EMPIRICAL EVIDENCE DISCONFIRMS

THE BIOPSYCHIATRIC ONTOLOGY

OF MENTAL DISORDERS

A DOCTORAL PAPER
PRESENTED TO THE FACULTY OF
THE
GRADUATE SCHOOL OF PROFESSIONAL PSYCHOLOGY
OFFICE OF GRADUATE STUDIES
UNIVERSITY OF DENVER

IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE
DOCTOR OF PSYCHOLOGY

BY
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JUNE 30, 1998

Acknowledgements

I want to thank several people who have supported me, influenced my thinking about this topic, and helped me to pose my questions and arguments in a more thoughtful and presentable way than they might otherwise be expressed. My parents raised me to explore and question everything, and have celebrated my attempts to grow and understand the world even when I've gone against the grain. I thank my parents and stepparents for their moral support, for supporting my education, and for being so interested in my studies and professional development.

I would like to thank Alberto Pieczanski, M.D., for helping me to find my path, for his care, for exemplifying the passion for the craft of therapy, and for the stimulating discussions that helped fuel my growing interest in this area of research.

Thomas Wehr, M.D., put up with my provocative and challenging behavior in research meetings at NIMH for far longer than most would have done as I began to have misgivings about the assumptions of biopsychiatric research and treatment. I thank him for his respect, his tolerance, his thoughtfulness, and the many opportunities he gave me to be a part of a rigorous biopsychiatric research team.

Early in the writing of this paper, I received some much-needed encouragement from Stanton Peele, Ph.D., and a corrective rap on the knuckles from Thomas Szasz, M.D. Also, David Gilles-Thomas, Ph.D., Howard Lambert, Ph.D., and Jacob Pomerantz, Ph.D., were unflinching and insightful in their criticism and the work is greatly improved because of their input. Finally, I'd like to thank my committee, Ralph Fisch, Ph.D., Lupe Samaniego, Ph.D., and Howard Lambert, Ph.D., for their time, support, and effort in helping me to produce this paper.

Truth is a river that is always splitting up into arms that reunite. Islanded between the arms, the inhabitants argue for a lifetime as to which is the main river.

–Connolly

Where it is a duty to worship the sun it is pretty sure to be a crime to examine the laws of heat.

–Morley

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ABSTRACT

Although serious mental disorders are popularly referred to as the result of "biochemical imbalances," a great deal of biopsychiatric research invalidates this notion. Evidence indicates that mental and physiological phenomena are mutually determined, but that conceptual and linguistic limitations make the understanding of a parallel mental and physical expression difficult to grasp. Biopsychiatric research is critically reviewed and reconceptualized as showing that while mental disorders are expressed physiologically, this does not determine causality. Recent studies show that both damaging and therapeutic interpersonal experiences create lasting changes in brain physiology. Additionally, genetic, morphological, and functional brain research has yielded more equivocal correlations with mental disorders than are customarily reported in the popular press. Treatment studies indicate that clinical improvement of reputedly biochemical disorders often occurs independent of any pharmacological effects. However, economic incentives by pharmaceutical companies and medically oriented health insurance companies may bias clinicians' treatment approaches toward pharmacological interventions. The confusion between a biopsychiatric epistemology of mental disorder and a biopsychiatric ontology of mental disorder is clarified, emphasizing that a particular method of inquiry does not determine the essence of what is being studied.

CHAPTER 1: Introduction

In the study of ideas, it is necessary to remember that insistence on hardheaded clarity issues from sentimental feeling, as it were a mist, cloaking the perplexities of fact. Insistence on clarity at all costs is based on sheer superstition as to the mode in which human intelligence functions.
–*Whitehead*

We make trifles of terrors, ensconcing ourselves into seeming knowledge, when we should submit ourselves to an unknown fear.
–*Shakespeare*

The present study will show that the biopsychiatric paradigm of mental illness—that severe mental disorders are caused by biochemical and/or anatomical defects—is based on inferential errors about the relationship between physiology and mental experience, and is not confirmed by empirical research. In this chapter, a brief introduction to the history of biopsychiatry and its critics will be followed by examples of media accounts of mental illness that reflect a biopsychiatric zeitgeist that does not accurately portray scientific research. The second chapter is an exploration of the philosophical and inferential errors of biopsychiatric thought. The biopsychiatric *a priori* is critiqued as an "illness" metaphor that is not completely in accord with the mental, physiological processes that the metaphor is used to describe. The difference between an epistemology of mental disorder and an ontology of mental disorder is highlighted. The third chapter includes research evidence showing that the biopsychiatric epistemology (the study of the biochemical and anatomical concomitants of mental phenomena) is inadequate as a method for determining the causes of mental disorders; and that the biopsychiatric ontology (the belief that the essence of mental illness is a biochemical or

disease process) is not supported by biopsychiatric research. The fourth chapter is a critique of research comparing pharmacological and psychotherapeutic treatments, and outlines a more parsimonious conceptualization of mental illness, and improved treatment research methodology.

Historical Overview of Biopsychiatry and its Critics

In 1989, former President George Bush proclaimed the 1990s to be "The Decade of the Brain." In this decade, a powerful surge in biological research was meant to increase our understanding and effective medical treatment of brain dysfunction (Scientific American, 1992). Besides research on degenerative diseases such as Parkinson's disease, and organic dysfunction such as epilepsy, it was hoped that new insights into complex behavioral problems such as schizophrenia and alcoholism would lead to better treatments. These insights might come, in part, from technological advancements in brain imaging that had been made possible by innovations in the defense industry.

The biopsychiatric approach to understanding the mind, sometimes called "biological reductionism," is an attempt to find the basis of mental process in the brain's biochemical activity and electrical impulses:

> In this decade of the brain, we are learning how the brain's machinery works, down to the biophysics of single cells. Struggling to oust magical, occult powers from matter, Descartes set in motion the reduction of mental functions to mechanical processes that is only now coming to fruition. (Leahey, 1997, p. 110)

Biopsychiatry has had a long history, being practiced by the "protopsychologists" in the 5th century, BC, and more recently by the humoralists of the 17th century, and the early neurologists of the late 19th century (Foucault, 1988; Leahey, 1997; Zuckerman,

1995). Nevertheless, biological reductionism, as an adequate and sufficient epistemology for understanding the mind, also has had its critics. Descartes, for instance, felt that some mental processes might be mechanistic and automatic, but that there was also a human consciousness utterly separate from the physical, mechanistic world. In the 1600s, the humoralists debated whether the origin of melancholia was genetic and chemical (temperamental and humoral) or whether qualities of melancholia were "free from any constraint of substance" (Foucault, 1988, p. 120). In his 1890 book, *Psychology*, William James wrote this critique of his biopsychiatric colleagues:

> 'Ohne Phosphor, kein Gedanke,' [without phosphorus, no thought] was a noted war-cry of the 'materialists' during the excitement on that subject which filled Germany in the [18]60s. The brain, like every other organ of the body, contains phosphorus, and a score of other chemicals besides. Why the phosphorus should be picked out as its essence, no one knows. It would be equally true to say, 'Ohne Wasser, kein Gedanke,' or 'Ohne Kochsalz, kein Gedanke'; for thought would stop as quickly if the brain should dry up or lose its NaCl as if it lost its phosphorus. . . . The phosphorus-philosophers have often compared thought to a secretion. "The brain secretes thought, as the kidneys secrete urine, or as the liver secretes bile," are phrases which one sometimes hears. The lame analogy need hardly be pointed out. . . . But we know of nothing connected with liver- and kidney-activity which can be in the remotest degree compared with the stream of thought that accompanies the brain's material secretions. (James, 1948, p. 132)

A century later, Richard Lewontin, a Harvard geneticist and zoologist, noted that

> We no longer think, as Descartes did, that the world is *like* a clock. We think it *is* a clock. . . . But that is not a universal direction for the study of all nature. A lot of nature. . . cannot be broken up into independent parts to be studied in isolation, and it is pure ideology to suppose that it can. (Lewontin, 1991, p. 14-15)

Critics of biopsychiatry often have attacked inferences about the nature of mental disorders that are based on analogical or metaphorical explanations, rather than scientific, empirical evidence. For example, Szasz has criticized the medical model that describes mental illnesses as a subclass of (medical) illnesses. He has argued that there are essential

differences in how the two types of problems satisfy the medical concepts of “symptoms” and “signs”:

> There can, in the absence of [symptoms], be no mental illness. Since it is obvious that this is not true for bodily illness—diseases such as asymptomatic and undiagnosed hypertension or coronary atherosclerosis immediately spring to mind—it is difficult to see how psychiatrists can, in good faith, maintain that mental illness is like any other illness. . . .
>
> [Unlike a medical symptom, a] mental symptom *does not point* to a possible illness; *it is* (the same as) a mental illness. (Szasz, 1990, p. 93, 97, italics in original)

Although a proponent of new antidepressant drug technology, Kramer (1993) has also noted the limitations of the biopsychiatric ontology:

> Biologists do not know what depression is. The reigning model at the cellular and chemical level, the biogenic-amine hypothesis, is demonstrably false or incomplete. Understanding of minor mood disorders, or normal variants, is even more primitive. . . . The biological study of the self is so primitive as to be laughable. (p. 283)

Kramer indicated that despite recent research efforts, the ontology, or essential nature, of mental disorders such as depression remains a mystery. He also pointed out the limits of the biological epistemology, or method of seeking such knowledge, that biopsychiatrists employ. Lipowski (1989, cited in Gabbard, 1992) criticized the biopsychiatric epistemology more pointedly:

> It confuses the distinction between etiology and correlation, and cause and mechanism, a common confusion in our field. It gives the patient a misleading impression that his or her imbalance is *the* cause of his or her illness, that it needs to be fixed by chemical means, that psychotherapy is useless, and that personal efforts and responsibility have no part to play in getting better. . . . To assume, as we all do, that biochemical processes underlie mental activity and behavior does not imply that they are the causal agents but rather constitute mediating mechanisms. (Gabbard, 1992, p. 992)

Objections such as these notwithstanding, criticisms of both the biopsychiatric epistemology and ontology have been overwhelmed by research and media attention

embracing the technologies of brain imaging and psychopharmacology. The “Decade of the Brain” initiative has profoundly influenced the American public’s concern with the biological basis of psychological problems. Increasingly, the understanding and treatment of psychological problems in terms of their physiological correlates is being supported above other approaches to mental health, both economically and politically (Breggin, 1991; Faenza & Guida, 1996; Krupnick et al., 1996; Mu™oz, Hollon, McGrath, Rehm, & VandenBos, 1994; National Alliance for the Mentally Ill [NAMI], 1997a, 1997b; Peele, 1995; Pincus et al., 1998; Ridgewood Financial Institute, 1997). In addition to economic and political support, the biopsychiatric approach to mental disorders has received a great deal of media coverage, and has benefited from the efforts of the pharmaceutical industry’s educational and advertising programs. The extent of this publicity has led some clinicians to become concerned about the status of biological psychiatry and the public’s exuberance about the latest “disease of the month” (Abbey & Garfinkel, 1991; Antonuccio, 1995; Antonuccio, Danton, & DeNelsky, 1995; Breggin, 1991, 1994; Dumont, 1991; Gabbard, 1992; Hayes & Heiby, 1996; Shorter, 1995; Walters, 1992; Yapko, 1997).

The relief of having a simple, biological reason for one’s difficulties is a powerful motivator to seek medical diagnosis. Weiner (1993) found that the diagnosis of illness results in more favorable treatment by others than does a judgment of personal failure; and it is on this basis that the biopsychiatric ontology may be an attractive model of psychological problems. The purpose of this paper is to present recent neurobiological evidence showing that the underlying assumptions of the biopsychiatric approach are erroneous, and that these assumptions lead to misinformation about, and limited

standards of care for, mental disorders. Furthermore, the biopsychiatric epistemology has yielded evidence that disconfirms its superiority over other approaches as a method for understanding and treating the causes of mental disorders. An exclusion of such disconfirming data from biopsychiatric theory-building promotes a scientifically unsupported ontology of emotional and behavioral problems.

