Expectations and Illness: Depression as a Culture-Bound Syndrome in North America

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Abstract

Clinical depression has been unilaterally construed as a biochemical imbalance in serotonerigic systems. The over-simplification of disease reflects economic, political, and social forces that pathologize normal behaviors to manufacture illness. This paper considers evolutionary and dynamic systems biology to advance the idea that subclinical depression is an illness within culture that manifests biologically, as opposed to being organically created and sustained. The classic medical model underestimates psychosocial elements of depression. Patient narratives show the limitations of the medical model and suggest a need for a new depression paradigm, which is the biopsychosocial model. This paper is critical of both the biological etiology of depression and the social and cultural elements that create and sustain depressive episodes.

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La dépression clinique a toujours été interprétée comme un déséquilibre du système sérotonergique. La simplification excessive de cette maladie est reflétée par les différentes sphères économiques, politiques et sociales qui pathologisent les comportements normaux en des comportements maladifs. Cette étude se sert des systèmes biologiques évolutifs et dynamiques pour avancer l'idée que la dépression subclinique est une maladie qui se manifeste biologiquement à l'intérieur même de la culture, par opposition à ce quelle soit organiquement créé et maintenue. Le modèle médical classique demeure fermé aux éléments psychosociaux de la dépression. Des entrevues avec les patients ont démontré les limites du modèle médical traditionnel et suggère la nécessité d'établir un nouveau paradigme à la dépression, tel que celui du modèle biopsychosocial. Cette étude est importante et cruciale car elle se penche non seulement sur les étiologies biologiques de la dépression mais met également l'emphase sur les éléments sociaux et culturels qui engendrent et maintiennent les périodes dépressives.

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Introduction

Clinical depression is an affliction unlike a broken leg or tuberculosis which presents the same way in all individuals regardless of time, place, gender, age, or culture. Instead depressive experiences and symptoms are diverse, manifesting themselves in highly variable ways. There is no single medical articulation of what constitutes depression. Depression is defined in several ways. Among the most common sets of criteria for diagnosing depression are those published by the American Medical Association (AMA) in the *Diagnostic and Statistical Manual of Mental Disorders*, DSM-VI TR, the World Health Organization (WHO) in the *International Classification of Disease*, IDC-10, and World Organization of National Colleges, Academics, and Academic Association of General Practitioners/ Family Physicians (WONCA) in collaboration with the WHO in the *International Classification of Health Problems in Primary Care*, ICHPPC-2. This paper employs the DSM-IV TR criteria, used most commonly by North American practitioners, in establishing the parameters of depression.[1]

Several aspects of depression pertaining to cultural and social aspects of the disease, which include spiritual questions, feelings of alienation, and existential concerns, are not captured in the DSM nosology. These more nebulous aspects of depression are sometimes voiced in milder variants of depressive experiences such as dysthymic disorder and sub-clinical depression. Not all individuals who consider themselves, or are considered by others, to be depressed meet the necessary number of symptoms on the list to be considered depressed by the DSM-IV. Still, they clearly suffer and present with depressive-like behavior.

In the DSM-IV TR, "depression" is an all-encompassing term, refering to several degrees and variants of depression ranging from major clinical to subnormal mood disorders such as minor depression, clinically referred to as dysthymia. The depression may consist of single or recurrent depressive episodes with intermittent periods of mania, as seen in bipolar affective disorder and its less severe form on the mood disorder spectrum, clinically referred to as cyclothymia. Culturally, the concept of depression in North America has expanded beyond its DSM definition, referring not to a debilitating sadness, but to a general lack of happiness. Some depression literature suggests that the depressive condition includes normal aspects of modern life which have become medicalized and pathologized to create a disease status.

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[1] As several existing disease nosologies define depression in different ways, this lack of consensus suggests that the medical community lacks a clear framework as to scope, breath, depth, and parameters of the depressive condition.

This paper surveys a selection of depression narratives ranging from accounts of severe and acute depressive episodes to milder depression experiences, while paying particular attention to how identity is affected by explanatory models and depression paradigms.

The narratives explore different ways of understanding depression. They range from interpretations of biomedical disease resulting from low serotonin levels to an illness within culture. The diverse selection of patient narratives not only highlights biological aspects of the disease but also includes cultural components contributing to the disease's complex etiology and pathogenesis. An expanded view of what constitutes the depressive condition (namely a lack of happiness as opposed to pathological sadness) challenges the vocabulary and paradigm of traditional explanatory models. The traditional medical model will come to be seen as an unhelpful frame work to advance an understanding of depression due to its linear reasoning and reductionism. The inadequacy of the traditional medical model creates a need for a new paradigm of understanding and approaching depression. This need is fulfilled by the biopsychosocial model. This new paradigm is able to account for the diverse and highly individual symptom presentations of the depressive condition in the postmodern era. The new biopsychosocial model of depression accounts for the interaction of science and culture in the production of disease.

The dominant paradigm of understanding depression in the West is informed by a biomedical model which attributes the disease to particularly low serotonin levels. The medical model of depression carries with it certain benefits and limitations. One benefit is the destigmatizing label of disease. This understanding removes individual blame from the sufferer. The disease model challenges an older view of mental illness as a personal moral failing. While viewing depression as a disease removes fault from the sufferer, it simultaneously places the sufferer in a more passive role. The construction of depression as a purely biochemical problem removes a significant amount of individual agency and control from the sufferer. The sufferer is afflicted with bad biochemistry, which only drugs can normalize. Therefore, according to this view, the sufferer is a helpless victim incapacitated by a disease over which he or she has no control.

The biomedical model has historically reduced depression to an account of serotonin abnormalities. The biomedical model is unable to account for the diverse presentation of illness experiences captured by patients' narratives. Accounts of different biomedical models for depression show how the reductionist approach is an inherent limitation of the medical model in addressing the diverse symptoms of clinical depression. In addition, I will discuss the role of the pharmaceutical industry in shaping the biomedical model as a dominant paradigm for understanding

clinical depression. In attempts to control chemical imbalances, the pharamaceutical industry has actively shaped the biomedical model as a dominant paradigm for understanding clinical depression.

Alternatives to the biomedical model are anthropological and sociological models of depression. These frameworks emphasize social and cultural disease etiologies over biological factors underlying biochemistry and genetics. These models challenge the legitimacy of the milder variants of depression as a biomedical disease, suggesting instead that the experiences people report are reflective of cultural fragmentation and social disconnectedness. Such feelings of separation are products of internalizing cultural expectations and unmet social standards.

These anthropological and sociological models challenge the notion of mental illness as a biomedical disease. Unlike historical views of depression and mental illness which see these conditions as moral failings in which the afflicted are solely responsible for their disease states, these models attribute responsibility for the disease states not to individuals but to the society in which we live. Therefore, even from within the cultural climate that sets the stage for milder variants of depression, people make free and autonomous choices that contribute to their lack of happiness. This discussion is framed by an evolutionary perspective on depression which suggests that depression and depressive behaviors are signposts indicating that energies and resources are poorly allocated in one's life, and that individual resources and energies would best be invested elsewhere.

When depression is considered from an evolutionary perspective, the sufferer gains a certain amount of agency and control that is absent in the medical model. The evolutionary model requires individuals to recognize poor investment of resources and make wiser choices for themselves. People must take responsibility for their individual happiness and acknowledge how their own decisions contributed to their current position. The medical model affords an opportunity to avoid the discomfort of taking responsibility for unfavorable outcomes, while the biopsychosocial perspective asks for confrontation of these unpleasurable aspects. In terms of attributing responsibility to people for the state of their mental health and happiness, the evolutionary perceptive offers a middle ground between older cultural ideas of holding the individual fully responsible and the biomedical model in which the person has no responsiblity for his or her disease state.

At the core of depression is the diagnosis of major depression. However, as one moves from core to periphery, the diagnosis of milder variants of depression occur along the edges of the

diagnosis category. This paper is less concerned with challenging the core construction of major depression as a biomedical disease but rather examines how the biomedical construction of depression destabilizes towards the periphery of the diagnosis category. Towards the periphery of the depression category, I will argue that the despondency, discontentment, suffering, and pain that patients report do not have biological causality. Rather, according to this new biopsychosocial model, the causes of such suffering are products of culture, expectation, and individual choice. This paper offers a challenge to the traditional biomedical model of understanding the disease. Sub-acute depressive experiences are more nebulously defined and do not neatly mesh with the DSM-IV TR criteria. The medical model is therefore unable to offer a useful paradigm for understanding and fails to provide a useful vocabulary for analysis. During the transition from the prototypical view of depression towards the borders of the diagnosis to milder variants, the construction of depression as a biomedical disease destabilizes.

The predominant biomedical model is inherently limited by its focus on serotonin and its inability to account for cultural aspects of the disease. A way to reconcile this limitation is to approach depression from a biopsychosocial perspective in which multiple disease etiologies across biological and social media are recognized. Such a paradigm is cognizant of biocultural co-evolution dynamics that produce disease and illness states.

In the case of milder variants of depression, a biopsychosocial model is useful in providing a vocabulary and framework for discussion in which afflicted individuals can engage in a self-reflective dialog. First, the individual acknowledges lifestyle decisions he or she made in addition to expectations held which contribute to the present state of unhappiness. After acknowledging decisions made, the individual must take responsibility for his or her choices and must take ownership of present unhappiness. In light of newly gained personal information gleaned from a self-reflexive dialog, the individual must make new decisions and life style choices, and/or modify expectations to alleviate and reduce discontentment, displeasure, and lack of happiness instead of claiming bad biochemistry and circumstance beyond individual control.

The proposed biopsychosocial model of depression is not at variance with previous depression research investigating biological platforms implicated in maintenance of the disease. Rather, the biopsychosocial model, working from a dynamic systems biology perspective, situates numerous well-documented biochemical relationships, which are pieces of the depression puzzle, within the context of holistic body function. Uniting previously competing theories into a single unified explanatory model, this new depression paradigm articulates and accounts for incongruities

in previous individual theories. The proposed biopsychosocial model draws upon the *neuroendocrine theory of depression*, also referred to as the *stressor model of depression*, coupled with the *neurogenetic theory of depression*. While aspects of these models are grounded in the biology of the organism, their theoretical basis is non-reductionist as they take into account interactions with the environment. When taken together, these theories, which culminate in a biopsychosocial model of depression, not only shatter the dominant biomedical model of depression as a serotonin deficiency disorder, but also offer a deep understanding of the complex etiology.

The standard medical model of depression is presented in the first chapter, and is then deconstructed across the next three chapters. The intermediate chapters consider cultural, philosophical, and evolutionary elements of depression which are absent in the medical model. The last chapter provides a technical and biologically-grounded account of depression that goes beyond the medical model in accounting for biochemical factors of depression.

Chapter 1: The Medical Model & Science of Depression

This chapter presents the classical medical model of depression in its entirety from how it is defined in disease nosologies to theories of biological causality. In defining the disease, the medical field has reached no consensus concerning the symptom constituting depression. Similarly, in searching for the biological origin of the disease, there is a lack of consensus concerning disease pathophysiology. The lack of consensus, notwithstanding the medical model, constructs depression as a disease resulting from biochemical imbalances which are responsible for patterns of symptoms presentation characterized by DSM-IV, ICD-10, and ICHPPC-2. This view of depression is significant because it is the dominant paradigm for understanding and interpreting depression in Western culture. Furthermore, this depression paradigm is important to this paper as its inherent assumptions and limitations are discussed and contrasted to other depression paradigms in later chapters. Examining the scientific reductionism of this model is the first step to gaining a greater understanding of depression beyond the dominant biomedical model.

Approaches to defining depression within the medical model.

Three separate published standards of criteria demonstrate the lack of consensus pertaining to the diagnostic criteria for diagnosing depressive disorder. At the core of the depression category is major depression, which is the most severe form of the disease. The criteria for diagnosing major depression remains more or less consistent across each set of diagnostic criteria. Transitioning from the core to the periphery of the diagnostic category less severe forms of depression are encountered. The criteria defining less severe depressive conditions fluctuate. When taken together the criteria for diagnosing milder depression and subnormal mood disorders produce a somewhat nebulous understanding of the condition. Three separate published standards of criteria, DSM-VI TR, IDC-10, and ICHPPC-2, revel the lack of consensus pertaining to the diagnostic criteria for diagnosing depressive disorder. After the analysis in this section, the duration of the paper will only refer to the aspects of the DSM-IV TR criteria when probing how depressive disorder is understood in North America. Since the DSM is a critical text in American psychiatry it is important to understand noy only how the DSM classifies depression in relation to other texts, but also to understand its history and the forces that have shaped the construction of this text.

The DSM: A brief history.

The DSM was developed to provide psychiatrists with objective terms and a consistent vocabulary to communicate with each other. This document bases its categories and diagnoses on statistical models. The disease taxonomy is limited by the methodology used to create the models. "The process by which [the DSM] gained its ascendancy is long and involved and reflects the status of psychiatry and of the American Psychiatric Association as both a political, professional and scientific organization."[2] DSM criteria and classifications reflect snapshots in psychiatric thinking and tensions within the field. Classifications emerge from professional committee meetings, tasks forces, compromises, input from the American Psychological Association (APA), and engagement of expert opinion within the psychiatric community. The DSM by no means represents a consensus of opinion in the field and does not reflect the spectrum of opinion in mental health regarding psychopathology or social functioning issues.

Critics challenge that the DSM invents illness categories and 'deviant behaviors,' as some of its diagnoses lack objective, verifiable, biological criteria. Therefore, the classification of illness seems arbitrary. The DSM allows the definition of mental disorders to change over time, which may be reflective of social norms and social thinking. For example, prior to 1973, homosexuality was listed as a psychiatric diagnosis, but this listing was later removed. Different editions of the DSM reflect different trends, psychiatry, radical paradigm shifts, tensions in the field, and the political and economic climate in which decisions were taken.

DSM-I was the first addition published in 1952, classifying roughly 60 disorders. DSM-II was published in 1968. In the era between World War II and the mid 1970s, a psychosocial model "informed by psychoanalysis, social thinking, and biological knowledge, was the organizing model for American psychiatry."[3] This approach was reflected in both early DSM additions. The psychosocial approach or psychodynamic model was fluid in that it "did not clearly demarcate the mentally well from the mentally ill."[4]

The psychosocial model at times was an amalgam of Freudian personality and intrapsychic conflict theory blended with Meyerian psychobiology that privileged the role of the environment. Supporting these foundations was the work of Karl Menninger who posited the "personality-

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[2] Kirmayer, Lawrence. Personal email communication. May 10, 2006

[3] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 399.

[4] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 399.

environmental struggle."[5] The psychosocial/psychodynamic framework held that the boundary between well and ill are fluid because a well person can become ill "if exposed to severe enough trauma."[6] In this model, mental illness exits along a continuum of severity and is the result of an "untoward mixture of noxious environment and psychic conflict."[7] Therefore, the presentation of mental illness is psychogenic, meaning psychologically medicated.[8] For Menninger, mental illness was "the failure of the suffering individual to adapt to his or her environment."[9] The central approach emphasizes "understand[ing] the meaning of the symptoms and undo[ing] its psychogenic cause, rather than manipulate[ing] the symptom directly (through medication, suggestion, etc.)."[10] Later "as biological insights into the nature of psychotherapy accrued, the prefix 'bio' was added to 'psychosocial' to give us the now- familiar 'biopsychosocial' model."[11]

The classificatory structure DSM-I and DSM-II focused on distinction between *psychosis* and *neurosis*. In this era, psychosis was operationalized to mean a severe mental disorder in which there was a complete break from reality, generally involving hallucinations and delusions. Neurosis, on the other hand, was operationalized to mean a milder mental disorder in which reality became distorted, but not completely disconnected. Typical neurosis included anxiety and depression.

In the era before the publication of DSM-III, the profession was is a state of crisis over broader disputes and outside attacks, which questioned the legitimacy of the profession. At this time, the profession existed in a climate of shrinking resources and support in which an antipsychiatry critique was mounting. From 1965 to 1972, the NIMH decreased its funding by 5% every year.[12] The profession lacked a 'common language' and needed to "map its professional

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[5] Menninger, K. Psychiatry in a Troubled World: Yesterday's War and Today's Challenge. New York: Macmillan, 1948.
[6] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410.
[7] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410.
[8] Grob, G. "The Forging of Mental Health Policy in America: World War II to the New Frontier." Journal of the History of Medicine 42 (1987): 410-446.
[9] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 400.
[10] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 400.
[11] Engel, G.L. "The Need for a New Medical Model: A Challenge to Biomedicine." Science 196 (1977): 129-136
[12] Brodie, H.K.H., and M Sabshin. "An Overview of Trends in Psychiatric Research: 1963-1972." American Journal of Psychiatry 130 (1973): 1309-1318 in Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 403.

jurisdiction."[13] Outside bodies asked that the profession be more accountable for its practices. A 1978 report on mental health issues by the Carter administration criticized the lack of mental health research productivity,[14] and the Federal Employee's Health Benefits program, underwritten by Aetna and Blue Cross, cut reimbursement and coverage in mental health. Robert Laur, Vice president of Blue Cross, stated that psychiatry "compared to other types of [medical] services [had] less clarity and uniformity of terminology concerning mental diagnoses, treatment modalities, and types of facilities providing care...One dimension of this problem ar[o]se from the latent or private nature of many services; only the patient and the therapist have direct knowledge of what services were provided and why."[15]

These concerns were amplified by federal Senator Jacob Javits. Javits remarked that it was the congressional view that the "existing mental health care system does not provide clear lines of clinical accountability."[16] The issues of diagnostic reliability, treatment outcomes, and accountability for those outcomes had come under public scrutiny. It was the view of some in the profession that the fluidity of the psychosocial model was responsible for professional shortcomings leading to these sorts of critiques.

The research base was more descriptive than quantitative. In order to justify the profession, doctors needed "explicit diagnostic criteria in order to gather homogenous research samples for clinical trials."[17] Medication was "creat[ing] a need for more experimentally and empirically based psychiatry"[18] that almost by definition would have to be quantitatively and not fluidly constructed.

Many "bemoaned psychiatry's drift away from medicine" [19] because medicine is science, and science has an air of objective validity. A faction within the profession "defended the classical

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[13] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 408.
[14] Report to the President from the President's Commission on Mental Health, vol I: Number 040-000-00390-8. Washington DC: US Government Printing Office, 1978 in Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 403.
[15] "Blue Cross VP says MH prospects Cloudy." Psychiatric News August 6, 1975. 1 in Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 403.
[16] "Javits says MH hurt by role confusion." Psychiatric News December 16, 1977. 1 in Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 403.
[17] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 404.
[18] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 404.
[19] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 402.

medical model of disease as an appropriate model of psychic illness."[20] Classic scientific approaches would quiet the external critics and lend an air of legitimacy to the psychiatric enterprise that was lacking in the public's opinion.

> *The ideological power of science cannot be underestimated as a contributing factor in the hegemony of the discourse of descriptive diagnosis in contemporary psychiatry. The seeming objectivity of science is science's own justification.*[21]

This approach to mental illness was in tension with the psychosocial model. "If [mental illness] is conceived psychosocially, psychiatric illness is not the province of medicine, because psychiatric problems are not truly medical but social, political, and legal." If underlying pathology cannot be identified to "explain mental illness, [then] the disturbances cannot be called diseases in the conventional medical sense."[22] Thomas Szasz used this line of reasoning to claim that mental illness was a 'myth.'[23] If it is a myth, and there are no diseases per say, then psychiatry cannot operate as a medicinal discipline. At this point in history, the profession decided to take a more biologically oriented approached to circumvent implosion.

The solution to these problems was the publication of DSM-III in 1980. The events leading to the publication of DSM-III represented an ideological power struggle in the profession between those who valued the psychodynamic approach and those who favored the conventional medical model. In the formation of DSM-III, compromises were made on both sides; however, psychodynamically-oriented practitioners had to surrender up the most ground as their point of view was virtually obliterated. This process was brokered though numerous committees, sub-committees, tasks forces, and expert involvement. APA involvement was present in this process.

The DSM-III discarded the psychodynamic model in favor of the conventional medical model. The word 'neurosis' and all it implications in the psychodynamic approach was dropped from DSM-III. The text became *atheoretical.* One of the missions of DSM-III was to improve diagnostic reliability which meant that the manual "would emphasize easily observable

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[20] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 402.
[21] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 408 following the work of Haberman, J. "Technology and Science as Ideology," in Towards a Rational Society: Student Protest, Science and Politics translated by J. Shapiro. Boston: Beacon press: 1970.
[22] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 402.
[23] Szasz, Thomas. The Myth of Mental Illness: Foundations of a Theory of Personal Conduct New York: Harper & Row, 1961.

symptoms."[24] The categorization of the manual was to be based on "best available evidence," which means etiology would not be used to classify unless the etiology was "proven."[25] The limitation of this approach is that people who have the same diagnosis may not share the same etiology or cause for their psychiatric label. This may mean that people in the same diagnosis category who have the same disorder may be treated differently because their illnesses have different origins/etiologies. Yet because the symptoms are the same, they are labeled together. The DSM does not include treatment information. Treatment is linked to etiology which is linked to particular views of illness, which at this time was either psychodynamically- oriented or in line with the medical model's view of discrete pathologies. The DSM is said to be atheoretical since it lacks etiological and treatment components. The DSM's role was not to address these theoretical issues but to provide a consistant vocabulary for professionals to communicate with each other.

The new direction of the DSM allowed for sharp distinctions to be made between mental states and behaviors that were normal and abnormal. The medical model allowed mental disorders to be "conceived as discrete pathological entities, each with its own natural history,"[26] which allowed for a "significant narrowing of psychiatry's clinical gaze."[27] In total, DSM-III is credited as being a "remedicalizing" instrument within American psychiatry.[28]

The transition from DSM-II to DSM-III also represented a tension between clinicians and researchers. "Research investigators replaced clinicians as the most influential voices in the profession."[29] This shift is consistent with the desire to run clinical trials and to use medication to treat illness in a similar fashion as other branches of medicine. DSM-III solved a number of problems for psychiatrists, but brought with it numerous limitations due to a narrowed medical gaze.

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[24] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 405.
[25] Task Force on Nomenclature and Statistics: Progress Report, March 1, 1976, in Papers of the Task Force on Nomenclature and Statistics. Washington, DC. Archives of the American Psychiatric Association in Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 405.
[26] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 402.
[27] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 399.
[28] Pasau, R.O. "The Remedicalization of Psychiatry." Hospital and Community Psychiatry 38(1987): 145-151 in Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 399.
[29] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 400.

In the view of psychiatrist, Mitchell Wilson, the narrowed gaze of the new medical model limited the discourse about mental illness in three ways.[30] First, "depth of mind" had been lost, as only "superficial and publicly visible symptoms" were addressed. Second, time was "shortened from a lifetime to a moment." Extended evaluation was reduced to a short interview, where psychiatry used to consider the development of the person and the unfolding of their symptoms within the greater context of the patient's life. Lastly, and most importantly, the type of information that was considered clinically relevant about a patent significantly narrowed. "Personality and the ongoing development of character, unconscious conflict, transferences, family dynamics, and social factors [were] aspects of a clinical case that [became] deemphasized."[31] DSM-III represented a radical shift in thinking, which set up some of the limitations for how mental health is approached today.

Subsequent versions of DSM-III are methodologically similar to the watershed in psychiatry, which occurred between DSM-II and DSM-III. The DSM-IIIR was published in 1987 and witnessed minor revisions of criteria. The DSM-IV was published in 1994 but went through a text revision in 2000, making the DSM-IV the latest working addition of the DSM. The DSM-V is scheduled to be published in 2011.

The DSM is a central text in American Psychiatry. Its criteria have meshed with the ICD since ICD was in its 9th addition, making the DSM an important text internationally. Despite its importance, the text has been widely criticized by scholars, clinicians, and researcher as being unscientific and arbitrary, particularly in the categorization of personality disorders.[32] One research psychologist even called for Congressional hearings regarding the DSM and potential harm its labels create.[33] While these considerations may be a matter of opinion and rhetoric, a more serious issue regarding the DSM is the potential bias in the development of its categories and criteria. A recent study found that *all* of the expert psychiatrists involved in developing and writing DSM criteria for mood disorder (which includes depression) have had financial ties to pharmaceutical companies that sell medications to treat the disorders for which they are writing operational

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[30] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410.
[31] Wilson, Mitchell. "DSM-III and the Transformation of American Psychiatry: A History." American Journal of Psychiatry 150.3 (1993): 399-410. 400. following the work of Reise, M.F. "Are psychiatric Educators 'Losing the Mind?' American Journal of Psychiatry 145 (1988): 1061-1067.
[32] Kirk, S. A., and Kutchins, H. The Selling of DSM: The Rhetoric of Science in Psychiatry. New York: Aldine de Gruyter. 2002.
[33] Caplan, Paula J. and Lisa Cosgrove Eds. Bias in Psychiatric Diagnosis. Oxford: Jason Arnson. 2004.

guidelines and criteria.[34] A serious flaw, this bias may privilege the views of the pharmaceutical industry, leading a professional and supposedly an atheoretical text to favor the treatment of affective disorders, such as depression, with drugs instead of considering other options. If this criticism is true, then mental illness has been constructed to meet the needs of one stakeholder in depression at the expense of patients.

The DSM-IV TR has been referred to as the bible[35] of American Psychiatry. What this text says about mental illness is important, as the text has the power to shape clinical practice and public perceptions of disease. Understanding the information that the DSM holds requires understanding its history, methodologies, and limitations. While it has been compared to the bible and has the blessing of the APA, the DSM has significant flaws.

DSM-IV TR.

To diagnose psychiatric disorders, this disease taxonomy provides a multi-axial assessment tool, which accounts for aspects of patients' lives that may shade the overall diagnosis. For example, the multi-axial systems account for personality, other medical conditions, social circumstance, and global functioning. The DSM-IV TR contains criteria for the diagnosis of depressive disorder, which is a category that encompasses several disorders of depressed mood ranging in severity. On the more severe end of the spectrum is major depression, or unipolar depression, which may occur in a singular episode or in recurrent episodes. To meet the criteria for major depression, a person must experience five out of the nine symptoms listed for a period of two weeks or longer. The symptoms include: depressed mood; diminished interest or pleasure in activities, also referred to as *anhedonia*; loss of energy or fatigue; feeling of guilt; recurrent thoughts of suicide or suicidal behaviors; diminished ability to concentrate or indecisiveness; psychomotor agitation or retardation; insomnia or hypersomnia; and change in appetite.[36] These criteria exist in addition to caveats for diagnosis which maintain that one of the symptoms must be depressed mood or anadonhia, and that the symptoms must be causing a great enough degree of distress to impair social and/or occupational functioning. The symptoms should not be due to psychology effects of drugs, such as drug abuse or prescribed medications, or be the result of a

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[34] Cosgrove, L., Krimsky, S., Vijayarghavan, M., and Schneider, L. "Financial ties between DSM-IV Panel members and the Pharmaceutical Industry." Psychotherapy and Psychomatics 75(2006): 154-160.
[35] Vedantam, Shankar. "Experts Defining Mental Disorders Are Linked to Drug Firms." Washingtonpost.com 20 April, 2006, A07.
[36] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorder: DSM-IV TR. 4th ed. Washington: American Psychiatric Association, 1994.

medical condition such as hyperthyroidism. Lastly, the symptoms should not be related to grief and bereavement for a lost loved one.

Major depression also includes bi-polar depression, formally referred to as manic depression. Bipolar depression is characterized by periods of depression followed by periods of mania and hypermania, in which patients are happy, hyperactive, and experience delusions of grandeur.

On the less severe end of the spectrum is the diagnosis of minor depression, which occurs when two to four symptoms are present and linger for at least two weeks. Dysthymia can be diagnosed when three or four of the symptoms are present, one of which must include depressed mood, for a period of two years or longer.

Cyclothymic disorder is a less extreme chronic bipolar disorder consisting of periods of mood that cycle between mild depression and hypomania, which are interdispersed with periods of normal mood lasting no more than two months. Symptoms may last a few days to several weeks; however, the cycling must be present for two years. This diagnosis has one caveat: the systems on the depressive end of the spectrum must not fulfill the criteria for major depressive disorder. While this disorder is part of the depressive disorder category, it rests on the bipolar spectrum and therefore is not a central focus of the paper, though this disorder, like variants of unipolar depression, is nebulously defined and is diagnosed though a different set of criteria in the ICD-10.

ICD-10.

The *International Classification of Disease*, IDC-10, has been referred to as the European definition for the classification of disease. Regarding depression, the ICD-10 uses similar criteria to the DSM but includes an additional symptom of loss of confidence or self-esteem.[37] This set of diagnostic criteria pays particular attention to lowering of mood and reduction of energy leading to decreased activity. Additionally, the ICD-10 highlights the presence of somatic symptoms. Somatic symptoms of depression include psychomotor retardation, agitation, lack of appetite, lack of libido, weight loss, physical pains, and gastrointestinal upset.[38] These criteria pay more attention to physical rather than psychological symptoms of depression. The ICD-10 categorizes depression based upon severity, in which a depressive episode may be categorized as mild, moderate, or severe.

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[37] World Health Organization. International Statistical Classification of Disease and Related Health Problems: ICD-10. 10th ed. Vol. 3. Geneva: World Health Organization, 2005.

[38] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 18.

In mild depression, two or three symptoms are present. The patient is distressed, but still able to function in his or her professional and personal life. In moderate depression, four or more of the symptoms are present, and the patient has difficulty performing ordinary activities. In severe depression, several of the symptoms are present, and the presentation of these symptoms is "marked and distressing."[39] Therefore, a severely depressed person is unable to perform the tasks of daily living. At this level of depression, typical symptoms include the loss of self-esteem and feelings of worthlessness and guilt. Somatic systems are generally present in addition to suicidal ideations. Interestingly, melancholia is listed as one of the descriptors in the guide lines for diagnosing clinical depression. The ICD-10, as opposed to the DSM, tends to associate certain symptoms with particular levels of depression. All symptoms must be present for least two weeks before a diagnosis can be made. The only exception is in the case of severe depression when the diagnostics can be made sooner if the symptoms have a rapid onset.

ICDPPH-2.

In the *International Classification of Health Problems in Primary Care,* ICHPPC-2, depression is defined as having two core systems, which are depressed mood and decreased interest, in addition to one of the following symptoms: suicidal ideations, indecisiveness, worthlessness or guilty feelings, insomnia, morning tiredness, anxiety or irritability, and psychomotor agitation.[40] A study in the Netherlands found that the ICHPPC-2 were harmonious with DSM-IV criteria for the diagnosis of major depression.[41] Similar to the DSM-IV definition, this study shows that the core of the depressive diagnosis, major depression, is stable and easier to categorize than the conditions of less acute depression towards the periphery.

The ICHPPC-2, is an interesting text when considered from the psychiatric perspective, as more and more psychiatric conditions are being diagnosed and even treated in the primary care

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[39] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 19.

[40] Classification Committee of WONCA (World Organization of National Colleges, Academics, and Academic Association of General Practitioners/ Family Physicians) in collaboration with the World Health Organization. International Classification of Health Problems in Primary Care: ICHPPC-2-Defined. 3rd ed. Oxford: Oxford University Press, 1983.

[41] Weel-Baumgarten EM van, Bosch WJ van den, Hoogen HJ van den, Zitman FG. "The Validity of the Diagnosis of Depression in General Practice: Is using criteria for Diagnosis as a Routine the Answer?" British Journal of General Practice 50 (2000): 284-287 in Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 19.

setting.[42] Primary care physicians play an important role in the diagnosis and treatment of depression either by managing the case in their practice or by referring to specialists. Often, primary care doctors or family physicians are a patient's first contact with a health care system. The patient's treatment is governed by the primary care physician's perception as to what symptoms constitute depression and how these symptoms manifest. The constructions and beliefs of the physician will shape the patient's understanding of his or her symptoms experience through a designation of an illness label which is subject to a physician's understanding of a disease category.

The *DSM* focuses on psychological symptoms of depression while the *ICD-10* highlights somatic symptoms of depression in addition to psychological symptoms. Depending upon how a patient presents his or her pains to a primary care physician, and how that physician understands depression, a diagnosis may or may not be made. For instance, a patient may come in complaining of generalized pain, headache, gastrointestinal upset, sleep disturbances, and fatigue. The patient may not use psychological language to describe his or her suffering. Instead, he or she uses idioms of distress that are physical as opposed to psychological. A primary care physician must either treat these disturbances as separate issues or probe at the root cause which may be psychological in origin. This is why patient presentation and physician understanding of depression is important in the diagnosis of depression. The presence or lack of an illness label will affect how the patient makes sense of his/her experience, and depending upon the nature of the symptoms, will affect identity. This example highlights how the medical understanding of what constitutes a disease influences intimate aspects of patient experience. These issues are especially relevant in primary care as it has been estimated that 70% of SSRI class antidepressant prescriptions are written by family practice and primary care doctors rather than psychiatrists.[43]

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In addition to the several modes of defining depressive disorders, several biological theories complete to explain the pathophysiology of depression. The *traditional* biomedical paradigm makes certain that the disease is unilaterally construed of as a biochemical problem in

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[42] Classification Committee of WONCA (World Organization of National Colleges, Academics, and Academic Association of General Practitioners/ Family Physicians) in collaboration with the World Health Organization. International Classification of Health Problems in Primary Care: ICHPPC-2-Defined. 3rd ed. Oxford: Oxford University Press, 1983.

[43] Grinfeld, M.J. "Protecting Prozac." California Lawyer 79 (1998) 36-40 in Glenmullen, Joseph. *Prozac Backlash.* New York: Touchstone. 2000, 17; Pollock, E.J. "Managed Care's Focus on Psychiatric Drugs Alarms Many Doctors." Wall Street Journal, Dec.1, 1995 in Glenmullen, Joseph. *Prozac Backlash.* New York: Touchstone. 2000, 17.

neurotransmitter systems. The section below presents biological theories of depression that only address disease pathophysiology as a complete explanation for symptoms experiences.
In the final chapter, biological theories of depression are returned to from a dynamic systems biology perspective which contextualizes specific out-of-balance chemical relationships within global body function across multiple body systems. The biological theories of depression presented below focus on out-of-balance chemical relationships in isolation from other bodily systems. The theories presented below are scientifically reductionist and prevent a larger understanding of depression.

Biological theories of depression.

The medical model attributes both the physical and psychological symptoms of depression to biochemical abnormalities. Therefore, normalizing biochemistry to that of 'normal species functioning' should successfully treat the problem. Research has traditionally focused on aspects of neuronal transmission with particular emphasis on neurotransmitter levels and receptor activity. Pharmacology breakthroughs in the wake of accidental drug discoveries have been critical in illuminating the pathopsychology of depression and have given rise to several neurochemical theories of depression. Gradually, research has shifted to examining how neuron physiology affects neurochemcial balances. Later research has focused on studying receptor subtypes. In a different vein of research, attention has focused on sleep quality, patterns, sleep wake cycles, and circadian rhythms, as sleep is dramatically affected in depression. Altering sleep quality and quantity has been observed to produce anti-depressant affects.[44] All of these investigations into depression limit the scope of inquiry to observing changing in body system. These modes of inquiry do not examine how body systems interact with the enviroment, or how body systems relate to one another in disease.

Neurochemical theories of depression.

