35]	1985	Arthritis clinic	Fibrositis/fibromyalgia (31)	26.1	4.3
Bouckoms et al.[36]	1985	Inpatient neurosurgery	Pain >6 mo (62)	24.2	
Haley et al.[37]	1985	Pain clinic	Chronic pain (63)	49.2	
Katon et al.[38]	1985	Seattle inpatients	Pain >1 year (37)	32.4	
Muse[39]	1985	Pain clinic	Pain >6 mo (64)	1.5	12.5
Fishbain et al.[28]	1986	Pain clinic	Pain >2 years (283)	4.6	23.3
Goldenberg[40]	1986	Arthritis clinic	Fibrositis/fibromyalgia (82)	13.4	
Large[41]	1986	Psychiatric consultation	Pain >6 mo (50)	6.0	28.0
Chaturvedi[42]	1987	Outpatient psychiatry	Pain >3 mo (203)	6.9	43.3
France et al.[43]	1987	Inpatient pain program	Low back pain >6 mo (73)	46.6	6.8
Love[44]	1987	Private practice	Low back pain >6 mo (68)	25.0	
Benjamin et al.[45]	1988	Outpatient pain clinic	Chronic pain (106)	33.0	
Walker et al.[46]	1988	Laparoscopy patients	Pelvic pain >3 mo (25)	28.0	

Note: Table 2 represents populations of chronic pain patients in which major depression (M) or a dysthymic disorder (D) were diagnosed according to the DSM-III criteria. Modified from R.H. Dworkin and M.J. Gitlin, *Clin J Pain* 1991; 7:79-94.

pain management program in the Mayo Clinic, 25 were "definitely" and 39 were "probably" depressed. In the same Department of Psychiatry and Psychology, Maruta and coworkers[48] found that in a different group of 100 inpatients, 34 patients were "definitely" depressed, 20 were "probably" depressed, and 46 were not depressed. Similarly, Krishnan et al.[49] diagnosed depression in 43.7% of 71 consecutive patients with chronic low back pain admitted to the inpatient program at Duke Medical Center.

Depression worsens the effect of pain on social and occupational functioning.[50,51] Depressed patients with chronic pain have consistently been found to be less active than their nondepressed counterparts.[52,53] The presence of depression in addition to pain codetermines course and outcome, physical impairment, and disability.[54] Depression reduces the likelihood of response to pain treatment and increases the utilization of medical services[55] in patients with pain. When depression is recognized and treated early in patients who present for treatment of chronic pain, expensive diagnostic and therapeutic procedures such as multiple surgeries may be avoided.[56]

A 1962 study[57] analyzed the intertwining of chronic pain and depressive syndromes in rheumatological diseases. In most patients with both conditions, depression had no clearcut antecedent factors. In other patients, clinicians judged that pain served to focus emotions during a difficult life situation. In still others, depression was attributed to chronic pain. Only rarely, according to the authors' analysis, did both conditions coincide by chance.

An explanation for the hypothesized increased prevalence of chronic pain in depression may lie in the biochemical features common to both disorders. These include involvement of serotonergic and noradrenergic systems, hypercortisolemia, and subnormal suppression of cortisol production in response to dexamethasone.[43,58,59]

Patients with chronic severe pain, such as postherpetic neuralgia or phantom or stump pain, experience distinct psychopathological sequelae compared with those who have hereditary, metabolically determined depression (formerly called "endogenous depression"). Patients with chronic pain typically show signs and symptoms of irritability, dysphoric mood, narrowing of interests, and reduced capacity for experience, known as the "algogenic psychosyndrome."[17] In contrast, in patients with severe depressive states, anhedonia, early morning awakening, indecisiveness, suicidal tendencies, existential despair, and in some cases psychotic features are more prominent. Thus, the presence of a long-standing, clearcut somatic source of pain in combination with the psychopathological picture of an algogenic psychosyndrome supports a clinical conclusion that pain is the cause and depression the result.