Apart from any criticisms, the massive efforts in biological and pharmaceutical research have yielded an advancement in the understanding of biological processes and the chemical amelioration of symptoms. These advances appear to provide evidence for the validity of the epistemology; yet, a large body of scientific evidence supports a more complex ontology than is currently in style. Nevertheless, the public, the government, the mental health guilds, and the insurance industry have been solidifying a consensus about the ontology of, and thus the legitimate treatments for, mental illness. As mental disorders increasingly are seen as primarily biological processes, biological treatments attain a preeminence (Breggin, 1991; Brown, 1990; Consumers Union, 1995; Critser, 1996; Faenza & Guida, 1996; Farber, 1990; Gabbard, 1992; Gergen, 1990; Kaiser, 1997; Karon & VandenBos, 1994; Krupnick et al., 1996; Modrow, 1996; Mu™oz et al., 1994; Peele, 1990, 1995; Pincus et al., 1998; Podvoll, 1990; Ridgewood Financial Institute, 1997; Sarbin, 1990; Szasz, 1990). For example, current mental health insurance capitation policies emphasize short-term medical interventions, and often provide greater coverage for prescriptions and primary care physician visits than for open-ended psychotherapy treatment. However, as the present study will show, the scientific evidence actually does not support the theoretical basis for such an approach to treatment, nor necessarily its clinical superiority. Nevertheless, a narrow range of treatment options,

promoted by economic, political, and legal inducements, may prevent the advancement of knowledge and treatment methods outside of accepted parameters of study (Critser, 1996; Gibeaut, 1996; Nash, 1997; Peele, 1995; Shute, 1997).

Contemporary Media Portrayals of Mental Disorders

The media are the conduits by which laypersons, and perhaps many clinicians, are informed about advancements in understanding what mental disorders are and how they can be alleviated. Much mental health research follows a narrow, biological epistemology of serious mental disorders; thus media accounts of this research contribute to clinicians' and the public's misunderstanding of the complexity of these disorders. In addition, articles appearing in magazines and newspapers have a dramatic, clear, and persuasive tone that often misrepresents the equivocal and tentative results that are evident in primary sources (Breggin, 1991). Examples of this misrepresentation of research are abundant and easy to find by comparing press clippings with original research.

Case example of the miscommunication of research findings.

A recent article in *Time* magazine reported the discovery of a dramatic anatomical difference in the brains of "people suffering from hereditary depression" (Gorman, 1997). The author concluded that this "latest finding" would "perhaps one day, help prevent the millions of Americans who may have inherited a propensity to depression from falling into the downward spiral of despair." The article in *Time* was written about a study published in *Nature* (Drevets et al., 1997), in which the authors had used a combination

of PET and MRI techniques to compare the average brain structure size and function of depressed, bipolar, and control groups.

The first problem in translating the original study to the popular press article was in a reification of measures of depressed affect into a genetic disease. This form of reductionism is based on dubious genetic evidence that has been contested in the scientific literature (Genetics Workgroup of the National Institute of Mental Health [GW-NIMH], 1997). In the *Time* article, it occurred in the use of the phrases "hereditary depression" and "inherited a propensity to depression." In the *Nature* study, Drevets et al. referred to heredity once, in their introductory remarks: "Both bipolar and unipolar disorders can be heritable illnesses associated with neurochemical, neuroendocrine and autonomic abnormalities. The neurobiological basis for these abnormalities has not been established" (p. 824). Yet, there is a lack of clear scientific evidence that forms of depression are genetically transmitted. The word "hereditary," and its synonym, "heritable," means "passing, or capable of passing, naturally from parent to offspring through the genes" (Random House, 1987). Rather than using the words "hereditary" or "genetic" throughout the rest of the article, Drevets et al. used the more ambiguous word "familial." This may have been done because their criteria of subject selection did not have a material, genetic basis, but relied on family history of a parent or sibling having either "probable or definite" affective disorders. Because so many complex traits, including religion and political party, are expressed in strong familial patterns (Lewontin, 1991), the criterion of probable or definite depression or bipolar disorder diagnosis in parents is not sufficient (nor, strictly speaking, necessary) to establish a genetic, hereditary link for depression between parent and offspring.

The second problem in translating the original study to the popular press article was that the anatomical measurements of the subgenual prefrontal cortex (SPFC) were made on expanded groups of subjects that included medicated subjects, subjects in remission, and subjects who *did not* have family members with depression, none of which was mentioned in the *Time* article. This is further evidence that the anatomical differences in this study are not attributable to "hereditary depression." In any case, the interpretation in *Time*, that "one portion of the brain is significantly smaller and less active in. . . hereditary depression" is not supported by the *Nature* study because the study was not actually about hereditary depression.

The third problem with the translation from the *Nature* study is related to the fact that the *Time* article does not mention that there were three groups in the study; i.e., that there was a bipolar disorder group as well as a unipolar group and a control group. Although the bipolar group showed reduced metabolism in the SPFC while in the depressed phase, it showed significantly increased activation in the manic phase, relative to control subjects and to bipolar subjects in the depressed phase. Anatomically, the brain volume was substantially smaller in the bipolar subjects relative to controls; but metabolically, the area's function during mania episodes more than compensated for this anatomical difference. Additionally, although the bipolar group had substantially smaller SPFCs than the control group, 8 out of 21 of the bipolar subjects in the study had "remitted," and 2 of the remitted subjects were unmedicated. Therefore, the reduced volume did not necessarily preclude normal levels of metabolic activity *or* normal behavioral and affective functioning. One bipolar subject was tested in both mood states, and showed a markedly symmetrical metabolism in the depressed and manic phases. This

led Drevets et al. to speculate that changes in SPFC function might be mood-state dependent, i.e., that changes in SPFC function were caused *by* mood state, not that mood state changes were caused by SPFC function. As will be discussed in Chapter 3, volume differences may also have been the result of changes in extraneuronal space rather than a reduction of neural tissue.

In summary, the *Time* article makes inferences about the reasons for and consequence of the anatomical differences that are not justified by the *Nature* article. The pervasive bias toward publishing definitive and exciting reports of biological differences between normals and subjects at the expense of accuracy is reflected in yet another passage about the metabolic rate difference: “The subgenual prefrontal cortex was almost 8% less active in depressed patients than in the controls” (Gorman, 1997). In fact, Drevets et al. first found a 7.7% difference, then replicated the procedure with a second group (allowing them to use a one-tailed t-test for the statistical analysis) and found a 6.6% difference. Instead of averaging the two numbers to slightly over 7%, Gorman rounded up the higher number to “almost 8%.” Although Gorman ends the *Time* article with caveats that this research can not identify people at risk for mental illness because of the variation between individuals, the dramatic tone of the article misrepresents the complex findings. One might summarize the *Time* article as saying that people with hereditary depression have smaller SPFCs than normal people. However, a more appropriate summary of the research might be that whatever anatomical and functional difference in SPFC may exist, on the average, between depressed and normal people, this difference may not preclude normal behavioral functioning or rates of brain activity that

offset a reduction in size. Because of limits in the study's methodology, the evidence does not support a genetic cause for the anatomical or behavioral differences.

Genetics in research versus genetics in the mass media.

The NIMH Genetics Workgroup recently published a 94-page report on the state of the art in mental health genetics research (GW-NIMH, 1997). The report contains 468 scientific references, and includes summaries of the molecular genetics research of such disorders as schizophrenia and bipolar affective disorder, two mental disorders whose genetic basis is commonly presumed to be an established fact rather than a hypothesis. Yet the NIMH Genetics Workgroup found that the molecular genetic evidence is weak or "suggestive" at best for bipolar affective disorder:

> Methodological criticisms have been raised about many of the earlier studies, and multiple failures to replicate have been reported. . . . The inability to obtain more compelling evidence may have resulted because: (1) genes on [chromosomes] 18 and 21 confer susceptibility to bipolar disorder, but they have such a small relative effect on risk that a very large sample is required for detection; (2) genes on 18 and 21 confer susceptibility in a small number of families (failures to replicate reflect the confounding effects of genetic heterogeneity); or (3) the reported positive results are due to chance. Unfortunately, these three explanations are currently indistinguishable. (pp. 49-50)

The same general finding held true for schizophrenia as well, which, like bipolar affective disorder, has been the subject of many molecular genetics studies:

> Only two studies have reported linkage evidence meeting a genome-wide *P* value of 5%. . . . The first study reported linkage to 5q. . . . however, numerous nonreplications have been published, and a combined re-analysis of several data sets, among them the original report, excluded a susceptibility locus from 5q. Analyses of additional markers in a new sample. . . led to exclusion of linkage to 5q. The second is a chromosome 6p linkage. . . . Analyses of 713 families contributed by 14 research groups worldwide failed to find more than suggestive linkage evidence to this region. Nonreplications of 6p linkage have been reported. An additional concern is that the markers implicated by the studies reporting suggestive evidence lie within a very large chromosomal region (over

> 30 Mb). . . . Several population-based association studies have implicated different candidate genes, but nonreplications exist for each. Reports of an association between trinucleotide repeat expansions and schizophrenia have not been followed by identification of a specific expanded gene. In summary, the strongest linkage evidence to date support the existence of schizophrenia susceptibility loci on chromosomes 6 and 8; however, the magnitude of the statistical evidence and the existence of nonreplication demonstrate that these are clearly not confirmed, convincing findings. The inconsistent results may reflect the effects of small relative gene effects, genetic heterogeneity, or Type I error. Reported linkages to other chromosomes (3, 5, 9, 20, 22) are less compelling. (pp. 63-64)

The lack of replicated evidence for genetic causes of serious mental disorders, coupled with suggestions in the mass media that these disorders are genetically based, indicates that substantial inferences are being made that are not based on this research. The evidence of high comorbidity in first-degree relatives and twins is evidence that some mechanism of "transmission" is occurring in many mental disorders. Although genetic and temperamental factors are passed from parent to child (Buss & Plomin, 1984), the great behavioral variance between genetically identical individuals supports a view contrary to the genetic disease model: Regardless of any putative genetic determinants, environmental and/or accidental factors are crucial in determining the incidence and course of mental disorders (Motulsky, 1997). While media reports of genetics research focus on the part of behavioral variance attributed to genetic or influence, the singularity of this biological focus in the media helps create an ontology of mental disorder that has important consequences:

> The knowledge of the genetic transmission of bipolar illness often triggers and maintains fear and a decision not to have children. Patients who already have children feel guilty and tend to explain the latters' behavior on the basis of possibly having inherited the illness. (Jacobs, 1982, p. 452)

While all behavior occurs within a complex web of influences, including genetic influences, a repetitive singling out of biological causes by the media may influence the

public to conceptualize and seek treatment through a narrow and inaccurate conceptualization of mental disorders.

Case examples of biopsychiatric bias in the mass media.