Neurochemical theories of depression arose from accidental discoveries of drugs that were being developed for other purposes but were found to have psychotropic properties capable of

[44] Henner, G., Klingberg, S., Schwarwler, F., and Schweinsberg, M. "Direct Comparison of Total Sleep Deprivation and Late Partial Sleep Deprivation in the Treatment of Major Depression," Journal of Affective Disorders 76 (2000): 85-93; Voderholzer, U., Hohagen, F., Klein, T., Jungnickel, J., Kirschbaum, C., Berger, M., and Riemann, D. "Impact of Sleep Deprivation and Subsequent Recovery Sleep on Cortisol in Unmedicated Depressed Patients," American Journal of Psychiatry 161.8 (2004): 1404-1410; Henner, G., and Schwarzler, F. "Therapeutic use of Sleep Deprivation in Depression," Sleep Medicine Reviews 6.5 (2002): 361-377.

elevating mood. The mechanism of action in these drugs revealed neurochemical balances implicated in depression.

In the 1950s, Iproniazid was the first monoamine oxidase inhibitor (MAOI) to be used as an anti-tubercular treatment. As was soon discovered, this drug elevated mood and relieved the symptoms of depression. MAOIs function as monoamine (MA) agents, meaning they increase the effects of the MA[45] neurotransmitters, which include serotonin (5-HT), norepinephrine (NE), epinephrine (E), and dopamine (DA), by blocking the activity of the enzyme degrading these neurotransmitters in the synaptic cleft. By blocking the enzyme that destroys these neurotransmitters, the neurotransmitters remain in the synaptic cleft for a longer period of time, causing greater activity in postsynaptic receptor sites. Following this discovery, MAOIs were developed for the treatment of clinical depression. Through understanding the mechanism of action of MAOIs, low levels of 5-HT, NE, E, and DA were believed to be involved in depression's pathology.[46]

Tricyclic antidepressants (TCAs) are another family of antidepressant drugs, which affect all of the MAs and are more selective then MAOIs, as TCAs have shown selective potentiation of 5-HT and NE.[47] The discovery of TCAs came while researching anti-psychotics medication for the treatment of schizophrenia. The drug was not found to have anti-psychotic properties but was able to elevate mood.[48] TCAs are named for their molecular structure, which is comprised of three fused rings that block the reuptake of monoamines from the synaptic cleft. Collectively MAOIs and TCAs have given rise to the *monoamine hypothesis of depression.*

The research on mood conducted by Joseph Schildkraut revealed a different neurochemical approach to depression. Schildkraut found that emotion and mood were strongly regulated by NE, E, and DA. Collectively, these chemicals are referred to as catecholamines. Schildkraut used the evidence that TCAs and MAOIs increased synaptic catecholamine levels to propose an integrated theory known as *catecholamine hypothesis* in a 1965 *American Journal of Psychiatry* article.[49]

The most famous neurochemical theory of depression is the *serotonin hypothesis.*

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[45] MAs are sometime referred to as biogenic amines.
[46] McKim, William A. Drugs and Behavior: An Introduction to Behavioral Pharmacology. 5th ed. New Jersey: Pearson Educational, Inc., 2003. 273.
[47] McKim, William A. Drugs and Behavior: An Introduction to Behavioral Pharmacology. 5th ed. New Jersey: Pearson Educational, Inc., 2003. 276.
[48] McKim, William A. Drugs and Behavior: An Introduction to Behavioral Pharmacology. 5th ed. New Jersey: Pearson Educational, Inc., 2003. 273.
[49] Schildkraut's J. "The Catecholamine Hypothesis of Affective Disorders: A Review of Supporting Evidence," American Journal of Psychiatry 122 (1965): 509-22.

According to this theory, low levels of 5-HT are thought to be the principally responsible neurotransmitter for causing and sustaining the depressive condition. This idea was first proposed by Arvid Carlsson in 1969[50], and by 1971, the first selective serotonin reuptake inhibitors (SSRIs) were developed in Sweden.[51] SSRIs function as 5-HT agonists by increasing the time the 5-HT spends in the synaptic cleft by preventing its re-absorption. This class of antidepressants has fewer side effects and was generally found to be more tolerable than first generation antidepressants. The lack of side effects contributed to the popularity of the SSRI class of antidepressant. Additional aspects contributing to the popularity of SSRI drugs, and a serotonin mediated view of depression, are discussed in connection with the pharmaceutical industry in the next chapter.

Since the discovery of single effect drugs, which only work on one neurotransmitter system, research has focused on the MA system leading to the development of NE reuptake inhibitors (NERIs) and dopaminergic reuptake inhibitors. The MA system continues to be an area of investigation in the biological basis for depression with new theories focusing on the efficacy of postsynaptic receptors, presynaptic autoreceptors and heteroreceptors, second messengers, and gene transcription factors.[52] Regardless of the specific neurotransmitters or complement of chemicals under investigation, the methodology is the same. Chemical relationships implicated in the maintenance and pathophysiology of the disease are isolated and studied in a reductionist fashion. Unfortunately a reductionist approach may never yield meaningful answers because this approach lacks a complete understanding of the problem. Therefore, a complete solution will not emerge from this methodological framework.

Conclusions.

This chapter presents the mechanistic framework of the science of depression. This framework is the basis of how depression is viewed in popular culture, yet the same framework later becomes the subject of much critique in the paper. The diagnostic criteria and biological theories of depression presented in this chapter all articulate components of the experience, but none manage to summarize its entirety. In considering how difficult it is to operationalize and define depression, Andrew Solomon compares establishing clinical parameters for depression to establishing clinical

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[50] Healy, David. The Anti-depressant Era. Cambridge, Mass.: Harvard University Press, 1997. 43-77.
[51] Healy, David. The Anti-depressant Era. Cambridge, Mass.: Harvard University Press, 1997. 43-77.
[52] Goldstein, David J., and Potter, William Z. "Biological Theories of Depression and Implications for Current and New Treatments." Pharmacotherapy of Depression. Ed. Domenic A. Ciraulo, and Richard I. Shader. Totowa, N.J.: Humana Press, 2004. 13.

parameters for hunger. "It's trying to come up with clinical parameters for hunger, which affects us all several times a day, but which in its extreme version is a tragedy that kills its victims."[53] A certain amount of hunger in the day is normal, but at certain point it becomes a health problem and interferes with how we want to live. The same can be said for sadness. Sadness is part of life, but taken to an extreme, it affects health and who we become as people.

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The second chapter discusses how different stakeholders in depression, namely patients, physicians, and the pharmaceutical industry, benefit if depression is constructed in biological terms consistent with research presented in this chapter. The remainder of the second chapter focuses on how these benefits turn into burdens.. The later portion of the chapter incorporates illness narratives to show how traditional depression paradigms shape identity, illness understanding, and treatment modality sought, which are based upon the suffer's understanding of illness. Relying on a single incomplete definition of depression, as encapsulated by neurochemical theories of depression, will manifest in a single incomplete treatment of the disease. Purely biological treatments are not able to effectively treat the disease since depression does not have a purely biological etiology as suggested by the medical model presented in the chapter. Non-biologically constituted etiologies of depression are the subject of the third chapter.

[53] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 23.

Chapter 2: The Drivers for the Biochemical Construction Depression & the Classic Understanding of Depression in America

Even though the particular nature of the pathophysiology of depression is debated, depression is unilaterally conceived as a biochemical problem, resulting in part from the way the DSM was constructed. The first half of the chapter examines the drivers for the biological construction of depression and the early days of pharmacology research. The later half considers how a purely biological construction of depression becomes burdensome and a detriment to patients.

The medical model of depression removes stigma and blame from mental illness. The pharmaceutical industry benefits since a biochemical characterization of depression necessitates finding a biochemical solution. This view of depression drives drug sales. Through the construction of the DSM, psychiatrists have been urged to see depression as a biological problem with discrete pathology. This view of disease drives drug prescription. Primary care physicians benefit as the diagnosis can be used to eliminate uncertainty in the therapeutic relationship. Research indicates that physicians diagnosis problems which they can treat,[54] and depression, when biochemically constructed, is easy to treat. The treatment consists of a pill. Patients benefit from a medical understanding of depression since the medical model prevents victim blaming. No responsibility for suffering is attributed to the individual. Each group benefits, first from the diagnosis of depression and second from the construction of that condition as a biochemical imbalance.

Early psychopharmacology research, which influenced the paradigm shift in psychiatry from DSM-II to DSM-III, contributed to present labeling and understanding of depression. In the early 20th century, drug research and disease classification in mental health occurred simultaneously. Drug response helped to define disease categories. Drug response also helped to understand underling disease mechanisms and important biochemical features of disease. Out of the early research, the one-drug/one disease model emerged. Though ultimately proven false, this model was useful in the beginning. Some still have an affinity for it today as an explanatory model because, in the words of psychiatrist Peter Kramer, it is "so irresistibly simple."[55] After this model gained prominence, mental health issues were though of as single-effect diseases like diabetes. This view is incorrect and overly reductionist. However, despite its inadequacy, it is an easy paradigm to

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[54] Goldberg D, and Huxley P. Common Mental Disorders. London: Routledg, 1992. 44 in Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 102.
[55] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 45.

market and understand. The one-drug/one disease model and the early days of psychopharmacology research both contribute to the overly simplistic and inaccurate view of depression today.

The second half of the chapter examines how the biochemical construction of depression affects how patients understand themselves and their disease through the usage of illness narratives. Flowing from an understanding of disease, the narratives show the varying kinds of treatments patients seek based on their construction of their illness. The narratives reflect an understanding of illness consistent with the traditional medical model of depression presented in the first chapter. The narratives show the ways in which biological constructions of depression are internalized by patients. The internalization of a particular understanding of depression shapes not only disease experience and self-understanding but also identity and membership in groups. These narratives show the effects of the pharmaceutical driver in constructing depression biologically.

Patients have internalized the messages disseminated by the industry and use completely biological metaphors to understand their disease experience. These constructions not only benefit the pharmaceutical industry by turning patients into consumers, but also benefit patients as this illness model prevents suffers from being blamed for their condition and ultimately from taking responsibility for their condition. Sadly, an incomplete characterization of disease leads to an incomplete treatment modality as reflected in the narrative of Elizabeth Wurtzel.

According to this narrative, the traditional biomedical model benefits patients by removing culpability, yet it also acts as a hindrance by preventing appropriate treatment. To provide better care to patients, an older disease paradigm must be dropped in favor of a model that is better able to account for the complete depressive experience. This new model will both account for aspects of depression captured by the DSM-IV and also provide a frame work for the management and characterization of sub-acute depression. Establishing parameters around sub-acute depression, a major shortcoming of the traditional medical model, must be addressed in a new paradigm.

Drivers and benefits in the biological construction of depression.

In seeking to understand the disease experience of depression, as well its ubiquitous presence in western culture, it is necessary to examine the role different cultural agents play in the construction of the disease. "The concept of depression is being supported and sustained by a wide

variety of commercial, professional, organizational, and cultural factors."[56] Each draws different benefits, but while some groups and people prosper from this construction, others are hurt. The section below begins the discussion of differential benefits and burdens experienced by shareholders in depression.

The pharmaceutical industry.

The pharmaceutical industry has a vested interest in ensuring that disease is constructed and understood in a particular fashion. Antidepressant drugs are the most prescribed and sold psychotropic drugs. Therefore, how the concept of depression is created and sustained will influence antidepressant sales. The industry will profit if disease categories are expanded to include as many patients as possible. This orientation may lead to medicalizing personality type and pathologizing normal behavior. Normally, diagnostic decisions are made though official channels like the World Health Organization, the American Psychiatric Association, and small committees of experts arriving at a consensus that is both evidence-based and transparent.[57] However, these supposedly evidence-based and transparent decisions are heavily influenced by the industry.[58] Industry-sponsored supplements in professional journals for anxiety and depression medication are common; although, the accuracy and value of some of these supplements may be of dubious value due to inadequate peer review.[59] Through publications such as these, the industry controls and influences the dissemination of a particular view of depression. This kind of literature, peer-review journals, shapes how clinicians understand depression, and in turn how patients come to understand depression through communication with their physician and direct-to-consumer-advertising.

The industry masterminds a covert and subtle way to market disease through direct-to-consumer-advertising . Not limited to only TV commercials and magazine advertiments, the industry relies on an entire orchestration of events and timing. Christopher Dowrick recounts the work of Brendan Koerner who gives an example of how a drug company ran a segment of its marketing campaign for a new drug. To position a drug for social anxiety disorder, a company

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[56] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 96

[57] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 96.

[58] Cosgrove, L., Krimsky, S., Vijayarghavan, M., and Schneider, L. "Financial ties between DSM-IV Panel members and the Pharmaceutical Industry." Psychotherapy and Psychomatics 75(2006): 154-160.

[59] Bero, L.A. "The Publication of Sponsored Symposiums in Medical Journals." New England Journal of Medicine 327 (1992): 1135-1140.

spent $30 million dollars in one year. This astronomical amount of money included the cost of hiring a high profile New York public relations firm.

> *[The] firm plaster[ed] bus shelters across the United States with pictures of a dejected looking man playing with a teacup, under the slogan 'Imagine being allergic to people.' For generalized anxiety disorder, the same public relations firm undertook a major media drive in 2001, involving eminent psychiatrists and patient groups. Women's magazines were inundated with stories of young women beset with worries about money and men. On the day of Paxil's approval for generalized anxiety disorder, a patient group called 'Freedom from Fear' released a telephone survey which revealed that sufferers spend nearly 40 hours per week worrying – the equivalent of a full time job. The press contact for this survey was SmithKline's public relation firm.*[60]

Direct-to-consumer advertising when done transparently is one issue. It is another to sell drugs though product placement, suggestion, and innuendo. The fashion and cosmetic industry use clever and covert methodologies such as these to create a desire and need for a product. However, when such methodologies are adopted by the pharmaceutical industry illness becomes manufactured. Paxil was once marketed as an anti-depressant. However, SmithKline realized that they could increase their profits if the drug could be applied to other disorders. This required manufacturing the disorders along with the drugs to treat them.

Antidepressants are easier to market if depression is understood in simple mechanistic terms because the treatment is easier to comprehend. Simplistic mechanisms lead to the perception that the disease is easier to treat than if a simple mechanistic relationship is lacking. If depression is characterized by low serotonin levels, then a serotonin agonist, such as an SSRI would be viewed as an effective means of treatment. If an inversely proportional relationship exists between happiness and serotonin levels, then normalizing serotonin levels through a serotonin agent will make sad people happy again. This simplistic relationship is the classic portrayal of depression in pharmaceutical advertising in America.[61]

Early psychopharmacology: The one-drug/one disease model.

Largely due to psychopharmacology's one-drug/one disease model, early psychopharmacology research set the stage for looking at issues in mental health as single effect diseases. This model was based on selective response to Lithium and reinforced by some of the

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[60] Koerner, I.M. "First You Market the Disease…Then You Push the Pills to Treat It." Guardian G2 (2002):8-9 in Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 96.

[61] Eli Lilly Corporation. "Depression Hurts." January 2006 <http://www.depressionhurts.com>

early work of Donald Klein. Fifty plus years ago, doctors had far fewer categories for diagnosing mental disturbances and far fewer medications to treat them with. Research focused on breaking down categories of disturbances in to diseases with definable patterns. These parameters were based upon selective drug response. Selective drug response though advances in pharmacology, was the mechanism by which early disease taxonomy was made possible. Drugs became more important in psychiatry. The more popularized role of drugs in psychiatry is reflected in the structure of DSM-II's evolution to DSM-III. In DSM-III the focus was on biochemical imbalances, which made drugs a more important aspect of treatment than in the past.

Before the development of Lithium, Emil Kraepelinian, Freud's contemporary, theorized and "showed that manic-depressives have a different course of illness from that of patients suffering from schizophrenia; he assumed that both diseases had a biological basis."[62] Lithium proved that he was correct. Lithium was proof that manic depression and schizophrenia were two separate diseases. Selective response to Lithium "performed an extraordinary 'pharmacological dissection,' defining for the all world the boundaries of a particular disorder."[63] This distinction "caused American psychiatrists to expand their use of the diagnosis."[64] The performance of "Lithium made it look as if medications would be splitters – definers of illness."[65] However there has never been a drug that split and separated disorders the way lithium did.

Subsequent drug developments have not split categories. Instead they have acted as 'lumpers,' blending and confusing categories together, "none more so than Prozac. Within a couple of years of its introduction, Prozac was shown to be useful in depression, OCD, panic anxiety, eating disorders, premenstrual syndrome, substance abuse, attention-deficit disorder, and a number of other conditions."[66] Multiple medication response across disease categories challenges existing disease nosology and makes illness difficult to classify and categorize as discrete entities. Furthermore it challenges conventional wisdom and the integrity of the present disease nosology. Since Prozac is useful in treating these disorders, is the natural conclusion that low serotonin levels are implicated in each disease's pathophysiology? As Kramer observes, OCD and dysthymia "are classified in contemporary psychiatry as discrete entities, one related to anxiety and the other to

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[62] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 44.
[63] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 45.
[64] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 45
[65] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 45
[66] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 45.

depression; but a countervailing movement, based in part on observed drug effects, characterizes them as related disorders."[67] Illness categories are becoming larger and less clearly defined.

Based upon this line of evidence, Kramer asserts that medication "do[es] not treat specific illness;"[68] rather it "alter[s] neurochemcial systems."[69] In this case, we have the power to free medications from their traditional use in treating illness and to redirect their potent effects towards harvesting benefits in other directions. Steroids can be used to help asthmatic patients breath more easily, while they can also allow athletes to artificially gain competitive muscle mass over the competition. Cocaine can be used as a topical anesthetic in eye surgery, but it can and is used to achieve other pleasurable ends. The view that behavioral active medication does not treat illness per sey, but modifies neurochemical systems, is a bridge from conventional mediation usage to cosmetic neurology and cognitive enhancing technologies. Cosmetic neurology is a form of personality enhancement in which psychotropic drugs are used to act as mood brighteners and change certain aspects of personality. A more in-depth discussion of cosmetic neurology occurs in the third chapter. Using medication to alter neurochemistry instead of to treat specific illness expands what can be treated with medication, thus creating an important shift in approach to mental health issues. As medication alters neurochemical systems, it can also modify personality and correct illness.

The view that medication does not treat illness but alters neurochemical systems is a powerful statement about how and in what context people will seek the effects of drugs, in addition to how a society understands the role of drugs in treating illness and in shaping the course of lives. "In clinical pharmacology, contemporary technology plays a dominant role in shaping ideology. What we look for in patients depends to a great degree on the available medications."[70] This perspective is analogous to Solomon's view that "As soon as we have a drug for violence, violence will be considered an illness."[71] The larger point is that "We pathologize the curable, and what can easily be modified comes to be treated as illness, even if it was previously treated as personality or mood."[72] The emerging question is if drug response indicates illness. In a classic understanding of disease presented in the first chapter, the previously accepted answer to this question was "yes."

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[67] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 46.
[68] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 45.
[69] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 45.
[70] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 35.
[71] Solomon, A. The Noonday Demon: An Atlas of Depression. Scribner: New York. 2001, 27
[72] Solomon, A. The Noonday Demon: An Atlas of Depression. Scribner: New York. 2001, 27

However, with the emergence of cosmetic neurology and the discussions of culture, philosophy, and ideology in subsequent chapters, the answer to this question becomes a resounding "no."

In the early days of behavioral pharmacology, drug development and differential response to medication were expected to ease difficulties in categorization and diagnosis of mental disturbances. Early efforts in pharmacology focused on how drugs could be useful in classifying disease. For example, a pioneer in psychopharmacology, Donald Klein, "worked backwards from drug response to diagnosis – sometimes creating new categories,"[73] in the course of his research. Most of Klein's patients were in-ward patients who were unresponsive to psychotherapy. Klein "medicated them with what ever was on hand, often matching medication to patient on the basis of one or another small clues."[74] He did his research in a time when "no one knew which diagnostic distinctions were relevant to medication choices, and moreover, there were few medications to try."[75] Klein "took on all comers and tried to say something about them based on their response to medication."[76] This approach was useful in charting new territory in the early days, but is unhelpful today. A patient's condition can not be determined based upon a response to medication. Response to medication no longer indicates that someone is ill, particularity if the mediation has enhancing effects. The medication would effect everyone, and surely not everyone is ill. Furthermore, some would suggest that what is being labeled as illness such as premenstrual syndrome (PMS), are not legitimate illnesses. Instead, PMS has been manufactured and therefore dose not really exist. "There are many grey states between full-blown depression and a mild ache unaccompanied by changes of sleep, appetite, energy, or interest; we have begun to class more and more of these as illness because we have found more and more ways to ameliorate them. But the cut off point is arbitrary."[77] The cut off point and the classification system for that matter may be arbitrary. Despite the unhelpfulness the one-drug/one-disease model, this view prevails in the popular and pharmaceutical discourse on depression. Enabling depression to be presented as if it were a single-effect illness and providing an easier and cleaner way to consider and frame problems of biology, the one-drug/one-disease model is "so aesthetically pleasing as to be irresistible"[78] to the pharmaceutical industry. Such a model appears to tie depression up into a neat little package. Depression becomes more manageable when viewed as a disease of low serotonin levels rather than

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[73] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 72.
[74] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 72.
[75] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 72.
[76] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 72.
[77] Solomon, A. The Noonday Demon: An Atlas of Depression. Scribner: New York. 2001, 27
[78] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 45

a complicated stress induced change in dynamic body function presented in chapter 5. "The serotonin thing is part of modern neuromythology."[79] In this vein, Solomon says that the hype around serotonin "is a potent set of stories."[80] Yet, these are the stories told by the pharmaceutical industry, and these are the stories patient tells themselves. The one-drug/one-disease model is no longer a valid way of approaching mental illness. Cosmetic neurology has blurred the lines between illness and wellness. Not all who take medication are sick in the classical sense. Rather this trend in medication use may be reflective of a sick society rather then a sick individual. The way depression can be viewed as a cultural illness is the topic explored in chapter 3.

The primary care physician.[81]

The pharmaceutical industry exerts control over the public perception of depression by not only influencing the biochemical construction of the disease, but the clinical discourse between professional collegues and patients and physicians. In *Beyond Depression,* Dowrick makes a claim that the diagnostic concept of depression differs between general practitioners and psychiatrists, as the diagnosis may fulfill different sets of needs.[82] For the general practitioner, diagnosing depression is a 'welcome opportunity' to "reduce the complexities of the problems that our patients present."[83] Based upon Dowrick's research as a generalist contending with psychiatric issues of patients, he concludes that generalists "are more likely to make a diagnosis if we feel we understand a particular problem and, most importantly, if we have some means at our disposal to treat it."[84] In his research Dowrick sites the work of David Goldberg and Peter Huxley who have demonstrated that both doctor and patient opt for easier pathways of communication when confronted with emotional distress in the therapeutic relationship, even if these pathways do not address the heart of the issue.

> *The doctor does not have to elicit and then manage emotional distress, and the patient does not have to face up to their own distress, and perhaps own partial responsibility for their*

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[79] David McDowell of Columbia University quoted in the text of in Solomon, A. The Noonday Demon: An Atlas of Depression. Scribner: New York. 2001, 22.
[80] Solomon, A. The Noonday Demon: An Atlas of Depression. Scribner: New York. 2001, 22.
[81] This section draws heavily from the research and analysis of Christopher Dowrick in Chapter 4: Drivers to Diagnoise of Beyond Depression.
[82] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 102.
[83] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 102.
[84] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 102.

current predicament. Both take refuge in safer roles: the doctor as a fighter of supposed organic disease, and the patient as a victim.[85]

While Dowrick suggests that this is a caricature of the past, he feels that "it is now very tempting to subsume complex problems within the label of depression and reach for the prescription pad with a sigh of relief."[86] Family doctors may use the diagnosis of depression "in part to negotiate our way out of consultations we find difficult."[87] In a study that compared family doctors' attitudes toward depression and their clinical behavior, no correlation was found between confidence in personal diagnostic ability and the actual level of diagnosis.[88] However, the study did find association between the doctor's ability to correctly identify depression and three attitudinal variables which were: a preference for treating depression with psychotherapy rather than antidepressants; a sense of ease in managing depression; and, the belief that the depression could be successfully treated in general practice. The identification of depression by this group of family doctors was not an independent variable since the diagnosis depended on individual beliefs, attitudes, and skills, which all relate to personal confidence in managing depression. "In other words, these doctors were more likely to make a diagnosis of depression if they believed that could manage and treat it." [89]

In *Beyond Depression,* Dowrick analyzes and provides transcriptions of audiotaped conversations between general practitioners and patients who are considered to have symptoms inadequately explained by physical pathology.[90] Dowrick uses these conversations to show how the diagnosis of depression can "create or impose order and understanding in the midst of confusion and chaos"[91] and is therefore a "convenient way out of the impasse [general practitioners] often find themselves in."[92] Interpretations of audiotaped transcriptions show how physicians can "turn raw human suffering (unbearable by the doctor) into depression (an illness, which is treatable, and

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[85] Goldberg D, and Huxley P. Common Mental Disorders. London: Routledg, 1992. 44 in Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 102

[86] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 103.

[87] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 103.

[88] Dowrick C, Gask L, Perry R, Dixon C, Usherwood T. "Do General Practitioners' Attitudes Towards Depression Predict Their Clinical Behavior?" Psychological Medicine. 30 (2000):413-419

[89] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 104.

[90] Dowrick C, Ring A, Humphris G, and, Salmon P. "Normalization of Unexplained Symptoms by General Practitioners: A Functional Typology." British Journal of General Practice 54 (2004): 165-170.

[91] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 104.

[92] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 104.

therefore bearable by the doctor.)"[93] In these ways, general practitioners may use the diagnosis of depression to safeguard a 'sense of professional competence;' however, these diagnoses are not necessarily always beneficial to patients. Rather, these cases are illustrative of how patients can be "shoe-horned into a diagnosis which may be convenient for the doctor but does little to address [patient] needs."[94] In this manner, depression may come to be a waste basket diagnosis.

While the physicians have a relationship with the patient, they also have a relationship with the pharmaceutical industry. The extensive body of literature in bioethics, anthropology, and sociology examining the role of the pharmaceutical industry, though pharmaceutical representatives visiting doctor's offices, to the practice of industry gift giving, suggests that these practices have not had a neutral effect of physician prescribing behavior. This interaction is part of the scientific and social construction of depression.

The patient.

Merely naming a pattern of symptoms as disease confers benefits to a suffer. It provides certainty, order, and predictability to what was otherwise interpreted as chaos.[95] As symptoms become a diagnosis that moves to treatment and prognosis, certainty is created in the medical gaze. This is one of the ways in which psychological comfort is gained though having a diagnosis. The unknown becomes known. Once someone has an illness label, they transition into a different social space as a result of the label. Sick people have more attention paid to their individual needs. Others offer them support. They are allowed to avoid personal and professional responsibilities without consequence.

The patients benefits from an illness label and continues to garner additional benefits if the illness is constructed in purely biochemical terms. A biochemical imbalance means that the afflicted is not responsible for their disease state. Claiming bad biochemistry means that the suffering is no one's fault. The medical model destigmatizes the depressive experience. This is an important paradigm shift from the past when depression was considered to be a sign of moral failing in the Middle Ages, and an indication that a person lacked reason during the Enlightenment. In the

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[93] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 106.
[94] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 108.
[95]Foucault, Michel. "Lecture One," Power/Knowledge: Selected Interviews and Other Writings, 1972-1977. New York: Pantheon. 1980; Foucault, Michel. The Birth of the Clinic: An Archaeology of Medical Perception. New York: Vintage books. 1975.

Middle Ages depressives and melancholics were seen as sinners because their suffering indicated that they had fallen from God's grace and were thus being punished. During the Enlightenment, the afflicted were viewed to be no better than animals because they were thought to lack reason. The perceived lack of rationality was justification for the harsh treatment of behavioral operant-conditioning approaches to discipline in British asylums.[96] The medical model offered gentler treatment of the afflicted, as sufferers were not seen as responsible for their condition. The condition was chemically driven and therefore beyond the circumstances of their control.

In the medical model, while the depressive is not responsible for their condition, they are also not in control of their condition. The only way a person can exercise some degree of control is to take drugs to alter his or her chemical state. In taking drugs, a person's agency remains limited. The person is a passive vessel in which the drugs act to transform pathological biochemical imbalances into normal ones. A contrasting view of responsibility for illness is presented when depression is examined from an evolutionary perspective in chapter four.

The evolutionary view emphasizes social navigation and good decision making, which requires taking responsibly. The medical model allows patients to avoid facing ugly aspects of life and to avoid taking responsibility for their role in producing an ugly state of affairs. In this model, sufferers can blame outside causes for their unhappiness instead of themselves.

* * *

Collectively these drivers contribute to a certain understanding of depression that in turn shapes the illness experience. Who people are is shaped by what they believe. The pharmaceutical industry gives form to what people believe by perpetuating certain views of the root causes of mental illness and clinical depression. This industry has the ability to sculpt physician attitudes and ultimately clinical behavior, which has a direct affect on the care patients receive, possibly influencing how patients understand themselves later in life. The patient's understanding is captured in the illness narrative.

The value of illness narratives.

The way patients understand the etiology and pathophysiology of their disease shapes their illness narrative, which later shapes how they understand themselves and their identity. The metaphors that patients use to describe diseases in Western biomedicine are rooted in their beliefs

[96] I have relied heavy on views and research of Andrew Solomon in Chapter 8: History of The Noonday Demon: An Atlas of Depression.

about the science of their disease. The science of the disease refers to the processes occurring in the body on a biochemical level. Beliefs about the biological processes shape social construction of disease and may influence symptom presentation and construction of the personal narrative, in addition to medicalization of the disease on a clinical level.[97] In short, an understanding of disease has the ability to shape personal identity. In other words, the etiology, diagnosis, and prognosis, plus additional beliefs about the disease processes, are socially modified by how one constructs views of science which underpins a disease. Patients incorporate their biochemical view of disease into understanding themselves by understanding what is going on in their body and life through illness narratives.

Through illness narratives, disease is located on both biological and social levels depending on the meaning we ascribe to it. The parameters of disease are defined in both biological and social spheres, according to what disease is, what it has done to society, and how it has shaped life experiences, ultimately shaping who people are. In *The Illness Narratives*, Kleinman uses the metaphor of a sponge soaking up "personal and social significance"[98] to describe the way in which an ill person's life trajectory becomes redirected and embodied by illness. For Kleinman, "this intimate type of meaning transfers vital significance from the person's life to the illness experience."[99] The construction of meaning in chronic illness is particularly important as the sufferer's life becomes an ongoing uphill climb just to be healthy or, perhaps more dangerously stated, *normal*. For some, depression is a chronic condition that is managed and incorporated into a tapestry of meaning across a lifetime. For others, depressive episodes punctuate, but not direct, the course experiences. The narratives presented in this chapter reveal a biological understanding of depression. Furthermore, these narratives demonstrate the success of pharmaceutical advertising campaigns, highlighting how their message that depression is a biochemical imbalance, particularly in serotonin system, has been internalized.

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[97] Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books. 1988. 18.
[98] Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books. 1988. 31.
[99] Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books. 1988. 31.

Serotonin alone.

Alfred Myer, author of the depression memoir, *Listening to Paxil - Narrative of Antidepressant Use,* understands his depression in purely biological metaphors and attributes his disease to serotonin alone.

> *I realized it was too early--not in the day but in the century--to go down to Harry's for a serotonin cocktail, ice and a dash of bitters, please, to match my cold and melancholic mood. "Transmission fluid's low," I'd explain, meaning that the spaces between nerve cells in parts of my brain weren't sufficiently lubricated with serotonin for certain messages to slide through.*
>
> *But my imaginary bartender wouldn't require an explanation. He would just need to look and listen to me: my eyes vacant and unrefreshed by a good night's REM sleep; face set in a fierce grimace, like one of those Chinese opera masks; voice strained; and remarks--when I bothered or managed to articulate them--caustic, vituperative, and gloomy.* [100]

When aspects of life and experience are viewed as separate units that can be plucked from the rest to be manipulated and reinserted, the self becomes fragmented. Myer speaks of pieces of himself and his body; he does not speak of himself as a united whole. A reductionist biochemical understanding of disease that focuses on just one or two processes to the exclusion of others enables this fragmentation. Patients experience increasing difficulty in viewing the self in holistic terms and in extracting meaning leading to a certain type of narrative, which portrays a fragment self. The construction of the illness narrative embedded within a personal history and rich ethnographic context changes because the ethnographic context has been lost. Kleinman suggests that illness narratives typically include a reinterpretation of symptoms within a "changing systems of meaning which are embodied in lived experience" and can be understood in a context of relationships.[101] However, Myer chooses to frame the context of his illness only in relationship to serotonin.

In focusing only on the chemistry of the disease, not even on his experiences of physical systems, Myer loses some aspects of social meaning and personal context. Myer has focused on a scientific understanding that is so biochemically reductionist that he has lost aspects of meaning by avoiding context, social connectedness, and relationships to things outside the self. He has bought into an understanding of the disease which changes the way he sees his disease experience, what is happening to him, and ultimately himself as a person embedded in an ethnographic context. Myer no longer puts the focus on his experience of symptoms, only on the altered biochemistry. In

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[100]Myer, Alfred. "Listening to Paxil." PsychologyToday.com. 14 May, 2005 <www.psychologytoday.com/ articles/pto-19960701-000038.html>

[101] Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books. 1988. 18.

shifting the medical gaze more inwardly, not only the self, but also aspects of the corporeal self, are objectified and reified. In this instance, Myer's serotonergic system becomes the fragmented aspect. The process of fragmentation is a barrier to seeking whole person care and help for illness on a variety of levels.

The narratives of Elizabeth Wurtzel and Lauren Slater describe another biochemical attribution of depression that is reductionist. While Myer's narrative does not reference non-biological etiology, the narratives of Wurtzel and Slater deny elements of cultural causality. Instead these narratives maintain that their disease state is brought about by biology alone. Since biochemistry is viewed to be the problem, only a biochemical solution is sought in treatment. Later chapters make the argument that depression's etiology is not governed by biochemistry alone, and biological underpinnings of depression are not governed by abnormalities in the serotonin system alone.

Biochemistry and nothing else.

Elizabeth Wurtzel, in the opening pages of her depression memoir, *Prozac Nation*, describes the chaos of depression:

> *Some catastrophic situations invite clarity, explode in split moments: You smash your hand through a windowpane and then there is blood and shattered glass stained with red all over the place; you fall out a window and break some bones and scrape skin. Stitches and casts and bandages and antiseptic solve and salve the wounds. But depression is not a sudden disaster. It is more like a cancer: At first its tumorous mass is not even noticeable to the careful eye, and then one day-wham!-there is a huge, deadly seven-pound lump lodged in your brain or your stomach or your shoulder blade, and this thing that your own body has produced is actually trying to kill you. Depression is a lot like that: Slowly, over the years, the data will accumulate in your heart and mind, a computer program for total negativity will build into your system, making life feel more and more unbearable...*[102]
>
> *...The pain you feel in the course of a major clinical depression is an attempt on nature's part (nature, after all, abhors a vacuum) to fill up the empty space. But for all intents and purposes, the deeply depressed are just the walking, waking dead.*[103]

Wurtzel uses purely biological metaphors to explain her disease experience. She writes of cancer, stitches, cuts, bandages, broken bones, and scraped skin. She is using the language of a biologically degrading system. Wurtzel's narrative highlights the physically lived experience of symptoms. The

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[102] Wurtzel, Elizabeth. Prozac Nation: Young and Depressed in America. New York: Riverhead Books. 1994. 21.
[103] Wurtzel, Elizabeth. Prozac Nation: Young and Depressed in America. New York: Riverhead Books. 1994. 22.

pain of the 'walking, waking dead' is linked to 'nature's part' in filling up the vacuum, which is an atomistic reference organically attributed to the disease. In the second half of the memoir, Wurtzel presents her disease, which she describes in the first part of the memoir, as a biochemical issue and seeks a pharmacological solution, which provides insight into how she sees what is happening within her.