Causal Relationships

The causal relationship of pain and depression has been the subject of long-standing controversy. In the clinical context, it is critical to establish a correct diagnosis before speculating about causal relationships. A proper psychiatric diagnosis is possible through a standardized interview by a trained clinician or through a systematic evaluation by a qualified psychiatrist or psychologist. Questionnaires may be helpful to gather demographic data, complaints, and information on the degree of disability, and even to quantitate psychiatric morbidity.[60]

Provisional acceptance of a variety of plausible hypotheses may be more helpful in understanding the constellation of chronic pain and depression than relying upon only one mechanism. My unpublished analysis of a case series of more than 2,000 chronic pain patients has shown that in over 90% of patients there were multiple disposing, initiating, and perpetuating factors such as physical or psychological trauma, infection, or cancer, rather than a single cause.

Psychodynamically, pain has been interpreted as a compromise between a forbidden wish and its punishment.[61] Engel[62] described a history of childhood neglect and abuse in "pain-prone personalities." Such persons exhibited inwardly directed aggression, and their pain served a communicative function. Childhood hospitalization is a risk factor for both depressive illness and intractable pain in adults.[63]

The cognitive mediation model of Rudy, Kerns, and Turk[64] claims that the presence of pain is not a sufficient condition for the subsequent development of depression. These authors hypothesized that the reduction of instrumental activities along with a decline in personal mastery is the link between pain and depression. In 100 consecutive referrals to an outpatient pain management program, they found that perceived life interference and reduced self-control were significant variables. Besides the relatively typical history of the pain-prone personality,[62,64] the severity of pain influences its interference with activity and quality of life.

The scar hypothesis claims that previous episodes of depression due to a genetic or acquired susceptibility predispose some individuals to a depressive episode after the onset of pain.[65] Patients with pain and depression have been reported to have an increased of rate of prior depressive episodes.[66] Higher prevalence rates of clinical depression have also been reported in the families of patients with pain than in different control groups.[67]

Temporal order may provide information about the cause of pain and depression. In certain patients, the signs and symptoms of pain and depression develop simultaneously.[57,68] According to the antecedent hypothesis, depression precedes chronic pain. In a systematic review by Fishbain,[69] however, 9 of 13 studies failed to support this hypothesis, while one study had mixed results. In a 10-year follow-up of metal workers, Leino and Magni[70] found that depressive symptoms predicted future musculoskeletal disorders, but not vice versa. Over a 3-year period, Von Korff and colleagues observed that depressed patients developed severe headaches and chest pain more often than controls.[71]

The consequence hypothesis (the belief that depression follows pain) was supported by the results of 15 studies related to chronic pain and by another three investigations of patients with intermittent pain. In Fishbain's review,[69] depression appeared more likely to follow than to precede pain. The discussion of whether pain precedes depression or depression leads to pain reminds me of asking which came first, the chicken or the egg. The enigma cannot be solved by linear deterministic thinking, yet it does not seem to be unsolvable.

Constellations of pain syndromes with depressive disorders can be regarded as dynamic systems within which the elements interact bidirectionally. With increasing severity of pain and progressively worsening impact on work, motor activity, and social role performance, the system may evolve to display new qualities. In a representative sample of the Hungarian population, pain-associated disability was found in 37% and of this subset, 30% reported depressive symptoms.[72] The limitations that result from pain are manifest in different ways in different areas of the body. These limitations tend to be greater for back pain and lower for facial pain.[73] Formal certification of disability may lead to further deterioration.[54,74] Pain is a cognitive, sensory, and emotional experience and a motivational and

interactional force. For many patients with pain and depression the complexity theory (Table 3) may be a more appropriate conceptual framework than conventional, sequential models of nociception.[75]

Table 3
Simple versus complex pain states

Simple	Complex
Monocausal	Multifactorial
Unidirectional	Bidirectional
Stimulus-response	Interactions
Linear	Nonlinear
Causal sequence	Network
Deterministic	Nondeterministic

Note: A simple pain usually has a clear, single cause and can be framed within a stimulus-response model. In contrast, complex pain states have a multifactorial origin. The link between stimulus and pain experience is linear in the case of simple pain, whereas in complex pain conditions there are multiple associations among elements, between which there may be nonlinear and nondeterministic relations. The terms "causal sequence" and "network" illustrate the fundamental differences.

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