Embedded within media accounts of mental illness are two implicit assumptions: (a) an epistemological assumption that knowledge of complex mental and behavioral processes can be increased by studying brain physiology; and (b) an ontological assumption that the essential nature of psychological phenomena is a biochemical process. In other words, the root of serious psychological disturbances is a biochemical imbalance; the proper study of the basis for these disturbances is a biochemical study; and the proper treatment is a biochemical treatment. Thus, a recent college course description for a class entitled, "Neuroscience in the 1990s: The 'Decade of the Brain'" stated that "illnesses such as schizophrenia are now understood to be the result of physical abnormalities in the brain that can be treated with drugs" (Jobe, 1996). An article in *Parade* magazine quoted Dr. Bruce Waslick of the New York State Psychiatric Institute saying, "Attention deficit is a real disease, a brain disorder. . . Something different is going on in these kids' brains" (Ubell, 1997, p. 5). A hospital magazine article quoted a physician as saying, "We try to make our patients aware that their obesity is a disease, that it is incurable, and that they will need maintenance assistance for the rest of their lives" (cited in Peele, 1995, p. 118). A brief article in *Men's Health* magazine quoted the actor, Rod Steiger, who has suffered from depression as saying, "while you might snap out of the social depression caused by a lost job, clinical depression doesn't go away. It's caused by a chemical imbalance. And you might need drug therapy to correct it, just as diabetics need insulin" (Staff, 1997, p. 42). Alza Corporation, a

pharmaceutical company that produced a brochure designed to recruit subjects for research protocols, explained that “studies indicate that ADHD does not stem from the home environment, but from biological causes.” The pharmaceutical company Eli Lilly’s promotional leaflet for its antidepressant, Prozac®, was headlined, “Like diabetes or arthritis, depression is a physical illness.” Eli Lilly also recently produced a booklet on “Understanding the inner workings of obsessive-compulsive disorder (OCD).” It stated that obsessions and compulsions constitute “a common medical illness,” and that this medical illness is “a biochemical imbalance that affects the way the brain influences a person’s thoughts, feelings and actions.” Nevertheless, Eli Lilly also stated that “it is difficult for scientists to determine which comes first—the changes in brain chemicals or the OCD.” SmithKline Beecham, another pharmaceutical company, produced a brochure called, “Depression: Getting the help you need.” The brochure said “Major depression requires prompt medical treatment. . . . Depression is an illness, just as diabetes and arthritis are illnesses. Having depression is <u>not</u> your fault and it’s <u>not</u> a sign of weakness” (emphasis in original). Another of SmithKline Beecham’s brochures, on anxiety disorders, said that anxiety disorder is “a medical condition” and “obsessive-compulsive disorder is as common an illness as asthma or diabetes.” An internet website called “HealthGuide Online!” stated that “Just like heart disease is an illness of the heart, and asthma is an illness of the lungs, schizophrenia is an illness of the brain” (HealthGuide, 1998). A nationally syndicated radio show called *Loveline* featured a caller with bulimia concerns. The show’s host said, “Fifteen years ago you were a nutball. Now it’s recognized as a legitimate, bona fide, medical disorder” (Carolla, 1996). An article about addiction in *Time* magazine stated that “drug dependence has a clear biological basis. . . .

Addiction is a disorder of the brain no different from other forms of mental illness" (Nash, 1997). An article in *The Medical Post* pointed out that "patients with panic disorder are at increased risk for other medical conditions" (Rich, 1996). And in response to a reader's question in *Parenting* magazine about a 5-year-old child who "rarely smiles or gets excited," Snyderman advised that "if neurological and psychiatric exams reveal a condition such as clinical depression, obsessive-compulsive disorder or extreme mood or temperament changes, anti-depressants may be useful, since these illnesses often stem from biological or hereditary factors" (Snyderman, 1997).

Media and pharmaceutical companies' accounts of the biological basis and medical status of mental disorders are ubiquitous. Moreover, while there has been some questioning in recent years about the medication of emotional and social problems, especially in young children (Huffington, 1997; Ubell, 1997; Zachary, 1997), there is very little support in the popular press for the idea that major mental disorders such as depression and schizophrenia result from psychological, developmental, and social factors of individuals and their environment. Additionally, the biochemical-basis justification for the medical treatment of severe emotional disorders has diffused into more subtle and uncodified problems. In the academic press, there are reports of drugs being used to treat not only reputed biological dysfunction but also problems such as jealousy, narcissistic rage, conduct disorder, and "imagined ugliness" (Abramson, 1983; Gross, 1991; Phillips, McElroy, Keck, Pope, & Hudson, 1993; Rifkin et al., 1997). The assertion of the biopsychiatric approach, as the ontology of psychological problems rather than an epistemology of research, is exemplified by pharmaceutical companies' claims that stressful life events, poor parenting, and problems at home do not facilitate OCD,

depression, or ADHD; but that these problems are biological, medical illnesses. The National Alliance for the Mentally Ill (NAMI), an organization that claims 168,000 members (and which is sponsored by over a dozen of the largest pharmaceutical companies in the U.S.) actively lobbies for the biomedical research of psychological problems. It defines these problems as "no-fault" biological brain disorders (NAMI, 1997a).

In answer to objections raised about the biopsychiatric approach to the research and treatment of depression, Eli Lilly recently produced a leaflet for patients called, "Facts about Prozac," with the following information:

> Certain antipsychiatry groups are the source of much of the misleading and inaccurate news coverage surrounding Prozac. These groups have a long history of opposition to psychiatry and medical treatments for mental illnesses, including depression. Members of these groups view psychiatry and psychiatric medicines as competition for their costly self-help programs. Consequently, they have gone to great lengths to discredit health care professionals and effective medical treatments. . . . The anti-Prozac campaign has been thoroughly discredited by the medical and scientific communities and various major news media sources. Well-respected news sources, such as *Time* magazine, *The Wall Street Journal*, and *60 Minutes*, have undertaken investigations of these antipsychiatry groups. In every case, these investigations revealed highly questionable practices and the groups' self-serving motivations (Eli Lilly and Company, 1995).

This study will show that much medical, scientific research actually discredits many of the claims made by pharmaceutical companies such as Eli Lilly about the nature of mental illness and the relative effectiveness of pharmacological treatments. For example, one researcher recently published a book based on Freedom of Information Act requests for Eli Lilly's own research documents and FDA memos, discrediting Lilly's claims about the relative effectiveness and the safety of Prozac→ (Breggin, 1994). Breggin's findings have been reinforced by other researchers, including members of the

World Health Organization (Medawar, 1997). Increasingly, biopsychiatric research itself is discrediting much of the promotional material generated by pharmaceutical companies.

In the Decade of the Brain, the promotion of biomedical technology for the treatment of emotional problems has been linked with a massive and successful effort to define these problems as illnesses, specifically biological illnesses. Grassroots organizations, pharmaceutical companies, scientists, and the popular press all have promulgated this biopsychiatric view concurrently with research designed to improve the understanding and treatment of psychological problems through a medical frame of reference.

Despite this campaign to legitimize the study and treatment of mental illness as a medical discipline, empirical evidence indicates that psychological problems (even profound and chronic disturbances in functioning such as schizophrenia, depression, and addiction) are not fundamentally biological diseases; nor are they best understood or treated as chemical imbalances, or "no-fault" illnesses. The ontology that psychological problems are biologically based may be the result of inferential errors about cause and effect and a biased view of the research. For example, the empirical evidence indicates a correspondence between certain psychological and physiological measures, but not that biological processes are the "prime mover" of serious mental disorders.

While the study of biological processes correlating with mental disorders provides important information about the way the brain works when people are suffering from psychological distress, the research yielded by the Decade of the Brain has coincided with an unfounded ontological shift. Rather than being conceptualized as a study of physiological correlates, biopsychiatric research results have been portrayed as evidence

that mental disorders fundamentally are diseases of the brain and ought to be treated that way. Philosophically and empirically, this shift is not supportable. Philosophical shortcomings of the biopsychiatric method will be reviewed in the next chapter. Neurobiological and genetic evidence against a biopsychiatric ontology of mental disorder will be presented in Chapter 3. The research and treatment implications of this evidence will be presented in Chapter 4.

CHAPTER 2: Philosophical and Conceptual Considerations

The body is a thing, the soul is also a thing; man is not a thing, but a drama—his life. Man has to live with the body and soul which have fallen to him by chance. And the first thing he has to do is decide what he is going to do.
–Ortega y Gasset

Science commits suicide when it adopts a creed.
–T.H. Huxley

Mental Illness and the Mind-Brain Split

Foucault (1988) chronicled the history of mental illness in Europe from the end of the sixteenth century, and discovered that the split between psychological and physical treatments for madness is a relatively recent phenomenon that occurred substantially later than the Cartesian philosophy that is reputed to have spawned it. Through the Age of Reason in 18th century Europe, it was thought that the mind and body were ordinarily a unity that madness split (although not completely) into dissociated parts. For example, in the case of mania, intense bodily sensations and movements could make one's mind blind to various ideas or perceptions; or in the case of depression, physical inertia could be accompanied by horrible or violent thoughts and feelings that were out of sync with the quiescent bodily state (Foucault, 1988). Yet, according to Foucault's description, these derangements and dysharmonies were not considered in terms of causal relations. It was not the body's humors that caused the madness, although the humors might well be out of balance. Nor was madness caused by a moral failing or weakness that perturbed the body, albeit that a person might stop assuming his or her responsibilities as a citizen. Rather, madness was at once an expression of the whole person, expressed through mind

and body alike (Lewontin, 1991). In this regard, Foucault describes the experience of "passion" as it was seen from the classical period through the 18th century—as a unity between the mind and body that is difficult to convey in ordinary language:

> Passion indicates, at a new, deeper level, that the soul and the body are in a perpetual metaphorical relation in which qualities have no need to be communicated because they are already common to both; and in which phenomena of expression are not causes, quite simply because soul and body are always each other's immediate expression. Passion is no longer exactly at the geometrical center of the body-and-soul complex; it is, a little short of that, at the point where their opposition is not yet given, in that region where both their unity and their distinction are established. . . .
>
> If it is true that there exists a realm, in the relations of soul and body, where cause and effect, determinism and expression still intersect in a web so dense that they actually form only one and the same movement which cannot be dissociated except after the fact; if it is true that. . . there are qualitative, as yet unshared kinds of *a priori* which subsequently impose the same values on the organic and on the spiritual, then we see that there can be diseases such as madness which are from the start diseases of the body and of the soul, maladies in which the affection of the brain is of the same quality, of the same origin, of the same nature, finally, as the affection of the soul. (Foucault, 1988, p. 88)

As will be shown, this pre-modern conceptualization of mind-body relations yields a more parsimonious and empirically supported model of mental disorder than does the current biopsychiatric approach. Namely, there are psychological experiences, including mental disorders, that are expressed in the mind and brain, and that are not separate such that one process causes the other. However, this holistic view began to change during the Age of Reason, along with an increase in the physical confinement of deranged citizens and greater interest in scientific hypotheses about physical, organic dysfunction. By the nineteenth century, this separation grew more complete: physical treatments (for the physical diseases of the nerves) were "devised by an innocent determinism" while psychological treatments (for the moral guilt of unconscious

impulses) were organized around “culpable freedom” and responsibility (Foucault, 1988, p. 182).

Current debates about mental health display the same tension between the “no-fault” physical manifestations of illness on the one hand, and the moral responsibility of the capacity to change on the other. The biopsychiatric ontology is an embrace of the former perspective; psychotherapeutic paradigms tend to embrace the latter perspective, with a few exceptions of ceding serious mental disorders to the biopsychiatric approach. More recently, there has been a call for integrating the split between the two treatment approaches of medication and psychotherapy; yet this development derives less from a coherent philosophy of mental disorder than from a pragmatic appeal to economics and an attempted reconciliation of rival guilds.

A coherent ontology of mental illness must give a parsimonious account of the empirical evidence produced by multiple epistemologies. By accomplishing this, the study of mental disorders avoids being restricted by the insufficiencies of any one approach. Before proceeding to an examination of the empirical evidence against the biopsychiatric ontology, the fundamental philosophical error of the biopsychiatric epistemology—that studying brain physiology will yield an accurate understanding and ultimate control over mental illness—must be demonstrated. In doing so, it will be clear that this epistemology of mental disorder is driven by an *a priori* conceptualization rather than by empirical evidence; and that the epistemology is unlikely to succeed as the foundation for understanding mental disorder, although it may produce a useful technology of treatment. While the empirical evidence confirms the limitations of the biopsychiatric approach, understanding the philosophical and logical basis for the

epistemology's insufficiency as a model for understanding mental disturbance will provide a constructive roadmap for better research methodologies, a more complete understanding of mental disturbance, and more effective forms of treatment.