> *I would fall into these spells of depression for no reason, at the least likely times, times I ought to be happy. I told her about the black wave, that the feeling was literally physical, that the sensation was palpable, as if I'd drunk a bottle of tequila and taken some shitty windowpane fluid and just lost my mind, that I was sure it was chemical. I wanted psychotropic drugs, I told her. I wanted her to prescribe me something that would make the rushes of misery stop. I wanted to break the black wave.*[104]

To this biochemical presentation of disease the psychiatrist replied:

> *Elizabeth....there is no pill in the world that's going to make you feel better. We have no way of measuring whether you have any sort of deficiency or not. The way we diagnose people for mental illness is purely anecdotal, and we prescribe medication that we believe will suit the patient best by trial and error.....so I would love to help you if I could. But I assure you from what you've told me, and from what I am reading here, that your problem is not chemical...*
>
> *It's not atypical of your generation to look for the chemical cure for everything. Wouldn't it be nice if we could all take happy pills and make the bad go away? We live in a drug culture, both legal and otherwise. But I'm not going to lie and tell you that some pill would help you when I know it wouldn't. From what you've told me about your parents, especially your father, you've grown extremely detached over the years, as a defense mechanism. You don't need drugs, Elizabeth. What you really need is a close, caring relationship. You need to trust somebody. You need to think that people are okay.*[105]

The psychiatrist's response challenges Wurtzel's construction and attribution of her depression in suggesting that no pill could help her. At first glance, the psychiatrist does not seem subscribe to the biochemical theory of depression; but much more likely, the psychiatrist is trying to address the complex etiology of the disease, which extends well beyond chemistry and goes into culture. Wurtzel's generation lives in a drug culture in which biology is seen as the problem, as opposed to constructing the problem in the way a society functions. This framing of biology results in the need for drugs or other medical care to treat social problems. In such a context, pharmacological solutions are sought.

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[104] Wurtzel, Elizabeth. Prozac Nation: Young and Depressed in America. New York: Riverhead Books. 1994. 147.
[105] Wurtzel, Elizabeth. Prozac Nation: Young and Depressed in America. New York: Riverhead Books. 1994. 148.

Lauren Slater, in her depression memoir, *Prozac Dairy*, writes about the power of the pill. Referring to Prozac, she attributes all the good things that have happened in her life to the biochemical changes in the brain brought about by her new course of drug therapy.

> *I fell in love one day, only it was not with a person; it was with my pill...Prozac brought me to pumpkin muffins, yellow fin tuna, and plum sauce. Prozac brought me to Harvard, where they accepted me to study.....Riding on the back of Prozac, I felt the hospitals were far away. My life became quiet but rich, a fine piece of music by Mozart. What happened is this: I got used to health, then I got good at it. Ivy League school. Friends and lattés, hey. Hey, it's really OK...I decided to accept Prozac completely, to declare it an essential and inseparable part of me, my permanent partner in life.*[106]

Revealing a powerful belief in the biochemical etiology of depression, Slater's narrative is an example of exactly what Wurtzel's psychiatrist was referring to when she described the current drug obsessed culture. Slater's narrative is not unlike Wurtzel's as both represent memoir writers of a younger generation of depression who have been raised in a culture of pills. Both view their depression in fully biochemical terms, shunning the idea that events in their life may be even partly responsible for their depression, even if these trigger events were responsible for the altered biochemistry. Both come from troubled families, suggesting that they have been depressed since they were children and that biochemistry is to blame for their problems more than issues surrounding abuse and a troubled household. Effective drugs would be an easy quick fix. The problem is that drugs may not be able to 'fix' their problems. Pharmaceuticals are not always effective no matter how much people want them to be, believe them to be, hope them to be, or allow themselves to be told that they are the answer. The belief in biochemistry and the willingness to engage in a model of disease, illness, and wellness medicated by substance as opposed to individual agency is incredibly powerful. Slater reveals this belief structures when she writes of childhood distress.

> *When I was very young, I made my own pills from colored sheets of drawing paper. I would tear off little bits and worry them between my thumb and forefinger until a small ball formed, and then I'd swallow my paper pills. I would lie down in the floor of the basement, next to the bottle, and wait for healing to happen. I loved my paper pills and went so far as to bottle them in empty jam jars. Red pills, green pills, pink pills, pills for my stomach, my head, my ears, my crotch. Sometimes I took several a day, and they moved through me, soothing every inch, lending color to the bits of blandness in my body, even to my scat.*[107]

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[106] Slater, Lauren. Prozac Diary. New York: Penguin Books. 1998. 104.
[107] Slater, Lauren. Prozac Diary. New York: Penguin Books. 1998. 102.

This atomistic understanding of the world is not only influenced by western science but also by an industry that will profit for perpetuating such an understanding of the world. "Implicit in the first-level meaning of symptoms are accepted forms of knowledge about the body, the self, and their relationship to each other and to more intimate aspects of our life worlds." [108] This construction of depression makes people want to buy psychotropic drugs to help themselves. Herein lies part of the danger. The biochemical understanding of depression has been suggested to patients by the pharmaceutical industry in hopes of influencing an understanding of disease that supports drug sales. In shaping the patient's view of the science underpinning depression, the industry also shapes individual identity. How a patient understands the science of a disease shapes the construction of the illness narrative, which in turn influences how patients see themselves. This interaction influences the treatment modality sought.

Patients, based upon what they believe to be occurring, construct a story of what has happened to them, which includes elements of their identity. As patients begin to focus on the biochemistry exclusively, they fail to focus on other parts of themselves which are quite critical. Wurtzel's psychiatrist points to this problem. She stresses that Wurtzel needs love, relationships, and connectedness with people, not drugs. If people believe their problems to be chemical, they will seek chemical solutions.

In *Prozac Diary*, Slater writes about an evening she spends in the Harvard libraries researching scholarly literature on Prozac. She records a list of quotations that she found powerful, both in meaning and in explanation. Among her recordings, she includes, though unreferenced, Elizabeth Wurtzel's metaphor of depression as a virus that takes over the computer system. However, she also includes quotations that reflect an atomistic understanding of the depression.

> *While correlation does not imply causation, we believe that if a patient is cured by a serotonin-specific chemical, then there are probable anatomical illness correlates in the brain.*[109]

> *In light of these findings, the patient's past, the stories of self, is no longer relevant. We do not need to explain mental illness in the context of history. We can place it, and its cures finally in the context of chemicals.*[110]

These quotations illustrate dangerous modes of constructing depression, as they focus on one aspect of disease to the exclusion of other factors. Wurtzel's psychiatrist begins to touch upon one of the

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[108] Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books. 1988. 11.
[109] Slater, Lauren. Prozac Diary. New York: Penguin Books. 1998. 108.
[110] Slater, Lauren. Prozac Diary. New York: Penguin Books. 1998. 108.

larger issues explored in this paper: how a disease model may give rise to a treatment modality that is not able to meet all of the patient's needs and is therefore inappropriate. The traditional medical model of depression was a critical step in articulating a biological underpinning of mental illness in the public eye. Research has moved beyond the reductionism of this model; however, this model is championed for the short term benefits it brings while the negative long term consequences have gone largely unnoticed.

Conclusions.

The diagnosis of depression is driven by patients, physicians, and the pharmaceutical industry. The illness narratives above show how medical models presented in chapter one influence patient understanding of disease, as each believes himself or herself to be the victim of bad biochemistry, which is causing the depressive condition. In general, the biochemical theories in the first chapter are unable to account for aspects of suffering and experiences highlighted by Wurtzel's psychiatrist. The limitation of the traditional medical model is unable to address depression co-factors, such as environment, culture, personality, social history, and relationships. In some ways, these limitations are benefits to stakeholders in depression; however as the critical reflection is developed, the medical model generates both winners and losers. Patients are the ultimate losers in the reductionist construction of depression, while other entities benefit greatly. This chapter explored how stakeholder benefits from the construction of the symptoms experiences as illness, which is underpinned by a biochemical imbalance.

The collective symptoms of fatigue, pain, irritability, anhedonia, insomnia, depressed appetite, loss of sexual interest, and fixation on death are understood as biology gone awry. These experiences are eloquently expressed in biological metaphors in illness narratives. The once poetic language of the 19th century melancholia had been blended with mechanistic metaphors of disease progression informed by beliefs about biochemical processes. The narratives in this section focused not only on changes in physical states of appetite, outlook, pleasure, social interaction, and beliefs about the future, but also on the attribution of the altered physiological states, which lead to symptoms presentation. These patient narratives present a view of depression, understood as a biochemical disease, in which serotonin is largely responsible for causing suffering and in which the patient bears no responsibility at all.

* * *

Chapter three departs from a medical construction of depression to consider how depression is a product of the environment and the times, more specifically, a product of modern culture and currently fragmented societies. When depression is viewed from a social constructivist perspective, the search for depression's etiology expands beyond biological media. Anthropological and sociological discussions of depression focus on how culture affects the labeling, manifestation, and trajectory of illness.

The narratives presented in the next chapter present people questioning themselves, their identity, the status quo, and the working of the society they inhabit. Here, the afflicted are uncertain of their identity, their faith, their place in the world, and the meaning of life. These largely unresolved existential questions are not only demanding to think about, but also create uncertainty, fretting, and unrest. In North American society, these feeling have been interpreted as symptoms of illness. What unfolds in chapter three is not only a discussion of depression, but also a normative social critique. If depression's etiology runs through both biological and social media, the social media requires equal criticism as that of the biological media. Just as biologists dissect and analyze tissue, so also must members of society be willing to dissect and analyze facets of culture Cultural anthropology and sociology are the means by which analysis of social media is accomplished.

Chapter 3: Beyond Biology - Depression as a Philosophical and Cultural Disease.

When depression is viewed from an anthropological and sociological perceptive, the focus shifts away from chemicals toward pathological elements of modern society. Anthropological and sociological depression paradigms champion the social construction of depression and illness categories. This construction challenges the traditional medical model and critiques American culture. Studying how a society forms illness categories reveals important pieces of information about that society. To study the disease from a cultural perspective, it is necessary to critically reflect on cultural norms and values. Along these lines, "the society-wide response to each problem also tells us much about the value structure of American society."[111]

The illness narratives in this chapter look beyond chemical aspects of depression and present depression as a philosophical and cultural constitution of disease. In the first half of the chapter, depression takes the form of people struggling within themselves to resolve philosophical questions. The fact that philosophical questioning causes some unrest, and that this kind of unrest is pathologized, says something about North American culture, reflecting a societal norm that suffering in any form is unacceptable. In the second half of the chapter, depression takes the form of people struggling within a culture to fit in and to be perceived as valuable or desirable to others. These narratives probe pathological elements of modernity, personality, consumerism, competition, capitalism underpinning expressive individualism, and the workings of society as a whole. These narratives show how "we manage as medical problems the symptoms resulting from social sources of distress and disease."[112]

These narratives challenge DSM diagnostic criteria by questioning the biochemical construction of depression as monolithically portrayed by the pharmaceutical industry and by raising the question of which symptoms are truly illness related. An alternative to understanding these experiences as illness is to re-categorize them as aspects of normal life that are both challenging and unpleasant. In popular culture, challenging and unpleasant aspects of life associated with suffering have been labeled as illness.

The classification of these experiences as pathological is a function of the drivers in the biological construction of depression discussed in the previous chapter. Problematizing difficult yet normal aspects of life expands the patient pool and creates a new market for antidepressant drug

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[111] Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books. 1988. 21.

[112] Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books. 1988. 21.

sales. People who encounter difficulty, hardship, and failure in their life can abdicate responsibility for the status of their life through the traditional medical model. Through this model, sufferers can blame their sadness, misfortune, and lack of success on illness instead of viewing their current situation as a product of their own expectations and decision-making. The next chapter focuses on taking responsibility for unpleasant experiences and looks at how taking responsibility affects treatment modalities. This chapter focuses on how depression, particularly milder variants, have been problematized by our culture to be understood as illness. The concerns voiced in patient narratives are philosophical and social in nature, yet they have come to be understood as symptoms of an illness.

Collectively, the narratives presented in this chapter are in the more nebulous region of the diagnostic category, if they can be diagnosed at all. Moving from the core of the diagnosis category towards the periphery, depression becomes increasingly difficult to quantify and understand. These narratives illustrate the lack of congruity between the symptoms experiences, cultural understanding, and DSM diagnostic criteria. They show how the category destabilizes further away from the diagnosis of major depression. Not all forms and sub-types of depression are identical. Depression varies in intensity and duration. Sub-clinical variants of minor depression cannot be treated in the same fashion as each other or major depression. Not all forms of suffering are symptoms of depression. Unpleasant life experiences cannot unilaterally be considered symptoms of illness.

After reading these narratives, several questions must be addressed: Is depression only a biological construct? If so, is it only a problem of biochemistry? If it is only a matter of biochemicals, how can only serotonin be responsible? How accurate is the traditional medical model? The narratives, when analyzed together, shatter not only the serotonin myth, but also the traditional biomedical model of depression. This selection of narratives reveals far too intricate and complex disease etiologies to be brought about by a single biochemical imbalance or by a biological underpinning that is free of a cultural context.

Depression as a Philosophical Disease.

The narratives in this section present depression as a philosophical or spiritual uncertainty, which is interpreted by today's culture as a symptom of illness. Suggesting a new way to view disease than previously discussed, these narratives require a critical look at the cultural climate in which categorization occurs. This collection of narratives challenges the serotonin myth.

Carl Elliott, in *Pursued by Happiness and Beaten Senseless* presents several narratives adapted from Maureen O'Hara's essays, which highlight a sense of alienation when one is alone in a crowd, the sense of "spiritual emptiness, the search for a sense of self, [and] alienation in the midst of abundance."[113] In these narratives, depression is not mentioned, popular American culture would clearly consider these people to be depressed or ill in some regard.

> *Jerry feels overwhelmed, anxious, fragmented, and confused. He disagrees with people whom he used to agree with and aligns himself with people he used to argue with. He questions his sense of reality and frequently asks himself what it all means. He has all kinds of therapeutic growth experiences: Gestalt, rebirthing, Jungian analysis, holotropic breathwork, bioenergetics, the Course in Miracles, twelve-step recovery groups, Zen meditation, Eriksonian hypnosis. He has been to sweat lodges, to the Rajeesh ashram in Poona, to the Wicca festival in Devon. He is in analysis again, this time with a self-psychologist. Although he is endlessly on the lookout for new ideas and experiences, he keeps saying that he wishes he could simplify his life.*[114]

> *Beverly comes into therapy torn between two lifestyles and two identities. In the California city where she goes to college, she is a radical feminist; on visits to her Midwestern home town she is a nice sweet, square conservative girl. The therapist asks her when she feels most like herself. She says, "When I am on the airplane.*[115]

Both narratives unmask the experience of alienation and the desire to connect to something outside the self. Alienation, "isn't a purely internal matter; it isn't just in the alienated person's head. It is a mismatch between a person and something outside of himself."[116] The disconnect can occur on a variety of levels. Elliott makes a distinction between *personal*, *cultural*, and *existential alienation*. Each disconnect highlights a different aspect of the way people relate to others. *Personal alienation* can be experienced as the failure to conform to social expectations of people in a similar circumstance. This form of alienation may be either internal or external. External alienation refers to not fitting in, like being a punk rocker at a debutante ball. Internal alienation refers to feeling differently from others in similar social settings, like feeling differently than all your other prep-school classmates feel (or you think they feel). *Cultural alienation* speaks to the inability to engage with a certain way of life, like Cambodian refugees living in Canada, or a Western physician treating patients who understand disease in terms of demonic possession and restless ancestors. In cultural alienation, one does not possess the tools, skills, or ability to construct the world as others see it in order to seamlessly function in that environment. *Existential alienation* refers to the kind of

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[113] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 7-12.
[114] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 7-12.
[115] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 7-12.
[116] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 8.

"alienation involved in questioning the very terms on which life was built."[117] Calling into question how people formulate and define life, existential alienation probes at questions of self-construction, attitudes towards cultural value systems, and the driving belief structure used to interpret the world. Existential alienation can be thought of as a philosophical crisis.

Jerry seems to experience more existential alienation, while Beverly seems to experience cultural alienation. Each desires to connect to a larger "something," a kind of "something" that each cannot put his or her finger on. They just want to be happy. The quest for meaning, the ups and downs of every day life, are normal. The mental states described by Beverly and Jerry are not inherently pathological. Yet both Beverly and Jerry have sought the help of mental health professionals. Their experiences of every day life have been pathologized. Jerry and Beverly are coming to grips and trying to reckon with aspects of their modern life, which includes feelings of alienation. Does this reckoning process of self-searching mean that they are ill? The narratives do not speak of disease, illness, biological or psychological abnormality, or skewed biochemistry. They are asking questions on a meta-level as they confront emptiness or soullessness. By the standards of modern culture and perhaps biomedicine, Jerry and Beverly could be categorized as depressed, but it would not be unlikely that an SSRI would benefit them, just as an SSRI would not be beneficial to Elizabeth Wurtzel. The medical gaze of others creates a disease label, and a niche for depression to occupy. It also provides an escape for confronting difficult aspects of life. Jerry and Beverly do not seem to be happy, but are they really depressed?

Are personal, cultural, and external uncertainty forms of depression? Or, has daily life become so pathologized that normal developmental events, that may be unpleasant, have come to be seen as conditions in need of treatment? For a long time, the question to treat a problem as spiritual or psychiatric has gone unanswered in the field of psychiatry and mental health.[118]

Consider the depression narrative recounted by Elliott in *A Philosophical Disease*, the story of an Irish Catholic Priest, who has lost his faith in God. Elliott has abstracted the priest's narrative from "Madness and Religion," an essay by Irish psychiatrist M.O'C. Drury.

> *The priest was an elderly considerate man with a gift for his work, but he had lost his faith. He had come to believe that his sermons were being delivered without true feeling, and that he no longer had any faith. Saying Mass had become a great burden for him, and he felt*

[117] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 9.
[118] O'Reilly, M.L. "Spirituality and Mental Health Clients." Journal of Psychosocial Nursing & Mental Health Services 42.7 (2004): 44-53; Baetz, M., Griffin, R., Bowen, R., Koenig H.G., and Marcoux, E. "The Association Between Spiritual and Religious Involvement and Depressive Symptoms in a Canadian Population." Journal of Nervous & Mental Disease 192.12 (2004): 818-822; McLaughlin, D. "Incorporating Individual Spiritual Beliefs in Treatment of Inpatient Mental Health Consumers." Perspectives in *Psychiatric* Care 40.3 (2004): 114-119.

that he should have never been ordained. He would awake each night at 3 am and lie in bed until sunrise worrying about the state of his soul. He lost his appetite and began to have stomach pains...The priest was showing the classical signs of depression: depressed mood, guilt, sleep loss, appetite loss, and preoccupation with death. Yet he did not regard his condition as a medical problem...After the first course of ECT the priest's abdominal pain disappeared. Within a week he was saying Mass again. After seven courses of ECT he was sleeping well and had gained ten pounds. His spiritual problems disappeared.[119]

What does depression mean for the Irish Priest? Is questioning the status of one's soul a serotonin problem? Is alienation a serotonin problem? Elliott links alienation to "incongruity between the self and external structures of meaning – a lack of fit between the way you are and the way you are expected to be, say, or a mismatch between the way you are living a life and the structures of meaning that tell you how to live."[120] The lack of congruity has the propensity to be personally stressful. The biological parameters of stress and the connections between stress and depression are touched upon in chapter four and discussed at length in the final chapter. After exploring how stress affects the body and brain, though cortisol feedback inhibition, from a biopsychosocial perspective, a question remains: In cases like these, can medicine treat the soul?

Alienation, incongruity, spiritual searching, and the quest for meaning are not always included in the etiology of depression discourse, and are most definitely not discussed in the medical model. Once again the face of depression makes a different expression as it manifests in another person. Elliott presents the narrative of a friend and colleague at McGill, Benjamin Freedman, who passed away in 1997.

Benjy was a loyal friend, ferociously intelligent and darkly funny, a complicated man of deep moral integrity. Yet for the first couple of years that I knew him, he periodically descended into very black moods. He would come into his office, close the door, draw the blinds and sit all day in a semi-darkness. Sometimes he was irritable and would get into bitter arguments with his close friends. I do not think Benjy would disagree with me when I say that he was probably clinically depressed. In fact, he once told me as so much himself. He had recently suffered the deaths of two close family members. But Benjy was also a deeply devout Orthodox Jew. He was secure in his faith as anyone I have ever known. He loved his family and was at home in his community. When Benjy and I talked about existential questions like these, questions about alienation from your own culture and not knowing who to be or what to do with your life, he would shake his head and laugh. He told me once he had no idea what I was talking about.[121]

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[119] Elliott, Carl. Bioethics, Culture and Identity: A Philosophical Disease. New York: Routledge, 1999, 49.
[120] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 8.
[121] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 10.

In the narrative of Benjamin Freedman, depression takes a different form. Freeman's narrative is free of alienation, philosophical crisis, grappling with modernity, consumption, and competition, yet the idea of illness prevails. If Dr. Freedman had sought medical attention, an SSRI would likely have been perscribed. The causes for the men in the last two narratives to be considered depressed are totally opposite, yet the condition is treated the same way.

Conclusions.

The narratives of the Irish Priest and Benjamin Freemen juxtapose the etiology of existential alienation as an etiology for clinical depression. This grouping of narratives collectively questions aspects of the social understanding of depressive symptoms that are rooted in philosophical turmoil which have come to be seen as pathological because western culture is intolerant to anything but happiness. "The cultural meanings of illness shape suffering as a distinctive moral or spiritual form of distress," while "local cultural systems provide both the theoretical framework of myth and the established script for ritual behaviour."[122] To this issue, Solomon writes that "If you read these pages [of *The Noonday Demon*] closely, you can learn how to be depressed: what to feel, what to think, what to do."[123] The narratives of philosophical depression presented above have not been ritualized since none of the narratives match the social scripting of what Americans make depression out to be as communicated in movies, media, pop-culture and advertising. Prototypal depression narratives are consistent with the traditional medical model of depression presented in the first chapter and essentialized by narratives in the second chapter. The narratives presented in chapter two, which cast serotonin as the biochemical basis of depression, have been highly ritualized because they conform to the publicized view of what depression is.

Contempoary society has been told, by the pharmaceutical industry, what depression is and how to think about it. The narratives in the pervious chapter incorporated the broadcasted view of depression into their illness narratives, while the narratives in this section have not. Some of the narratives in this section may not even be considered illness narratives, as they may be normal life experiences that have been pathologized.

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[122] Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books, 1988. 26.

[123] Solomon, A. The Noonday Demon: An Atlas of Depression. Scribner: New York. 2001, 400

The section above reflected on narratives intolerant to a certain kind of suffering. The narratives below present cultural intolerance to modes of being and personality type. From this perspective, depressive illness may act as a "clue to a broader cultural condition, a symptom not so much of the patient's illness but of the society in which he lives."[124]

Depression as a cultural disease.

Ideas about what constitutes the status quo, the good life and normal, are always changing. Americans have an expectation that normal is a prosperous, self actualized life that is free of sadness. Historically, periods of sadness and reflection on sadness were normal and were not incompatible with living the good life.[125] The view of what constitutes the good life has changed. "Melancholy was a central cultural idea, explaining and organizing the way people saw the world and one another and framing social, medical, and epistemological norms."[126] Now melancholy is a disease. Emily Dickenson wrote of loss and said, "There was a funeral in my brain."[127] Today people may be able to relate or even share Dickenson's sentiment; but, they use different language and metaphors depending upon how they understand themselves, their culture, and what is happening. Rather than poetry, they use the language of disease.

American norms.

Today's modern world is fragmented. We live in neighborhoods but do not know our neighbors. We have jobs, but no meaningful work. We live in family units, but feel no sense of connectedness to them. The seasons change along with the seasonal fruits and vegetables, yet no matter the day, the same produce is available in the supermarket. We are no longer bound to the cycles of nature. We have become alienated from things we once knew.

We are modern urban hunter-gathers driving down the highway to buy electronics and other objects for our lifestyle. We need to have the right jeans, the expensive bedspread, and the modern dinning room table with matching place settings from Ikea that define us as people. We must wear our stylish clothing while we listen to our iPods as we walk down the street looking at the signs and

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[124] Elliott, C. Bioethics, Culture and Identity: A Philosophical Disease. Routledge: New York. 1999, 52.
[125] Radden, Jennifer. The Nature of Melancholy: From Aristotle to Kristeva. Ed. Jennifer Radden. Oxford: Oxford University Press, 2000.
[126] Radden, Jennifer. The Nature of Melancholy: From Aristotle to Kristeva. Ed. Jennifer Radden. Oxford: Oxford University Press, 2000. 1.
[127] Dickson, Emily. "There was a funeral in my brain." The Complete Poems of Emily Dickenson. New York: Everyman Pocket Library, 1993. 128-29.

the stores, which tell us how to live in the modern age. We have become consumers, bombarded at every turn with messages telling us what we should consume based upon the life styles we lead.

We are perpetually told through advertising which products to buy to improve ourselves because we are never good enough. Advertising is successful when we internalize the message that we need the product, good, or service, and that without it, we are deficient, or that this product will make us better than we already are. Either way, we, the consumer, are always at a deficit-- always in need of improvement. We receive the message that we are lacking in some capacity on a daily basis. When this message is internalized, we see ourselves as deficient, and consumption serves as a mechanism to fill the deficiency.

North Americans strive to be successful on every frontier of life. They should have meaningful work in which they are able to make a contribution, a warm family life, and a community of their peers to enjoy during their leisure time. They should be charming, charismatic, and flexible, always a good-sport, a hard-worker, and a real go-getter. Americans seek to be confident, self-assured, and authentic. Within their community of peers, their family, and themselves, people face a perpetual push for self-improvement and betterment in order to attain fulfillment. This never-ending cycle translates into fierce competition and constant one-upmanship. Part of being successful is not just keeping up with the Jones, but out doing the Jones. In this bifurcated construction, people emerge as either winners or losers. Americans strive to be the winner; however, someone must also be the loser. Only one employee is boss at the office, one house is the biggest on the block, one soccer team wins the state finals, and one child gets the lead in the school play. According to these cultural values, which are competitive, individualistic, and materialistic, people evaluate their lives, degree of success, and social worth. People seek to become these things, as these cultural values set the criteria for what the good life is and how to live it.

A shy person wants to become more outgoing, less inhibited, and spontaneous, all of which are culturally valued traits. With the right solution, the former-wallflower at the cocktail party can become the life of the party--the social butterfly she has always sought to be but never had the courage to become. After all, who would not want to envision himself or herself, the true self, as desirable, valuable, popular, and sexy? It is possible for people to believe that they are desirable, valuable and sexy even if culture defines what constitutes these things differently, in which case people are setting out to become their own creation. Alternatively, people can say, I want to be

these things, whatever they are, and I will let my culture define them, and then I will become them. For this approach in North America, people found Prozac.

Transformation through Prozac? Or medicating personality type?

Prozac has the ability to change personality. The SSRI has activating and energizing effects, which can sculpt personality to the dominant bubbly and outgoing social norms.

> *Scholars have worried that Prozac treats the self rather than proper disease, that it alters personality, that it feeds dangerously into the American obsession with competition and worldly success, and that it offers a mechanistic cure for spiritual problems.*[128]

Some people take Prozac to allow them to be the person that they want to be. In this context, cosmetic neurology emerges. The term cosmetic psychopharmacology was coined by Peter Kramer in *Listening to Prozac*, and refers to the use of psychotropic drugs, not to treat illness per say, but to act as mood brighteners improving a person's psychiatric well-being. Carl Elliott has referred to this state of being as 'better the well.' Through this medication, less pleasant aspects of modern life can be solved with a pill. Those who lack the outgoing personalities, motivation at work, creativity, and a zest for life can take a pill to transform their personality to one that is more socially desirable, which will allow them to achieve the life they have always wanted.[129] Prozac's transformative properties on personality have been well documented and have blurred the line between illness, wellness, and enhancement.[130] The transformative properties of Prozac bring medicalization of personality type and pathologize the normal to a higher level.

One of Dr. Kramer's patients, in *Listening to Prozac,* reported that she "feels like a different person" when she is on Prozac. She said "This is who I am. I feel strong. I feel resilient. I feel confident."[131] After going off Prozac she said, "I am not myself."[132] The drug allows people to 'feel more like themselves.'[133] In some cases, this means feeling like an entirely different person, a person who is not defeated, who accomplishes goals, and who is valued by culture. This medication allows people who do not have a culturally valued personality type to attain one. In the words of Dr. Kramer, "Prozac seems to help patients who he would not have previously thought to be

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[128] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 8.
[129] Narratives of this sort fill the pages of Listening to Prozac.
[130] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997.
[131] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 3.
[132] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 3.
[133] Elliott, Carl. "Introduction," Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 3.

clinically depressed – people who were shy, unhappy, emotionally rigid, or socially isolated."[134] The self can be transformed and remade with Prozac.

In an essay from the book, *Prozac as a Way of Life*, Carl Elliott voices his worry that this kind of transformation is inauthentic. Elliott does not believe that this kind of medication can allow people to become their true selves; rather, it helps people conform to dominant cultural norms. He points out that modern life pulls individuals in "different often contradictory moral directions,"[135] because aspects of modern life "fracture the unified self."[136] We value authenticity, integrity, being true to ourselves "over time and circumstance, and that, with some qualifications, we ought to be morally committed to maintaining that unity,"[137] as failing to do so would render us insincere and disingenuous. All the while, we receive societal messages "that encourage us to adopt a flexible, adaptable identity."[138]

To draw from the nuanced terminology of Carl Elliott, modern workers are expected to be highly plastic in their ability to learn new skills sets as the job market ebbs and flows, working on short term contracts and forever selling themselves to employers as they climb onward and upward or just struggle to survive. The cyber world offers people the freedom to create a disembodied personality that may be very different from how they are in real life.[139] Cosmetic surgery allows people to alter their face, body, and image. And now, psychiatry can allow people to alter even their personality. In Elliott's eyes, people are not making autonomous choices but instead allowing culture to work through them. If individuals do not posses socially valued traits and buy into these cultural values, therein lays the pressure to *become*.

This tension that Elliott identifies cuts though all of American history as it is "a tension between the values of self-improvement and personal achievement, on one hand, and, on the other, the values of stability, loyalty to your roots, and remembering where you came from."[140] These

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[134] Elliott, Carl. "Introduction." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 3.
[135]Elliott, Carl. "Introduction." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 8.
[136] Elliott, Carl. "Introduction." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 8.
[137] Elliott, Carl. "Introduction." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 8.
[138] Elliott, Carl. "Introduction." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 8.
[139] Elliott, Carl. "Introduction." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 8.
[140] Elliott, Carl. "Introduction." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 9.

tensions manifest in the language in which people discuss mental illness, identity, and Prozac's relation to the two.

While we are told to be true to ourselves, which in theory would allow us to be the people we are or want to be, we are told every day *who* we should be as the single standard of beauty, femininity, masculinity, and success is prompted in media and advertising. Those who buy into the approach to cosmetic neurology are accepting a manufactured notion of self and the becoming process. They do not value their appearance unless they are the single standard of beauty of the commercialized super model, trying to become what *she* is even if that is not who *they* are. Regardless of the merits of what people seek to become, Prozac allows them "to become." Prozac allows for a transformation of identity.

Julia narrative: A woman transformed.

Julia, one of Dr. Kramer's patients in *Listening to Prozac,* becomes the person she wants to be and now leads the lifestyle she wants to have because Prozac transformed her. Dr. Kramer describes Julia's life as having 'definite form to it.'

> *She had completed training as a registered nurse, married had children, and had taken a short-day job at a nursing home, a position that allowed her to be back at the house to greet her children on their return from school. But there were problems on every front. She demanded extraordinary control in the household. The beds had to be made just so. The children had to be organized before leaving for school. Julia's husband was uncomfortable with her inflexibility and she found herself raising her voice to him and the children more than was right. Also, the nursing home job was beneath the level of her abilities. Julia was not challenged but she saw no way out.*[141]

Julia had come to Dr. Kramer because she heard about the transformative properties of Prozac, and she wanted the drug. However Dr. Kramer initially wanted "to avoid medicating Julia for what looked like marital dissatisfaction,"[142] as he hoped these sorts of problems "would respond to a reassessment of her own or the family's needs in therapy."[143] Therapy did not help.

Early in the course of Julia's therapy, Dr. Kramer made suggestions to help Julia modify aspects of her life to help her in meeting her expectations. Suggestions of this nature included her husband taking on more household responsibilities, after-school programs for the children, or a nanny. Dr. Kramer thought the additional time might allow Julia to find a career in which she could find fulfillment. However, Julia felt that her problems could not be solved in such a mundane

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[141] Kramer, Peter D. Listening to Prozac. New York: Penguin Books. 1997. 24.
[142] Kramer, Peter D. Listening to Prozac. New York: Penguin Books. 1997. 24.
[143] Kramer, Peter D. Listening to Prozac. New York: Penguin Books. 1997. 24.

fashion, which was previously also suggested by her husband. "If she were not at home, the straightening would not be up to her satisfaction, and the children would not be neat and scrubbed in a way that pleased her."[144] Her satisfaction was a matter of what was pleasing to her.

Before presenting in Dr. Kramer's office, Julia sought out previous medical help. An internist put her on anti-anxolitic medication for what he referred to as "situational reaction associated with depressive overtones."[145] In Kramer's opinion, this was "a label for a problem that does not quite rise to the level of illness but that nonetheless seems to call for treatment."[146] However, her gynecologist understood Julia's problems as premenstrual syndrome, for which he tried several different treatments ranging from water pills to plant remedies, which normalize hormone level, and higher doses of anxiety medication, which had little effect on Julia. Kramer felt that "as a psychiatrist, [he] was in no better position to categorize Julia's problems than her psychologist, internist, or gynecologist had been. [His] preference, as [he] ha[s] said, was not to call her ill at all, but to focus on some intimate aspect of the self."[147]

In DSM-IV, sub-acute clinical depression is dysthymic disorder, a category for patients who do not quite meet the standards of major depression. But dysthymia refers to people who suffer from depressed mood 'for most of the days than not' for two plus years, and who have disturbances of sleep, appetite, energy, concentration and the like when depressed. In Kramer's estimation, "Julia did not have those sort of disturbances [as described in the DSM], and her depression was not at all constant."[148]

Julia's other doctors had all noted her depressive tendency, yet she was not clinically depressed. Kramer speculated about where her need for control, inability to communicate with her husband, and frustration with her children came from. Could it be a defense against the fear of having her inadequacies laid bare? What about family pathology? Could her husband be undermining her, feeding her anxiety such that she stayed home instead of joining the work force? "Her styles, her preferences, her sense of priority, her perfectionism were so pronounced that she was continually angry at her children and husband and, given the impossibility of instilling her standards in them, stalemated in her career."[149]

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[144] Kramer, Peter D. Listening to Prozac. New York: Penguin Books. 1997. 24.
[145] Kramer, Peter D. Listening to Prozac. New York: Penguin Books. 1997. 24.
[146] Kramer, Peter D. Listening to Prozac. New York: Penguin Books. 1997. 24.
[147] Kramer, Peter D. Listening to Prozac. New York: Penguin Books. 1997. 25.
[148] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 25.
[149] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 24.

Julia's psycho-social worker provides perspective and insight into Julia's experience which accord well with Dr. Kramer's percepts of Julia's experience.

> *When Julia first came to the office, her distress related to frustration over her stalled career and certain personal issues – unresolved family-of-origin conflicts that had re-emerged in her marriage. Julia's father, a businessman, had been a high-strung perfectionist; the son of a depressed mother, he was the more nurturing of her parents. Julia says her mother was more passive and distant. Julia's older sister seemed to stumble from failure to failure, and as a result, Julia was moved to care for her and to identify with her competent father. The conflict in Julia's own marriage, as the social worker formulated the case, involved gender-role conflict. Identifying with her father, Julia secretly, or even unconsciously, felt herself to be more competent then her spouse. At the same time, not least for her own sense of security, she wanted to maintain the illusion that her husband was like her father, strong and decisive. The social worker saw Julia's obsessionality – and her paralysis in her career and home life – as an expression of inner conflict over control in the family; she was torn by a wish to let her husband take the lead, opposed by repeated urges to barge in and do things right. These same conflicts emerged in her handling of the children, whom she pushed hard while telling herself she was giving them their head.*[150]

Julia not only lacked these insights and found talk therapy unhelpful, but also wanted what she came there for, medication. After all other avenues and treatment failed, Dr. Kramer put Julia on Prozac. Prozac seemed to be the solution. Julia reported the experience of being on medication to be 'like night and day.'

> *The children behaved more obediently, and when Julia remarked on the change, they told her she was yelling less. Her husband became more cooperative as Julia became more pleasant with him. Then she noticed that she had markedly more energy.....There were ups and downs. Some weeks, Julia reported having been nervous with her children and having yelled excessively. These were fluctuations often correlated with particular stressors. For instance being home on weekends was harder than responding to the structure of work. And that structure of work was changing. First Julia quit her part time job. She chose instead to do hospital shift work on an on-call basis – a particularly disruptive way to live, but she felt, the best way for her to re-enter the career path for hospital nursing. She began to specialize in pediatric nursing and found she could enjoy the unpredictability of young children in a way that had been impossible for her in earlier years. She believed that without medicine she would have never been able to take this step, accompanied as it was by complex care taking arrangements for her own children and a need often to overlook a degree of chaos in the home.*[151]

After Julia had stabilized for five or six months, the dosage was lowered, and Julia reported "I'm a witch again."[152] Dr. Kramer noted that "she felt loosely – pessimistic, and gray and demanding.

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[150] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 31.
[151] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 28.
[152] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 28.

She was up half the night cleaning."[153] She said she did not feel like herself anymore. As the medication dosage was upped, she returned to her normal self again, or at least the self that was pleasing to her and others.

Kramer characterized Julia's problems as stemming form "martial or inner conflict,"[154] while Julia experienced her problems as resulting form a medical condition. She believed that "if she were well the turmoil in the family would disappear. And that is just what happened."[155]

Essentially, Julia had a normal life, and like any normal life, it is not perfect. Her problems were not pathological, yet they caused her to suffer. Julia had expectations of what her life would be like, and it did not turn out that way. Instead of modifying her expectations and changing her behavior, she turned to a biomedical model for understanding her suffering. She turned to medication to solve her problems. While Kramer and Elliott see Julia's transformation as the product of enhancement technology though cosmetic neurology, she understands her transformation as one of healing. The intervention of Prozac transformed her from a state of illness to a state of health.

> *To Julia the story was entirely different. As so often happens, the pill rectified the illness. If there was a chance in the world that Julia might see her difficulty in adjusting to married life as anything but a result of a 'biological disorder characterized by compulsiveness and depression,' her relapse and rescue by the increased dose of medication ended it.*[156]

Julia's narrative represents, from a patient's perspective, the benefits in considering life problems as biomedical disease. In the biomedical model, patients are not responsible for their suffering, and they bear no responsibility for their disease state. Rather, bad neurochemistry is to blame. This model renders its sufferers as passive victims, who are helpless, and therefore not responsible for their suffering. With this view comes limited agency on the part of the sufferer to change or ameliorate his or her condition. Julia's problems appear to be solved, regardless of the merits of the solution.

A different perspective on transformation and the medicalization of personality type.

While Elliott worries that such transformations are inauthentic, David DeGrazia argues just the opposite. For DeGrazia, Prozac and "personality cosmetics" are an opportunity for people to

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[153] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 28.
[154] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 27.
[155] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 27.
[156] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 32.

become a product of their own grand design, the ultimate in self-creation.[157] Prozac has become like any other tool in self-modification. Dark eyeliner allows women to become that smoky-eyed woman of mystery. Plastic surgery, bobby pins, hair color, push-up bras, and wigs allow women to become something of their own choosing. Everyone wants to be successful and valuable; everyone wants to be fulfilled. These props and accessories of daily living now seem to include Prozac. However, tools that allow people to biochemically alter their personality to fit in are quite disturbing as they cut into the core of identity.

Some people use their own definition to operationalize success and value. They define who they want to become and then become that vision regardless of what their surroundings hold to be successful and valuable. This kind of transformation does not seem worrisome, and perhaps appears to be the kind of authentic self-creation that DeGrazia identified. Others know that they want to be perceived as successful and valuable, but they do not know what that really means, so they turn to their culture and surroundings to define it. Then they strive to become the culturally-operationalized definitions of success and value. This kind of transformation may be the hollow, inauthentic transformation of identity that Elliott addresses.

Conclusions.

Julia has social and familial troubles, but are these troubles the face of illness? When people are not able to conform to a cultural ideal or stereotype, society says they are incomplete or damaged. Our culture dictates that they require fixing. What happens when the defective component is deeply tied to personal identity? When the worried-well seek treatment, they are seeking to change who they are. Who they are seems in some way unpleasing to them or appears to be blocking them from achieving life expectations, dreams, and goals. They are dissatisfied with their life. When a traditionally sick person seeks treatment, aspects of his or her identity will change as well. However changing the identity was not the goal of the treatment. The traditionally ill are trying to heal, which requires transitioning from the social space of sickness to a functional member of society. This journey of healing will no doubt have an effect on identity; however, the person's identify was not deemed the problem in the first place. Cosmetic neurology for the worried-well allows identity to be named the problem in need of treatment.

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[157] DeGracia, David. "Prozac, Enhancement, and Self-Creation." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 35.

Conclusions.

A collective review of depression narratives shatters the serotonin myth and the biomedical model's ability to provide a helpful vocabulary and explanatory mechanism to understand the highly individualized and varied symptoms presentation in clinical depression. The DSM does not use the language of alienation, soullessness, and existential concern. When narratives are analyzed together, they reveal a more complex disease etiology and pathogenesis beyond mere abnormalities of the biological system and serotonergic neurotransmission. In this chapter, people struggle within themselves and within larger cultural frameworks. After considering the diverse selection of patient narratives, the organic basis of depression remains unclear, if it can be biologically attributed at all.

Are low serotonin levels to be blamed for these people's unhappiness? If low serotonin levels cause depression, and these people are depressed, either by their standards or society's, then is the reasonable conclusion that they have a biochemical abnormality. After considering the above narratives, a single biochemical deficiency is not the likely trigger for the priest's lack of faith, Benjamin's black moods, Beverly's comfort on an airplane, Jerry's disagreements with old friends, and Julia's need for organization. Clearly other elements are at work. The neglected element is culture. Cultural expectations and attitudes are shaping what people consider to be disease.

True depression can be organically attributed according to a dynamic systems biology perspective; however, pathologizing unpleasant aspects of normal life as depressive disorder will not reveal a biological etiology for that kind of suffering and unrest. Depression has an organic basis, but not everything often called depression is truly depression. Depression is more than a biochemical disease, so it needs to be understood as a complex interaction of biology, environment, and culture that causes suffering. Tensions in any one of these areas will translate into problems, as evidenced by the patient narratives.

A culture that has unattainable expectations for living the good life will cause its people to endlessly quest to achieve them. People will never achieve them and will, therefore, feel that they perpetually fall short. Today's culture has unhealthy expectations for its members. When depression is only looked at only biologically, tensions in the environment and culture are ignored. An incomplete understanding of depression poses a great danger to patients because an incomplete understanding will lead to an incomplete treatment.

The selection of narratives forces people to consider how life's challenges and disappointments are medicalized. Our identity is easily jarred when we acknowledge that we are not the people we want to be or strived to become. We must be very careful about what we call a

disease so that people will not receive unnecessary or inappropriate treatments. Treatment for depression ranges from electroconvulsive therapy (ECT) to medication, to different kinds of talk therapy. Each has documented benefits, and treats different aspects of the self. Each treatment modality has appropriate uses in certain circumstances, as well as detrimental effects in unwarranted circumstances. Depending on the view of illness, people have many ways to transform themselves, many ways to heal, and many ways *to become*.

* * *

The discussion and critical reflection in this chapter expand the etiology of depression beyond biology to look at problematic elements of culture, which cause people to be unhealthy. From this perspective, depressive experiences are understood as cultural diseases and later recast as unpleasant aspects of normal life. A question that is raised throughout this chapter, and comes to a head at the chapter's close is: In the course of normal life should people alter their expectations, or should they medicate the problems away? If people seek to live an extraordinary life, should they change their expectations at all, or should they perish trying? These questions are explored in the next chapter, which takes an evolutionary perspective in considering depressive disorder. From this perceptive, depression is conceived as an adaptive advantage in navigating difficult social situations that challenge fitness. According to the evolutionary perspective, developing insight into social problems that cause unrest is the key to solving them. Solving social difficulties will improve, not only fitness but also quality of life. Taking medication that ameliorates the pain may blunt insight, and therefore block patients from realizing the benefits of depression when it is used as a tool for social navigation.

Chapter 4: An evolutionary perceptive.

Evolutionary theorists have several postulates regarding depression's existence in modern culture. First, depression has been theorized to serve a purpose, but that purpose is no longer served in modern times. Second, modern life stress is "incompatible with the brains we have evolved, and depression is the consequence of doing what our brains did not evolve to do."[158] Third, depression serves a useful function for individuals in society, and benefits can be gained from being depressed. Fourth, genes implicated in depression are also implicated in other useful behaviors that are so essential to our functioning that the net benefit out weighs the burden.[159] Of these evolutionary approaches to depression, the third postulate is the focus of this chapter, with brief consideration of a genetic basis for depression described by the forth postulate.[160]

As depression is prevalent in different cultures and populations throughout the globe, evolutionary theorists argue that its frequency is too high for it to be 'a simple dysfunction.'[161] Therefore, depression must serve some sort of adaptive function and is neither maladaptive nor pathological. The first half of the chapter presents the *social navigationn hypothesis*. According to the *social Navigationn hypothesis* (SNH) proposed by Watson and Andrews, depression plays a role in social problem-solving. Support for this hypothesis is culled from psychology literature. The genetic basis of depression is considered in an a*daptationist* depression theory, while *alternative* a*daptationist* theories consider different aspects of the social environment mentioned in the SNH. The focus remains on the SNH hypothesis because it challenges and later destabilizes the purely biological construction of depression. This perspective offers a unique insight into the treatment and management of depressive episodes.

The second half of the chapter explores how evolutionary perspectives on depression interface with American values tough narratives. This exploration focuses on taking responsibility for suffering as a means to increase agency. Increasing agency creates opportunities to solve social problems, which cause suffering and depressive episodes. This selection of narratives shows how taking responsibility is difficult given North American values. Additionally, these narratives show how taking responsibility and engaging in social problem-solving can combat depression. This

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[158] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 404.
[159] This presentation of research draws from the structuring of ideas presented by Solomon in Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001.403-404.
[160] The evolutionary postulates presented in this paragraph relied on research presented by Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 404
[161] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 403.

discussion raises the question of how to persist in the face of difficulty, a questions with implications for both mental health and personal identity.

Subscribing to a socially constructed view of depression as articulated by the social Navigationn hypothesis provides two options to end the depressive experience. One is to resolve the social conflict by strategizing to overcome it. Another approach is to accept defeat and surrender. In some cases, working though the depression to fight towards a goal may be a healthy course of action. In other instances, surrendering up may be more appropriate as it will lead to a healthier outcome. The difficulty lies in deciding which course of action is realistic and which is unreachable. These decisions have great impact on identity, who people become, and how people do or do not transform as a result of their expectations.

The previous chapter explores personal transformations though medication, while this chapter explores the idea of transformation though wise decision-making and action taking.

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The evolutionary perspective looks at social transformations of identity and becoming, which are fundamentally different than transformations though cosmetic neurology considered in the last chapter. In agreement with this perspective and this paper, other transformative processes and ways to *become* do exist and can alter social identity without changing elements of personality In this chapter, the journey of becoming and the challenges people face in their everyday lives will be analyzed from an evolutionary perspective, in which depression serves an adaptive function if sufferers use this opportunity to gain insight. This chapter highlights how the process of insight-gathering has been pathologized, medicalized, and medicated based upon cultural norms.

An example of this kind of transformation is training a person must undergo to enter a profession. There trainee's personality will not fundamentally change once they are an accredited individual however they perceive themselves, and how others perceive them will change. Consider a student in training for a medical career. Through the process of medical school and residency, a future physician becomes a physician. Before she has undergone the training, she can picture future versions of herself and her identity as a physician but cannot yet incorporate the persona of physician into her identity. Her experience of medical training is one of becoming and is an essential component of her identity as it entails achieving a life-long dream. William May wrote, "No one can watch a physician nervously approach retirement without realizing how much he has

needed his patients to be himself."[162] Any process of *becoming* involves trials and tribulations. If the process of becoming is tedious or blocked in any way, and people are prevented from completing the process of becoming, people may not have the opportunity to be the who they want to be. The outcome of failing at a dream may cause different forms of alienation from how people envision themselves and locate themselves with in a social milieu.

In North America, a cultural expectation, perhaps flowing from the Constitutional right to pursue happiness, asserts that people need to be happy all the time. Perpetual happiness, even if Americans have a right to it, is not a realistic expectation, especially when people do not realistically appraise personal abilities and capabilities. When people over-estimate themselves and fail, of course they feel disappointed, dejected, and depressed. Is the sadness people feel after being unrealistic with themselves and experiencing a poor outcome the symptom of an illness?

* * *

Everyone wants to be a certain kind of a person, to set goals and satisfy expectations, to dream about the future and how to get there. Julia, from the narrative presented in the last chapter, wants to be a certain kind of a person, which for her means being a certain kind of wife and mother. For others, being a firefighter or helicopter pilot is essential to how they envision themselves. Alternative modes of transformation and becoming (by non-pharmaceutical means) are explored in this chapter, illustrating how people can transform their identity, without modifying the essential self, but yet still influencing personal and social identity. Looking at non-pharmaceutical transformations is important to the reflection on depression because these transformations address personal expectations and matters of identity, which are previously unexplored in the literature.

Evolving into being a particular kind of person is different from fundamentally changing one's identity. Selecting activities to thrill and enhance is different from cosmetic neurology. The previous chapter examined a kind of pharmacology where drugs fundamentally change building blocks of how people react to the world and how others react to those medicated individuals. Hobbies, careers, and dreams shape who people are and how they interact, but hobbies and careers do not shape the essential self which includes a sense of humor or an ability to relate to others on a personal level. Julia was not looking to enhance herself through growth; she sought to change a fundamental aspect of her essential self. This fundamental change had subsequent affects on her identity. The next section explores how identity changes in transformations of the non-essential self

[162] May, William. "Code and Covenant or Philanthropy and Contract?" On Moral Medicine: Theological Perspectives in Medical Ethics. Ed. Stephen E. Lammers and Allen Verhey. 2nd ed. Grand Rapids, Michigan: William B. Eerdmans Publishing Company, 1998. 130.

though growth and experiences, as opposed to through modifications of the essential self through medication.

Evolutionary perspectives of social Navigationn.

The *social Navigationn hypothesis* (SNH) is a comprehensive theory about the adaptive significance of depression. The SNH draws upon evolutionary theory to suggest that depression is not maladaptive as it plays an important role in resolving conflicts within a social milieu through two complementary problem-solving functions, which are the *social rumination function* and the *social motivation function*. The *social rumination function* allows people to focus cognitive resources on "planning ways out of complex social problems"[163] while the *social motivation function* motivates the social network or depressive's partner to help.

The modern social environment is highly complex and different from the ancestral environment. Changes in the social environment could account for the prevalence and intensity of depression. "Modern social complexity and dynamism probably increase the context for ruminative and motivational depression, because people face an ever-changing array of fitness enhancing opportunities, but are blocked from or do not understand how to access them...The ruminative and motivational functions of depression may correlate with so-called minor (sub-clinical) and major (clinical) depression, respectively."[164] The SNH is able to account for depressive symptomology at varying intensities.

Social rumination function.

Through the cognitive changes in depression, the *social rumination function* enhances the capacity for accurate social analysis and problem-solving capability, thereby allowing the depressive (depressed person) to focus cognitive resources on "planning ways out of complex social problems."[165] Based on evolutionary theories of emotional pain (which is analogous to physical pain), emotional pain signals problems in the social environment, which, if unaddressed, could have detrimental fitness consequences. Waston and Andrews propose that "emotional pain forces the individual to consider a wider range of strategic options than would otherwise be considered,

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[163] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 2.
[164] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis. Journal of Affective Disorders 13 (2001): 2.
[165] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis," Journal of Affective Disorders 13 (2001): 1.

including costlier and riskier ones."[166] Therefore it can be predicted "that depressives will mentally stimulate a greater number of possible solutions to their social problems than non-depressives, they should consider a greater range of strategic options."[167] This style of problem-solving is a function of not only the amount of time spent processing the problem, but also the manner in which the problem is processed.

Scholarship has indicated that the ability to resolve cognitively demanding social problems was important in structuring unique aspects of human intelligence over time.[168] Watson and Andrews use this work to suggest that "people should have evolved psychological adaptations governing the allocation of cognitive resources toward finding solutions."[169] Depressive symptoms are generally accompanied by anhedonia. From the evolutionary perspective, anhedonia serves a purpose as it removes distracters by allocating time to cognitive analysis and problem-solving. The loss of interest in sex may free individuals "from pleasure based attachments that may impede adaptive changes in social relationship."[170] The loss of pleasure in daily life activities indicates that the problem is so important to fitness that the flexible pursuit of pleasure will delay resolution to the problem.

Evolutionarily, the psycho-motor retardation and loss of energy in depression not only reduces the likelihood of encountering a predator while one is not functioning optimally, but also is another way to remove activities that are not targeted at solving the critical problem. In support of this view, Lemke and colleagues have found that psychomotor retardation positively correlates with anhedonia.[171]

Depressives are often involved in complicated social situations, outcome of which has dramatic effects on personal fitness. Therefore, depressives must be both realistic and conservative in making plans to resolve the social problem. Resolving the social problem requires complex

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[166] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis. Journal of Affective Disorders 13 (2001): 4.
[167] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis, Journal of Affective Disorders 13 (2001): 4.
[168] Alexander, R.D. "Evolution of the Human Psyche." The Human Revolution. Ed. P. Mellars and c. Stringer. Edinburgh: University of Edinburgh Press, 1989: 455-513; Humphrey, N.K. " The Social Function of Intellect." Growing Points in Etiology. Ed. P.P.G. Bateson, and R.A. Hinde. Cambridge :Cambridge University Press, 1976: 303-317.
[169] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 5.
[170] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 4.
[171] Lemke, M.R., Pohl P., Koethe, N., Winkler, T. "Psychomotor Retardation and Anhedonia in Depression." Acta Psychiatrica Scandinavica 99 (1999): 252-256.

calculations often involving third parties in which reactions of other people and mental states need to be assessed. Research has shown that depressives may be less biased about their phenotypic quality than non-depressives.[172]

The attribution style of depressives is referred to as the *depressive attribution style* and is an important part of the social rumination function because it provides accurate mechanisms for social analysis. Depressives exhibit different attribution styles for attributing successes and failures than non-depressives. Non-depressives have a *self-serving bias* (SSB) in which they attribute personal success to their abilities and failures to bad luck or lack of effort but never lack of ability.[173] Non-depressives are more likely to attribute the success of others to chance and the failures of others to lack of ability.[174] This pattern of attribution in depression is reversed. Depressives attribute their success and the failures of others to chance or luck, and their failures and the success of others to skill and ability. This specific pattern of attribution is referred to as the *depressive attributional style* (DAS).[175] Research has shown that the DAS is a more accurate attributional style[176] because the SSB is distorted from 'strategic self-enhancement.'[177] For example, depressives evaluate people (including themselves) more even-handedly for personality traits, future outcomes, and reasons for success and failures.[178]

Depressives should not be outperforming non-depressives in all cognitive domains, as depression is only an adaptive advantage is social problem solving. Depressives perform poorly on demanding cognitive tasks of a non-social nature, which include intelligence tests, learning and

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[172] Joiner T.E., Schmidt, N.B., Singh, D., 1994. "Waist-to-hip Ratio and Body Dissatisfaction Among College Women and Men: Moderating Role of Depression Symptoms and Gender." The International Journal of Eating Disorders 16 (1994): 199-203.

[173] Sedikides C. "Assessment, Enhancement, and Verification Determinants of the Self-evaluation Process." Journal of personality and social psychology 65 (2003): 317-338.

[174] Sedikides C. "Assessment, Enhancement, and Verification Determinants of the Self-evaluation Process." Journal of personality and social psychology 65 (2003): 317-338.

[175] Sweeney, P.D., Anderson K., and Bailey, S. "Attributional Style in Depression: A Meta-analytic Review." Journal of personality and social psychology. 50 (1986): 974-991.

[176] Ackermann , R., and De Rubies R.J. "Is Depressive Realism Real?" Clinical Psychology Review 11(1991): 565-584.

[177] Sedikides C. "Assessment, Enhancement, and Verification Determinants of the Self-evaluation Process." Journal of personality and social psychology 65 (2003): 317-338; Sedikides C., Campbell, W.K., Reeder, G.D., and Elliott, A.J. "The Self-serving Bias in Relational Context." Journal of Personality and Social Psychology 74 (1998): 378-386.

[178] Brown, J.D. "Evaluations of Self and Others: Self-enhancement Basis in Social Judgment." Social Cognition 4 (1986): 353-376; Tabachnik, N., Crocker, J.,and Alloy, L.B. "Depression and Social Comparison, and the False-Consensus Effect." Journal of Personality and Social Psychology 45 (1983): 688-699; Ahrens, A.H., Zeiss, A.M., and Kanfer, R. "Dysphoric Deficits in Interpersonal Standards, Self-efficacy, and Social Comparison." Cognitive therapy and Research 12 (1988): 53-67; Alloy, L.B., and Ahrens, A.H. "Depression and Pessimism for the Future: Biased Use of Statistically Relevant Information In Predictions for Self Verses Other." Journal of Personality and Social Psychology 52 (1987): 366-378.

memory tasks[179], reading compression, and organization and clustering tasks.[180] This poor performance is to be expected since cognitive resources of depressives are focused elsewhere. Depressives not only have a more accurate attribution style but also out perform non-depressives on social problem-solving tasks[181] and more accurately judge the control they have in contingent outcomes than non-depressives.[182] Since depressives are more socially dependent and vulnerable, they have a greater incentive to make accurate behavioral and mental status predictions than non-depressives who are less vulnerable.

Social motivation function.

Depression has a *social motivation function* which secures the help and support from partners of the depressive. This function is very important, especially if partners were initially reluctant to give help. "The costs associated with the anhedonia and psychomotor perturbation of depression can persuade reluctant social partners to provide help or make concessions." [183] The two mechanisms through which this occurs are *honest signaling* or passive *unintentional fitness extortion*. Depression gets its motivational power through the costs it imposes on the depressive and on close social partners, as each has a vested positive fitness interest in the normal functioning of the depressive. [184]

In the honest signaling hypothesis, the social partners are motivated to help by virtue of the costs imposed on the depressive. The social partner perceives that the depressive behavior is a genuine signal of need, or a cry for help, and acts out of virtue. The honest signaling hypothesis sees the costs imposed on the self as opposed to partners as the crucial factor for eliciting help.

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[179] The biological underpinning for diminished performance in these tasks as it pertains to hippocampus functioning and neurogensis are discussed in chapter five.

[180] Hartlage , S., Alloy, L.B., Vazquez, C., and Dykman, B. "Automatic and Effortful Processing in Depression." Psychology Bulletin 113 (1993): 247-278.

[181] Yost, J.H., and Weary, G. "Depression and the correspondent inference bias: evidence for more effortful cognitive processing." Personality and Social Psychology Bulletin 22 (1993): 192-200; Lane, J.D., and DePaulo B.M. "Completing Coyne's Cycle: Dysphorics' Ability to Detect Deception." Journal of Research in Personality 33 (1999) 311-329.

[182] Ackermann , R., and De Rubies R.J. "Is Depressive Realism Real?" Clinical Psychology Review 11 (1991): 565-584.

[183] Paraphrased from Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 1.

[184] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigation Hypothesis." Journal of Affective Disorders 13 (2001): 2.

However, according to the motivation by fitness extortion function, help is elected through imposing escalating costs on others, and any costs imposed on the self are incidental.[185] The partner intervenes because he or she feels that the price of intervention, which may require some form of acquiescence, is less than the cost of continued escalation without intervention. In this manner, depression can motive a single partner or an entire social network.

Depressive episodes can only motivate members of the social network to act if they have a positive fitness interest in the depressive. Either motivational hypothesis predicts that depressives would be in a greater state of depression when they are experiencing problems with partners who have high fitness interests in them. Evidence for this hypothesis was found in a study examining the mental health of caregivers of Alzheimer's patients.[186] Caregivers were asked to rank the helpfulness of their social circle. In this study, high levels of current upset and distresses were coupled with high levels of helpfulness and support from the caregivers' social network in the past. High levels of social network helpfulness in the past was a better predictor of depression in caregivers than a history of recent upheaval with a minimally helpful social network. This finding supports the social motivation function of the SNH; however, this finding is somewhat at variance with other research, which indicates that a strong social network buffers depression.[187]

Implications of the SNH.

The SNH constructs depression as an adaptive problem-solving tool in cases of extreme social distress. Depressives confronted with social problems that are difficult to resolve perceive that their social situation is unpleasant and difficult to change. Feelings of entrapment and helplessness have been referred to by depression researches as *hopelessness.*[188] Rather then hopelessness, Watson and Andrews suggest that *desperation* is the more appropriate term as it "does not imply that a problem is perceived to be unsolvable. It implies that the problem is important to solve, it so far has resisted solution, and resolution may require risky or unusual strategies."[189] It is well-documented that strong social support and improvements in social

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[185] Hagen, E.H. "The Function of Postpartum Depression." Evolution and Human Behavior 20 (1999): 325-359.
[186] Pagel, M.D., Erdly, W.W., and Becker, J. " Social Networks We Get With (and In Spite of) a Little Help From Our Friends." Journal of Personality and Social Psychology 53 (1987): 793-804.
[187] Paykel, E.S. "Life Events, Social Support and Suppression." Acta Psychiatrica Scandinavica Suppliment 377 (1994): 50-58.
[188] Abramson, L.Y., Metalsky, G.I., and Alloy, L.B. "Hopelessness Depression: A Theory-Based Subtype of Depression." Psychology Review 96 (1989): 358-372.
[189] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigation Hypothesis." Journal of Affective Disorders 13 (2001): 5.

relationships boost recovery from depression.[190] An alternative resolution to solving the problem is to class it as unsolvable. Practitioners have noted that depressive symptoms dissolve when the afflicted patients end their quest for the unattainable.[191] According to the SNH, when the social problem is solved, the depression should end. Solving the problem or classifying it as irresolvable are two ways in which resolution can be achieved.

Based upon the SNH, Watson and Andrews recommend neo-Darwinian forms of informative therapy and social problem-solving therapy to treat depression rather than antidepressant medication. "The SNH implies that anti-depressant medications risk handicapping the client's ability to navigate and control their social environment; this could, in the long run, hinder the depressive from making key improvements in quality of life."[192] Therefore, interfering with depression could hamper improvements in social situations, so depressives must endure the experiences in order to gain insight to ultimately better their situation. However, some may feel that this view endorses suffering[193] or 'healing through the dark emotions.'[194]

This construction of depression can easily be misinterpreted and abused, leading to increased suffering. Using the SNH as justification, depressives could be told to address their problems by themselves instead of being supported by clinicians and networks. While the SNH should never be used as a justification to withhold appropriate treatment for depression, it challenges cultural values of suffering and threatens drivers that construct depression as a biochemical disorder. According to American values, the lack of total and utter happiness is seen as an illness, while the SNH contends that temporary suffering has a purpose and will lead to a net gain of happiness in the end.

While some may find that the idea of healing through the dark emotions offers a glorification of suffering, it is worth noting that medical science and the institution of medicine

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[190] Andrews, B., and Brown, G.W. "Stability and Change in Low Self-esteem: The Role of Psychological Factors." Psychology Medicine 25 (1995): 23-31; Brown G.W., Adler Z., and Bifulco, A. "Life Events, Difficulties and Recovery Form Chronic Depression." British Journal of Psychiatry 152 (1988): 487-498; Brugha, T.S. Bebbington, P.E., Stretch, D.D., MacCarthy, B., and Wykes, T. "Predicting the Short-term Out Come of First Episodes and Recurrences of Clinical Depression: A Prospective Study of Life Events, Difficulties, and Social Support Networks." Journal of Clinical Psychiatry 58 (1997): 298-306.

[191] Nesse, R.M. "Is Depression an Adaptation?" Archives of General Psychiatry 57 (2000): 14-20; Price, J.S., Sloman, L., Gardner, R., Gilbert, P., and Rhode, P. "The Social Competition Hypothesis of Depression." British Journal of Psychiatry 164 (1994): 309-315.

[192] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 5.

[193] Kramer, Peter. "The Valorization of Sadness: Alienation and the Melancholic Temperament." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press. 2004. 48-58.

[194] Greenspan, Miriam. Healing Through the Dark Emotions : The Wisdom of Grief, Fear, and Despair. Boston: Shambhala, 2003.

have long asked patients to suffer in the short-term in order to gain long-term benefits. In chemotherapy, patients are asked to endure toxins pumped though their bodies that make them sick, lose their hair, and weaken their immune system, all in the name of healing. The SNH requires patients to endure unpleasant feelings in hope of soliciting insights to problems that will ultimately restore happiness. Moreover, the evolutionary view of depression empowers the afflicted. It does not victimize them, strip them of their agency, or make them passive suffers as biochemical models of depression do. The SNH locates the ability to heal within the individual and in their relationships. The patient, as opposed to a pill, is the instrument of healing. While this view of depression empowers, it also requires taking responsibility for suffering.

The SNH is able to account for irregularities in the depression literature. For example, in some randomized clinical trails of antidepressant medication, the placebo arm showed the greatest therapeutic gains.[195] These findings would be predicted by the SNH as insights and would not be blunted with medication. Therefore, the non-medicated patients could work themselves out of the depression and restore their social functioning, while medicated patients would be prevented from social problem-solving. In medicated patients, the social rumination and motivation functions of depression were thwarted perhaps by diminished anhedonia. Based upon findings such as these, Watson and Andrews concluded that, drugs should not be given unless "causative social problems also are being addressed,"[196] as medication may "emasculate the ruminative and motivational functions of a potential adaptive depression."[197]

The SNH accounts for the finding in the literature that milder variants of depression are less responsive to medication than more severe depressive episodes.[198] The origins of milder variants of depression are socially-based according to the SNH. A biochemical attribution of symptoms is a misattribution in which a biochemical solution is sought over a social solution. Therefore, the root

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[195] The National Institute of Mental Health funded a double blind randomized controlled clinical trail comparing sertraline, hypericum perforatum (the active ingredient in St. John's Wort) and Placebo, in the United states. The study involved 340 adult outpatients with Major Depression. At the two and eight week primary efficacy measures neither treatment group could be differentiated from the placebo group. At the conclusion of the study, full response to treatment was highest in the placebo group (32% of patients) as opposed to either the hypericum (24 % of patients) or sertaline which is an SSRI (25 % of patients) group. Hypericum Depression Trial Study Group. "Effect of Hypericum Perforatum (St. Johns Wort) in Major Depressive Disorder: A Randomized Controlled Trail." Journal of the American Medical Association 287 (2001):1807-14.

[196] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 11.

[197] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 11.

[198] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 1-14.

cause of the depression is likely missed. As illustrated in this scenario, when a problem is misunderstood, the solution is not found, and the 'disease' does not respond to medication.

These findings coupled with the SNH support the argument that deeper levels of depression are more biochemically-based while less severe forms of depression have multiple etiologies, which are often rooted in social media. Based on the SNH, finding indicate that at one point, all forms of depression were socially grounded, and some depressions continue to become biologically rooted at the level of major depression.

The last chapter examines the interaction between biological and social media through biopsychosocial depression theories, which show how problems in social media can take root in biological media. In such instances, depression whose initial etiology is social deepens in severity and gains additional etiology in biological media. At this point, chemical interventions are necessary to balance body systems. Although, changes in social systems may positively affect biological systems, thereby normalizing biochemical irregularities associated with pathophsyiology of depression. Medication should not be given if the social life is out of balance, because abnormal biochemistry has not yet been manifested. Even when abnormal biochemistry persists, behavioral changes can successfully alter biochemical irregularities, making medication, in some cases, unnecessary. When an out of balance social life crosses over into creating an out of balance body, biological treatments need to be considered in addition to social ones. Towards the periphery of the diagnosis category, milder variants of depression have their origins in disharmonious social spaces and become biologically rooted as depression deepens towards the core of the category.

A genetic perspective, an adaptationist view of depression.

The evolution of depression genes appears to be maladaptive according to the prevailing medical view; however, such genes must have conferred a net benefit in order to endure. Two possible explanations for this evolution are the *adaptationist view* and the *maladaptive byproduct hypothesis*. According to the maladaptive by-product hypothesis, genes that coded for depression also coded for other traits (pleiotropy) whose benefits out-weighed the negative costs of depression and therefore endured. Akiskal proposes that depression is a by-product of a human adaptation for sensitivity to suffering.[199] The adaptationist view counters that depression is an adaptation, and therefore is not maladaptive as the medical model suggests. One such adaptationist view was

[199] Akiskal, H.S. "Dysthymia and Cyclothymia in Psychiatric Practice a Century After Kraepelin" Journal of Affective Disorders 62 (2001): 17-31.

explored in the SNH. The extent to which the maladaptive by-product hypothesis is false depends upon the degree to which the adaptation view of depression is true. The truth of these theories is inversely proportional to each other, as they are polar opposites.

Alternative adaptationist hypothesis.

Alternative adaptationist hypotheses take a non-genetic perspective of depression and use theories similar to the SNH as they suggest depression plays an important function in social problem solving. Alternative adaptationist hypotheses include the *social yielding hypothesis* and the *strike hypothesis*. According to the social yielding hypothesis, depression is an adaptation that benefits the loser in a conflict as it helps the loser do three important things. First, depression stops the loser from engaging in competition against the winner, which has already proved to be fruitless. Second, the loser accepts the loss. Third, depression signals submission on the side of the loser, indicating to the winner to stop oppressive behavior that was part of the competition.[200] In this manner "depression forces the acceptance of a fitness-limiting situation, especially loss of rank."[201] From this perceptive, prolonged depression represents a maladaptive ability to accept loss in a competition that cannot be won, but the depressive symptoms themselves are not maladaptive.

In the *strike hypothesis,* depressive episodes are seen as mechanisms by which the depressive can gain a greater degree of investment from a partner that may be exploiting them. The strike hypothesis suggests that depression solves 'dyad-specific problems,' while the SNH suggests that motivational aspects of depression play a role in "solving problems that have a far more systemic basis in the social network,"[202] which are not dyad-specific at all.