The Biological *A Priori* and the Justification for Treatment

Searle (1992) has commented that the epistemology of mental health research can not determine its ontology; "on the contrary, in the study of the mind as elsewhere, the whole point of the epistemology is to get at the preexisting ontology." In other words, attempting to understand the nature of mental disorders by looking at their biochemical phenomena does not make mental disorders, themselves, biochemical phenomena. Rather, the biopsychiatric epistemology reveals only a small piece of the ontology of mental illness. Critics have argued that this confusion is what has happened in the biopsychiatric study of the mind. That is, the biopsychiatric study of mental disorder has been an outgrowth of an *a priori* ontological view, rather than being a scientific approach toward constructing an ontology of mental illness through multiple epistemologies. Biological research on mental disorders has been driven in part by the premise that the basis of serious mental disorders is biological. In this view, an *a priori,* and unfalsifiable background assumption of both positive and negative research findings is that mental disorders are biologically based. This assumption prevents epistemological flexibility and the accommodation of the biopsychiatric paradigm to new evidence, both of which are necessary for a science to grow.

While the biopsychiatric epistemology provides a method for understanding and treating mental and behavioral phenomena by exploring biological correlates of these

phenomena, the biopsychiatric ontology is an *a priori* belief that mental and behavioral phenomena are reducible to and emergent from biochemical processes. Because the biopsychiatric ontology attributes cause to biochemical processes, it suggests a treatment approach that addresses the presumed physical basis, rather than the emergent mental expression, of mental disorder. On the other hand, the claim that mental illnesses are physically *expressed* arises from the empirical evidence yielded by the epistemology. Because the biopsychiatric epistemology is merely a method or approach to understanding mental disorder, it does not attribute cause as much as it provides a means for establishing cause at the biochemical level of expression, irrespective of the other levels at which one might study the expression of mental disorder. The epistemology directs research to understanding the biochemical phenomena concomitant with mental disorder. The epistemology, itself, does not suggest a treatment approach.

The Misattribution of Cause

The science of biopsychiatry is a search for evidence relating to the biochemical processes correlated with behavioral measures. While it is commonplace in psychological research that correlation does not equal causation, the advent of multiple regression analysis, popularized by Jacob Cohen (Cohen & Cohen, 1975), led some researchers to believe that this form of statistical analysis can yield causal evidence. The reason for this belief derives from the fact that through this method, the quantity of variance of some effects (independent variables) could be partialled from others in determining relationships with dependent variables. The partialling of variance yields the appearance

of “purer” measures of relative association between effects or factors. However, Cohen & Cohen warned that this technique does not imply causality:

> Again, we disavow the causal implication of the term “effect,” which is not logically defensible with nonexperimental [i.e., nonorthogonal] IVs. The reader is invited to take it as a mathematical metaphor and may prefer to substitute the more neutral word “difference.” Causal interpretations are never warranted by statistical results, but require logical and substantive bases. (p. 200)

In using phrases such as “assumed causal priority of the variables” (Cohen & Cohen, 1975, p. 99), Cohen has emphasized that causal ordering in regression analysis is a “logical” process and a hypothesis-based, *a priori* assumption by the investigator, not an empirically derived *result* of analysis. Data analytic models can not denote cause. Two hundred years earlier, philosopher David Hume argued essentially the same point: that while we assign causes to objects, in actuality a cause is merely an attitude we take toward objects (i.e., that the constant conjunction of two different events gives rise to an *expectation* of reoccurrence of one event given another). If one occurrence precedes another, the former is attributed to be the cause. Thus, if we observe that a reduction in the metabolism of serotonergic neurons precedes behavioral symptoms of depression or aggression on numerous occasions, we attribute the reduced secretion as the cause of depression or aggression, and predict future conjunctions of the physical and psychological event. Empirically, constant conjunction and its modern namesake, correlation, do not establish cause. The logical meaning we make of such correlational or statistical analysis establishes cause (Hume, 1967; Ayer, 1980). It is at this level of attribution that errors are made in biopsychiatric theory-building. Accurate causal attributions lead to the prediction and control of events, and so they are crucial for the development of a scientific technology. Yet, such a scientific technology can also

succeed under conditions of inaccurate causal attribution. This can happen when one variable of interest is attributed to be the cause of another, but where in actuality the variables are not independent, but mutually or reciprocally determined. In this case of "pseudocausation," the two variables are not actually separable (logically, correlation or constant conjunction between variables require independence between variables; Boss, 1983). Thus, the statement "psychomotor retardation is caused by depression" is pseudocausal because depression is not independent of, but partly defined by, psychomotor retardation. Similarly, the statement "depressed affect is caused by serotonergic dysfunction" is pseudocausal if depressed affect is dependent on or partly defined by such dysfunction. The causal question is begged: What causes the serotonergic dysfunction that is sometimes present in depression?

Ostensibly, the accuracy of causal attributions can be measured empirically by testing hypotheses. Behavioral psychology is the prototypic method for this endeavor, in that behavioral psychology involves the measurement of behavioral events or data to aid in the control and prediction of future behavioral events. Naturally, the constant conjunction of two events, X and Y, even if one precedes the other, can itself be caused by the constant conjunction of a third event (*ad infinitum*) with X and/or Y. Thus, it is possible that the reduced metabolic activity of serotonergic neurons sometimes seen in conjunction with depressive symptoms is, along with those symptoms, caused by other events. Therefore, the attribution of a causal relationship does not rule out a superordinate cause or set of causes that impinges either positively or negatively on the causal relationship of interest (Meehl, 1991). For example, low serotonin has been associated with depression, social rejection-sensitivity, and aggressive behavior, and high serotonin

has been associated with confidence and dominance behaviors (Kramer, 1993). From this association, one might infer that serotonin function causes fluctuations in mood and behavior. However, primate research has indicated that the experimental manipulation of social dominance hierarchies, or social status, among monkeys predicts serotonin function in expected directions (Raleigh, McGuire, Brammer, & Yuwiler, 1984). Specifically, experimentally increasing a monkey's social dominance through the experimental manipulation of social interaction coincides with an increase in that monkey's serotonin production. Thus, a third variable of social status might be considered causal in relation to the variables of serotonin and mood/behavior. Naturally, a host of other variables might influence any or all of these factors concurrently. Accurate causal attributions, replicated by further research, can still beg the causal question. Therefore, in establishing the ontology of mental illness as biologically based, two complications arise concerning causal attributions: whether a variable is a cause or a pseudocause; and whether a causal variable acts as a "surrogate" (Cohen & Cohen, 1975) for some unknown superordinate cause. Logically, cause is partly determined by the temporal ordering of events. In the biopsychiatric ontology, biological dysfunction must precede mental or behavioral disturbance as a necessary condition for cause. As will be shown, the non-independence and non-linear temporality of physiological and mental events precludes this temporal ordering, creating problems for the biopsychiatric ontology of mental disorders.

The Decontextualization of Behavior

In addition to the problems with causal attributions in biopsychiatric research, there are also relevant technical issues having to do with definition, measurement, and analysis. The methods of defining, measuring, and analyzing mental or behavioral events require a great deal of inference, and the limits these inferences place on a scientific psychology have been extensively reviewed by Meehl (1991). Our presumption that a behavior is a stable, definable, measurable, and bounded *thing* (e.g., the response-event of pressing a lever) facilitates causal attributions for that behavior because constant conjunction (a prerequisite for causal attributions) can only be established by the repetition of functionally identical events (e.g., behavioral operants). For the attribution of causation, this functional identity must be established by the definition or delimiting of the event. Yet, the context of events is constantly changing, so defined behaviors are always artificially bounded and decontextualized to some degree (Cohen & Cohen, 1975; Meehl, 1991). The difficulty that this presents was pointed out succinctly by William James: “mental facts cannot be studied apart from the physical environment of which they take cognizance” (James, 1948, p. 3). While behavioral psychology attempts to include a limited number of contextual stimuli when defining behaviors, the biopsychiatric epistemology of severe mental disorders relies on a radically decontextualized construct of biochemical process (Szasz, 1990).

The creation of decontextualized constructs of mental illness simplifies the causal modeling process (i.e., by obviating environmental factors, and focusing on human physiology) but is the result of an *a priori* decision, not empirical evidence. Even with less extreme narrowing of variables of interest, the reduction of experimental, contextual

"noise" is always accompanied by the loss of meaningful "signal" because in the behavioral sciences, there is always a multiplicity of influences on a dependent variable (Cohen, 1994; Cohen & Cohen, 1975).

Further problems emerge in the interpretation of research outcome data. The focus on a low likelihood of a false positive (low alpha error) as a meaningful outcome measure has been challenged on the basis that it does not take into account the size of the effect, only the probability of the research effect given that in the real world such a relationship between variables does not exist (Cohen, 1994; Cohen & Cohen, 1975). In other words, the "significant difference" concept does not mean that the difference is substantial in any way, but that it is highly probable that it is not a totally spurious finding. With a large enough sample size, literally any two variables will be significantly different or correlated. Therefore, the finding of a significant difference can not confirm a hypothesis of effect (Cohen, 1994).

It also has been argued that the statistical correlation of two variables is actually irreconcilable with real-world causal prediction because statistical correlations vary depending on the attributes of the entire sample rather than on the individual attributes that actually underlie causes:

> Causality operates on single instances, not on populations whose members vary. The effect of A on B for me can hardly depend on whether I'm in a group that varies greatly in A or another that does not vary at all. (Cohen, 1994, p. 1001)

So, the definition of a decontextualized behavioral event allows scientific manipulations and hypothesis testing, yet even the basis for understanding the outcomes of such experimentation is open to debate. Research evidence utilizing null-hypothesis significance testing with non-orthogonal, clinical variables neither demonstrates a causal

relationship between variables, nor indicates the importance of a relationship if any pertains. Cause can be inferred from the experimental manipulation of temporally separable, independent variables. If behavioral variables and their physiological concomitants are neither temporally separable nor independent, no causal attributions can be made about the biological basis of mental disorders.

Compounding these inferential limitations of biopsychiatric research methodologies are the inferential errors of mistaking significance testing for power analysis, and of mistaking sample-wide variance statistics as predictive of specific clinical cases. These errors can cause researchers to overstate the ability to generalize statistically measured relationships between decontextualized variables to the prediction and control of individual human experiences.