In contrast to the SNH, the social yielding hypothesis sees the social rumination function to be useful, as it does not require enhanced problem-solving capabilities. The SNH constructs depression as a way to get out of fitness-limiting situations. In short, it helps the depressive strategize to win by suggesting "that persons who have lost social status may need enhanced social analysis and motivational abilities to mitigate their loss."[203] Alternative adaptationist hypotheses

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[200] Gilbert, P., and Allan, S. "The Role of Defeat and Entrapment (Arrested Flight) in Depression: An Exploration of An Evolutionary View." Psychology Medicine. 28 (1998): 585-598; Price, J.S., Sloman, L., Gardner, R., Gilbert, P., and Rhode, P. "The Social Competition Hypothesis of Depression." British Journal of Psychiatry 164 (1994): 309-315.
[201] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigationn Hypothesis." Journal of Affective Disorders 13 (2001): 3.
[202] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigation Hypothesis." Journal of Affective Disorders 13 (2001): 3.
[203] Watson, Paul J., and Andrews, Paul W. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigation Hypothesis." Journal of Affective Disorders 13 (2001): 3.

provide explanations for the social origins of depression, which is constructed in terms of individual relationships to the environment and not pathological biochemical relations.

* * *

The theories outlined in the first half of this chapter are useful in exploring how depressives navigate their afflictions in the narratives presented below. In the second chapter, the narratives represented depressives who navigated their problem biochemically and did not seek insight-building due to their understating of their suffering. In the third chapter, the narratives discussed afflicted patients who considered issues in their environment to be causative of their suffering, with the exception of Julia's narrative; however, the discussion of her narrative highlighted these aforementioned issues, even if she had a different view of her experience. Now in this selection of narratives, insight-building is the tool used to work though depression.

Depression Narratives.

Evolutionary views of depression are given voice in narratives through patients taking control of their situation. Sufferers transition from passive to active roles and become the instrument of healing through lifestyle and social decisions they make. This selection of narratives shows different ways patients take responsibly for their happiness, identity, overall health, and pathways in life.

The evolutionary view of depression does not enter into the popular discourse. Only one depression memoir-writer, Andrew Solomon, acknowledges the evolutionary perceptive. The evolutionary view is likely under represented because it requires sufferers to take more responsibility than they would like to, and it opposes a biological construction of depression. This tension is explored by looking at different sections of Solomon's memories and personal illness narratives, in which relevant sections are analyzed in relation to the social navigation theories presented above. All narratives in this chapter are taken from Solomon's book. This selection of narratives examines how the afflicted seek to end their suffering by harnessing control within their social space and by making critical decisions about their transformation of identity into people who want to be both self-actualized and healthy. Within these narratives unfolds a discussion of responsibility, personal identity, and becoming in American culture.

The discomfort of responsibility.

In a chapter of *The Noonday Demon*, Solomon talks about alternative treatments for depression, ranging from complementary and alternative medicine, to allopathic remedies, to

outlandish solutions. In this section, he includes suggestions from his readers about his depression since publishing his *New Yorker* Article. A woman from Tucson wrote (and Solomon reports that it is his favorite) "Have you ever considered leaving Manhattan?" Upon considering this thought, Solomon states that "Leaving Manhattan would most assuredly lower my stress level." According to the SNH, abandoning a situation or pursuit is one way to end the stress of social navigating and associated suffering. However, Solomon does not abandon Manhattan. Perhaps the Manhattan lifestyle is too essential to Solomon's identity to abandon, even if it imposes a cost. Clearly, he has chosen to endure the stress for the kind of person that he wants to be. In staying, he elevates his stress level, which contributes to his depression, but if remaining affects his identity, he must endure the pathway. For these kinds of decisions, people must take responsibility for what they chose to endure, even if it causes suffering. In order to climb Mt. Everest without supplemental oxygen, climbers must be willing to breathe the thin air. In order to live in Manhattan, city dwellers must be willing to breathe the smog and endure the pace. In these situations, people can not have it both ways.

The model used to explain depression has significant implications regarding personal responsibility for mental health. Recalling the paralyzing fear and lethargy of a depressive episode Solomon wrote:

> *I can't sit in a movie theater" I said at one stage when someone tried to cheer me up by inviting me to a film. "I can't go outside," I said later. I didn't have a rationale for these feelings, didn't expect to melt at the movies or to be turned to stone by the breeze outside; I knew in principle that there was no reason why I couldn't go outside; but knew that I couldn't do it as surely as I now know that I can't leap tall buildings in a single bound. I could (and did) blame my serotonin.* [204]

In evoking the serotonin theory of depression, Solomon bore no responsibility for the depressive episode and resulting fear. He was the victim. Earlier in the memoir, Solomon presented an understanding of the biological basis for depression which is consistent with the stressor model of depression. Here he addressed the links between environmental stress and depression, with the suggestion that stress may cause depression through cortisol pathways. The association between depression and stress will be revisited and expanded upon in the final section of the paper, which addresses depression from a biopsychosocial perceptive.

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[204] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 305.

To a certain degree people are able to control stress levels by the decisions they make. Solomon made a choice to live in Manhattan and must take responsibility for this choice and the resulting stress. It is easier to blame serotonin than to blame oneself for personal decisions. Considering the empirical evidence indicating that stress causes depression, electing to partispate in stressful activities may be a significant point of responsibility to take for decisions that affect mental health and happiness.

Stress is a known cause of depression. This section discusses how personal decisions can cause stress, while the next chapter reviews scientific evidence that shows how stress causes depression using the stressor model of depression, which is tied to the neurogenic and neuroendocrine depression models. Depression, when considered from an evolutionary perspective, forces people to confront and reduce acute stressors responsible for causing their depression. Not confronting the stressors exacerbates the problem, requiring people to take responsibility for their unhappiness and the related personal decisions. Unlike the biomedical model, the evolutionary perceptive does not allow its sufferers to be passive. Rather, the evolutionary view empowers the afflicted with a sense of agency to improve their mental health and ameliorate their suffering. The point of the evolutionary model is to take responsibly by gaining insight and by acting in an adaptive manner to insure survival.

Not all variants of the depressive condition are induced by stress or environment; however, depression clearly does not only have an organic base. As shown in the final section, a biopsychosocial paradigm of depression accounts for the influence of mental states on physical states. Interaction with the environment is part of the disease pathogenesis, which is influenced by the decision people make.

If health is influenced by individual's decisions, people must take responsibility for those decisions, knowing that these choices will shape both mental and physical wellness. If depression serves an evolutionarily adaptive function of a sign post, then in time of duress, depressives must recognize the folly of their previous decisions as to make better decisions in the future. Acting in a manner to rectify duress requires an agency that comes from taking responsibility. Just as people can make fruitless decisions, they also can make fruitful decisions, which means recognizing their agency as decision-makers who have some degree of control over their lives. Agency means letting go of the biomedical model's passivity and blaming personal decisions rather than serotonin levels.

The violinist – Giving up and healing.

Depression may act as a sign post indicating the need to change non-productive behaviors. In other words, if someone is failing at something, why persist? Solomon tells the story of a "woman who had been trying to make her way in the world as a professional violinist, despite the discouragements of her teachers and colleagues, and who suffered from an acute depression that was only minimally responsive to medication and other therapies. When she gave up music and switched her energies to an area to which her abilities were better suited, her depression lifted."[205] The lift in mood would be predicted by the SNH. To admit defeat and class a situation as unsolvable is painful and may have profound consequences on personal transformation; however, such an admission increases personal fitness functioning and provides opportunity to explore other fitness enhancing pursuits.

What people want is not always personally beneficial or necessary. The evolutionary perspective of depression provides a vocabulary and paradigm for unraveling these concerns. The strength of the evolutionary model is granting an opportunity to harness a locus of control to heal and function, as opposed to feeling helplessly trapped by biology or unsolvable situations.

Claudia Weaver – Sticking to it and healing.

The narrative of Claudia Weaver in *The Noonday Demon* is a story of empowerment and victory. Claudia realizes that she is "lucky," as not every one has the experience of healing from depression.

> *I feel slightly artificially up. When I was ten milligrams lower on my medication, the depressive moments would come in and they were very disturbing and disruptive and really painful and hard to get out of, although I could pull out of them and would. And I don't feel the same sense of smoothing sailing that I had while I was planning the wedding. If I felt reasonably safe, I would go off the medicine; but I don't feel safe. I find it increasingly hard to draw the line between the depressive and the non-depressive me. I think the depressive tendency is much stronger in me even than the actual depression. Depression is not the be-all and end-all of my life. You know, I'm not going to lie on my bed for the rest of my life and suffer. The people who succeed despite depression do three things. First, they seek an understanding of what is happening. Then they accept that this is a permanent situation. And then they have to somehow transcend their experience and grow from it and put themselves out into the world of real people. Once you've done the understanding and the growth, you realize that you can interact with the world and live your life and carry on with your job. You stop being so crippled, and you feel such a sense of victory! A depressive person who can put aside navel gazing is not as insufferable as one who can't. At first, when I realized I would spend my life doing a mood dance, I was very, very bitter about it.*

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[205] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 410.

But now I feel like I am not helpless. This has become a major focus of my life: How can I grow from this? Maybe this hurts me now, but how can I learn from this.[206]

Elements of Weaver's narratives sound like mind-over-matter rhetoric, but they also give a person some degree of control and agency over what is occurring in their life. While some derive comfort from the biomedical model, which removes personal blame, others derive solace from Weaver's perspective, knowing that they can do something about their depression. Deciding to take action may take the form of Weaver's realization, pursuing insight-building personally or with professional help. Taking action also means seeking pharmacological treatment if the state of depression has deepened beyond the level at which social Navigationn and problem-solving will yield solutions.

* * *

Deciding when to endure hardship to achieve a goal is a dilemma present in every life. Setting goals allows people to become who they want to be. Meetings these goals, or not, has tremendous impact on personal identity. So, when should people be willing to endure, and when should they give up? This choice depends on how badly people want their goal and what they are willing to put up with. The formulation goal, the degree to which people are willing to pursue it, and sacrifices they are prepared to make along the way must all be considered. Above all, people must consider how realistic they have been when setting their goals. The evolutionary perspective encourages realistic goal setting regarding identity, achievement, and happiness as a function of these factors. Being realistic is a dimension of being responsible. Both the violinist and Claudia Weaver were realistic in their appraisals of self, which led to the restoration of personal happiness, even though it was achieved by opposite means – one stuck to it and one gave up.

* * *

The social navigation hypothesis in action.

At a London cocktail party, one woman recounted her pathway of recovering from suffering to Andrew Solomon. The narrative is not an illness narrative so much as it is a story of personal decision-making and triumph. For ease of discussion, this narrative will be referred to as the narrative of the London cocktail party lady.

I had terrible depression. I did not like the idea of medication. I realized that my problem was stress-related. So I decided to eliminate all the causes of stress in my life. I quit my

[206] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 157.

job. I broke up with my boyfriend and never really looked for another one. I gave up on my roommate and now I live alone. I stopped going to parties that run late. I moved to a smaller place. I dropped most of my friends. I gave up, pretty much, on make- up and clothes. It sounds bad, but I am really much happier and much less afraid than before. And I did it without pills.[207]

This narrative raises several points of consideration. In the traditional medical model, if someone heals without taking medication, was he/she sick to begin with? Based upon how illness and depression are constructed in the first chapter, the answer to this question is no. Illness by definition in the medical model is a biochemical disturbance. That definition makes this narrative difficult to reconcile with the traditional model. If she was sick, how can she heal without pills? Either the woman in the narrative did not have an illness, and could therefore 'recover' without drugs, or she was incorrect in her assessment that she had recovered. However, the evolutionary model suggests a third possibility. Perhaps, she did have an illness and was able to alter her depressive biochemistry by a means other than drugs, suggesting that depression is not a purely biochemical problem. Immediately, the difficulties and limitations of constructing depression as a purely biochemical issue come into focus through discussion raised by this narrative. The traditional medical model lacks the vocabulary and scope to address a full consideration of this narrative, due to an overly reductionist framework.

In the traditional model, drugs are the only way to fix biochemical irregularities, as these kinds of irregularities are perceived as the only issue. However, other issues contribute to depression. The discussion must not stop with a consideration of biochemistry. This narrative raises the possibility of modifying depressive biochemistry without drugs or, on a grander scale, locates the problem outside of a biochemical domain altogether. Non-pharmacological interventions are effective in the treatment of depression because depression is a biopsychosocial concern. Depression's etiology runs though non-biological media. Non-pharmacological treatments can modify internal biochemical states. One such way is effective social Navigationn, as it leads to problem-solving and ultimately to a reduction in stress. Stress is at the core of depression. The mechanisms by which social problem-solving and non-pharmacological interventions can alter depressive biochemistry are reviewed at length in chapter 5. In brief, behavioral interventions in depression are targeted at reducing stress, as stress is a trip wire for depression on a biological level though cortisol cascades and neuroendocrine feedback.

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[207] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 125.

Returning to the original question of how someone can heal from depression without taking medication, the evolutionary perspective incorporated with a biopsychosocial understanding embraces this possibility because these frameworks are not limited to a biochemical discourse. This woman's narrative illustrates the social Navigationn hypothesis in action. Depression acted as an adaptation to help her end her sadness. Her depression gave her pause for thought, and provided an opportunity for critical reflection about her life, likes, dislikes, and toleration levels. After reflecting, she acted, and was no longer depressed. She made radical decisions about her life and someone responded, "That's completely crazy. That's the craziest thing I've ever heard. You must be crazy to be doing that to your life."[208] Yet, she is happy. In taking this approach, she defied the status quo. This kind of behavior is threatening. It is easy to label those that defy the norm and threaten a more standard way of life as crazy, thus discounting their actions without considering their meaning. "Is it crazy to avoid the behaviors that make you crazy? Or is it crazy to medicate so that you can sustain a life that makes you crazy?"[209]

She made a personal decision to live within the bounds of what she could tolerate. She modified her goals, expectations, and approach to life; she made a personal decision. When it comes to modifying life and reformulating goals and expectations, people must be transparent and honest with themselves in their decision-making process. Whatever the choice taken, individuals must be aware of how and why they have made a particular choice. The decision to endure or to avoid pain and the manner in which they chose to navigate adversity are based on the kind of life they want to lead and the kind of person they believe themselves to be. If they choose to take on more and turn to performance enhancing drugs to increase their capacity to do so, then wthey have made a conscious choice. They are not ill. Too often the cloak of illness is applied to those who turn to medication to sustain a life that they would be otherwise unable to live. The athlete who takes steroids is choosing to increase his capacity to perform, as an athlete is different than the asthmatic who takes steroids to act as broncodilators in order to breathe more easily. The asthmatic has a medical condition and illness in the classical sense while the athlete does not. Medication use is not synonymous with illness. This paper does not consider issues and ethics associated with performance enhancing drugs, but instead uses the discussion of cognitive performance enhancing drugs to reflect upon what people consider to be an illness and makes normative claims about the context of medication usage and what this means in North American society. Medication used to

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[208] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 125.
[209] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 125.

endure and enhance is synonymous with an illness label in today's culture. The view that medication inherently equals illness does not indicate that individual people are ill, but rather this phenomenon is symptomatic of an illness within society.

As people struggle to decipher what life problems to address and what to ignore, they may feel pressured to address all negative aspects in their lives, thus giving the appearance of having no choice at all. In such instances, they are allowing cultural expectations and pressures to work through them. Today's culture dictates that its members must achieve so that they can be successful, which means acquiring objects of material value. According to the pressures of society, only achievement will make people happy. Furthermore, society dicates that people must also achieve these standards effortlessly. Winning should not be a struggle. "It has been fairly well established that the advent of the supermodel has damaged women's images of themselves by setting unrealistic expectations. The psychological supermodel of the twenty-first century is even more dangerous than the physical. People are constantly examining their own minds and rejecting their own moods."[210] When people medicate themselves to achieve, they are not ill, but rather they allow an ill culture to affect them. In this respect, depression is not an illness of the body or mind, but an illness of the time. Medication will not be able to change this culture of disease.

The only problem within the individual is perhaps how people have chosen to live given personal limitations and preferences. To this effect, Wittgenstein articulated that the "sickness of a time is cured by an alteration in the mode of life of human beings, and it was possible for the sickness of philosophical problems to get cured only through a changed mode of thought on life, not through a medicine invented by an individual." [211] This refers to the decisions people make about how to live and who to become. This is a philosophical articulation of the social Navigationn hypothesis.

After cogitating on these issues and raising the coupling of questions about 'is it crazy to change your life and expectations to avoid medication', even to the point where you no longer recognize your life, or do you 'medicate to sustain a life that you otherwise would not be able to handle', Solomon reveals the choice he made for himself.

> *I could downgrade my life and do fewer things, travel less, know fewer people, and avoid writing books on depression – and perhaps if I made all those changes, I would not need*

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[210] Solomon, A. The Noonday Demon: An Atlas of Depression. Scribner: New York. 2001, 26.
[211] Wittgenstein, L. Remarks on the Foundations of Mathematics. ed G.E. Anscombe. Basil Blackwell: Oxford. 1956, 57.

medications. I might live my life within the bounds of what I can tolerate. It is not what I have opted primarily to do, but it is certainly a reasonable option. [212]

I lead [a life], full of adventure and complexity, [it] affords me such enormous satisfaction that I would have trouble giving it up. I would hate that more than almost anything. I would sooner triple the number of pills I take than cut my circle of friends in half.[213]

Many do not realize that they have options. Solomon realizes that he has options. He has chosen to exercise one of them. He knows that he is medicating himself to sustain a life that he otherwise would not have been able to live. The London cocktail party lady chose the other option. She has chosen to live within the confines of what she can tolerate. To recognize the existing options and then to choose one requires taking responsibility and ownership of personal suffering. Therefore, sufferers have agency to act and are not passive victims of biochemistry. People can no longer claim that their depression is not their fault simply because they have bad chemistry. However in these situations, referring to fault or blame is not entirely appropriate. No one is ill and no one deserves blame. Rather, people are only trying to understand what has happened, and why they are suffering. People are making personal lifestyle choices that are perhaps informed by dominant cultural values.

American cultural norms and social values foster individual competition and achievement. Within today's society Solomon choice is far more acceptable than the route of the London cocktail party lady. Societal pressures and the construction of depression as perpetuated by the pharmaceutical industry have skewed the view of this issue to be only a medical problem in need to a regiment of pill treatments. However, the suffering discussed in the narratives comes from failure, alienation, and bad life decisions, not flawed biochemistry. In these narratives people suffered because there was a miss match between what people expected to happen in their lives(expectations) and what actually happened (outcome). Today's culture urges its members to adopt non-realistic expectations that will never be fulfilled, but this is not a serotonin problem.

Personal life style choices that require medication should not be labeled as illness in the context of cosmetic neurology. The athlete who simply *desires* to be stronger and faster in competition must not be confused with the asthmatic who physically *needs* medication to be able to breathe while running. Response to medication does not prove illness in cases of enhancement technology. Sufferers need to realize that they have choices; taking medication for a life they

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[212] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 125.
[213] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 125.

otherwise could not lead is a choice. The afflicted must be cognizant of this choice instead of blindly moving forward.

> *Imagine a society that subjects people to conditions that make them terribly unhappy, and then gives them drugs to take away their unhappiness. Science fiction? It is already happening...In effect, antidepressants are a means of modifying an individual's internal state in such a way as to enable him to tolerate social conditions that he would other wise find intolerable.*[214]

The excerpt above is from Theodore Kaczynski's *Industrial Society and Its Future*, more commonly referred to as the "Unabomber Manifesto," highlights the tension between medication and social worlds. The Prozac phenomenon is not the first time society has medicated members of the population to preserve the status quo. In the 1950s and 1960s, women were medicated with Miltown, amphetamine, barbiturates, Librium, and Valium to keep them "in their place, to make them comfortable in a setting that should have been uncomfortable, to encourage them to focus on tasks that did not matter."[215] These pills used in this context have collectively been referred to as 'mother's little helpers.' In the era of Stepford wives, these pills were popular and widely prescribed. The Rolling Stones even wrote a song about the effect of these pills:

> *Things are different today,*
> *I hear ev'ry mother say*
> *Cooking fresh food for a husband's just a drag*
> *So she buys an instant cake and she burns her frozen steak*
> *And goes running for the shelter of a mother's little helper*
> *And two help her on her way, get her through her busy day*
>
> *Doctor please, some more of these*
> *Outside the door, she took four more*
> *What a drag it is getting old*
>
> *Men just aren't the same today*
> *I hear ev'ry mother say*
> *They just don't appreciate that you get tired*
> *They're so hard to satisfy, You can tranquilize your mind*
> *So go running for the shelter of a mother's little helper*
> *And four help you through the night, help to minimize your plight.*[216]

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[214] Kaczynski, Theodore. Industrial Society and Its Future, 1995. in Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 125.
[215] Kramer, Peter D. Listening to Prozac. New York: Penguin Books, 1997. 39.
[216] Jagger, Mick, and Keith Richards. "Mother's little Helper," Aftermath. The Rolling Stones. 1965.

People medicate themselves to stand the condition of their life. Alternatively, instead of medicating to endure the status quo, they could ask what is so horrible about their life that makes them sad and work to change that aspect. Changing one's way of life to be happy is the approach fostered by the social Navigationn hypothesis. The violinist, Claudia Weaver, and the London cocktail party lady all adopted this approach to end their suffering. Andrew Solomon chose an alternate pathway. However, he was cerebrally aware of the decision he made, as opposed to blindly medicating himself to be consistent with cultural norms. Each made a personal choice, and each was aware of other options. No one was a passive victim, and no one can legitimately claim that his or her problem resulted from bad biochemistry alone. Each actor had agency to act, and each made his or her own choice, which had the power to change each individual accordingly.

Giving up and sticking to it in America – the consequences on identity.

Giving up on a dream comes into tension with transformation of identity and a vision of the future self, which would result from achieving a dream. The decision that the violinist made was monumental. She knew that she could no longer endure the pathway she had chosen, so she stopped. Stopping the competition and hard work necessary to achieve a dream comes into tension with the American way of life. Part of American identity is the rags-to-riches story, pulling yourself up by the boots straps, being who you want to be: This cultural identity does not mesh with "giving up."

While today's culture expects competition, hard work, and successes, society has also become intolerant to less pleasant demands of working hard. Hard work is rigorous and may require a degree of suffering in order to archive. However, the expectation of perpetual happiness and effortless success limits the ability and willingness to endure. This tension is explained in the medical arena. Sufferers turn to medication to achieve their goals of transformation by modifying the essential-self or to blunt painful insights about their life-decision and pathways chosen.

Given the implications for responsibility, Americans appear less willing to embrace non-biological paradigms for understanding depression. The biological paradigm is free of blame and any kind of responsibility. The lack of responsibility renders people powerless to change their fate without pharmacological intervention. "If depression is an organic disease – then insurance covers

it and it is not your fault. However, if it is part of your own causality then the sufferer "receives no more protection than does stupidity."[217]

A society where people pursue careers for which they have little aptitude becomes a short-lived society lacking reproductive fitness. Some people are not suited for various pursuits and, therefore, must cultivate their interests elsewhere. However, this view of depression and the corresponding treatment modality of reducing the stressor that causes depression have implications on how people choose to lead their lives and act in the face of adversity.

People risk giving up too easily and the equal danger of going down with the ship. Under what circumstance is it wise to persist in the face of adversity, and when is persisting foolhardy? If the violinist only practiced once a month for 10 minutes and was frustrated and depressed due to her lack of progress, quitting would appear wise. An alternative approach would be to modify her work ethic. If the violinist had a rigorous work ethic and was not making progress, choosing a different profession might be wise. However, if the violinist thinks that being a professional violinist entails only playing at Carnegie Hall and the Boston Philharmonic and that local venues such as state theaters and private functions are the venue of amateur violinists, then her decision to quite might appear to be foolhardy. She could have had a good career as a professional violist even if she was not at the top of her profession. In such an instance, modifying her expectations may have been more appropriate than modifying her career choice altogether. The hypothetical situations consider coming to terms with personal limitations and the ensuing alienation one may feel after seeing what T.S. Eliot refers to as "seeing the moment of your greatness flicker."[218] People do not always become who they set out to be. Not everyone can become the most popular girl at school, woman in the office, or life of the party. In order for someone to be popular, someone else must be unpopular to validate that person's popularity. In the American model of success, people can only be successful if others are unsuccessful.

The evolutionary model emphasizes channeling efforts toward productive pathways and removing stressors. Quitting is not the only way to be productive and to avoid stress. Instead of quitting, modifying expectations so that abilities and self-projects harmonize can also lead to *becoming*, though with a different vision of the final product.

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[217] Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 361.
[218] Elliott, T.S. "The Love Song of J. Alfred Prufrock." 1917. The Waste Land and Other Poems. Ed. Helen Vendler. New York: Signet Classics, 1998.

The sign post view of depression in combination with North American values send the message that people should give up in the face of adversity to avoid suffering. Though not always a realistic expectation, North Americans seems to value effortless success.

Suffering, melancholia, and the sadness that flows from failed endeavors are not feelings that are culturally embraced. Rather these feelings are actively avoided. In avoiding stressors which are the requisite challenges, people must rise to the challenge in order to become who they set out to be; otherwise, people loose out on the opportunity to become that person. When people rise to the challenge, regardless if they succeed or not, thier, personal identity changes.

Achievement comes with sacrifice, difficulty, and the trials of becoming. To live in Manhattan means enduring the pace. To climb to the roof of the world (Mt. Everest) means breathing the thin air. To be a professional violist means enduring the days of struggling to make it, unless talent come naturally. Even talents that come naturally require some degree of cultivation, which may be rigorous, difficult, and un-pleasurable. By avoiding these stressors or ignoring the sign posts' messages to cultivate other aspects of life, people miss out on where that suffering can lead, which may be well worth the arduous journey. More importantly, if people give up on dreams, they also give up a piece of their identity. However, if who they want to be does not take into consideration a realistic appraisal of personal abilities, then opting out is a wise course of action.

* * *

Throughout history, society has been changed and improved by people doggedly following their dreams to become the people they want to be. Through a commitment *to becoming*, society has seen the first Black women to get a PhD in physics, the Nobel laureate, the UN goodwill ambassador, the physician, and the scholar.

What course of actions should people take when the dreams get large and unruly or seem impractical and disconnected from reality? What about the scholarly athlete who wants to be top in her field and also wants to compete at the Olympic level, all before the age of 30? What about dreams of becoming that seem less noble? Should people follow these dream or just give up? Achieving these aspirations and dreams includes a component of identity that a person acquires in the becoming process. Some aspirations may seem more intrinsically worthwhile than others. The intrinsic worth of a dream does not increase or decrease the role dreams play in forging the identity of a person if that person truly desires to become what they dream.

In Carl Elliott's critiques of American culture through looking at what mental illness reveals about a society, he writes that it is possible to recognize "a life to be a failure or a success, even if we aren't always able to say exactly why." [219] How people allocate their resources is a component in determining the success or failure of a life since "some lives are better than others, quite apart from the psychic well-being of the person who is leading them." [220] This statement regards the quality of the decisions to be the ultimate answer to the question of how people act in the face of adversity. An unsuccessful life does not necessarily mean quitting; it could indicate a life of poor decision making, such as refusing to give up and quitting too soon.

A different face of this articulation is a person challenging himself or herself to become a certain kind of a person. Even if a person fails, he or she rose to the challenge. Failing by commission means rising to the challenge, while failing by omission means never trying. These are two different kinds of failure. Twentieth century novelist, Walker Percy, whose characters are Elliott's archetypes for the discussion of modernity and alienation, writes that "We all know perfectly well that the man who lives out his life as a consumer, sexual partner, and 'other-directed' executive; who avoids boredom and anxiety by consuming tons of newsprint, miles of movie film, years of TV time; that such a man has somehow betrayed his destiny as a human being." [221] These persons did not rise to the challenge of becoming. They failed by omission. They were never willing to face the pain of failing, and in doing so never allowed themselves to be in a position to experience the high quality pleasure of succeeding--of *becoming*. Then, there is Solomon's violinist, who fails by commission. She tried and her dream did not work out. Each will experience some degree of alienation and unrest.

In considering this sort of spiritual unrest, Elliott recommends reflecting on the context of a person's life in order to help him or her.

> *By ignoring such matters as how a person lives his life, by steadfastly refusing to pass judgment on whether the ideals he lives by are worthy or wasteful or honorable or demeaning, psychiatry can say nothing useful about alienation. It places itself in the position of neutrality about the broader structures of meaning within the lives that are lived, and from which they might be alienated.* [222]

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[219] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 11.
[220] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 11.
[221] Percy, Walker. Sign Posts in a Strange Land. Ed. Patrick Samway. New York: Farrar, Straus and Giroux. 1991, 12-13.
[222] Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 11.

Psychiatrists can help patients by assisting them in social Navigationn leading to the successful resolution of a problem or the realization of a dream. This can be achieved through modulating expectations so that dreams can be realized in portions or in their entirety. This means charting a course of achievement with realistic benchmarks which identify and act upon requisite plateaus of achievement

This process might be life-long. In this context, mental health professionals can help structure a pathway to the potential attainment of a life target and can function as a midwife to the birthing of dreams. From this position, 'such matters of how a person lives' are not ignored, but individual and arbitrary judgment is not passed on the quality of a vision. The patient experiences incremental successes; and, the failures and hardship of an unruly unrealistic dream have been circumvented.

In this capacity, psychiatrists can help patients realize goals by assisting to identify steps along the way, thus allowing clients to move closer to the realization of their dream. In this process, patients may realize at different benchmarks or plateaus of achievement that they no longer must achieve the dream in the same manner it was first articulated. A side path may be taken or the goal may be disregarded as the need for fulfillment has been satisfied by achieving benchmarks in the vision of the dream. In this process, patients can find healing, resolution, fulfillment, a comfort level, and peace. Individuals can change directions and be completely fulfilled because the achievement of the intervening benchmarks has been met in the healing process.

Conclusions.

Acting in a manner that is both healthy and fulfilling in the face of adversity is the challenge presented by the evolutionary perspective. This approach to social Navigationn requires honestly engaging with the self to realistically appraise personal abilities to make plans for the future. How these challenges are met affects identity and transformation of future selves through decision-making, responsibility, and action-taking.

Approaching depression in this fashion means locating the source of the problem in a culture that has unrealistic standards for success. Such a culture is unhealthy because the unattainable standards lead to a quest for fulfillment that will never be realized. Inflated standards emerge from media depictions of fulfillment that have become cultural expectations for what constitutes the good life. The problem is not biology, but inappropriate expectations of what a normal life holds. An otherwise happy life punctuated by difficulty and sadness is not seen as a normal life but as a

problematic existence. For Americans, transient moments of happiness are not enough, for people are told that they must be happy all the time. The expectation is that healthy people are happy people. The normal bouts of sadness in everyone's life have been recategorized as a medical condition which requires fixing.

Instead what need fixing is society's outlook and expectations. In knowing when to modify the dream or pathway, people can still achieve a desired life target, though in a less grandiose fashion, and can still find fulfillment in the achievement. People can reach the goal in climbing the summit of a lesser mountain, a different mountain, or the same mountain with a different root. This metaphor for social navigation can only be achieved through insight and self-reflexive dialog, as opposed to through medication. Very few people can live up to the cultural expectations of what is considered 'happy.' Following in this logic, most would be considered sad and, therefore, ill. This misdiagnosis is precisely what the pharmaceutical industry hopes for.

The violinist's and Claudia Weaver's narratives are examples of how the evolutionary perspective powerfully shapes decision-making leading to healing. The problems are social, and the solution is appropriate social navigation. In this context, depression is not an illness, but a mechanism of adaptive functioning in a complex social world.

Individuals choose some of the complexities, as explored by Solomon's narrative. Fate is responsible for other complexities. In either case, when people stand at a crossroad, they must make decisions and hope for a good outcome. If the outcome is not bright, they must recognize and take responsibility for any actions that gave rise to unfavorable circumstances. People must understand that sadness is sometimes the result of poor decision-making or bad luck, not a medical condition. Sufferers are presented with many opportunities to harness agency and make better futures though making wise, well-calculated, well-educated, realistic decisions. These kinds of decisions have the power to transform social identities in a more potent way than transformation accomplished through medication, as cosmetic pharmacology not only transforms social identity but also modifies aspects of the essential self.

The evolutionary approach to life's difficulties (depression) allows the essential self to remain unaltered while people become self-actualized and actively seek fulfillment. To paraphrase from the work and ideas of Carl Elliott, it is possible to access a life as a success even if we are not able to say exactly why. People who have successfully socially navigated choose not to blunt the growing pains. They evolved as people, and they *became*.

* * *

In the face of difficulty, some such as the violinist and the London cocktail party lady will choose to modify their lives to live within the bounds they can tolerate. These narratives show the ways in which the social navigation hypothesis can be implemented. Some will lead a less grand life, but they will not depend on pharmacology to become self-actualized. Others such as Solomon will choose not to rearrange their life, but to rearrange themselves as to better handle their life. These personal decisions have enormous consequences on identity and the transformation of future selves.

Sufferers must realize all the choices open to them and must understand the difference between taking medication to enhance their abilities as people verus taking mediation to heal an illness. Biological irregularities are a part of major depression. The degree to which these abnormalities are present in minor and sub-clinical variants of depression are less clear. Society needs a new definition for illness. Not all forms of suffering constitute a medical condition. Therefore, members of society must open their eyes to a culture that forces its members to live in unhealthy ways. In this case, the individual members are not the sick ones persay. The illness spoken of is located in society and works though its members when cultural norms are internalized. As long as people feel that they have no control, they will passively take medication for a disease. When a certain amount of agency has been harnessed, people may either chose to socially navigate their lives without medication, or they may choose to take medication to allow performance at the desired level, but they are no longer 'sick.'

* * *

The next chapter presents the biological dynamics of the depressive episodes. The chapter is a scientific account of the biological mechanics of depression which locate abnormalities in the serotonin system within the context of holistic body function. Dynamic systems biology looks at how changes in one system affect other systems, which impact global functioning. The etiology and pathogenesis of major clinical depression are only understood through an emergent paradigm that is cognizant of biopsychosocial interactions.

Not all episodes of sadness are depression, and not all forms of depression manifest to the depth and severity of major depressive illness. The next chapter discusses the biochemistry of major clinical depression. Not everyone experiencing the suffering, pain, and unrest of depression has these biochemical events occurring because much of what is detailed in the scientific account of the depressive episodes occurs more frequently at the core of the diagnosis category. Most of peoples' experiences and troubles are towards the nebulous perimeter of the category, where

depressive biology has not yet manifested, as their problems are rooted in navigation of social and philosophical media. As the severity and intensity increases, the social and philosophical problems will cross over and manifest biologically. How this crossover occurs is explained by the *stressor model of depression.* The effect of stress is explored from a dynamic biological system perspective on the whole body, while neural specific responses are examined by analyzing the connection between the *stressor model of depression* and the *neurogenetic theory of depression* in tandem.

Chapter 5: Biopsychosocial Theories of Depression

This chapter substantiates claims made in pervious chapters that depression is not merely a serotonin deficiency disorder by providing expansive scientific evidence as to what occurs in the body during a depressive episode. Since the paper criticizes the standard account of depression, thereby creating a void concerning the biological foundations of the disease, this chapter seeks to fill that void by providing an alternate biological paradigm. The alternate biological paradigm is a full-scope account of depression's biochemistry from the biopsychosocial perspective. The biochemical discourse is not limited to serotonin, and is interactive with psychosocial elements of the disease. The technical analysis bolsters claims made in pervious chapters by providing scientific evidence showing the interaction between psychosocial elements of depression and biology.

* * *

This chapter challenges the common portrayal of depression as a serotonin deficiency disorder, and counters the dominant medical paradigm with a view of depression from a dynamic biological systems perspective. This perspective stresses the interplay of a variety of body systems in disease. The body functions as a dynamic system composed of numerous subsystems. The functioning of each subsystem is a component of homeostatic functioning of the body, or dynamic system. Each subsystem functions in relation to one another. Therefore, changing an aspect of the subsystem produces changes in other subsystems. The dynamic system must correspondently adapt to this fundamental change. The changes experienced in subsystems as a result of a fundamental change are referred to as *cascade changes*.