Ontological Metaphors: Limitations of the Mental Illness Concept

Complicating matters further, the process of defining behaviors has been described as a psycholinguistic contrivance. That is, the decontextualized definition of behavior as an observable, replicable *thing* is the result of a metaphorical process. Behavioral events in context do not have real boundaries or the possibility of replicability. Therefore, the attribution of such limits is a mental exercise performed by an observer about an event. The metaphor of *behavior = thing* is an example of an entity metaphor (Lakoff & Johnson, 1980). We conventionally think and speak in metaphor and analogy because these are powerful tools through which we increase our understanding of the world (Gambrill, 1990; Lakoff & Johnson, 1980). Still, all tools are limited in their utility. Understanding the use and misuse of metaphor can clarify the assumptions of the

biopsychiatric ontology. Lakoff & Johnson (1980) argue that “our ordinary conceptual system, in terms of which we both think and act, is fundamentally metaphorical in nature” (p. 3). Gambrill (1990) specifies that analogies “are often used in daily life to decide what to do in novel situations” (p. 155); in other words, to make the unfamiliar more familiar and the abstract more concrete. For example, the concept of *street corner* has no actual boundary or “thingness,” but we conceptualize and talk about it as an entity by convention. Ontological metaphors provide ways of describing experience so we can more easily think or talk about experience. By using metaphors, we understand ideas in terms of their similarity to other ideas. Ontological metaphors often take the shape of entity metaphors: understanding concepts more easily as things. There are a number of conventional metaphors that fit this description. For example, we conceive and talk about theories and arguments as if they were buildings. We say that the foundation is shaky, that the theory may fall apart, that we need to strengthen or buttress the theory, that it has a framework, that the theory can stand or fall on the basis of an argument, or collapse under the weight of contradictory evidence (Lakoff & Johnson, 1980). The use of metaphor elucidates some aspects of a concept while obscuring other aspects because the metaphor for the idea is not the same as the idea itself. Thus, if we understand the concept of theory only in terms of the building metaphor, we will be limited in our understanding because there are many ways in which theories are not like buildings. Metaphors can mislead even as they provide a coherent way of understanding something. Thus, describing someone’s theory in the metaphorical terms of a building may prevent one from conceiving it as a dynamic, growing “organism”: that it can feed on new data and mature into an adult theory that continues to develop and make changes, or that

might become infirm and need rehabilitation. This metaphorical distinction can also lead to different actions based partly on the ontological premise of the metaphor: One might be attempted to "demolish" a theory because of its many cracks, and weak foundation, rather than "nurse" it back to health. Similarly, conceiving of a behavior in terms of replicable units allows measurement and facilitates empirical study, but obscures the reality that in many important ways behaviors are not like replicable units. "The use of analogy becomes crooked argumentation when an analogy is used not as a guide to expectations, but as proof of a conclusion" (Thouless, 1974, cited in Gambrill, 1990, p. 156).

The concept "mental illness" is a metaphorical construct in which we understand emotional, psychological, or behavioral qualities by using the metaphor of physical illness (Goffman, 1961; Szasz, 1961, 1990). We say a person is suffering from the illness, that he or she has symptoms, we give a diagnosis, we prescribe a treatment, perhaps they undergo a remission, their condition may worsen, we may observe a syndrome of idiopathic etiology, etc. As with other uses of metaphor, this conceptualization provides a useful way not only to understand the concept, but also to act upon it.

The fact that a person's emotions or behavior are conceptualized through a medical metaphor rather than as Kantian things-in-themselves is irrelevant because, as Lakoff & Johnson argue, there is very little about the world that we do not understand through some kind of metaphor. A surgeon may use the metaphor of war in describing his or her operation on a tumor. The fact that the surgeon is not "really" going to war may not interfere with a successful outcome. On the contrary, the metaphor of war may provide a useful way to plan or *strategize* the *attack* on a tumor (and *surgical* strikes are

used in war). It is common for corporate executives who are developing business strategies to study famous battles or military heroes. In the same way, the metaphor of medical illness for emotional problems also may be quite useful in the understanding and treatment of such problems. The utility of this metaphor notwithstanding, it is imperative that the illness metaphor be understood as such so as not to limit or preempt other epistemologies that will lead to a more thorough understanding of the ontology of emotional problems (Searle, 1992). The fact is that emotional problems occur within a physiological context. However, this does not mean that the physiological context itself causes the emotional problems. "Even facts become fictions without adequate ways of seeing the facts" (Laing, 1967, p. 17). Gambrill (1990) states that

> Analogies create vivid images that are then readily available. Their vividness may crowd out less vivid but more accurate analogies and discourage a review of possible limitations of an analogy. . . . Analogies play upon our emotions. . . . They are one of many devices for creating conviction even though there are no rational grounds for the convictions. (p. 156)

A more rational approach to understanding mental illness requires a critical analysis of the ways in which the illness or disease metaphor breaks down in accurately describing the relationship between physiological and mental phenomena.

A number of authors, including Foucault (1987), Fromm (1956), Kierkegaard (Bretall, 1946), Laing (1967), Lewontin (1991), Peele (1981), Sartre (1994), Searle (1992), and Szasz (1990, 1996), have objected to the entity metaphor that conceives of human experience as a thing on the existentialist grounds of subjectivity, responsibility, agency, and choice. These authors highlight that beyond the metaphor's utility, there are important ways in which the entity metaphor does not accurately reflect psychological experience and behavior. For example, Fromm (1956) and Szasz (1996) have argued that

experience is more dynamic process than stable product. The “mind” of consciousness can be understood as its transitive verb form: to mind, or attend to, something (Szasz, 1996); and “love” is, likewise, something that is “done,” not merely a felt sensation (Fromm, 1956). Peele (1981) argues for an alternative to the reductionistic view of psychology, taking into account individual experiential factors, and not confusing “investigations of contributory factors in the basic sciences with complete accounts of the behaviors and mental states that these factors influence” (p. 807). Searle (1992) has pointed out that the assumption that reality is objective, observable, and testable “has proved useful to us in many ways, but it is obviously false, as a moment’s reflection on one’s own subjective states reveals” (p. 16). Despite the limitations and criticisms of the entity metaphor of mental process, Szasz (1990) has noted that there is little understanding among scientists and the lay public that the disease metaphor of mental illness is a metaphor rather than a matter of fact. Lewontin (1991) observed that “we have become so used to the atomistic machine view of the world that originated with Descartes that we have forgotten that it is a metaphor” (p. 14).

It is difficult to comprehend a complex concept such as *mental disorder* without referring to the disease metaphor. The illness/disease metaphor has become a nearly universal convention because that metaphor is rich, versatile, and functional as an analogy of that set of experiences. Yet, just as the war metaphor for business is incomplete and can lead to undesirable outcomes, the disease metaphor has similar flaws and limits that must be elucidated and corrected. The disease concept is metaphorical, whatever its richness or functionality. When this is adequately understood, the ontology of mental illness can be “opened up” to other epistemologies and treatments that are

empirically grounded and that take into account the ways in which mental disorders are not like diseases.

Clarification of the Mind-Body Problem

One of the obstacles to understanding that mental disorders are not really diseases is that mental states are expressed physically, as are diseases. Thus, unlike other metaphors, there is an apparent interface or point of "real" contact between the metaphor and the concept that the metaphor describes. That apparent interface is the biochemistry of mental function. In the *theories are buildings* metaphor, there are no actual bricks in theories that confuse the issue. In the *mental illness is a disease* metaphor, there *is* a complex physical process that corresponds with and is not separate from the mental process. The nature of this interface has vexed scientists and philosophers for centuries as the "mind-body" problem.

Boss (1983), Foucault, (1987, 1988), and Searle (1992) have argued that the idea of interface, correspondence, or correlation between mental and physical process is actually false:

> Even the most cautious brain researchers. . . cannot come to terms with the relationship between psyche and soma. When referring to the two they speak only of a "correlation," of "counterparts". . . . But a "correlation" is highly questionable as long as one of the two things correlated, the psyche, remains as indefinite as it is in physiology. Besides, the very notion of a "correlation" . . . assumes a previous dividing and objectifying of human existence into at least two phenomena which are thought of as independent of each other. Only things thus divided can correlate. . . No one proceeding from this dualistic mode of thought has managed to say anything comprehensible about this postulated relationship between the psyche and the nervous system. (Boss, 1983, pp. 28-29)

> Thus we are supposed to believe that if something is mental, it cannot be physical; that if it is a matter of spirit, it cannot be a matter of matter; if it is immaterial, it cannot be material. But these views seem obviously false, given everything we

> know about neurobiology. . . . The fact that a feature is mental does not imply that it is not physical; the fact that a feature is physical does not imply that it is not mental. (Searle, 1992, pp. 14-15)

Searle also claims that "biological processes produce conscious mental phenomena, and these are irreducibly subjective" (p. 98). Yet, the mind-body relationship is more complicated than that. Irreducibly subjective conscious mental phenomena also produce biological processes, as will be discussed in the next chapter. The conceptualization of mental process as emergent from brain process promotes the view that even "irreducibly subjective" mental illness is caused by biological processes; but Searle's contention that mental phenomena are "emergent" from brain physiology is incomplete. Brain physiology is also an emergent process of mental phenomena. As will be shown in the next chapter, biopsychiatry's materialist epistemology favoring cause-effect interpretations provides plenty of evidence that changing brain physiology "leads to" changes in mental phenomena; but also that changing mental phenomena "leads to" changes in brain physiology. The evidence for the reciprocal nature of mental and biochemical interventions justifies a radical shift in the biopsychiatric ontology. Viz., it has been assumed that a constant conjunction of mental and physiological states implies that one causes the other; specifically, that deranged physiological processes cause mental disorders. But the evidence does not support the hypothesis that mental disorders are caused by biochemical "imbalances" because there is adequate evidence that mental processes can also cause changes in biochemical functioning. As Foucault (1988) described, there is no causal interface, but rather one reality observed by two different approaches to human experience. The biochemical and experiential realities of mental illness are neither related nor separate because they are, in fact, a unity.

As will be shown, the claim of biological primacy in mental illness is not supported by research data. To the contrary, recent developmental and longitudinal research supports an experiential primacy just as adequately: that early problematic experiences (expressed physiologically) lead to later emotional problems that are also expressed as physiological patterns of activity in the brain. What this means for biopsychiatry is that while drugs can affect mental experience, their use is not justified by the ontological claim that mental illness is (or is caused by) a biochemical imbalance. While researchers and the media claim the biochemical "basis" of mental illness as a fact, Kazdin (1992) has noted that data can "only be taken as proof of a hypothesis if no conceivable alternative hypothesis could account for the results or if the predicted relations would be obtained if and only if the hypothesis were true" (p. 4). As it turns out, an alternative hypothesis does account for the results and predicted relations of biopsychiatric research at least as well as the medical model does. That is, the diagnoses and symptomatology of mental disorders are correlated with various physiological measures not because mental disorders are caused by biochemical changes, but because biochemical changes and mental disorders result from mental experiences that are expressed biochemically.

Finally, one of the keystones of the biopsychiatric epistemology is genetics research because cause proceeds temporally; and ontologically, nothing precedes genetic (biochemical) causes of mental disorders, if such causes are found. Nonetheless, the discovery of genetic factors that predict incidence of mental illness symptoms has been elusive; and the evidence for the strong popular and academic claims of genetic causation has not yet been produced by brain researchers (GW-NIMH, 1997). In keeping with the

determinist, anti-moral stance of nineteenth-century scientific psychiatry, proponents of biopsychiatry, including NAMI, hope that molecular genetics research will exonerate patients and their families from being held responsible for their mental disorders (Leshner, 1992; NAMI, 1997a). Yet, at a meeting of the American Association for the Advancement of Science, Arno Motulsky, professor of medicine and genetics at the University of Washington, explained that one of the goals of molecular genetics research is to understand the mechanisms of gene expression that lead to disease specifically so that people can take more responsibility for the environmental influences:

> There are some genes they say [that if they] are defective you'll always get the disease. . . . But most genes require some environmental factor [for the disease to be expressed]. . . . A common disease every baby is tested for is phenylketonuria (PKU). Now, that disease causes mental retardation if you have phenylalanine in your diet. If you reduce phenylalanine in the diet, the disease doesn't produce any symptoms. So even that disease is an environmental disease. . . . In fact, take an environmental disease like a fracture. You say, "well that's clearly environmental," but in fact there are genetic factors that have something to do with the density of your bones. If your bones are very sturdy, you're less likely to have a fracture in the same amount of trauma than someone who has thinner bones. . . . One way of thinking about the interaction of heredity and environment [is that] genetics gives us a more rational, logical way of doing preventive medicine. If we work out the genetic factors that predispose some people to environmental factors that bring out the disease, and if we know what these environmental factors are, we can pick those people to which we can direct our preventive therapy much better than just saying it's for everyone. And that's one of the goals of genetics in complex diseases. (Motulsky, 1997)

Thus, one of the effects of genetics research on mental disorders may be to increase the focus on environmental influences once people at greater genetic risk are identified. By Motulsky's reasoning, NAMI's assertion that mental disorders are "no-fault" biological illnesses because they are genetic is similar to asserting that a leg broken while skiing was the "no-fault" result of a genetic propensity. The extent to which mental

phenomena are genetically influenced will also reveal complementary causal influences: those of the individual's social environment.