Irregularities of the serotoninergic system are a cascade change that is the result of a greater fundamental change in the way the body manages stress. While serotonin abnormalities are part of the depression, they are not the only part of disease worthy of extensive research, development, and discourse. This chapter situates changes in serotonin levels in the context of numerous biochemical changes in the body through exploring the neuroendocrine response to stress. An overview of the *stressor model* and *neurogenic theory of depression* are presented through the lens of dynamic system biology.

The stressor model of depression may be considered part of a dynamics systems biological perspective as it looks at the effects of perceived physical and psychological stress on the entire body in addition to system specific responses. Considering the larger picture of how stress responses connect to the onset and maintenance of depression highlights the complexity of changes

occurring in the body extending beyond the serotonergic system. Changes in serotonin levels are part of a cascade of systems-specific responses as opposed to the fundamental biochemical changes that are responsible for causing depression.

In considering the body as a complete functional unit, as opposed to an amalgam of subsystems, dynamic systems biology offers a more effective way to normalize serotonin levels and other neuro/biochemical disturbances associated with depression than the traditional medical model. While past methodologies sought to balance cascade effects (such as serotonin levels) without addressing the root causes, this paradigm addresses and seeks to correct the fundamental change in the body that gives rise to cascade effects in other systems. Intervention at the level of the fundamental event responsible for causing cascade effects is required. The earlier the intervention in a cascade, the less far-reaching its effects will be, thereby diminishing the severity and number of systems affected.

A strong body of evidence indicates that stress hormones are implicated in the onset and maintenance of depressive episodes. Deregulation of the stress response system through cortisol hyperactivity and loss of neuroendocrine negative feedback control are theorized to be at the core of depression's pathophysiology.[223] Stress response deregulation is the fundamental change that creates cascade effects in all other body systems though the stress hormone cortisol, corticotropin-releasing hormone (CRH), and the hypothalamic-pituitary-adrenal (HPA).

Boosting serotonin levels is one way to influence depressive biochemistry. However, after considering biochemical pathways affected by stress and their connections to depression, alternate modes of intervention outside the current biomedical model may be affective in altering the pathophysiology of depression. The current medical model emphasizes serotonin, but does not address the underlying problem of stress.

When one embraces the paradigm and approaches depression from a biopsychosocial standpoint, one must also relinquish the traditional medical model that places serotonin at the core of the problem. Traditional pharmacological treatments, such as SSRIs, would no longer be a first line treatment for depression. Instead treatments would center around the core of this issue: stress. In this paradigm, cortisol blocking medication would replace SSRIs as a pharmacological first line treatment. Therapeutics and other treatment modalities would target reducing stressors and the

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[223] Habib K.E., Gold P.W., and Chrousos G.P. "Neuroendocrinology of Stress." Endocrinology & Metabolism Clinics of North America 30.3 (2001): 712; Gold, P.W., Wong M.L., and G.P. Chrousos G.P. "Stress System Abnormalities in Melancholic and Atypical Depression: Molecular, Pathophysiological, and Therapeutic Implications [editorial]." Molecular Psychiatry 1 (1996): 257-264.

effects of the stressor on the body through biochemical and behavioral means. Treatments may include modifying expectations, changing social Navigationn strategies, and entering into talk therapy targeted at modifying behavior to reduce stress.

* * *

In considering a complete physiological response to perceived stress and understanding how stress impacts the nervous and neuroendocrine system, a new way of looking at depression emerges. The new perspective shatters the old paradigm and brings a higher level of complexity to depression discourse. While this complexity requires an expanded technical vocabulary and attention to the non-linear aspects of how body systems connect, the purpose of this discourse is not to gain a technical mastery of non-reductionist biochemical disease process, but to appreciate how a scientific discourse shapes beliefs about disease and well-being. In adapting a different biochemical view of depression, the social location of the disease changes and climate in which cultures is viewed shifts in response to a change in discourse. What follows below is a presentation of fact that makes this paradigm shift evidence-based and empirically grounded. Previous chapters suggest a body of evidence for a new view of depression, and this chapter provides evidence to substantiate previous claims of what depression is and is not. Depression is the result of stress deregulation. Depression is not the result of serotonin abnormalities.

An Overview of changes in the body due to stress.

The body reacts to stress in two ways. The involuntary autonomic nervous system (ANS) is fast acting and immediately responds to stressors. The neuroendocrine system through the hypothalamic-pituitary-adrenal (HPA) axis is slower acting and prepares the body to respond to prolonged (chronic) stress.

The autonomic nervous system.

The fast acting *autonomic nervous system* is broken into two parts that function in opposite but complementary ways. The *sympathetic nervous system* prepares the body to deal with an acute stressor by marshalling stored energy though inhibition of energy storage functions such as glucongenesis; promoting energy release by increasing metabolism of stored products; focusing attention on perceived threat; enhancing vigilance; boosting cerebral blood flow and glucose usage; increasing cardiovascular out put; increasing respiration rates; delivering energy substrates to muscle; decreasing hunger and feeding behaviors; inhibiting reproductive physiology and behavior;

and suppressing immune function. In short, catabolism is increased and most of the body's fuel is dedicated to neural, cardiac, and muscle-skeleto systems.[224] Neurochemically, the increase in catabolism translates into basic metabolic changes including secretion of epinephrine by the adrenal medulla and norephinephrine by the sympathetic nerves. [225] This response to stress is organized by the sympathetic nervous system is referred to as the *flight or fight response.*

The *parasympathetic nervous system*'s main function is to return the body to a state of normalcy or *homeostasis* after a period of excitement. The main function of the parasympathetic nervous system is to 'rest and digest,' thereby off-setting the flight or fight response. The ability to re-establish homeostasis after periods of change is referred to as *allostasis.*[226] In other words, systems are turned on when they are needed and turned off when homeostatic balance has been achieved. However, rebalancing responses may be insufficient, and the cost to maintain homeostasis may be too high. In this situation, body wear and tear leads to disease.[227] The *allosteric load* refers to the 'wear and tear' a body endures to achieve allostasis and to return to homeostatic balance.[228]

The neuroendocrine system.

Research examining nonspecific generalized responses to stress began as early as 1936 when Selye identified adrenal hypertrophy, thymolymphatic dystrophy, and gastric ulceration as classic systems of prolonged stress response.[229] This research highlights the important of glucocortiod hormones secreted by the adrenal cortex and thus implicates the HPA axis.

The HPA axis is part of the neuroendocrine system that acts in concert with the nervous system. The HPA axis is a slower acting system then the ANS. The HPA axis is involved in regulating digestion, the immune system, energy usage, and the body's reaction to stress. The key components of the HPA axis are the paraventricular nucleus (PVN), which is part of the hypothalamus. The hypothalamus is a brain region responsible for regulating metabolic and

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[224] Chrousos G.P., and Gold P.W. "The Concepts of Stress and Stress System Disorders: Overview of Physical and Behavioral Homeostasis." Journal of the American Medical Association 267 (1992):1244-1252.
[225] Selye, H. "A Syndrome Produced by Diverse Nocuous Agents." Nature 138 (1936):32-36.
[226] Sterling, P and Eyer, J. "Allostasis: A New Paradigm to Explain Arousal Pathology." Handbook of Life Stress, Cognition and Health. Ed. S. Fisher and J. Robinson. New York: John Wiley & Sons, 1981.
[227] Selye, H. "Syndrome Produced by Diverse Nocous Agents." Nature 138 (1936): 32.
[228] Schulkin, J., Gold, P.W., and McEwen, B.S. "Introduction of Corticotrophin-releasing Hormone Gene Expression By Glucocorticoids: Implications for Understanding the States of Fear and Anxiety and Allostatic Load." Psychoneuroendocrinology 23 (1998): 219-243.
[229] Selye, H. "Forty Years of Stress Research: Principal Remaining Problems and Misconceptions." Canadian Medical Association Journal 115 (1976): 53-56.

autonomic functions. The hypothalamus links the nervous system to the endocrine system though neurohormones and hormone secretion cascades. The PVN region of the hypothalamus contains neuroendocrine neurons which make and secrete vasopressin and corticotrophin releasing hormone (CRH).[230] These two peptides, or short proteins, regulate the anterior lobe of the pituitary gland, and facilitate the secretion of adrenocorticototrophic hormone (ACTH). ACTH acts on the adrenal cortices, located just above the kidney. The adrenal cortices produce glucocortiods, cortisol, and corticosteroid hormone, which are released into the blood stream.[231] Corticosteroid hormone release is also facilitated by the release of epinephrine by the adrenal medulla, which further supports autonomic nervous system response.[232]

Corticosteroid hormones influence both subsystems of the ANS though high and low type affinity receptor subtypes (CRH-1 and CRH-2) that are co-localized in limbic neural circuitry. CRH-1 and CRH-2 "drive in anti-parallel fashion the sympathetic and parasympathetic components of the stress response system."[233] Mineralcorticoid receptors (MR) or the CRH-1 receptor subtype participate in the flight or fight response in preparing the body for stress. MRs mediate "higher brain function involved in control of sensitivity and/or threshold, while glucocorticoid receptors (GR) facilitate termination of the stress response"[234] through the CHR-2 receptor subtype in the parasympathetic nervous system, which facilitates late-sustained coping mechanisms.

Cortisol acts in the maintenance of energy levels though regulating the metabolism of proteins, carbohydrates, and fats, in addition to balancing the effects of insulin during sugar anabolism or catabolism, cardiovascular function, blood pressure, and reduction of immuno-inflammatory response. Therefore, cortisol provides the body with adequate fuel to deal with the stressful event for a sustained time period.[235] When the amount of cortisol in the blood stream is sufficient, the hypothalamus and anterior pituitary release less CRH and ACTH, and the adrenal

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[230] Some times corticotrophin releasing hormone (CRH) is referred to as corticotrophin releasing factor (CRF). For the purposes of this paper the two can be used interchangeably, but for consistency CRH will be used.
[231] Chrousos G.P. "Stressors, Stress, and Neuroendocrine Integration of the Adaptive Response: The 1997 Hans Selye Memorial Lecture." Annals of the New York Academy of Sciences 851 (1998): 311-335.
[232] Habib K.E. "Role of Brain-adrenal-gastric Axis in Modulating Gastric Functions during Acute Stress in Male Albino Rats." MSc Dissertation (Physiology), Minio University Faculty of Medicine, El-Minio, Egypt, in Habib K.E., Gold P.W., Chrousos G.P. "Neuroendocrinology of Stress." Endocrinology & Metabolism Clinics of North America 30.3 (2001): 695-728; Habib KE, Negro PJ, Dib A, et al. "Endogenous Opioids Contribute to Gastric Ulcerogenesis During Stress in Male Sprague-Dawley Rats." Gastroenterology 116 (1999): A179.
[233] Van Pragg, Herman M., de Kloet, Ron, and van Os, Jim. Stress the Brain and Depression. Cambridge: Cambridge University Press. 2004, 145.
[234] Van Pragg, Herman M., de Kloet, Ron, and van Os, Jim. Stress the Brain and Depression. Cambridge: Cambridge University Press. 2004, 145.
[235] Straug R.O. "Health Psychology." Stress and Health. Ed. Jessica Bayne. New York: Worth Publishers, 2002.

cortex releases less cortisol. However, in the case of a problem with negative feedback regulation and inhibition cortisol production, the stress system response becomes deregulated.

Glucocorticoids and cortisol are the final products of the HPA pathway. Their affect on target tissues are described above. Glucocorticoids also play a regulatory role in basal control of HPA activity by terminating the stress response through negative feedback control of HPA in the inhibitory effects of neurotransmitter GABA to the PVN[236] by CHR-2 receptor action, which is slow acting. Feedback control also occurs through fast acting CRH-1 receptors (MR), which are responsive to low levels of glucocortiods, thereby limiting the duration of tissue exposure to CRH, which has catabolic, lipogenic, anti-reproductive, and immunosuppressive effects on the body as brought on by stress.

If the stress response is not quelled by allosteric regulation, the stress response becomes sustained or augmented, causing target tissue overexposure to cortisol. In this situation, the body acts as if it were under stress, when there is no longer a stressor. The short term advantages of the stress response involving cardiovascular output, respiration, digestion, energy utilization, cessation of reproductive behaviors, and immuno-suppression turn into detriments in the long-run because these responses were designed to be short-lived. Cortisol, increases in concentration when the HPA axis is stimulated for long periods and has been used as a quantitative measurement of the degree of stress in one's life.[237]

In the context of the HPA axis and sympathodrenal system, stress has the ability to "influence virtually every cell in the body."[238] Should this system experience difficulty in the form of hyperactivity or deregulation the entire body is affected, as cortisol acts on a number of target tissues.

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All of the brain regions and pathways mentioned above have additional functions, as they are part of interlocking subsystems. When the stress response system goes awry, important secondary, tertiary, and quaternary effects produce multidimensional cascade changes, some of which even feed back on themselves. The process of stress regulation described above is linear.

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[236]Korte S.M., Bouws G.A., and Bohus B. "Central actions of corticotropin-releasing hormone (CRH) on behavioral, neuroendocrine, and cardiovascular regulation: Brain corticoid receptor involvement." Hormones and Behavior 27 (1993):167-183; Michelson D., Chrousos G.P., and Gold P.W. "Type I Glucocorticoid Receptor Blockade Does Not Affect Baseline or Ovine Corticotropin-releasing Hormone-stimulated Adrenocorticotropic Hormone and Cortisol Secretion." Neuroimmunomodulation 1 (1994): 274-277.

[237] Kalat, J.W. Biological Psychology. Ed. J. Strandberg. 7 ed. Belmont: Wadsworth/Thomson Learning, 2001. 335-362.

[238] Gold, P.W., Goodwin, F.K., and Chrousos, G.P. "Clinical and biochemical manifestations of depression: Relation to the neurobiology of stress." New England Journal of Medicine 319 (1988): 348-353.

The discourse and analysis of secondary, tertiary, and quaternary effects of stress deregulation is not linear due to the volume of components necessary to gain a complete nuanced understanding and due to the way the components interrelate. The mechanisms underpinning particular relationships are just beginning to be researched and studied in a non-reductionistic context. The present research on neuropeptide Y is illustrative of this point.

Neuropeptide Y.[239]

Research on neuropeptide Y (NPY) reveals that this hormone is implicated in the stress-depression-cortisol puzzle. NPY is involved in the "regulation of centrally mediated functions,"[240] as it has been observed to affect memory processing,[241] feeding behavior,[242] and circadian rhythms via the pathway from the thalamic ventrolateral geniculate to the hypothalamic suprachiasmatic nucleus,[243] in animals. Mammals injected with NPY eat excessively, likely due to modulation of the hypothalamic feeding center.[244] NPY affects anterior pituitary hormone secretion, autonomic nervous system control, and other neurotransmitter systems.[245]

Relating to affective disorders, three studies have found that NPY mediates anxiolytic effect in rats,[246] and alterations of central NPY are present in both stress and mental illness.[247] More

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[239] The research present in this section relied heavily on a paper by Husum, H., Mikkelsen, J.D., Hogg, S., Mathe, A.A., Mork, A (2000), and the section on neuropeptide Y in a paper by Habib K.E., Gold P.W., and Chrousos G.P. (2001) paper.

[240] Husum, H., Mikkelsen, J.D., Hogg, S., Mathe, A.A., and Mork, A. "Involvement of Hippocampal Neuropeptide Y in Mediating the Chronic Actions of Lithium, Electroconvulsive Stimulation and Citalopram." Neuropharmacology 39.8 (2000): 1463-1473.

[241] Flood, J.F., Hernandez, E.N. and Morley, J.E. "Modulation of Memory Processing by Neuropeptide Y." Brain Research 421 (1987): 280–290.

[242] Stanley, B.G., Chin, A.S. and Leibowitz, S.F. "Feeding and Drinking Elicited By Central Injection of Neuropeptide Y: Evidence For a Hypothalamic Site(s) of Action." Brain Research Bulletin 14 (1985): 521–524; Levine, A.S. and Morley, J.E. "Neuropeptide Y: A Potent Inducer of Consummatory Behavior in Rats." Peptides 5 (1984): 1025–1029.

[243] Huhman, K.L., Gillespie, C.F., Marvel, C.L. and Albers, H.E. "Neuropeptide Y Phase Shifts Circadian Rhythms in Vivo Via a Y2 Receptor." Neuroreport 7(1996): 1249–1252; Biello, S.M., Golombek, D.A., Schak, K.M. and Harrington, M.E. "Circadian Phase Shifts to Neuropeptide Y in Vitro: Cellular Communication and Signal Transduction." Journal of Neuroscience 17 (1997): 8468–8475.

[244] Heilig, M., and Widerlov, E. "Neurobiology and Clinical Aspects of Neuropeptide Y." Critical Reviews in Neurobiology 9 (1995): 115-136.

[245] Habib K.E., Gold P.W., Chrousos G.P. "Neuroendocrinology of Stress." Endocrinology & Metabolism Clinics of North America 30.3 (2001): 704.

[246] Heilig, M., Söderpalm, B., Engel, J.A. and Widerlöv, E. "Centrally Administered Neuropeptide Y (NPY) Produces Anxiolytic-like Effects in Animal Anxiety Models." Psychopharmacology 98 (1989): 425–429; Britton, K.T., Southerland, S., Van Uden, E., Kirby, D., Rivier, J. and Koob, G. "Anxiolytic Activity of NPY Receptor Agonists in the Conflict Test." Psychopharmacology *(Berlin)* 132 (1997): 6–13; Wahlestedt, C., Pich, E.M., Koob, G.F., Yee, F. and Heilig, M. " Modulation of Anxiety and Neuropeptide Y–Y_1 Receptors by Antisense Oligodeoxynucleotides." Science 259 (1993): 528–531.

[247] Calogero, A.E., Gallucci, W.T., Gold, P.W., et al. "Multiple Feedback Regulatory Loops Upon Rat Hypothalamic Corticotropin-releasing Hormone Secretion: Potential Clinical Implications." Journal of Clinical Investigation 82

specifically, a clinically significant negative correlation has been observed between NPY levels in CSF and anxiety scores of depressed persons,[248] indicating that anxiety is a core component of the depressive syndrome, and underpinning several other affective disorders. Accordingly, the psychopathologic states of anxiety and depression "may share a common biologic basis because both respond to classic antidepressant treatment. Local microinjections of NPY into the central nucleus of the amygdala reproduced the anxiolytic-like effect of intracerebroventricular injections but [do] not affect food intake,"[249] thereby indicating the dual effects can be separated.

Husum and colleagues believe that NPY effects on centrally mediated functions in depressed persons suggest a connection "between [the] disruption of normal NPYergic neurotransmission and the symptoms observed in depressed patients."[250] However, due to a lack of evidence, no support for the correlation between depression and polymorphic alleles of the NPY gene can be found in the literature at this time. Instead, Detera-Wadleigh and colleagues suggest that deregulation of the NPY system may be the result of a secondary event (as opposed to a primary event).[251] While this idea appears promising, it has not yet been consistently demonstrated, as cerebrospinal fluid (CSF) sampling for the level of NPY-like immunoreactivity (NPY-LI) in plasma were found to be either reduced[252] or unchanged[253] in depressed persons. However,

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(1988): 767-774; Castro, M., and Moreira, A.C. "Regulation of Corticotropin-releasing Hormone Secretion by ACTH at Different Times after Adrenalectomy." Brazilian Journal of Medical and Biological Research 29 (1996): 1573-1578.

[248] Heilig, M., and Widerlov, E. "Neurobiology and Clinical Aspects of Neuropeptide Y," Critical Reviews in Neurobiology 9 (1995): 115-136; Heilig, M., Söderpalm, B., Engel, J.A. and Widerlöv, E. "Centrally Administered Neuropeptide Y (NPY) Produces Anxiolytic-like Effects in Animal Anxiety Models." Psychopharmacology 98 (1989): 425–429; Munglani, R., Hudspith, M.J., and Hunt, S.P. "The Therapeutic Potential of Neuropeptide Y: Analgesic, Anxiolytic and Antihypertensive." Drugs 52 (1996): 371-389; Wettstein, J.G., Earley, B., and Junien , J.L. "Central Nervous System Pharmacology of Neuropeptide Y." Pharmacology and Therapeutics 65 (1995): 397-414.

[249] Habib K.E., Gold, P.W., and Chrousos, G.P. "Neuroendocrinology of Stress," Endocrinology & Metabolism Clinics of North America 30.3 (2001): 695-728

[250] Husum, H., Mikkelsen, J.D., Hogg, S., Mathe, A.A., and Mork, A. "Involvement of Hippocampal Neuropeptide Y in Mediating the Chronic Actions of Lithium, Electroconvulsive Stimulation and Citalopram." Neuropharmacology 39.8. (2000): 1463-1473.

[251] Detera-Wadleigh, S.D., de Miguel, C., Berrettini, W.H., DeLisi, L.E., Goldin, L.R. and Gershon, E.S. "Neuropeptide Gene Polymorphisms in Affective Disorder and Schizophrenia." Journal of Psychiatric Research 22 (1987): 581–587.

[252] Nilsson, C., Karlsson, G., Blennow, K., Heilig, M., and Ekman, R. "Differences In the Neuropeptide Y-like Immunoreactivity of the Plasma and Platelets of Human Volunteers and Depressed Patients." Peptides 17 (1996): 359–362; Hashimoto, H., Onishi, H., Koide, S., Kai, T., and Yamagami, S. "Plasma Neuropeptide Y in Patients With Major Depressive Disorder." Neuroscience Letters 216 (1996): 57–60; Widerlöv, E., Lindström, L.H., Wahlestedt, C., and Ekman, R. "Neuropeptide Y and peptide YY as Possible Cerebrospinal Fluid Markers for Major Depression and Schizophrenia, Respectively." Journal of Psychiatric Research 22 (1988): 69–79; Widerlöv, E., Heilig, M., Ekman, R., and Wahlestedt, C. "Possible Relationship Between Neuropeptide Y (NPY) and Major Depression — Evidence From Human and Animal Studies." Nordisk Psykiatrisk Tidsskrift 42 (1998) 131–137; Widerlöv, E., Wahlestedt, C., Håkanson, R. and Ekman, R., "Altered Brain Neuropeptide Function in Psychiatric Illnesses With Special Emphasis on NPY and CRF in Major Depression." Clinical Neuropharmacology 9 (1996): 572–574.

increased levels of CSF NPY-LI in depressed persons who responded to electroconvulsive therapy (ECT) has also been observed.[254]

Electroconvulsive stimulation (ECS) is an adaptation of human electroconvulsive therapy (ETC) but modified for animals. ECS research found that administration of ECS significantly increased NPY-LI levels in the hippocampus and cortical regions.[255] Evidence indicates that "different treatments, effective in the alleviation of depression, lead to neurochemical changes consistent with an increase in NPYergic neurotransmission in areas relevant for behavioral activation and perception of emotional states."[256] In addition to ECS, antidepressant medication of the SSRI type has been observed to have the aforementioned effects.

Interestingly, NPY also has antidepressant-like actions. NPY "was demonstrated to reduce the duration of immobility in the rat forced swim test,"[257] which is widely accepted as a screening tool used to detect and differentiate the treatments that have antidepressant-like actions from the effects of anxiolytic compounds.[258]

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[253] Berrettini, W.H., Doran, A.R., Kelsoe, J., Roy, A. and Pickar, D., "Cerebrospinal Fluid Neuropeptide Y in Depression and Schizophrenia." Neuropsychopharmacology 1(1987): 81–83; Roy, A., "Neuropeptides in Relation to Suicidal Behaviour in Depression." Neuropsychobiology 28 (1993): 184–186; Gjerris, A., Widerlöv, E., Werdelin, L. and Ekman, R. "Cerebrospinal Fluid Concentrations of Neuropeptide Y in Depressed Patients and In Controls." Journal of Psychiatry and Neuroscience 17 (1992): 23–27.

[254] Mathé, A.A., Rudorfer, M.V., Stenfors, C., Manji, H.K., Potter, W.Z. and Theodorsson, E. "Effects of Electroconvulsive Treatment on Somatostatin, Neuropeptide Y, Endothelin, and Neurokinin: A Concentrations in Cerebrospinal Fluid of Depressed Patients: A pilot Study." Depression 3 (1996): 250–256.

[255] Stenfors, C., Mathé, A.A. and Theodorsson, E., "Chromatographic and Immunochemical Characterization of Rat Brain Neuropeptide Y-like Immunoreactivity (NPY-LI) Following Repeated Electroconvulsive Stimuli." Journal of Neuroscience Research 41(1995): 206–212; Stenfors, C., Mathé, A.A. and Theodorsson, E. "Repeated Electroconvulsive Stimuli: Changes in Neuropeptide Y, Neurotensin and Tachykinin Concentrations in Time." Progress in Neuro-Psychopharmacology and Biological Psychiatry 18 (1994): 201–209; Wahlestedt, C., Blendy, J.A., Kellar, K.J., Heilig, M., Widerlöw, E. and Ekman, R. "Electroconvulsive Shock Increase the Concentration of Neocortical and Hippocampal Neuropeptide Y(NPY)-like Immunoreactivity in the Rat." Brain Research 507 (1990): 65–68; Mathé, A.A., Gruber, S., Jimenez, P.A., Theodorsson, E. and Stenfors, C. "Effects of Electroconvulsive Stimuli and MK-801 on Neuropeptide Y, Neurokinin A, and Calcitonin Gene-related Peptide in Rat Brain." Neurochemistry Research 22 (1997): 629–636.

[256] Weiner, E.D., Mallat, A.M., Papolos, D.F. and Lachman, H.M. "Acute Lithium Treatment Enhances Neuropeptide Y Gene Expression in Rat Hippocampus." Brain Research, Molecular Brain Research 12 (1992): 209–214; Zachrisson, O., Mathé, A.A., Stenfors, C., and Lindefors, N. "Region-specific Effects of Chronic Lithium Administration on Neuropeptide Y and Somatostatin mRNA Expression in the Rat Brain." Neuroscience Letters 194 (1995): 89–92; Mathé, A.A., Jousisto-Hanson, J., Stenfors, C. and Theodorsson, E. "Effect of Lithium on Tachykinins, Calcitonin Gene-related Peptide, and Neuropeptide Y in Rat Brain." Journal of Neuroscience Research 26 (1990): 233–237; Widdowson, P.S., and Halaris, A.E. "Chronic Desipramine Treatment Reduces Regional Neuropeptide Y Binding to Y_2-type Receptors in Rat Brain." Brain Research 539 (1991): 196–202.

[257] Husum, H., Mikkelsen, J.D., Hogg, S., Mathe, A.A., and Mork, A. "Involvement of Hippocampal Neuropeptide Y in Mediating the Chronic Actions of Lithium, Electroconvulsive Stimulation and Citalopram." Neuropharmacology 39.8. (2000): 1463-1473.

[258] Porsolt, R.D., Anton, G., Blavet, N. and Jalfre, M. "Behavioural Despair in Rats: A New Model Sensitive To Antidepressant Treatments." European Journal of Pharmacology 47(1987): 379–391; Porsolt, R.D., Le Pichon, M., and Jalfre, M. "Depression: A New Animal Model Sensitive to Antidepressant Treatments." Nature 266 (1977): 730–732.

Coming full circle in the stress-depression-cortisol puzzle, exposure to CHR leads to reductions of NPY and gonadotropic-releasing hormone (GnRH) secretion from the hypothalamus, followed by later reductions of pituitary gonadotropin secretion.[259]

According to the role NPY plays in the stress-depression-cortisol interaction, every axis of the body acts in concert. The linear analysis, essential in the traditional medical model and glorified by the pharmaceutical industry, is unable to provide a useful vocabulary to discuss the dimensionality of the changes occurring. In the story of NPY, other actors and subplots are worthy of their own story in the stress-depression-cortisol puzzle; however, they were not explored as the focus was on NPY. Every brain region, neurochemical, hormone, and cascade secretion mentioned above has its own story. In the discussion of depression and stress, the same complement of brain regions, neurochemicals, and hormones are mentioned. As research persists, all the ways that they relate to each other are becoming clearer.

* * *

The purpose of this section is not solely to inform the reader of the role of NPY in depression, as much as it is to show the depth and complexity of the systems at work. NPY is but one neuromodulator of centrally-mediated functions. Other important functions are also affected by stress and CRH exposure and do not relate to each other in clear ways.

For instance, stress is a known immunosuppressant.[260] Detailed work in this field has revealed more nuanced meanings to the blanket statement that stress is a known immunosuppressant. Stress may increase humoral immunity while it suppresses cellular immunity. This response is mediated by glucocorticoids, helper-T cells, and cytokine production. Acute stress launches proinflammatory responses through release of CRH and the mast cell-histamine axis.[261] This change is beneficial in the sort term but not in the long term. Increases in cortisol decrease white blood cell counts, thereby impairing immune response.[262] In instances of sustained stresses, the proinflammatory response has the propensity to launch a vicious feedback cycle due to escalating level of cortisol.

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[259] Chrousos GP, and Gold, P.W. "The Concepts of Stress and Stress System Disorders: Overview of Physical and Behavioral Homeostasis." Journal of the American Medical Association 267 (1992): 1244-1252.
[260] Elenkov, I.J., and Chrousos, G.P. " Stress Hormones, Th1/Th2 Patterns, pro/anti-inflammatory Cytokines and Susceptibility to Disease," Trends in Endocrinology and Metabolism 10 (1999): 359-368.
[261] Elenkov, I.J., and Chrousos, G.P. "Stress Hormones, Th1/Th2 Patterns, pro/anti-inflammatory Cytokines and Susceptibility to Disease," Trends in Endocrinology and Metabolism 10 (1999): 359-368.
[262] Walport L. Malignant Sadness: The Anatomy of Depression. New York: The Free Press, 1999.

A proinflammatory response means that the body is sending a signal to all systems that it is under stress, which means that cortisol is being secreted. High levels of cortisol have been observed to lesion and atrophy the hippocampus. Hippocampal lesioning is further perceived as a stress, and the body responds to the stressor by secreting more cortisol. Hence the vicious feedback cycle continues along with escalating hippocampal lesioning, cell death, and atrophy.[263] Hippocampal damage is a significant aspect of the pathophysiology of major depression. This phenomenon factors into the neurogenetic theory of depression; cascade effects to the hippocampus are examined in detail later in the chapter. As the stress-depression-cortisol puzzle unfolds in this chapter, the interconnectedness of all of the aforementioned systems and neurochemicals remain significant.

Gross anatomical effects and implications for sequelae.[264]

Outside the brain, cortisol has been observed to have gross anatomical effects though numerous subsystems. Gross effects of cortisol have been observed to promote insulin resistance, atherosclerosis, impaired growth, and bone loss.[265] Stress leads to differential activation of vagal and sacral parasympathetic efferents know to mediate gut responses and thereby to influence digestion.[266] As discussed in relation to NPY, stress influences feeding behavior. Analyzing these data together creates massive implications for the far reaching effects of stress on the digestive tract. To recap, stress has been observed to influence feeding behavior, gut responses, and insulin uptake. Food intake and ability to harvest nutrients and energy have consequences for dynamic system functioning, as factors that influence digestion, also have secondary, tertiary, and quaternary effects on excretion, fluid levels, and energy utilization. Effects on energy utilization are significant as they moderate activity levels, lethargy, and feelings of malaise.

Outside the brain, these changes are accompanied by increased prolactin secretion which is also released during both male and female orgasms, milk production in women, and uterine contractions during child birth, and pancreatic glucagons, which facilitate glucose uptake into cells. The gross anatomical effects of cortisol hyperactivity or recurrent stress provide interesting and compelling evidence situating CRH irregularities at the beginning of melancholic depression. An

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[263] Kalat, J.W. Biological Psychology. Ed. J. Strandberg. 7 ed. Belmont: Wadsworth/ Thomson Learning, 2001. 335-362.

[264] Research presented in this section relied heavily on a review article written by Habib K.E., Gold P.W., and Chrousos G.P. (2001).

[265] Meyer, S.E., Chrousos, G.P., and Gold, P.W. "Major Depression and the Stress System: A Life Span Perspective." Development and Psychopathology 13 (2001): 565-80.

[266] Habib KE, Negro PJ, Dib A, et al. "Endogenous Opioids Contribute to Gastric Ulcerogenesis During Stress in Male Sprague-Dawley Rats." Gastroenterology 116 (1999): A180.

autopsy study on depressed patients found greater numbers of PVN, CRH, AVP neurons, suggesting a robust and reinforced stress response axis. Imaging studies have found depressed patients to have decreased metabolic activity in the subgenual medical prefrontal cortex, and marked hippocampal atrophy. [267] The meaning of these findings will be discussed in the section that examines hippocampal neurogenesis.

Patients with melancholic depression and or stress hyperactivity may sustain somatic sequelae. Sequelae pathological conditions result from a prior disease, injury, or attack· Sequelae associated with melancholic depression and/or stress hyperactivity including innate and T helper 1-directed immunosupression, osteoporosis, and pathology associated with metabolic syndrome X. Metabolic syndrome X is cluster of metabolic disorders resulting from the primary disorder of insulin resistance. As mentioned earlier, insulin resistance is facilitated by high levels of CRH.

A mineral bone density study of young persons (both male and female) with recurrent depression found clinically significant loss of bone mineral density when compared to a normal population.[268] Another study found osteoactivity of depressed persons to be similar to patients who have Cushing's syndrome,[269] which is characterized by overproduction of cortisol. A frequent co-morbid diagnosis in Cushing syndrome is depression.

As the discussion of depressive pathology broadens, a package of symptoms, emotional states, and neurochemistry relate to each other in complex and intimate ways. All are associated with cortical exposure and HPA hyperactivity. As the story continues, the same brain regions, chemical compounds, and drugs are discussed again and again. With each mention, a new connection and dimension of the interaction will be articulated.

Conclusions.

Given the many acute and sustained effects stress has on the body, the stress-response system was designed to be time-limited as it accompanies antireproductive, antigrowth, catabolic, and immunosuppressive effects, which offer temporary benefits that are detrimental in the long run. In chronic stress, cortisol hyperactivity, or deregulation of the stress system are affects which were

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[267] Gold, P.W., and Chrousos, G.P. "The Endocrinology of Melancholic and Atypical Depression: Relation to Neurocircuitry and Somatic Consequences." Proceeding of the Associaion of American Physicans 111 (1999): 22-34.
[268] Michelson, D., Stratakis, C., Hill, L., Reynolds, J., Galliven, E., Chrousos, G., and P. Gold "Bone Mineral Density in Women with Depression." New England Journal of Medicine 335 (1996): 1176-1181.
[269] Michelson, D., and Gold, P.W. "Pathophysiologic and Somatic Investigations of Hypothalamic-pituitary-adrenal Axis Activation in Patients with Depression." Annals of the New York Academy of Sciences 840 (1999): 717-722.

supposed to be temporary but are prolonged and harmful. The stressor model of depression seeks to explain the pathophysiology of clinical depression through the effects of sustained stress responses.

The purpose of describing the stress response in such detail is to show the complexity and interconnectedness of body systems. A change in one biochemical relationship has cascade effects not only in that particular system, but in other body systems as well. To reduce a multifactorial problem such as depression to a single serotonergic issue is unhelpful and ultimately detrimental in understanding and treating depression. The traditional medical model over-looks root cause, and instead focuses on medical secondary, tertiary, and quaternary aspects of the disease. The issue in need of attention, discourse, and analysis is stress pathways in the body, and more holistically framed, in culture.