As mentioned in the previous chapter, Searle (1992) stated that the epistemology of mental health research can not determine the ontology of mental illness. That is, the method of study can not determine what the object of study's essence is. Biopsychiatric researchers' focus on biochemical variables does not mean that the underlying nature of mental disorders is biochemical. Boss (1983) argued that

> Natural science insists on trying to define and clarify a set of phenomena to which it has no access, the phenomena of human existence. This doggedness completes the effect of fascination and intimidation with which the marvels of natural scientific manipulation have entranced mankind in the age of technology. In the final analysis, this power to manipulate has tended to blind natural scientific researchers to their own theoretical transgressions. (p. 30)

Thus, it may be that the power and utility of the biopsychiatric epistemology in producing desirable technologies has yielded an illusory ontology of mental illness in the current culture. Regardless, both the epistemology and the ontology suffer from grave logical and inferential errors about the relationship between biochemistry and mental events. A flawed epistemology might yield a useful technology of treatment while being scientifically inaccurate by exploiting the nonindependence of physiological and mental variables: treating one variable would necessarily affect the other variable. Nothing useful can be stated about a biological cause of mental disorder if mental experiences are correlated with certain physiological processes because of an intrinsic unity of physiology and mental experience. A nonindependence of these factors would require transcending or merging these two classes of variables in the attribution of cause.

The biopsychiatric ontology of mental illness is an *a priori* background assumption justifying the biopsychiatric approach to research and treatment. This

ontology is based on the premise that mental processes are emergent from physiology, and that causal relationships follow this emergent path. The ontology is supported in part by metaphorical constructs that obscure important ways that mental processes are different from physiological processes such as disease. Additionally, the ascertainment of cause-effect relationships between biological and psychological processes requires independence and temporality between definable variables. If psychological experiences are not independent of their physiological "correlates," if such processes do not precede the mental experiences, or if mental experiences are not adequately defined (validated), causal inferences may not be drawn about the biological processes involved in mental disorders. These issues that challenge the biopsychiatric ontology of mental disorder are best addressed by a careful analysis of the empirical evidence, followed by the generation of more parsimonious alternative hypotheses.

CHAPTER 3: Empirical and Methodological Considerations

> The dangers threatening modern science cannot be averted by more experimenting, for our complicated experiments have no longer anything to do with nature in her own right, but with nature charged and transformed by our own cognitive activity.
>
> *–Heisenberg*

> We dance around in a ring and suppose,
> But the Secret sits in the middle and knows.
>
> *–Frost*

The biopsychiatric ontology of mental illness implies that some mental disorders are caused by biochemical dysfunction that may, in turn, be caused by genetic defects. However, recent studies show that psychological experiences are mediated or expressed physiologically, not that they are caused by a physiological process. Considerable research has demonstrated the effects that psychological experiences have on neurobiological processes. Physiological variables under study have included diverse systems (e.g., neurological function, pulmonary function, and immune response). The evidence indicates that psychological phenomena are the consequence of the interaction between individuals and their environments. This interaction—what we call *experience*—is a physiological process occurring within a genetic, neurobiological context. However, evidence that experiential interventions, like chemical interventions, predictably modify biochemical processes and neural structures undermines the special status of pharmacological compounds as being uniquely suited to address the physiological expression of mental disorders. In addition, the genetic context within which experience takes place is not an independent causal factor, but part of a matrix or

causal Gestalt that may not be suited to an analysis that conceptualizes genetics and experience as separate component causes of behavior.

Neurobiology of Experience

There is no way to experience something passively, without the active engagement of the central nervous system. Experiences are behavioral interactions with the environment, even when the body is at rest (Greenough, 1986). New experiences alter the activity of neuronal networks, increasing the "strength" of the synaptic connections in the particular sensory-motor network that is involved in a given experience. Repetition of these experiences further facilitates neuronal transmission within the relevant network. The strengthening of connection in such learning experiences is thought to be due, in part, to the activation of neurotransmitter-sensitive adenylate cyclase in the presynaptic membrane, which facilitates cyclic adenosine monophosphate (cAMP)-dependent protein phosphorylation of potassium (K+) channel proteins. K+ phosphorylation prevents repolarization of the action potential, resulting in a sustained and increased release of neurotransmitter (Kandel, 1989). Physiologically, short-term memory and long-term memory are thought to consist mostly of this kind of enhanced neurotransmitter release. However, long-term memory of experiences also involves the synthesis of gene-products—proteins and RNA—and this synthesis of gene products leads to significant changes in neuroanatomy. Bailey and Chen (1983, 1988, cited in Kandel, 1989) found that after behavioral sensitization training (which created long-term memories of electrical shock) in *Aplysia*, the number of pre-synaptic terminals in sensory neurons doubled. In addition, a far greater proportion (65% versus 41%) of the pre-synaptic

terminals now had an active zone from which vesicles could be released compared to the controls. Greenough (1986) reviewed a number of studies of the effects of postweaning-age and middle-age experiences on the neuroanatomy of rats. These studies showed that different environmental experiences exerted effects on the number of synapses, extent of dendritic branching, size of individual neuronal somata, number of glia, and the size and cellular composition of neocortical areas "beyond traditionally conceived periods of development" (Greenough, 1986, p. 391).

Long-term memory, like short-term memory, is facilitated by a phosphorylation of K+ channel proteins, but this phosphorylation is not caused by cAMP or direct neurotransmitter exposure. Rather, the functional and structural changes occurring in neurons that are repeatedly stimulated by sensitizing experiences are the result of changes in gene-expression, which is under the control of modulatory neurotransmitters such as serotonin (Kandel, 1989; Perry, Pollard, Blakley, Baker, & Vigilante, 1995). The implication of this mechanism is that experiences create memories through the entrainment and physical alteration of neural networks established by associated neurotransmitter release. Effectively, long-term memories are the alteration of neural function and structure caused by changes in gene-expression (phosphorylation of proteins), which is caused by a repeated release of transmitter or modulator influenced by the experience. In line with this model of neurobiological encoding of experience, Post (1992) posits that psychosocial stressors and their biochemical concomitants become encoded at the level of gene expression (by inducing activity of the proto-oncogene c-fos and other transcription factors that influence neuroanatomy and chemistry) in recurrent affective disorders. For example, psychosocial stressors related to separation and loss are

associated with the onset of depressive episodes, and these stress responses may either initiate long-term encoding or trigger previously encoded physiological processes that have been sensitized (Post, 1992). This sensitization model has been hypothesized to explain apparent “endogenous” depression episodes that occur subsequent to first onsets of depression, the great majority of which are provoked by a severe life event (Brown, Harris, & Hepworth, 1994).

The interaction between the individual and the surrounding environment influences gene expression through the neurological encoding of long-term memories. Further, the fact that experiences alter gene expression precludes simple inferences about the genetic basis of complex psychological experiences and behaviors. Thus, mental processes are fundamentally physiological, but brain structure and function are profoundly influenced by psychological experiences. Very early experiences exert a far-reaching influence on the brain development and psychological functioning of the growing infant. The neurobiology of these infant experiences has been extensively studied in attachment research.

Attachment, Trauma, and Neurobiology

Attachment research, which was initiated by Spitz (1950) and Bowlby (1969, 1973, 1980), has become a dominant subfield of developmental psychology. It encompasses both primate and human populations, and focuses on physiological, ethological, and social learning processes (Schore, 1994; Stern, 1985). The study of attachment behaviors concerns the behavioral interchange between infants and their primary caregivers; and how different styles of caregiver behaviors affect infants’

physiological arousal, psychosocial development, and coping styles. In recent years, a great deal of emphasis has been placed on physiological or biochemical correlates of mental disorders such as schizophrenia; but little attention has been paid to how these physiological manifestations may have been influenced by premorbid psychosocial (and thus, physiological) experiences.

In 1978, Walsh found a connection between grandparent death and concurrent birth of grandchildren who later became schizophrenic. In her study of 140 families with schizophrenic offspring, psychiatric controls, and normal controls,

> 41 per cent of the families in the schizophrenic group experienced a grandparent death within 2 years prior to or following the birth of the schizophrenic child. In contrast, this concurrence of events was found in 20 per cent of families in the disturbed nonschizophrenic group and in only 8 per cent of cases in the normal control group. (Walsh, 1978, pp. 459-460)

The difference between diagnostic groups was significant, and was not accounted for by overall differences in death rate among groups. Similarly, in a 1991 study, Liotti asked a group of 46 patients suffering from various dissociative disorders and a group of 119 controls who had other psychiatric disorders whether their mothers had suffered "the loss through death of one of her parents, a sibling, a child, or her husband in the two years before—two years after your birth" (cited in Liotti, 1992, p. 202). He found that approximately 62% of the dissociative patients and only 13% of the patients with other psychiatric diagnoses answered affirmatively. Liotti hypothesized that the mothers of children who later became dissociative patients "were mourning over a serious loss in the period during which their children were becoming attached to them" (Liotti, 1992, p. 202). Similarly, Walsh posited that the concurrent stresses of death and birth could impede both mourning and parenting processes. Main and Hesse (1990) found a similar

connection in which the unresolved losses of mothers predicted a disorganized style of attachment in their infants. In their study, 60% of mothers who experienced deaths of older family members before finishing high school had infants independently judged as disorganized, whereas only 21% of the mothers who hadn't experienced such losses had infants judged as disorganized. Main and Hesse (1990) found that the relationship between mothers' loss and the attachment style of their infants was mediated by the extent to which the mothers' mourning was unresolved as measured by a "Lack of Resolution of Mourning" scale: "Only three out of nineteen mothers (16%) showing no indices of unresolved mourning had disorganized infants. In contrast, eleven out of twelve unresolved mothers (91%) had infants who had been judged disorganized" (p. 170). The disorganized type of insecure attachment refers to infants who lack coherent strategies for responding to separation and reunion (Main & Solomon, 1986). This insecure pattern of behavior is most likely due to learned parent-child interactions, not genetic factors (Livesley, Jang, Jackson, & Vernon, 1993). Rather than referring to disorganized cognitions, this style includes idiosyncratic behaviors that indicate apprehension, unexpected alternations between approach and avoidance, and other conflict behaviors such as prolonged freezing of movement (Lyons-Ruth, 1996). Disorganized attachment status has been associated with later childhood aggression (Lyons-Ruth, 1996) and greater risk of suicidal behavior in adolescents (Adam, Sheldon-Keller, & West, 1996).

Early experiences organize the mind of the developing individual through the neurobiological encoding of these experiences. Recently, Perry et al.'s research on the neurobiology of infant and childhood trauma pointed to what he called "the use-

dependent organization of neural systems" (Perry et al., 1995). That is, unlike the experience-dependent neuronal changes that occur in adulthood, Perry et al. hypothesized that the changes that occur in the brains of very young children are more susceptible to becoming organized into semipermanent activation patterns by environmental interactions. Research on early attachment between infants and caregivers provide evidence for this hypothesis. Attachment research on humans and other primates clearly shows that mothers or other primary caregivers serve an arousal-regulating function for the infant; and the style of interactions around arousal regulation predict later behavioral characteristics in the young child (Schore, 1994; Stern, 1985). The relationship between primary caregiver and infant is quite specific, and substitutions by other familiar figures or adoptive parents may disturb this regulatory function. Even a relatively brief separation of thirty minutes has been shown to significantly elevate plasma cortisol levels in both mother and infant squirrel monkeys (Coe, Mendoza, Smotherman, & Levine, 1978). This response is not attenuated even when the mother and infant monkeys are kept in their home environment among familiar monkeys during their separation. The stress response also is not attenuated in the infants when other familiar females have "aunted" and held the infant during the brief separation. Like the human attachment research on behavior, this study of pituitary-adrenal function shows that there is a highly specific attachment relationship between infant and mother. This experienced relationship regulates arousal in a way that is biochemically expressed.