* * *

The first half of the chapter presented a broad view of how stress affects the body. Key components of the stress-depression-cortisol puzzle were introduced and some basic interactions were highlighted. The remainder of the chapter will focus on the hippocampus and connecting the stressor model of depression with the neurogenic theory of depression. In focusing on the hippocampus, the role serotonin plays is contextualized as the story comes full circle. Serotonin is an important component of the stress-depression-cortisol puzzle, yet after reflecting on how stress underpins depression, the stature of serotonin diminishes from how it is presented in popular cultural and the traditional medical model.

The Neurogenenic Theory of Depression.

The adult mammalian brain has the ability to grow and regenerate neurons throughout the lifespan. This phenomenon is referred to as neurogenesis, which is a daily process due to a basal rate of neurogensis required for healthy functioning. Higher rates of neurogenesis are associated with novel environments and learning and memory tasks. Diminished neurogenic rates are associated with cognitive deficits present in depression, difficulty in learning and memory tasks, unstimulating environments, depressive pathophysiology, and stress.

The role of the hippocampus is memory consolidation. Here the brain selects which short term memories will be stored and entered into long term memory. Un-stored memories are discarded. Hippocampus damage has been demonstrated to impair memory function, especially the formation of new memories, and to impair future learning. Memory failure and difficulty learning are symptoms of depression and have been observed in chronically stressed rats and depressed

people.[270] The neurogenic theory of depression provides a mechanism that is able to account for the cognitive changes associated with depression and is consistent with the approach presented by the stressor model of depression.

A stress-induced decline in neurogenesis is a factor in the onset of depressive episodes, as evidence indicates that stress may be the causal element in the onset of depression.[271] Numerous studies have demonstrated that depressed patients undergo numerous neurophysiological changes. Part of theses changes are tied to proinflammatory response of acute stress mentioned earlier in the chapter. Chronic stress damages the hippocampus in several ways. One, apoptosis, or cell death, occurs due to elevated cortisol levels, which result in hippocampal volume loss and fewer neurons. Two, neurogenesis rates are depressed, so the hippocampus is unable to compensate for the loss of neurons. The specific site of neurogenic impairment is the dentate gyrus, a subsection of the hippocampus. Three, dendritic arborazation, also called dendritic branching, occurs in Ammon's Horn, a subsection of the hippocampus. Dendritic branching is biologically significant because it reduces dendrite length, impairing the dendrite's sole function of picking up information (as it now spans a shorter distance) and transmitting it to the neuronal cell body. The cell body decides whether or not to act on the information inputs (stimulus) picked up by the dendrite.[272] In short, the flow of information, or signal transduction pathway, is disrupted. Hippocampal lesions form via these mechanisms. The lesions are perceived as a further stressor. CHR secretion increases, and a vicious feedback cycle begins. After repeated exposure to physical or psychological stress, the hippocampus atrophies as a result of the loss of CA3 pyramidal neurons[273] and hippocampal granule cells.[274]

Overall changes can be observed in the hippocampus, limbic system, basal ganglia, amygdala, and orbitofrontal cortex as a result of chronic exposure to stress. Reduction in brain volume and cortical thickness occurs as a result of neuronal death and failure to compensate tough neurogenesis. The rate of neurogenesis becomes depressed. The decrease in neurogenesis stops new hippocampal cells from forming, and thus the normal 'recycling' of brain cells stops.

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[270] Wolpert, L. Malignant Sadness: The Anatomy of Depression. New York: The Free Press, 1999.
[271] Kendler, K.S., Karkowski, L.M., and Prescott, C.A. "Casual Relationship between Stressful Life Events and the Onset of Major Depression." American Journal of Psychiatry 15 (1999): 837-841.
[272] McEwen, B.S. "Effects of Adverse Experiences for Brain Structure and Function." Biological Psychiatry 48 (2000): 721-731.
[273] Margarinos, A., McEwen, B., Flugg, G., and Funchs, E. "Chronic Psychosocial Stress Causes Apical Dendrite Atrophy of Hippocampal CA3 Pyramidal Neurons in Subordinate Tree Shrews." Journal of Neuroscience 16 (1996): 3534-3540; McEwen, B.S. "Stress and Hippocampal Plasticity." Annual Review of Neuroscience 22 (1999): 105-102.
[274] Tanapat, P., Galea, L.A., and Gould, E. "Stress Inhibits the Proliferation of Granule Cell Precursors in the Developing Denate Gyrus." Journal of Developmental Neuroscience 16 (1998): 235-239.

Recycling refers to the forming of new neurons to replace the dying ones. When recycling stops, neuronal volume decreases. The slowing of neurogenesis is related to actual cell death. Decreased neurogenesis is a result of stress induced and rises in cortisol levels, which reduces seteronergic transmission.

In studying how SSRIs manipulate serotonin levels, the connection between pharmacological treatments for depression and neurogenesis rates have begun to be understood. During development, serotonin has been observed to promote neurogenic effects in the brain,[275] while in adulthood, serotonin is involved in synaptic plasticity, through its actions on the 5-HT 1A receptor sites (which is a serotonin specific receptor subtype). The 5-HT 1A receptor is most densely localized in the hippocampus.[276] Antidepressant treatment therapies increase the activity of serotoninergic neurotransmition, which also increases neurogenesis rates. One study demonstrated that fluoxetine, a selective serotonin reuptake inhibitor, produced a 70% increase in dentate gyrus nerve cells in the adult rat brain.[277] Previous studies have demonstrated that antidepressant drugs facilitate the up regulation of the brain-derived neurotrophic factor (BDNF) in the hippocampus,[278] which promotes differentiation and survival of hippocampal neurons, not only during development, but also in adulthood. Furthermore, antidepressant treatment blocks the stress-induced down regulation of hippocampal BDNF expression that suppresses neurogenesis. The underlying molecular mechanisms of these therapies are not well understood.[279] However, serotoninergic neurotransmission is widely accepted as an important component of the neurogenic phenomenon.

More concretely understood is the drug effect on the neurotransmitter serotonin by the SSRI class of antidepressants, which are 5-HT agonisits. Agonisits function by increasing or potentiating the effects of a chemical or drug. 5-HT is a chemical abbreviate for serotonin. 5-HT agonisits function by preventing the reuptake of serotonin, allowing it to stay in the synaptic cleft longer. While the effect on 5-HT is clear, the time course delay of drug administration to onset of

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[275] Lauder, J.M., Wallace, J.A., & Krebs, H. "Roles of Serotonin in Neuroembryogenesis." Experimental Med-Biology 13 (1981): 477-506; Whitaker-Amitia, P.M. "Role of Serotonin and Other Neurotransmitter Receptors in Development: Basis for Developmental Pharmacology." Pharmacology Review 43 (1991): 553-561.

[276] Whitaker-Amitia, P.M. "Role of Serotonin and Other Neurotransmitter Receptors in Development: Basis for Developmental Pharmacology." Pharmacology Review 43 (1991): 553-561.

[277] Jacobs, B.L., Praag, H., and Gage, F.H. "Adult Brain Neurogenesis and Psychiatry: A Novel Theory of Depression." Molecular Psychiatry 5 (1999): 262-9.

[278] Nibuya, M., Nestler, E.J., and Duman, R.S. "Chronic Antidepressant Administration Increases the Expression of cAMP Response Element Binding Protein (CREB) in Rat Hippocampus." Journal of Neuroscience 16.7(1996): 2365-2372.

[279] Nibuya, M., Nestler, E.J., and Duman, R.S. "Chronic Antidepressant Administration Increases the Expression of cAMP Response Element Binding Protein (CREB) in Rat Hippocampus." Journal of Neuroscience 16.7(1996): 2365-2372.

therapeutic action remains mysterious since the therapeutic effects are not seen until two to three weeks later. Research suggests "that this is due to the time it takes for newly born dentate gyrus neurons to migrate and differentiate, and to extend their neuritis and become fully functionally integrated into the existing brain circuitry"[280] This hypothesis reconciles the difference in time between the drug's effect on 5-HT levels and the gain of therapeutic effects in antidepressant drug therapy.

Antidepressant medication is not the only successful way to treat depression, nor is it the only way to boost neurogenic activity. ECT has been observed to induce long-term structural and functional changes in the brain. ECT has been observed to promote hippocampal neurogenesis in the dentate gyrus region, as well as increase serotonergic neurotransmission. In ECT, an electrical current is passed though the brain that creates a seizure. Seizure activity has been found to promote hippocampal neurogenesis in the dentate gyrus and hilus, as studied by the BrdU labeling technique.[281] Scott and colleagues found "a net increase in neurogenesis within the hippocampal dentate gyrus following ECS treatment."[282] Electroconvulsive Shock (ECS) is the animal model of ECT. A later study found a dose-dependent mechanism between neurogenic rates and ECS administration.[283] In studies, cell proliferation and survival were monitored. Each found that new cells survived around 3 to 4 months, and were integrated into the brain circuitry. Madsen and colleagues found that of the new neural circuits formed, many new neurons were present, but also that new neurons made connections with preexisting neurons in the circuit. New neurons connecting with existing circuitry may be evidence of neurocorrective ability within the phenomenon of neurogenesis.

The ECT literature focused on the ability of seizures to cause neuronal birth; however, the literature also discussed the ability of seizures to cause neuronal death through apoptosis, also know as cellular suicide due to the release of hydrolytic enzymes within the lysosomes. "While no direct link between apoptosis and neurogenesis has been shown, several different manipulations that cause an increase in apoptosis in the dentate gyrus also cause an increase in neurogenesis."[284] These

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[280] Jacobs, B.L. "Adult Brain Neurogenesis and Depression." Brain, Behavior, and Immunity 16 (2002): 606.
[281] Scott, B.W., Wojtowicz, J.M., and Burnham, W.M. "Neurogenesis in the Dentate Gyrus of the Rat Following Electroconvulsive Shock Seizures." Experimental Neurology 165 (2000): 231-236.
[282] Scott, B.W., Wojtowicz, J.M., and Burnham, W.M. "Neurogenesis in the Dentate Gyrus of the Rat Following Electroconvulsive Shock Seizures." Experimental Neurology. 165 (2000): 231.
[283] Madsen, T.M., Treschow, A., Bengzon, J., Bolwig T.G., Lindvall, O., and Tingstrom, A. "Increased Neurogenesis in a Model of Electroconvulsive Therapy." Biological Psychiatry 47.12 (2000): 1043-1049.
[284] Scott, B.W., Wojtowicz, J.M., and Burnham, W.M. "Neurogenesis in the Dentate Gyrus of the Rat Following Electroconvulsive Shock Seizures." Experimental Neurology 165 (2000): 235.

processes could be linked. If so, neuronal death "may be a stimulus for increased neurogenesis,"[285] which indicates a compensatory mechanism. In this case, recycling is occurring with no net increase of neurons. Resultantly, hippocampal volume would not be increased, only maintained. The issue of neuronal volume is especially important in considering the stress-induced model of depression tied to the loss of neuronal volume as a function of stress. Scott concluded that ECT may reverse these losses "through the stimulation of neuronal proliferation" by seizure activity.[286]

Promotion of neurogenesis in the dentate gyrus of the hippocampus appears to contribute to recovery from clinical depression. The hippocampus is one of the few brain regions that undergoes adult neurogenesis.[287] As stress affects neurogenesis, the hippocampal nerves are particularly sensitive to the negative effects of stress. Serotoninergic function is implicated as the dentate gyrus has the highest concentration of 5-HT-1A receptor sites in the brain.[288] At this point, only correlational relationships link adult hippocampal neurogenesis to serotonergic input to the dentate gyrus. [289]

The emotional and cognitive consequences of depression could be attributed to changes in hippocampal functioning. Beyond a positive correlation of hippocampal volume loss (atrophy) and major depression,[290] the explicit nature of the observed changes in the hippocampus is unknown. The same is true of their pathogenesis. Currently, glucocorticoid-mediated neuronal loss is being addressed by the field,[291] which supports the stressor model of depression because glucocorticoids

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[285] Scott, B.W., Wojtowicz, J.M., and Burnham, W.M. "Neurogenesis in the Dentate Gyrus of the Rat Following Electroconvulsive Shock Seizures." Experimental Neurology 165 (2000): 235.

[286] Scott, B.W., Wojtowicz, J.M., and Burnham, W.M. "Neurogenesis in the Dentate Gyrus of the Rat Following Electroconvulsive Shock Seizures." Experimental Neurology 165 (2000): 235.

[287] Eriksson, P., Perfileva, E., Bjork-Eriksson, T., Alborn, A., Nordborg, C., Peterson, D., and Gage, F. "Neurogenesis in the Adult Human Hippocampus." Nature Medicine 4 (1998): 1313-1317.

[288] Kia, H.K., Miguel, M.C., Brisorgueil, M.J., Daval, G., Riad, M., El Mestikowy, S., Hamon, M., and Verge, D. "Immunocytochemical Localization of Serotonin 1A Receptors in the Rat Central Nervous System." Journal of Comparative Neurology 365 (1996): 289-305.

[289] Brezun, J. M., and Daszuta, A. "Depletion in Serotonin Decreases Neurogensis in the Dentate Gryus and the Subventricular Zone of Adult Rats." Neuroscience 89 (1999): 1001.

[290] Sheline, Y., Wany, P., Gado, M., Csernansky, J., and Vannier, M. "Hippocampal atrophy in recurrent major depression." Proceedings of the National Academy of Science USA 93 (1996): 3908 –3913.

[291] Brown, E S., Rush, A.J., and McEwen, B.S. "Hippocampal Remodeling and Damage by Corticosteroids: Implications for Mood Disorders." Neuropsychopharmacology 2 (1999): 474-484; McEwen, B.S. "Stress and Hippocampal Plasticity." Annual Review of Neuroscience, 22 (1999): 105-102; McEwen, B.S. "Effects of Adverse Experiences for Brain Structure and Function." Biological Psychiatry 48 (2000): 721-731; Sapolsky, R.M. "The Possibility of Neurotoxicity in the Hippocampus in Major Depression: A Primer on Neuron Death." Biological Psychiatry 48 (2000): 755-765.

are stress hormones and function in conjunction with adrenal corticoids.[292] A body of evidence connecting the theories is forming and is presented in the next section.

Beyond antidepressant drugs and ECT, certain behaviors have been observed to facilitate neurogenic activity. Learning and memory tasks are hippocampal-dependent, resulting in an up regulation of neurogenic activity.[293] Increased neurogenesis has been observed in response to cardiovascular activity such as running, but not swimming. The observed changes in neurogenesis rates have correlated with increases in granule cell long-term potentiation, which is a cellular model of learning and memory.[294] As mentioned earlier, novel environments and learning and memory tasks have also been observed to increase neurogenic activity. The most compelling evidence supporting the neurogenic theory of depression comes from the research connecting functional down regulation of neurogenic activity with onset of depressive symptoms as reviewed above.

Conclusions.

In summary, chronic antidepressant treatment increases 5-HT 1A function[295] and may increase neurogenic activity though activation of the 5-HT 1A receptor. The formation of new hippocampal cells could indicate an important adaptive functioning response to antidepressant drugs. This drug effect would oppose down-regulation of neurogenesis as well as stress induced atrophy. Antidepressant drugs likely induce an up regulation of neurogenesis that opposes the reduction of hippocampal volume, which leads to a reduction in function and possibly a depressive condition. ECT studies provide further evidence of neurogenesis opposing hippocampal volume loss, which ultimately leads to a depressive condition, under the stressor model of depression.[296]

How exactly seizure activity facilitates neurogenesis is still not well understood. As one possibility, the electrical activity exerts a compensatory mechanism of neural recycling that counters the loss of stress induced neuronal death.[297] The increase in neurogenesis maintains the

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[292]Tanapat, P., Galea, L.A., and Gould, E. "Stress Inhibits the Proliferation of Granule Cell Precursors in the Developing Denate Gyrus." Journal of Developmental Neuroscience 16 (1998): 235-239

[293] Gould, E., and Tanapat, P. "Stress and Hippocampal Neurogenesis." Biological Psychiatry 46 (1999): 1472-1479.

[294] van Praag, H., Kempermann, G., and Gage, F. "Running Increases Cell Proliferation and Neurogenesis in the Adult Mouse Dentate Gyrus." Nature Neuroscience 2 (1999b), 266 –270.

[295] Duman, R.S. "Novel Therapeutic Approaches Beyond the Serotonin Receptor" Biological Psychiatry 44 (1998): 324 –335.

[296] Madsen, T.M., Treschow, A., Bengzon, J., Bolwig T.G., Lindvall, O., and Tingstrom, A. "Increased neurogenesis in a model of electroconvulsive therapy." Biological Psychiatry 47.12 (2000): 1043-1049; Scott, B.W., Wojtowicz, J.M., and Burnham, W.M. "Neurogenesis in the Dentate Gyrus of the Rat Following Electroconvulsive Shock Seizures." Experimental Neurology 165 (2000): 231-236.

[297] Scott, B.W., Wojtowicz, J.M., and Burnham, W.M. "Neurogenesis in the Dentate Gyrus of the Rat Following Electroconvulsive Shock Seizures." Experimental Neurology 165 (2000): 231-236.

number of hippocampal neurons. The tie between these two treatments is that they both promote neurogenesis in the same brain region, the dente gyrus. *Some evidence suggests that ECT increases serotonin levels, which leads to the increase of neurogenesis, but no clear evidence supports this assertion. Further research will mostly examine the connection* between serotonin levels and ECT.

A new theory of depression must account for interdependencies of 'various functional subsets of the system' involved in neurogenesis and neuroplasticity. The stressor model appears to address all of these considerations. These findings indicated that a strong correlation exists between an increase in neurogenesis and a decrease in depressive condition. Biochemically, clinical depression appears to be an issue of HPA hyperactivity, with profound implications for hippocampal functioning and neurogenic capacity, rather than a serotonin deficiency disorder.

Evidence for the connectedness of both theories.

Cortisol, serotonin, and stress are interconnected in the onset and maintenance of clinically depressive episodes. Elevated cortisol levels are strongly tied to depression as half of all depressed patients have increased cortisol levels.[298] In Cushing's Syndrome, a disease characterized by high cortisol levels (hypercortisolemia), half of the patients develop clinical depression.[299] Depressed patients have high levels of CRH, as measured by cerebrospinal fluid concentrations, and they have decreased levels of dehydroepiandrosterone (DHEA), a hormone that acts as a cortisol antagonist.[300] Antagonists act to decrease the effect of a chemical or drug. Lack of cortisol antagonism indicates an increase in the effects of cortisol.

One study observed that rats exposed to chronic unpredictable stressors had increased cortisol levels and decreased 5HT-1A mRNA levels. 5HT-1A is a serotonin receptor subtype. A decrease in mRNA coding for 5HT-1A means fewer proteins are being made from the portion of the DNA coding for that protein, also referred to as down regulation. The study observed similar changes in the brains of depressed patients that committed suicide. Furthermore, this study was able to demonstrate that the functional down regulations of 5HT-1A receptors can be counteracted by the removal of the adrenal glands, thereby circumventing effects of the HPA axis. Gland removal eliminated elevated cortisol levels. Elevated cortisol levels are implicated in functional down

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[298] Walport L. Malignant Sadness: The Anatomy of Depression. New York: The Free Press, 1999.
[299] Seeley, R. R., Stephens, T. D., and Tate, P. Anatomy and Physiology. Ed. Martin J. Lange. 6 ed. New York: McGraw-Hill, 2003.
[300] Walport L. Malignant Sadness: The Anatomy of Depression. New York: The Free Press, 1999.

regulated of serotonin receptor subtype 5HT-1A. [301] In a similar vein, chronic unpredictable stress was also observed to decrease motor skills function, which is a symptom of depression noted in the DSM-IV TR.[302] The study noted that motor skill function returned to normal upon antidepressant administration to depressed rats in animal models. This study links biochemical models of depression with behavior symptoms of depression episodes.

Research has shown that patients who are unresponsive to SSRI antidepressants show dramatic improvement upon administration of cortisol suppressing medication.[303] Integration of this information suggests that more contributes to the depressive condition than merely low serotonin levels. Several ideas have been formulated about the role of stress during development, both pre-natal in the embryonic environment and post-natal in early development. One such study hypothesized that neural circuitry may be altered during development and negatively manifested though increased susceptibility to stressful stimuli.[304] Alternatively, several studies have investigated the role of neural reward mechanisms by looking at dopaminergic pathways implicated in depression. Along this line of reasoning, one study found that exposure to chronic unpredictable stress leads to a decreased responsiveness to rewarding stimuli,[305] which is another symptom of clinical depression. According to these findings, decreased responsiveness is a result of cortisol-induced suppression of the dopaminergic pathways.

Social psychology research complements reported biological evidence. One study demonstrated that stressful life events increase the risk of developing depression and the subsequent experience of depressive episodes.[306] Another study used self-report and report of a mother to

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[301] Lopez, J.F., Chalmers, D.T., Little, K,Y., and S.J. Watson. "Regulation of Serotonin$_{1A}$, Glucocorticoid, and Mineralcorticoid Receptor in Rat and Human Hippocampus: Implications for the Neurobiology of Depression." Biological Psychology 43.8 (1998): 547-73.

[302] Mizoguchi, K., Yuzurihara, M., Ishige, A., Sasaki, H., and T. Tabira. "Chronic Stress Impairs Rotarod Performance in Rats: Implications for Depressive State." Pharmacology, Biochemistry and Behavior 71 (2002): 79-84.

[303] Lopez, J.F., Chalmers, D.T., Little, K,Y., and S.J. Watson. "Regulation of Serotonin$_{1A}$, Glucocorticoid, and Mineralcorticoid Receptor in Rat and Human Hippocampus: Implications for the Neurobiology of Depression." Biological Psychology 43.8 (1998): 547-73.

[304] Meyer, S. E., Chrousos, G. P., and Gold, P. W. "Major Depression and the Stress System: A Life Span Perspective." Development and Psychopathology 13 (2001): 565-80

[305] Lin, D., Bruijnzeel, A.W., Schmidt, P., and A. Markou. "Exposure to Chronic Mild Stress Alters Thresholds for Lateral Hypothalamic Stimulation Reward and Subsequent Responsiveness to Amphetamine." Neuroscience 114.4 (2002): 925-33.

[306] Kendler, K. S., Karkowski, L. M., and Prescott, C. A. "Causal Relationship between Stressful Life Events and the Onset of Major Depression." American Journal of Psychiatry 156.6 (1999): 837-841.

record stressful life events, in addition to measuring cortisol levels, and concluded that undesirable life events were a robust predictor of depression.[307]

The connectedness of these theories suggests a need for a broader view of depression. To date, depression is posited as a biochemical problem in which the medical discourse is linear and reductionist. This approach to depression is unable to account for its complexities, interconnectedness of body subsystems, and interaction with the environment. A unified theory of depression, which can account for all dimensions of the issue though biological, psychological, and social media, is necessary. Depression must be approached from a biopsychosocial perspective.

Need for the biopsychosocial perspective

As stated in the introduction, when depression is viewed solely as a problem within the serotonin system, other systems in need of attention are ignored. On a biological level, an examination of the root cause is necessary to ascertain what is responsible for initiating cascade changes, as opposed to merely medicating the changes once they arise.

A study the HPA axis is necessary to see where it converges with existing knowledge and where it diverges from conventional understandings of the illness. Stress sits at the core of the depressive condition. Therefore, researchers must investigate what stress means on a biology level in addition to what causes stress on a psychological and social level. The stresses of the mind later become problems for the brain. This critical transition is ignored by the traditional medical model but is accounted for in a biopsychosocial paradigm of depression.

This paradigm examines culture, individual agency, and decision-making. It looks into social spaces to address psychological and social aspects of depression, which are ignored by the medical model. Psychological and social aspects of disease are difficult to quantify using traditional quantitative measures. Adopting the biopsychosocial paradigm means expanding research methodology to blend qualitative modes of inquiry with traditional quantitative measures. The biopsychosocial view requires departure from the status quo, since the current popular vocabulary and scientific depression discourse are inadequate to address the multidimensionality of depression, ranging from highly diverse and individual symptoms presentation, to a lack of medical consensus at the periphery of the diagnosis category, to dynamic systems biology.

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[307] Goodyer, I. M., Park, R. J., and Herbert, J. "Psychosocial and Endocrine Features of Chronic First-Episode Major Depression in 8-16 Year Olds." Biological Psychology 50.5 (2001): 351-57.

This chapter illuminates how inadequate the traditional medical model is at providing a useful framework for discussing depression on a biological level. When the scope of the depression discussion is broadened to probe interactions between biology, psychology, and social worlds, the medical model hinders the discussion instead of furthering it. The biopsychosocial paradigm links biological information across subsystems to gain an understanding of what is occurring in the body. This view is lost in the traditional medical model as only serotoneric neurotransmission was investigated. Furthermore, the biopsychosocial paradigm takes the next step to crosslink biological platforms to cultural and social components of health function presented in earlier chapters. The biopsychosocial paradigm presents a unified theory of depression that can finally account for the complete array of depressive experiences at varying intensity levels, as it appreciates how biology and cultural environments interact to forge states of illness and health. In seeking a complete understanding of the disease, the biopsychosocial view seeks complete solutions and a pathway of healing.

Conclusions.

The chapter examined the biology of depression from a dynamic systems biology perspective and reviewed the stressor model of depression as an alternate paradigm to the traditional medical model. The neurogenetic theory of depression fits within dynamic systems biology and helps contextualize the role that serotonin plays in the stress-depression cortisol puzzle. Upon reviewing the evidence presented in this chapter, depression can no longer be conceived as a serotonin deficiency disorder. Instead, the biological basis for depression seems to be underpinned by hypercortisolian and stress response dysregualtion. Its effects on the dynamic systems and hippocampal functioning are significant.

Several conclusions can be drawn from the research linking chronic stress and depression. Chronic stress and HPA hyperactivity seem to trigger depression. At a minimum, cortisol and CRH are depressogenic substances capable of maintaining a depressive episode.[308] The significant discovery of the connection between elevated cortisol levels and decreased serotonin function is able to account for the hypercortisolemia in half of depressed patients and the success of serotonergic pharmacological intervention. This discovery also offers an explanation to why many patients do not respond effectively to SSRI treatment because the cause of their low serotonin is not

[308] Goodyear, I. M., Park, R. J., and Herbert, J. "Psychosocial and Endocrine Features of Chronic First-Episode Major Depression in 8-16 Year Olds." Biological Psychology 50.5 (2001): 351-57.

just a mere lack of serotonin. Therefore, a drug that lowers cortisol levels is more effective for some patients than an SSRI. Normalizing cortisol levels prevents cascade effects, which alter serotonergic transmission. Cortisol suppression therapy is an earlier intervention and addresses the root cause of depression. Both cortisol and serotonin are implicated in depression, but only addressing low serotonin levels, they are not a complete treatment or always the most effective treatment.

More research is needed to investigate effective treatments for this debilitating disease. Part of this research means understanding root causes. An important direction for this research to take may come from realizing that categorizing depression as a single disease (especially a disease of low serotonin levels) is unhelpful. A careful review of literature recounting the stressor model of depression and how it fits in with the neurogenic theory of depression shatters the serotonin myth. While serotonin is part of depression's etiology and parthenogenesis though cascade effects, it is not the root cause of the disease. Depression is more multi-faceted than previously thought. The evidence presented in this chapter accounts for the wide range of patient experiences captured in the depression narratives in earlier chapter. Future research of disease etiology and pathogenesis needs to reflect this new direction.

* * *

The technical body of evidence presented in this chapter substantiates claims made in previous chapters that depression is not merely a serotonin problem, but instead results from biopsychosocial elements. Depression has an organic component that must not be allowed to trump psychosocial etiologies. As the paper has criticized existing accounts of depression, this chapter strives to provide an account of depression from a biological perspective that would not be vulnerable to these criticisms. The result was a highly technical account of depression that explored biological foundations of disease while avoiding the pitfalls of reductionist approaches to biology. With this new view of biological aspects of depression, the argument that depression is a biopyschosocial phenomenon has come full circle as this chapter has shown how biological and cultural elements interact to sustain or dissolves disease states as mediated by stress.

Conclusions:

People elect to take Prozac because it seems easy and pain free. The side effects of older anti-depressants impose greater costs on patients, which caused people to use them sparingly and only when they felt it was really necessary. The same constraints no longer exist with Prozac. Individuals no longer have to make benefit – burden calculations or weigh psychiatric gains against somatic disturbances. With Prozac, people can easily medicate themselves rather than endure the condition of their lives.

> *Prozac is so easily tolerated that almost anyone can take it and almost anyone does. It has been used on people with slight complaints who would not have been game for the discomforts of older antidepressants, the monoamine oxidase inhibitors (MAOIs) or tricyclics. Even if you're not depressed, it might push back the edges of your sadness, and wouldn't that be nicer than living with pain?*[309]

In the 50s and 60s, women took the barbiturate tranquilizer, Miltown, referred to as "mother's little helper" by The Rolling Stone to handle the unpleasant aspects of life, while in 90s and in the 21st century, North Americas take Prozac to meet the demands of their lives and surroundings. Cultural expectations of happiness are so great that people think that they are ill if they are not happy all the time. Instead of asking what aspect of life is making someone so unhappy and working on changing that aspect, many seek to preserve the status quo and change themselves instead. North American culture is so "imbedded with an expectation of happiness, and that, in consequence, we prefer to see negative emotional experiences as aberrant and deviant. In which case our decision to afford depression the status of diagnosis may derive so much from our scientific knowledge as from our system of values."[310]

In a cultural climate with no place for rest, melancholic reflection, or sadness, more people are likely to conform to the dominant cultural view, which sees these experiences as problematic instead of normal, though unpleasant, aspects of life. Those who expect the world to permit perpetual happiness will medicate accordingly to push back the edges of their sadness for two principle reasons. One, they genuinely believe that they are ill, and two, they see no great no harm in pushing back the edge of their sadness with medication. To believe these two statements is dangerous and harmful. However, the harms are seldom considered in the traditional medical model because such conversations lay outside the parameters of what the medical model can measure.

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[309] Solomon, A. *The Noonday Demon: An Atlas of Depression.* Scribner: New York. 2001, 27

[310] Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 12.

The medical model provides a limited discourse for depression because it only considers biochemical factors of disease. Even the biological factors considered by the medical model are reflected upon in a reductionist manner. The biological reductionism and focus on serotonin is no accident. The pharmaceutical industry is a powerful driver that has orchestrated disease parameters to be as broad as possible and then socially located the disease so that the majority of the population could fall within the disease's parameters. The pharmaceutical industry feeds off media messages and advertising. The public is told what products to buy for self-improvement because everyone is led to believe they are defective in some way. People are always being told that some product exists that can make them better than they already are. The public has been taught to be consumers, and consumers are taught that they are at a deficit if they are without a product, good, service, or medication. The pharmaceutical industry uses the same tactics as the retail industry to create demand for their products. David Healy advises that the way to sell medication is to first sell sickness.[311] Patients are the big losers who are harmed by this practice. The pharmaceutical industry profits from perpetuating these harms.

Normal people cannot meet inflated cultural expectations of the good life and are told that they are sick because they have unattainable expectations and are unhappy since they cannot meet their lofty dreams. These problems are psychosocial in nature and are solved by introspection, adjusted attitudes, and effective social navigation. The origins of these problems are socio-cultural, not biological. Therefore, biological treatments for this kind of suffering are inappropriate and may cause damage. First, biological treatments may not be effective for managing subclincial variants of depression, as studies have shown that mild depression does not respond to medication. Lack of medication response suggests that disturbances are not biologically constituted or non-sertonergic in nature. Second, as the social navigation hypothesis suggests, taking medication to blunt the pains of depression caused by poor social navigation prevents the problem, which is responsible for causing the depression, to be solved. Medication allows people to endure suffering instead of stopping the problem that originally caused the suffering. Depression is an adaptation allowing for better social navigation of complex problems that are important to fitness functioning. Wittgenstein explains that "sickness of a time," [312] if it is philosophical in origin, can only be cured by changing the way

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[311] Healy, David. The Anti-depressant Era. Cambridge, Mass.: Harvard University Press, 1997.
[312] Wittgenstein, L. Remarks on the Foundation s of Mathematics. ed G.E. Anscombe. Basil Blackwell: Oxford. 1956, 57.

people live and approach the world. Therefore "medicine invented by an individual"[313] will not be able to remedy the suffering.

When depression is viewed from a evolutionary perspective, the harms of medication come into focus. The evolutionary perspective forces depression to be considered in a non-conventional way. The evolutionary perspective coupled with normative cultural analysis posits that depression is an illness within culture as opposed to a problem with biochemistry.

Depression is a culture-bound construct. For example, Japan,[314] China,[315] and Asia provide greater tolerance for melancholia, a cultural space to reflect upon sadness, and permission to accept the transience of life. In these countries, melancholia is not seen as a problem; therefore, it is not pathologized and cured. In Japan, depression is treated with a completely different compliment of pharmaceuticals than in the West. How can one disease be medicated and managed in two completely different ways? In the United States, depression is treated with Prozac, while in Japan and Asia depression is treated with sedative hypnotics and barbiturates.[316] The disease is managed differently based upon geography because each culture has a different belief about what constitutes the good life and how to live it. North American culture is individualistic and values competitive, bold, out-going personalities. In Asia, notions of the good life center on community and blending individual wants with the wishes of partners and family. The dominant social norms of North America are not portable. Each society will see problems and devise treatments for those problems based upon culturally-specific notions of what constitutes the good life. Therefore, depression is not purely a biochemical manifestation. Treatment is determined by cultural geography. Consider Julia's narratives and the values she placed upon neatness and organization. She suffered because she was too tidy and organized, and those traits were not valued. "To be neat in a culture that prizes neatness may bespeak a very different, less aberrant biological state than maintenance of the same behavior in a culture that has adopted different values."[317] Constructing disease only around biological quantifiable parameters is to miss out on larger discussions of social determinants of health, what constitutes well-being, and the climate in which illness categories and classifications are being made.

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[313] Wittgenstein, L. Remarks on the Foundation s of Mathematics. ed G.E. Anscombe. Basil Blackwell: Oxford. 1956, 57.
[314] Kirmayer, Laurence J. "The Sound of One Hand Clapping: Listening to Prozac in Japan." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 164-193.
[315] Kleinman, Arthur. "Culture and Depression." The New England Journal of Medicine. 351.10 (2004): 951-953.
[316] Kirmayer, Laurence J. "The Sound of One Hand Clapping: Listening to Prozac in Japan." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 164-193.
[317] Kramer, Peter. Listening to Prozac. New York: Penguin Books, 1997. 39.

The transition from DMS-II to DSM-III marked a shift in psychiatric thinking. The psychosocial model was abandoned in favor of a reductionistic biomedical approach. With this shift in thinking came a shift in illness definitions, in terms of who was considered ill and in need of treatment. After considering limitations of the dominant medical model, psychiatric thinking must again evolve to blend biology and psychosocial thinking. A larger cultural backdrop of psychosocial issues has been ignored in mental health because it is not an easy way to promote disease. This critical omission limits research and analysis, and ultimately harms patients.

Steven Sharfstein, president of the American Psychiatric Association, in a 2005 essay to his professional colleagues proclaimed that "as a profession, [psychiatrists] have allowed the biopsychosocial model to become the bio-bio-bio model."[318] In further exploring this issue Sharfstein added that "if [psychiatrist] are seen as mere pill pushers and employees of the pharmaceutical industry, our credibility as a profession is compromised."[319] A purely biological model strips sufferers of their agency and ability to heal through non-pharmaceutical means. The era of suspicion has arrived where the medical profession must decide who is being considered ill and why. By what criteria are some people ill and others well? Do objective clinical criteria exit, or are psychiatric experts on the payroll of the pharmaceutical industry determining who is ill and who is well according to economic guidelines as opposed to the principles of beneficence and non-malificence? Future research must examine who these decision makers are and in what climate these decisions are made.