Real or perceived threats from the environment provoke arousal responses in the infant that are expressed behaviorally and through increases in a variety of sympathetic nervous system functions. When the caregiver has previously served as an effective

reducer of the infant's arousal, the infant's behavioral responses to these perceived threats include crying and seeking of the caregiver. Upon rejoining the effective caregiver, soothing behaviors such as holding, rocking, and speaking in a soft and comforting voice, reduce the arousal of the infant, further increasing feelings of safety and control over environmental stimuli.

Parents of infants who have a disorganized attachment style often suffer from unresolved traumas, and in general, maternal psychopathology predicts the insecure attachment of their infants (Liotti, 1992; Radke-Yarrow, Cummings, Kuczynski, & Chapman, 1985). The link between maternal experiences and infant attachment styles probably is mediated through social interaction, rather than autonomous chromosomal effects. For example, in Radke-Yarrow et al.'s (1995) study of 2 and 3-year-olds, paternal depression did not add to the effect of maternal depression on insecure attachment in a modified version of Ainsworth and Wittig's Strange Situation protocol (in fact, the group with both parents being depressed had a slightly lower incidence of insecure attachment than the group in which only the mother was depressed). However, presence of a father in the home did have a significant salutary impact on the risk of an insecure mother-child attachment, compared to a single-parent family. This indicates a socially mediated influence of parental emotional state on the child's affect and behavior. The effect of an unresolved traumatic experience on the ability of a mother to care for her infant may be mediated partly by genetic factors; however, the Main and Hesse (1990) study indicates that effective resolution of trauma ameliorates the impact of parental trauma's effects on infant attachment (although, presumably, some genetically mediated constitutional factor or factors might prevent effective resolution of mourning in some mothers). Radke-

Yarrow et al.'s (1995) study similarly shows that other salutary environmental factors can militate against insecure forms of infant attachment.

A number of empirical studies have shown an association between early abuse or trauma and subsequent neurobiological effects in humans that are not easily accounted for by genetic or congenital factors (see Schiffer, Teicher, & Papanicolaou, 1995, for a review). Schiffer et al. (1995) studied 20 paid volunteers who believed they came from "dysfunctional" families. None of the subjects were taking any psychotropic medication, and none met criteria for any DSM-III-R diagnoses. Half of the subjects reported a childhood history of significant trauma or abuse. During an auditory evoked potential procedure, subjects were asked to recall neutral and painful memories. The trauma group showed significant asymmetry in cortical activation during the two tasks; subjects with no history of significant childhood trauma did not. Specifically, during the neutral memory task, the trauma group showed a significantly greater left-hemisphere dominance that shifted to a significant right hemisphere dominance during the painful memory task. The no-trauma group showed no laterality in either condition. The degree of laterality was not correlated with the subjects' reported mood states during recall of the memories. This study of the enduring physiological effects of early experiences supports the hypothesis that differences between brain structure and function in people with psychiatric symptoms may be the result of different early developmental experiences.

Dopamine-_-Hydroxylase: Example of a Biological Mediator of Experience

In a study of the correlation between conduct disorder and low levels of serum dopamine-_-hydroxylase (DBH) in psychiatrically hospitalized boys, Galvin et al. (1991)

cited previous researchers who had hypothesized that DBH was “a genetic marker for a vulnerability to develop a childhood precursor of antisocial personality: conduct disorder, . . . solitary aggressive type” (CDSA; Galvin et al., 1991, p. 1). DBH is an enzyme that catalyzes the conversion of dopamine into norepinephrine within neurons. Increased production of norepinephrine, like that of cortisol, is associated with exposure to a stressor. Although Galvin’s study corroborated earlier findings that very low DBH was associated with conduct disorder, they also found a significant relationship between the “definite” or “possible” experience of abuse or neglect before the age of 36 months and later DBH levels. In a follow-up study, Galvin et al. (1995) found that subjects who were maltreated before 72 months had lower DBH activity than did those who were maltreated later or not at all. In both studies, when the timing of abuse or neglect was not specified, neither abuse nor neglect correlated significantly with later DBH levels. Only very early abuse and/or neglect were associated with the low DBH levels. The authors hypothesized that while low DBH is clearly associated with CDSA, there may be two types of children: those whose DBH is lowered by experiences of childhood maltreatment and those whose DBH is lowered by genetic factors (because there were some children with low DBH who did not have documented histories of maltreatment; Galvin, et al., 1995). It should be pointed out that there is also a possibility that these hypothesized types are not mutually exclusive categories, or that the boys without documented histories of early abuse or neglect nevertheless may have been maltreated.

As the authors suggest, reduction in DBH may be a biological sequela of the early abuse and/or neglect experience, and this reduction in DBH function may be an intermediary variable between early maltreatment and later conduct disorder.

Alternatively, it may be that the reduction in DBH function causes behavioral problems partly or wholly independent of maltreatment experiences, and is passed on genetically (Gabel, Stadler, Bjorn, Shindledecker, & Bowden, 1995) since serum DBH activity is genetically influenced (Gabel et al., 1995; Markianos, Rinieris, Hatzimanolis, & Stefanis, 1990; Ramchand, Wei, Ramchand, & Hennings, 1993).

In contrast to the hypothesis of a genetic set-point for DBH, two studies reported that although depressed individuals had significantly lower DBH, the levels increased when the depression remitted (Damase-Michel et al., 1991; Paclt & Koudelov↔, 1990). Another study reported that the association between low DBH and behavior disorders in young boys may have been highly contingent on the environmental context and who was rating the behaviors (Gabel, Stadler, Bjorn, Shindledecker, & Bowden, 1993).

These studies suggest a strong connection between low DBH and problematic behaviors or moods; but that the earlier hypothesis—that DBH is a genetic marker of a propensity for conduct disorder—was probably too simplistic. DBH function appears to be suppressed by early abuse or neglect, and this suppression may represent a biochemical epiphenomenon of the predictable relationship between being maltreated as a young child and later becoming antisocial or isolative. While there is evidence for genetic control of DBH activity, there also is evidence that DBH activity and conduct are significantly altered by early damaging experiences, and by later ameliorative ones (Damase-Michel et al., 1991; Gabel et al., 1993, 1995; Galvin et al., 1991, 1995; Paclt & Koudelov↔, 1990). Thus, DBH may function as a biochemical barometer of experiences as much as a genetically determined causal factor in conduct disorder or depression. Prospective studies that have adequate baseline measures of DBH and behavior problems

and that take into account changes in behavior following treatment, off-medication, would shed light on whether low DBH predicts experiential sensitivity to different contexts, or whether DBH activity increases subsequent to positive emotional and behavioral changes without pharmacological intervention. If either is the case, these results would indicate that DBH might be an experience-dependent biochemical marker for early abusive or neglectful relationships or depression as well as for the amelioration of these problems. This hypothesis emphasizes that biochemical processes may mediate the relations between a person's past experiences and future behavior, rather than acting as causal agents or genetic markers for that behavior. The biological study of the physiological mechanisms of experiences does not imply that physiological processes cause these experiences, although this epistemology may shed light on how experiences are physiologically expressed and "remembered."

Manipulating Biochemistry by Altering Psychological Experiences

A variety of studies have been published showing that physiological processes can be manipulated by changing mental experience. One prominent area of this research is in the field of psychoneuroimmunology. Psychological stressors are well-known to influence disease and tumor proliferation by suppressing immune response, and studies have shown that this effect on immunity can be direct, rather than occurring indirectly (e.g., through stress-related behavioral changes, blood flow changes, body temperature changes, etc.; Maier, Watkins, & Fleshner, 1994). While studies have documented the effects of naturalistic psychological factors such as health locus-of-control and causal attributions, respectively, on immune function in depressed patients (Reynaert et al.,

1995) and HIV-positive patients (Segerstrom, Taylor, Kemeny, Reed, & Visscher, 1996), a few studies have been conducted prospectively to show the effects of psychological interventions on physiology. Psychotherapy has been found to significantly enhance survival rates for heart attack survivors and cancer patients (Fawzy et al., 1993). For example, in Fawzy et al.'s study of a six-week, structured, therapy group for malignant melanoma patients, the therapy recipients had a significantly lower chance of reoccurrence and significantly lower mortality than the control group even though the therapy group was significantly older than the controls. Psychotherapy has also been shown to be effective in the treatment of epilepsy (Miller, 1994) and alopecia universalis (profound baldness that is thought to be caused by stress). Teshima, Sogawa, Mizobe, Kuroki, & Nakagawa (1991) treated two groups of alopecia patients with either a small dose of immunosuppressant chemotherapy or a combination of chemotherapy and psychotherapy (relaxation and image therapy). In the chemotherapy group, 1 of 5 patients improved (grew hair). In the chemotherapy and psychotherapy group, 5 of 6 patients improved.

Placebo treatments have been shown to reduce symptoms and relapse of depression (Elkin et al., 1989; Medawar, 1997; Peselow, Sanfilipo, Difiglia, & Fieve, 1992) and schizophrenia (Lewander, 1994) significantly and effectively when compared to drugs at effective dosages. These disorders are widely known to have physiological correlates, and some authors have questioned whether placebo effects in psychiatric disorders are the result of psychological epiphenomena such as expectation effects or the desire to please the therapist (see Butler & Steptoe, 1986). In a well-controlled placebo study of pulmonary responses in asthmatics, Butler & Steptoe (1986) found that

"asthmatic participants produced a bronchoconstrictive response to the [placebo] suggestion that they were inhaling an irritant chemical, and that this effect was blocked by placebo therapy" (p. 180). The airway responses were not related to either fluctuations in subjective distress or high trait anxiety. This study adds to the evidence that placebo responses are physiological processes, just as they are mediated by psychological expectations.

Differences in Brain Function Are Not Sufficient to Establish a Disease Process

Despite the questionable inference that differences in brain function or structure denote a primarily physical etiology that supercedes experiential influences, researchers have focused their efforts on studying neurobiology to develop strictly physical causal models of severe mental disorders (Chua & McKenna, 1995). These efforts have yielded an abundance of data, but no consistent findings of physical causes that are necessary or sufficient for diagnosis (Aylward et al., 1996; Stevens, 1997; Woods, Brennan, Yurgelun-Todd, Young, & Panzarino, 1995), and no evidence of a physical etiology independent of psychological process. Devous, Gullion, Grannemann, Trivedi, & Rush (1993) noted that between 1980 and 1990 there were at least 20 reports of alterations in brain activity in depressed patients compared with controls. Methodological inconsistencies between these studies were the rule, and findings were contradictory for global cerebral blood flow (gCBF) as well as for region-of-interest (ROI) differences, in both bipolar and unipolar patients. Devous et al. (1993) suggested that improved methodology might generate more consistent findings, and that researchers should: focus on ROIs rather than gCBF; increase sample size; and divide samples by age, gender, and diagnostic or

treatment subtypes (e.g., endogenous/exogenous, psychotic/nonpsychotic, medicated/ unmedicated, and unipolar/bipolar). Devous et al.'s research yielded a complex interaction between age, diagnosis, hemisphere, and ROI, and they concluded that "function is altered in different types of mood disorders" (p. 254). Whether this altered function points to a physical etiology or simply the physiological expression of a depressed mood highlights the danger of inferring a physical cause from the study of pathophysiology.