In an era of eroding trust, transparency in decision-making is important. The publication of DSM-V in 2011 will require expert consultants to disclose financial ties and conflict of interest information. The competing interests in establishing illness categories will be transparent. However, equally important is this transparency within individuals as they make decision about how they will live their lives and why. People must honestly evaluate what they are capable of and set reasonable expectations. If they chose to live beyond the bounds of their capabilities and take medication to do so, they are not ill but rather are misreading their abilities. Taking medication seems easier than critically reflecting on shortcomings, failures, and personal contributions to unhappiness.

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[318] Sharfstein, Steven S. "Big Pharma and American Psychiatry: The Good, the Bad, and the Ugly." Psychiatric News 40.16 (2005): 3.

[319] Sharfstein, Steven S. "Big Pharma and American Psychiatry: The Good, the Bad, and the Ugly." Psychiatric News 40.16 (2005): 3.

A biopsychosocial approach to depression means rethinking what kind of suffering can be legitimately classed as a biomedical condition, what kind of suffering is part of normal life, and what roles people play in bringing about their own unhappiness. Approaching depression from this perspective requires taking responsibility for happiness and personal decisions. A biopsychosocial approach to depression does not mean avoiding medication. The model advocates responsible use of medication. Medication can be used to treat illness, or it can allow people to sustain a life outside the bounds of what they are normally able to tolerate. These two uses of medication should not be confused, as medication usage is not synonymous with illness.

Reference List:

Abramson, L.Y., Metalsky, G.I., and L.B. Alloy. "Hopelessness Depression: A Theory-Based Subtype of Depression." Psychology Review 96 (1989): 358-372.

Ackermann , R., and R.J. De Rubies. "Is Depressive Realism Real?" Clinical Psychology Review 11 (1991): 565-584.

Ahrens, A.H., Zeiss, A.M., and R. Kanfer. "Dysphoric Deficits in Interpersonal Standards, Self-efficacy, and Social Comparison." Cognitive Therapy and Research 12 (1988): 53-67.

Akiskal, H.S. "Dysthymia and Cyclothymia in Psychiatric Practice a Century After Kraepelin." Journal of Affective Disorders 62 (2001): 17-31.

Alexander, R.D. "Evolution of the Human Psyche." The Human Revolution. Ed. P. Mellars and C. Stringer. Edinburgh: University of Edinburgh Press, 1989: 455-513.

Alloy, L.B., and A.H. Ahrens. "Depression and Pessimism for the Future: Biased Use of Statistically Relevant Information In Predictions for Self Verses Other," Journal of Personality and Social Psychology 52 (1987): 366-378.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorder: DSM-IV TR. 4th ed. Washington: American Psychiatric Association, 1994.

Andrews, B., and G.W. Brown. "Stability and Change in Low Self-esteem: The Role of Psychological Factors." Psychology Medicine 25 (1995): 23-31.

Baetz, M., Griffin, R., Bowen, R., Koenig, H.G., and E. Marcoux. "The Association Between Spiritual and Religious Involvement and Depressive Symptoms in a Canadian Population." Journal of Nervous & Mental Disease 192.12 (2004): 818-22.

Bero, L.A. "The Publication of Sponsored Symposiums in Medical Journals." New England Journal of Medicine 327 (1992): 1135-1140.

Berrettini, W.H., Doran, A.R., Kelsoe, J., Roy, A., and D. Pickar. "Cerebrospinal Fluid Neuropeptide Y in Depression and Schizophrenia." Neuropsychopharmacology 1 (1987): 81–83

Biello, S.M., Golombek, D.A., Schak, K.M., and M.E. Harrington. "Circadian Phase Shifts to Neuropeptide Y In Vitro: Cellular Communication and Signal Transduction." Journal of Neuroscience 17 (1997): 8468–8475.

"Blue Cross VP Says MH Prospects Cloudy." Psychiatric News Aug. 6, 1975. 1.

Brezun, J. M., and A. Daszuta. "Depletion in Serotonin Decreases Neurogensis in the Dentate Gryus and the Subventricular Zone of Adult Rats." Neuroscience 89 (1999): 1001.

Britton, K.T., Southerland, S., Van Uden, E., Kirby, D., Rivier, J., and G. Koob. "Anxiolytic Activity of NPY Receptor Agonists in the Conflict Test." Psychopharmacology *(Berlin)* 132 (1997): 6–13.

Brodie, H.K.H., and M. Sabshin. "An Overview of Trends in Psychiatric Research: 1963-1972." American Journal of Psychiatry 130 (1973): 1309-1318.

Brown, E. S., Rush, A.J., and B.S. McEwen. "Hippocampal Remodeling and Damage by Corticosteroids: Implications for Mood Disorders." Neuropsychopharmacology 2 (1999): 474-484.

Brown, G.W., Adler, Z., and A. Bifulco. "Life Events, Difficulties and Recovery Form Chronic Depression." British Journal of Psychiatry 152 (1988): 487-498.

Brown, J.D. "Evaluations of Self and Others: Self-enhancement Basis in Social Judgment." Social Cognition 4 (1986): 353-376.

Brugha, T.S., Bebbington, P.E., Stretch, D.D., MacCarthy, B., and T. Wykes. "Predicting the Short-term Out Come of First Episodes and Recurrences of Clinical Depression: A Prospective Study of Life Events, Difficulties, and Social Support Networks." Journal of Clinical Psychiatry 58 (1997): 298-306.

Calogero, A.E., Gallucci, W.T., Gold, P.W., et al. "Multiple Feedback Regulatory Loops Upon Rat Hypothalamic Corticotropin-releasing Hormone Secretion: Potential Clinical Implications." Journal of Clinical Investigation 82 (1988): 767-774.

Caplan, Paula J. and Lisa Cosgrove Eds. Bias in Psychiatric Diagnosis. Oxford: Jason Arnson. 2004.

Castro, M., and A.C. Moreira. "Regulation of Corticotropin-releasing Hormone Secretion by ACTH at Different Times After Adrenalectomy," Brazilian Journal of Medical and Biological Research 29 (1996): 1573-1578.

Chrousos, G.P. "Stressors, Stress, and Neuroendocrine Integration of the Adaptive Response: The 1997 Hans Selye Memorial Lecture." Annals of the New York Academy of Sciences 851 (1998):311-335.

Chrousos, G.P., and P.W. Gold. " The Concepts of Stress and Stress System Disorders: Overview of Physical and Behavioral Homeostasis." Journal of the American Medical Association 267 (1992):1244-1252.

Classification Committee of WONCA (World Organization of National Colleges, Academics, and Academic Association of General Practitioners/ Family Physicians) in collaboration with the World Health Organization. International Classification of Health Problems in Primary Care: ICHPPC-2-Defined. 3rd ed. Oxford: Oxford University Press, 1983.

Cosgrove, L., Krimsky, S., Vijayarghavan, M., and L. Schneider. "Financial Ties Between DSM-IV Panel Members and the Pharmaceutical Industry." Psychotherapy and Psychomatics 75(2006): 154-160.

Hypericum Depression Trial Study Group. "Effect of Hypericum Perforatum (St. Johns Wort) in Major Depressive Disorder: A Randomized Controlled Trail." Journal of the American Medical Association 287 (2001):1807-14.

DeGracia, David. "Prozac Enhancement, and Self-Creation." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press. 2004. 35.

Detera-Wadleigh, S.D., de Miguel, C., Berrettini, W.H., DeLisi, L.E., Goldin, L.R., and E.S. Gershon. "Neuropeptide Gene Polymorphisms in Affective Disorder and Schizophrenia." Journal of Psychiatric Research 22 (1987): 581–587.

Dickson, Emily. "There was a funeral in my brain." The Complete Poems of Emily Dickenson. New York: Everyman Pocket Library, 1993. 128-129.

Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004.

Dowrick, C., Gask, L., Perry, R., Dixon, C., and T. Usherwood. "Do General Practitioners' Attitudes Towards Depression Predict Their Clinical Behavior?" Psychological Medicine 30 (2000):413-419.

Dowrick, C., Ring, A., Humphris, G., and P. Salmon. "Normalization of Unexplained Symptoms by General Practitioners: A Functional Typology." British Journal of General Practice 54 (2004): 165-170.

Duman, R.S. "Novel Therapeutic Approaches Beyond the Serotonin Receptor." Biological Psychiatry 44(1998): 324 –335.

Elenkov, I.J., and G.P. Chrousos. " Stress Hormones, Th1/Th2 patterns, Pro/anti-inflammatory Cytokines and Susceptibility to Disease." Trends in Endocrinology and Metabolism 10 (1999): 359-368.

Eli Lilly Corporation. "Depression Hurts." January 2006 <http://www.depressionhurts.com>

Elliott, Carl. "Introduction," Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 3.

Elliott, Carl. "Pursed by Happiness and Beaten Senseless." Hastings Center Report 30.2 (2000): 7-12.

Elliott, Carl. Bioethics, Culture and Identity: A Philosophical Disease. New York: Routledge. 1999, 49.

Elliott, T.S. "The Love Song of J. Alfred Prufrock." 1917. The Waste Land and Other Poems. Ed. Helen Vendler. New York: Signet Classics. 1998.

Engel, G.L. "The Need for a New Medical Model: A Challenge to Biomedicine." Science 196 (1977): 129-136.

Eriksson, P., Perfileva, E., Bjork-Eriksson, T., Alborn, A., Nordborg, C., Peterson, D., and F. Gage. "Neurogenesis in the Adult Human Hippocampus." Nature Medicine 4 (1998): 1313-1317.

Flood, J.F., Hernandez, E.N. and J.E. Morley. "Modulation of Memory Processing by Neuropeptide Y." Brain Research 421 (1987): 280–290.

Foucault, Michel. "Lecture One." Power/Knowledge: Selected Interviews and Other Writings, 1972-1977. New York: Pantheon. 1980.

Foucault, Michel. The Birth of the Clinic: An Archaeology of Medical Perception. New York: Vintage books, 1975.

Gilbert, P., and S. Allan. "The Role of Defeat and Entrapment (Arrested Flight) in Depression: An Exploration of an Evolutionary View." Psychology Medicine 28 (1998): 585-598.

Gjerris, A., Widerlöv, E., Werdelin, L., and R. Ekman. "Cerebrospinal Fluid Concentrations of Neuropeptide Y in Depressed Patients and in Controls." Journal of Psychiatry and Neuroscience 17 (1992): 23–27.

Gold, P.W., and G.P. Chrousos. "The Endocrinology of Melancholic and Atypical Depression: Relation to Neurocircuitry and Somatic Consequences." Proceeding of the Association of American Physicians 111 (1999): 22-34.

Gold, P.W., Goodwin, F.K., and Chrousos, G.P. "Clinical and Biochemical Manifestations of Depression: Relation to the Neurobiology of Stress." New England Journal of Medicine 319 (1988): 348-353.

Gold, P.W., Wong M.L., and G.P. Chrousos G.P. "Stress System Abnormalities in Melancholic and Atypical Depression: Molecular, Pathophysiological, and Therapeutic Implications [editorial]." Molecular Psychiatry 1 (1996): 257-264.

Goldberg, D., and P. Huxley. Common Mental Disorders. London: Routledg, 1992. 44 in Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 102.

Goldstein, David J., and William Z Potter. "Biological Theories of Depression and Implications for Current and New Treatments." Pharmacotherapy of Depression. Ed. Domenic A. Ciraulo, and Richard I. Shader. Totowa, N.J.: Humana Press, 2004. 13.

Goodyer, I.M., Park, R.J., and J. Herbert. "Psychosocial and Endocrine Features of Chronic First-Episode Major Depression in 8-16 Year Olds." Biological Psychology 50.5 (2001): 351-57.

Gould, E., and P. Tanapat. "Stress and Hippocampal Neurogenesis." Biological Psychiatry 46 (1999): 1472-1479.

Grob, G. "The Forging of Mental Health Policy in America: World War II to the New Frontier." Journal of the History of Medicine 42 (1987): 410-446.

Greenspan, Miriam. Healing Through the Dark Emotions : The Wisdom of Grief, Fear, and Despair. Boston: Shambhala, 2003.

Grinfeld, M.J. "Protecting Prozac." California Lawyer 79 (1998) 36-40 in Glenmullen, Joseph. *Prozac Backlash.* New York: Touchstone. 2000, 17.

Habermas, J. "Technology and Science as Ideology," in Towards Rational Society: Student Protest, Science and Politics translated by J. Shapiro. Boston: Beacon press: 1970.

Habib, K.E. "Role of Brain-adrenal-gastric Axis in Modulating Gastric Functions During Acute Stress in Male Albino Rats." MSc Dissertation (Physiology), Minio University Faculty of Medicine, El-Minio, Egypt, in Habib, K.E., Gold, P.W., Chrousos, G.P. "Neuroendocrinology of Stress," Endocrinology & Metabolism Clinics of North America 30.3 (2001): 695-728.

Habib, K.E., Gold P.W., and G.P. Chrousos. "Neuroendocrinology of Stress." Endocrinology & Metabolism Clinics of North America 30.3 (2001): 695-728.

Habib, K.E., Negro, P.J., and A. Dib. "Endogenous Opioids Contribute to Gastric Ulcerogenesis During Stress in Male Sprague-Dawley Rats." Gastroenterology 116 (1999): A179.

Hagen, E.H. "The Function of Postpartum Depression." Evolution and Human Behavior 20 (1999): 325-359.

Hartlage , S., Alloy, L.B., Vazquez, C., and B. Dykman. "Automatic and Effortful Processing in Depression." Psychology Bulletin. 113 (1993): 247-278.

Hashimoto, H., Onishi, H., Koide, S., Kai, T., and S. Yamagami. "Plasma Neuropeptide Y in Patients with Major Depressive Disorder." Neuroscience Letters 216 (1996): 57–60

Healy, David. The Anti-depressant Era. Cambridge, Mass.: Harvard University Press, 1997. 43-77.

Heilig, M., Söderpalm, B., Engel, J.A. and E. Widerlöv. "Centrally Administered Neuropeptide Y (NPY) Produces Anxiolytic-like Effects in Animal Anxiety Models," Psychopharmacology 98 (1989): 425–429.

Heilig, M., and E. Widerlov. "Neurobiology and Clinical Aspects of Neuropeptide Y." Critical Reviews in Neurobiology 9 (1995): 115-136.

Henner, G., and F. Schwarzler. "Therapeutic Use of Sleep Deprivation in Depression." Sleep Medicine Reviews 6.5 (2002): 361-377.

Henner, G., Klingberg, S., Schwarwler, F., and M. Schweinsberg. "Direct Comparison of Total Sleep Deprivation and Late Partial Sleep Deprivation in the Treatment of Major Depression." Journal of Affective Disorders 76 (2000): 85-93.

Huhman, K.L., Gillespie, C.F., Marvel, C.L., and H.E. Albers. "Neuropeptide Y Phase Shifts Circadian Rhythms in Vivo Via a Y2 Receptor." Neuroreport 7 (1996): 1249–1252.

Humphrey, N.K. 1976. " The Social Function of Intellect." Growing Points in Etiology. Ed. P.P.G. Bateson, and R.A. Hinde. Cambridge :Cambridge University Press, 1976: 303-317.

Husum, H., Mikkelsen, J.D., Hogg, S., Mathe, A.A., and A. Mork. "Involvement of Hippocampal Neuropeptide Y in Mediating the Chronic Actions of Lithium, Electroconvulsive Stimulation and Citalopram." Neuropharmacology 39.8 (2000): 1463-1473.

Jacobs, B.L. "Adult Brain Neurogenesis and Depression." Brain, Behavior, and Immunity 16 (2002): 606.

Jacobs, B.L., Praag, H., and Gage, F.H. "Adult Brain Neurogenesis and Psychiatry: A Novel Theory of Depression." Molecular Psychiatry 5 (1999): 262-9.

Jagger, Mick, and Keith Richards. "Mother's little Helper." Aftermath. The Rolling Stones. 1965.

"Javits says MH hurt by role confusion." Psychiatric News December 16, 1977. 1

Joiner T.E., Schmidt, N.B., and D. Singh. "Waist-to-hip Ratio and Body Dissatisfaction Among College Women and Men: Moderating Role of Depression Symptoms and Gender." The International Journal of Eating Disorders 16 (1994): 199-203.

Kaczynski, Theodore. Industrial Society and Its Future, 1995. in Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001. 125.

Kalat, J.W. Biological Psychology. Ed. J. Strandberg. 7 ed. Belmont: Wadsworth/ Thomson Learning, 2001. 335-362.

Kendler, K.S., Karkowski, L.M., and C.A. Prescott. "Casual Relationship Between Stressful Life Events and the Onset of Major Depression." American Journal of Psychiatry 15 (1999): 837-841.

Kia, H.K., Miguel, M.C., Brisorgueil, M.J., Daval, G., Riad, M., El Mestikowy, S., Hamon, M., and Verge, D. "Immunocytochemical Localization of Serotonin 1A Receptors in the Rat Central Nervous System." Journal of Comparative Neurology 365 (1996): 289-305.

Kirk, S. A., and H. Kutchins. The Selling of DSM: The Rhetoric of Science in Psychiatry. New York: Aldine de Gruyter. 2002.

Kirmayer, Laurence J. "The Sound of One Hand Clapping: Listening to Prozac in Japan." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press, 2004. 164-193.

Kleinman, Arthur. The Illness Narratives: Suffering, Healing and the Human Condition. New York: Basic Books. 1988.

Korte S.M., Bouws, G.A., and B. Bohus. "Central Actions of Corticotropin-releasing Hormone (CRH) on Behavioral, Neuroendocrine, and Cardiovascular Regulation: Brain Corticoid Receptor Involvement." Hormones and Behavior 27 (1993):167-183.

Kramer, Peter. Listening to Prozac. New York: Penguin Books, 1997.

Kramer, Peter. "The Valorization of Sadness: Alienation and the Melancholic Temperament." Prozac as a Way of Life. Ed. Carl Elliott and Todd Chambers. Chapel Hill, NC: The University of North Carolina Press. 2004. 48-58.

Koerner, I.M. "First You Market the Disease...Then You Push the Pills to Treat It." Guardian G2 (2002):8-9 in Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004. 96.

Lane, J.D., and B.M. DePaulo. "Completing Coyne's cycle: Dysphorics' Ability to Detect Deception." Journal of Research in Personality 33 (1999) 311-329.

Lauder, J.M., Wallace, J.A., and H. Krebs. "Roles of Serotonin in Neuroembryogenesis." Experimental Med-Biology 13 (1981): 477-506.

Levine, A.S., and J.E. Morley. "Neuropeptide Y: A Potent Inducer of Consummatory Behaviour in Rats." Peptides 5 (1984): 1025–1029.

Lemke, M.R., Pohl P., Koethe, N., and T. Winkler. "Psychomotor Retardation and Anhedonia in Depression." Acta Psychiatrica Scandinavica 99 (1999): 252-256.

Lin, D., Bruijnzeel, A.W., Schmidt, P., and A. Markou. "Exposure to Chronic Mild Stress Alters Thresholds for Lateral Hypothalamic Stimulation Reward and Subsequent Responsiveness to Amphetamine." Neuroscience 114.4 (2002): 925-33.

Lopez, J.F., Chalmers, D.T., Little, K,Y., and S.J. Watson. "Regulation of Serotonin$_{1A}$, Glucocorticoid, and Mineralcorticoid Receptor in Rat and Human Hippocampus: Implications for the Neurobiology of Depression." Biological Psychology 43.8 (1998): 547-73.

Madsen, T.M., Treschow, A., Bengzon, J., Bolwig T.G., Lindvall, O., and A. Tingstrom. "Increased Neurogenesis in a Model of Electroconvulsive Therapy." Biological Psychiatry 47.12 (2000): 1043-1049.

Margarinos, A., McEwen, B., Flugg, G., and E. Funchs. "Chronic Psychosocial Stress Causes Apical Dendrite Atrophy of Hippocampal CA3 Pyramidal Neurons in Subordinate Tree Shrews." Journal of Neuroscience 16 (1996): 3534-3540.

Mathé, A.A., Jousisto-Hanson, J., Stenfors, C. and E. Theodorsson. "Effect of Lithium on Tachykinins, Calcitonin Gene-related Peptide, and Neuropeptide Y in Rat Brain." Journal of Neuroscience Research 26 (1990): 233–237.

Mathé, A.A., Gruber, S., Jimenez, P.A., Theodorsson, E. and C, Stenfors. "Effects of Electroconvulsive Stimuli and MK-801 on Neuropeptide Y, Neurokinin A, and Calcitonin Gene-related Peptide in Rat Brain." Neurochemistry Research 22 (1997): 629–636.

Mathé, A.A., Rudorfer, M.V., Stenfors, C., Manji, H.K., Potter, W.Z. and E. Theodorsson. "Effects of Electroconvulsive Treatment on Somatostatin, Neuropeptide Y, Endothelin, and Neurokinin: A Concentrations in Cerebrospinal Fluid of Depressed Patients: A Pilot Study." Depression 3 (1996): 250–256.

May, William. "Code and Covenant or Philanthropy and Contract?" On Moral Medicine: Theological Perspectives in Medical Ethics. Ed. Stephen E. Lammers and Allen Verhey. 2nd ed. Grand Rapids, Michigan: William B. Eerdmans Publishing Company. 1998, 130.

McDowell, David M., and Henry I. Spitz. Substance Abuse: From Principles to Practice. Taylor & Francis Group: New York. 1999.

McEwen, B.S. "Effects of Adverse Experiences for Brain Structure and Function." Biological Psychiatry 48 (2000): 721-731.

McEwen, B.S. "Stress and Hippocampal Plasticity." Annual Review of Neuroscience 22 (1999): 105-102.

McKim, William A. Drugs and Behavior: An Introduction to Behavioral Pharmacology. 5th ed. New Jersey: Pearson Educational, Inc., 2003.

McLaughlin, D. "Incorporating Individual Spiritual Beliefs in Treatment of Inpatient Mental Health Consumers." Perspectives in Psychiatric Care 40.3 (2004):114-119.

Menninger, K. Psychiatry in a Troubled World: Yesterday's War and Today's Challenge. New York: Macmillan, 1948.

Meyer, S.E., Chrousos, G.P., and P.W. Gold. "Major Depression and the Stress System: A Life Span Perspective." Development and Psychopathology 13 (2001): 565-80.

Michelson, D., and P.W.Gold. "Pathophysiologic and Somatic Investigations of Hypothalamic-pituitary-adrenal Axis Activation in Patients with Depression." Annals of the New York Academy of Sciences 840(1999): 717-722.

Michelson, D., Stratakis, C., Hill, L., Reynolds, J., Galliven, E., Chrousos, G., and P. Gold "Bone Mineral Density in Women with Depression." New England Journal of Medicine 335 (1996): 1176-1181.

Michelson, D., Chrousos, G.P., and P.W. Gold. "Type I Glucocorticoid Receptor Blockade Does Not Affect Baseline or Ovine Corticotropin-releasing Hormone-stimulated Adrenocorticotropic Hormone and Cortisol Secretion." Neuroimmunomodulation 1 (1994): 274-277.

Mizoguchi, K., Yuzurihara, M., Ishige, A., Sasaki, H., and T. Tabira. "Chronic Stress Impairs Rotarod Performance in Rats: Implications for Depressive State." Pharmacology, Biochemistry and Behavior 71 (2002): 79-84.

Munglani, R., Hudspith, M.J., and S.P. Hunt. "The Therapeutic Potential of Neuropeptide Y: Analgesic, Anxiolytic and Antihypertensive." Drugs 52 (1996): 371-389.

Myer, Alfred. "Listening to Paxil." PsychologyToday.com. 14 May, 2005 www.psychologytoday.com/ articles/pto-19960701-000038.html

O'Reilly, M,L. "Spirituality and Mental Health Clients." Journal of Psychosocial Nursing & Mental Health Services 42.7 (2004): 44-53.

Nesse, R.M. "Is Depression an Adaptation?" Archives of General Psychiatry 57 (2000): 14-20.

Nibuya, M., Nestler, E.J., and R.S. Duman. "Chronic Antidepressant Administration Increases the Expression of cAMP Response Element Binding Protein (CREB) in Rat Hippocampus." Journal of Neuroscience 16.7 (1996): 2365-2372.

Nilsson, C., Karlsson, G., Blennow, K., Heilig, M., and R. Ekman. "Differences In the Neuropeptide Y-like Immunoreactivity of the Plasma and Platelets of Human Volunteers and Depressed Patients." Peptides 17 (1996): 359–362

Pagel, M.D., Erdly, W.W., and J. Becker. " Social Networks We Get With (and In Spite of) a Little Help From Our Friends." Journal of personality and social psychology 53 (1987): 793-804.

Pasau, R.O. "The Remedicalization of Psychiatry." Hospital and Community Psychiatry 38(1987): 145-151.

Paykel, E.S. "Life Events, Social Support and Suppression." Acta Psychiatrica Scandinavica Suppliment 377 (1994): 50-58.

Percy, Walker. Sign Posts in a Strange Land. Ed. Patrick Samway. New York: Farrar, Straus and Giroux. 1991,12-13.

Pollock, E.J. "Managed Care's Focus on Psychiatric Drugs Alarms Many Doctors." Wall Street Journal, Dec.1, 1995 in Glenmullen, Joseph. *Prozac Backlash.* New York: Touchstone. 2000, 17.

Porsolt, R.D., Anton, G., Blavet, N., and M. Jalfre. "Behavioural Despair in Rats: A New Model Sensitive To Antidepressant Treatments." European Journal of Pharmacology 47 (1987): 379–391

Porsolt, R.D., Le Pichon, M., and M. Jalfre. "Depression: A New Animal Model Sensitive to Antidepressant Treatments." Nature 266 (1977): 730–732.

Report to the President from the President's Commission on Mental Health, vol I: Number 040-000-00390-8. Washington DC: US Government Printing Office, 1978

Price, J.S., Sloman, L., Gardner, R., Gilbert, P., and Rhode, P. "The Social Competition Hypothesis of Depression." British Journal of Psychiatry 164 (1994): 309-315.

Radden, Jennifer. The Nature of Melancholy: From Aristotle to Kristeva. Ed. Jennifer Radden. Oxford: Oxford University Press, 2000.

Reise, M.F. "Are psychiatric Educators 'Losing the Mind?' American Journal of Psychiatry 145 (1988): 1061-1067.

Roy, A., "Neuropeptides in Relation to Suicidal Behaviour in Depression." Neuropsychobiology 28 (1993): 184–186

Sapolsky, R.M. "The Possibility of Neurotoxicity in the Hippocampus in Major Depression: A Primer on Neuron Death." Biological Psychiatry 48 (2000): 755-765.

Schildkraut, J. "The Catecholamine Hypothesis of Affective Disorders: A Review of Supporting Evidence." American Journal of Psychiatry 122 (1965): 509-22.

Schulkin, J., Gold, P.W., and B.S. McEwen. "Introcuction of Corticotropin-releasing Hormone Gene Expression By Glucocorticoids: Implications for Understanong the States of Fear and Anxiety and Allostatic Load." Psychoneuroendocrinology 23 (1998): 219-243.

Scott, B.W., Wojtowicz, J.M., and W.M. Burnham. "Neurogenesis in the Dentate Gyrus of the Rat Following Electroconvulsive Shock Seizures." Experimental Neurology 165 (2000): 231-236.

Sedikides, C. "Assessment, Enhancement, and Verification Determinants of the Self-evaluation Process." Journal of personality and social psychology 65 (2003): 317-338.

Sedikides, C., Campbell, W.K., Reeder, G.D., Elliott, A.J. "The Self-serving Bias in Relational Context." Journal of personality and social psychology 74 (1998): 378-386.

Seeley, R.R., Stephens, T.D., and P. Tate. Anatomy and Physiology. Ed. Martin J. Lange. 6 ed. New York: McGraw-Hill, 2003.

Selye, H. "Forty Years of Stress Research: Principal Remaining Problems and Misconceptions." Canadian Medical Association Journal 115 (1976): 53-56.

Selye, H. "A Syndrome Produced by Diverse Nocuous Agents." Nature 138 (1936):32-36.

Sharfstein, Steven S. "Big Pharma and American Psychiatry: The Good, the Bad, and the Ugly." Psychiatric News 40.16 (2005): 3.

Sheline, Y., Wany, P., Gado, M., Csernansky, J., and M. Vannier. "Hippocampal Atrophy in Recurrent Major Depression." Proceedings of the National Academy of Science USA 93 (1996): 3908 –3913.

Shorter E, and P. Tyer. "Separation of Anxiety and Depressive Disorders; Blind Alley in Psychopharmacology and Classification of Disease." British Journal of Medicine 327 (2003): 158-160.

Slater, Lauren. Prozac Diary. New York: Penguin Books. 1998, 104.

Solomon, Andrew. The Noonday Demon: An Atlas of Depression. New York: Scribner, 2001.

Stanley, B.G., Chin, A.S. and S.F. Leibowitz. "Feeding and Drinking Elicited By Central Injection of Neuropeptide Y: Evidence For a Hypothalamic Site(s) of Action." Brain Research Bulletin 14 (1985): 521–524.

Straug, R.O. "Health Psychology." Stress and Health. Ed. Jessica Bayne. New York: Worth Publishers, 2002.

Stenfors, C., Mathé, A.A., and E. Theodorsson. "Chromatographic and Immunochemical Characterization of Rat Brain Neuropeptide Y-like Immunoreactivity (NPY-LI) Following Repeated Electroconvulsive Stimuli." Journal of Neuroscience Research 41 (1995): 206–212.

Stenfors, C., Mathé, A.A., and E. Theodorsson. "Repeated Electroconvulsive Stimuli: Changes in Neuropeptide Y, Neurotensin and Tachykinin Concentrations in Time." Progress in Neuro-Psychopharmacology and Biological Psychiatry 18 (1994): 201–209.;

Sterling, P., and J. Eyer. "Allostasis: A New Paradigm to Explain Arousal Pathology," Handbook of Life Stress, Cognition and Health. Ed. S. Fisher and J. robinson. New York: John Wiley & Sons. 1981.

Sweeney, P.D., Anderson K., and S. Bailey. "Attributional Style in Depression: A Meta-analytic Review." Journal of personality and social psychology. 50 (1986): 974-991.

Szasz, Thomas. The Myth of Mental Illness: Foundations of a Theory of Personal Conduct New York: Harper & Row, 1961.

Tabachnik, N., Crocker, J., and L.B. Alloy. "Depression and Social Comparison, and the False-Consensus Effect," Journal of personality and social psychology 45 (1983): 688-699.

Tanapat, P., Galea, L.A., and E. Gould. "Stress Inhibits the Proliferation of Granule Cell Precursors in the Developing Denate Gyrus." Journal of Developmental Neuroscience 16 (1998): 235-239.

Task Force on Nomenclature and Statistics: Progress Report, March 1, 1976, in Papers of the Task Force on Nomenclature and Statistics. Washington, DC. Archives of the American Psychiatric Association.

Van Pragg, Herman M., de Kloet, Ron, and Jim van Os. Stress the Brain and Depression. Cambridge: Cambridge University Press. 2004, 145.

van Praag, H., Kempermann, G., and F. Gage. "Running Increases Cell Proliferation and Neurogenesis in the Adult Mouse Dentate Gyrus." Nature Neuroscience 2 (1999b), 266 –270.

Vedantam, Shankar. "Experts Defining Mental Disorders Are Linked to Drug Firms." Washingtonpost.com 20 April, 2006, A07.

Voderholzer, U., Hohagen, F., Klein, T., Jungnickel, J., Kirschbaum, C., Berger, M., and D. Riemann. "Impact of Sleep Deprivation and Subsequent Recovery Sleep on Cortisol in Unmedicated Depressed Patients." American Journal of Psychiatry 161.8 (2004): 1404-1410.

Wahlestedt, C., Pich, E.M., Koob, G.F., Yee, F., and M. Heilig. " Modulation of Anxiety and Neuropeptide Y–Y_1 Receptors by Antisense Oligodeoxynucleotides." Science 259 (1993): 528–531.

Wahlestedt, C., Blendy, J.A., Kellar, K.J., Heilig, M., Widerlöw, E., and R. Ekman. "Electroconvulsive Shock Increase the Concentration of Neocortical and Hippocampal Neuropeptide Y(NPY)-like Immunoreactivity in the Rat." Brain Research 507 (1990): 65–68

Walport, L. Malignant Sadness: The Anatomy of Depression. New York: The Free Press, 1999.

Watson, Paul J., and Paul W Andrews. "Toward a Revised Evolutionary Adaptationist Analysis of Depression: The Social Navigation Hypothesis." Journal of Affective Disorders 13 (2001): 2.

Weel-Baumgarten, E.M. van, Bosch, W.J. van den, Hoogen H.J. van den, and F.G. Zitman. "The Validity of the Diagnosis of Depression in General Practice: Is using criteria for Diagnosis as a Routine the Answer?" British Journal of General Practice 50 (2000): 284-287 in Dowrick, Christopher. Beyond Depression: A New Approach to Understanding and Management. Oxford: Oxford University Press, 2004.

Weiner, E.D., Mallat, A.M., Papolos, D.F., and H.M. Lachman. "Acute Lithium Treatment Enhances Neuropeptide Y Gene Expression in Rat Hippocampus." Brain Research, Molecular Brain Research 12 (1992): 209–214

Wettstein, J.G., Earley, B., and J.L. Junien. "Central Nervous System Pharmacology of Neuropeptide Y." Pharmacology and Therputics 65 (1995): 397-414.

Widdowson, P.S. and A.E. Halaris. "Chronic Desipramine Treatment Reduces Regional Neuropeptide Y Binding to Y_2-type Receptors in Rat Brain." Brain Research 539 (1991): 196–202.

Widerlöv, E., Wahlestedt, C., Håkanson, R., and R. Ekman. "Altered Brain Neuropeptide Function in Psychiatric Illnesses With Special Emphasis on NPY and CRF in Major Depression." Clinical Neuropharmacology 9 (1996): 572–574.

Widerlöv, E., Lindström, L.H., Wahlestedt, C., and R. Ekman. "Neuropeptide Y and peptide YY as Possible Cerebrospinal Fluid Markers for Major Depression and Schizophrenia, Respectively." Journal of Psychiatric Research 22 (1988): 69–79

Widerlöv, E., Heilig, M., Ekman, R., and C. Wahlestedt. "Possible Relationship Between Neuropeptide Y (NPY) and Major Depression — Evidence From Human and Animal Studies." Nordisk Psykiatrisk Tidsskrift 42 (1998) 131–137.

Wittgenstein, L. Remarks on the Foundations of Mathematics. ed G.E. Anscombe. Basil Blackwell: Oxford. 1956, 57.

Whitaker-Amitia, P.M. "Role of Serotonin and Other Neurotransmitter Receptors in Development: Basis for Developmental Pharmacology." Pharmacology Review 43 (1991): 553-561.

World Health Organization. International Statistical classification of Disease and Related Health Problems: ICD-10. 10th ed. Vol. 3. Geneva: World Health Organization, 2005.

Wurtzel, Elizabeth. Prozac Nation: Young and Depressed in America. New York: Riverhead Books, 1994. 21.

Yost, J.H., and G. Weary. "Depression and the correspondent inference bias: evidence for more effortful cognitive processing." Personality and Social Psychology Bulletin 22 (1993): 192-200.

Zachrisson, O., Mathé, A.A., Stenfors, C., and N. Lindefors. "Region-specific Effects of Chronic Lithium Administration on Neuropeptide Y and Somatostatin mRNA Expression in the Rat Brain." Neuroscience Letters 194 (1995): 89–92.