In a PET-imaging study of the way brain function is altered during transient mood changes, Pardo, Pardo, & Raichle (1993) found consistent brain changes in normal volunteers (who were screened extensively for psychiatric disorders) when subjects felt sad (average rating of 8 on a 10-point scale) while thinking about personal losses. The authors summarized that "these data suggest that inferior and orbitofrontal activation may relate to 'on-line' experiential aspects of self-induced dysphoria" (p. 716). In their review of PET studies of depressed patients, Pardo et al. (1993) note a variety of findings, some that overlap with the findings in their normal, "experimentally sad" group, and one study that found no differences between depressed and control groups. This heterogeneity of findings makes comparisons between Pardo et al.'s study and depression studies difficult, although the authors suggested better overlap between the brain activity of these normal sad subjects and the orbitofrontal or medial frontal activation found in subjects with obsessive-compulsive disorder. In their discussion, Pardo et al. make a crucial point: neuroimaging studies that show a difference between psychiatric patients and normal controls do not necessarily show pathophysiology per se, but rather the physiology of the "on-line" experiential process. The implication of this study is that physiological markers

do not necessarily indicate either a physical “substrate” or causality, but rather the biological expression of psychological experiences.

Two studies of PET imaging before and after successful treatment of obsessive-compulsive disorder (OCD) confirm that experiential interventions, like chemical interventions, systematically modify brain function when they are effective. Baxter et al. (1992) found that glucose metabolism in the caudate nucleus of OCD patients responsive to behavior therapy changed to the same extent as caudate metabolism in patients responsive to fluoxetine, after 10 weeks of treatment. Nonresponders in both the fluoxetine and behavior therapy groups showed no such change in metabolic rate. In a replication of Baxter et al. (1992), Schwartz, Stoessel, Baxter, Martin, & Phelps (1996) found that after 8-12 weeks of behavior therapy, medication-free patients with OCD who responded to behavior therapy had a significant bilateral decrease in caudate glucose metabolism, that also was significantly greater than poor responders to the treatment. These two studies demonstrate that although mental function or disorder is expressed physiologically, this does not imply that a pharmacological intervention must be used to change this physiological expression. While changing biochemistry is not the raison d’être of psychotherapy, it nonetheless may be considered a biochemical intervention. Thus, the apparent distinction between “biological” psychiatric disorders and “psychogenic” psychiatric disorders may be more imagined than real, with psychological changes being expressed physiologically in every mental state, whether pathological, benign, or therapeutic. Further research may elucidate this hypothesis. In any event, it can be stated with some confidence that mental disorders treated with psychotherapy are being treated biochemically.

Brain Morphology Studies

Nonspecificity.

In reviewing studies of brain morphology, it is important to keep in mind that the plenitude of studies is notably bereft of replications. For example, while schizophrenia studies have dominated the field of brain morphology research, Goldman-Rakic & Selemon (1997) recently observed that "no one area of the brain has been found to be consistently compromised in schizophrenia patients" (p. 442). In a study of neuroleptic-naïve, first-episode schizophrenic patients versus controls, Pettegrew et al. (1991) found differences between groups in membrane phospholipid and high-energy phosphate metabolism in the dorsal prefrontal cortex, possibly indicating reduced synthesis and increased breakdown of membrane phospholipids, which might antedate the onset of anatomical changes in schizophrenia. Pettegrew et al. hypothesized that the differences might indicate abnormal brain development or premature brain aging in the schizophrenic patients. Evidence of blood platelet membrane phospholipid breakdown specific to schizophrenic patients, and not other psychiatric controls, was also found by another research group (Gattaz, Schmitt, & Maras, 1995). Goldman-Rakic & Selemon (1997) have hypothesized that the membrane phospholipid breakdown in schizophrenic patients may be the result of regressive processes in the neuropil (the space between neurons that contains blood vessels, glial cells, axons, and dendrites) rather than in neuron cell bodies, because a slight decrease in cortical gray matter thickness has been demonstrated in some schizophrenic brains (Lim et al., 1996) but has not shown to be the result of a decreased number of neurons (Casanova & Kleinman, 1990). Because adult experiences may

substantially enhance the makeup of the neuropil, and generate the growth of neuronal and other processes (Greenough, 1986), the hypothesis of a premature or irreversible brain-aging process may be too pessimistic.

In addition to morphological differences between schizophrenics and controls, a large number of brain imaging studies have found morphological differences between other psychiatric patients and controls, including: reduced caudate nucleus volume in OCD patients (Robinson et al., 1995; although Aylward et al., 1996, found normal caudate volumes); ventricular enlargement in bipolar men (Andreasen, Swayze, Flaum, Alliger, & Cohen, 1990; Swayze, Andreasen, Alliger, Ehrhardt, & Yuh, 1990) but not in women (Swayze et al., 1990); reduced frontal lobe volume and higher frequency of subcortical hyperintensities in periventricular white matter in severely depressed inpatients (Coffey et al., 1993); reduced subgenual prefrontal cortex volume in bipolar and unipolar patients (Drevets et al., 1997); widening of bilateral upper cortical sulci in women with endogenous depression, but narrowing of the right Sylvian fissure in women with non-endogenous depression (Baumann, Bornschlegl, Krell, & Bogerts, 1997); reduction of dopamine reuptake site densities in patients with social phobia (Tiihonen et al., 1997); and cortical gray matter deficits and sulcal and ventricular enlargement in chronic alcoholics (Jernigan et al., 1991; Pfefferbaum, Sullivan, Mathalon, & Lim, 1997).

Because very few studies have been replicated or have included multiple diagnostic groups, it has been difficult to determine whether these differences between patients and controls are diagnosis-specific or generalized to a variety of disorders. Woods et al. (1995) studied the magnetic resonance imaging (MRI)-scan reports of 536 inpatients in 10 DSM-III-R diagnostic categories, and 51 normal controls. While the

study had several methodological flaws, including lack of age-matching and a selection bias in referring patients to have MRI scans, several interesting findings emerged:

> Even after controlling for age, brain imaging abnormalities are present in increased numbers of inpatients in all major psychiatric diagnostic groups. The presence of imaging abnormalities in schizophrenic and affective disorder patients is well-documented, but the current results indicate that excessive ventricular enlargement and periventricular hyperintensities also appear to be present in. . . the general category of personality disorders. (Woods et al., 1995, pp. 52-53)

When covaried with age and compared with normals, ventricular enlargement was significantly greater for the schizoaffective, substance abuse, dementia/delirium, personality disorder, depressed nonpsychotic, and bipolar psychotic groups. Cortical atrophy was significantly less for the bipolar nonpsychotic group than for the control subjects. This study indicates that morphological differences between the brains of psychiatric patients and controls may be nonspecific, and highlights the need for psychiatric-control comparison groups in morphometric and brain function studies.

Elkis, Friedman, Wise, & Meltzer (1995) conducted a meta-analysis of ventricular enlargement and cortical sulcal prominence in mood disorders. They found significant differences for both variables between mood disordered patients and controls, with moderate effect sizes (d=0.44 for ventricular enlargement; d=0.42 for sulcal prominence). Patients diagnosed with mood disorders showed significantly less ventricular enlargement than patients diagnosed with schizophrenia, but the effect size of the difference between groups was small (d=-0.20). The authors concluded that “these results reinforce previous suggestions of the nonspecificity of structural brain changes in schizophrenia and mood disorders” (p. 735). Elkis et al. (1996) extended this finding by conducting an empirical study of normal controls and patients diagnosed with affective disorders and schizophrenia. They found no significant differences between normals and

either of the patient groups in terms of ventricular brain ratio (VBR); and they found no significant difference between patient groups in terms of sulcal widening (although both groups differed significantly from controls). Barr, Ashtari, Bilder, DeGreef, & Lieberman (1997) found that first-episode schizophrenia patients and temporal lobe epilepsy patients both had ventricular volumes that were significantly larger than controls, but that did not differ from each other. Lim et al. (1996) inferred that their finding of cortical gray matter volume deficit and lateral ventricular enlargement in schizophreniform patients "close to the onset of illness supports the role of preexisting structural brain deficits in the genesis of schizophrenia" (p. 1548). However, the study measured schizophrenic patients after the onset, and since ascertainment of onset time was not described, it is unclear how causal inferences can be made from the correlation between morphology and symptoms. In addition, DeLisi et al. (1992) did not find ventricular enlargement differences in a similar, but larger sample of schizophreniform and schizoaffective patients. These studies indicate that caution should be used in hypothesizing that a morphological difference between psychiatric patients and normal control subjects is indicative of disease-specific and etiological pathophysiology.

Unreliability of morphological differences.

Stability of ventricle size in schizophrenia has been measured in many studies in an effort to determine whether lateral ventricle size differences are of etiological significance. While a number of studies have demonstrated a sample-wide stability of computed tomography (CT) and MRI brain images over follow-up intervals between 1-8 years, the data in these studies actually indicate a great deal of change within individuals

during the interval. Extreme individual differences of greater than $\bar{3}$0%, and group differences between 13% and 39%, between time points are common in these studies (Illowsky, Juliano, Bigelow, & Weinberger, 1988; Nasrallah, Olson, McCalley-Whitters, Chapman, & Jacoby, 1986; Sponheim, Iacono, & Beiser, 1991; Vita, Sacchetti, Valvassori, & Cazzullo, 1988). Variation in individual ventricle size tends to show a regression toward the mean upon follow-up. Sponheim et al. (1991) have hypothesized that methodological problems have made intra-individual comparisons between scans invalid and that the apparent extreme changes in volume are measurement artifacts. By using a new measurement procedure that provided an estimate of the largest cross-sectional area of the lateral ventricles on both scans, Sponheim et al. again demonstrated no overall increase over time; yet still found instances of substantial decreases in composite VBR over time, including one schizophrenic patient whose composite VBR shrank from approximately 13.5 to approximately 9.5 over a two year interval.

In a large meta-analysis of 39 studies of VBR in schizophrenia, Van Horn & McManus (1992) found that in general, schizophrenics have higher VBR measures than do controls, but that this difference shrank considerably from early studies to later studies during the 1980s because of larger VBRs in control groups over time. They also noted that studies that used a sample that had been schizophrenic longer had larger VBRs; studies that adequately reported the sex of their subjects had lower schizophrenic VBRs (despite no gender effect), and studies that used Research Diagnostic Criteria (RDC) had lower schizophrenic VBRs. Because the difference between schizophrenic and control subjects' VBRs was shown to be substantially smaller than initially reported in the literature, Van Horn & McManus concluded that "the specificity and sensitivity of any

test using VBR as a criterion of schizophrenia (or of schizophrenic subtypes) has diminished, such that it is unlikely to be of any practical use in diagnosis" (p. 695).

In contradiction to studies that have shown a sample-wide stability of VBR in schizophrenics over time, a number of recent studies have shown progressive enlargement over time (DeLisi et al., 1995; Rapoport et al., 1997; Schwartzkopf, Olson, Coffman, & Nasrallah, 1990; Woods et al., 1990). Interestingly, DeLisi et al. found no correlation between progressive ventricle enlargement and cognitive or neuropsychological functioning. They also concluded that the ventricular enlargement was probably due to cortical or subcortical atrophy rather than primary enlargement of the ventricles. Woods et al. (1990) found that the enlargement occurred only for a subset of chronic schizophrenic patients, in an irregular step-wise pattern. Schwartzkopf et al. (1990) found third ventricle enlargement over time, but not lateral ventricle enlargement. Rapoport et al. (1997) found significant increases in VBR and lateral ventricle enlargement in adolescent patients with childhood onset schizophrenia compared with controls, although the two groups were significantly different for race, socioeconomic status, weight at second scan, and total cerebral volume.

Brain morphology studies in schizophrenia have yielded contradictory findings that are difficult to sum up. While it may be the case that there is an overall difference between the ventricle sizes in people diagnosed with schizophrenia versus normal controls, this difference appears small, with a great deal of overlap between normals and schizophrenics, nonspecificity for schizophrenia, and several studies showing no difference (Van Horn & McManus, 1992). The question of whether ventricles enlarge over time is complicated by measurement error, publication-date effects (Van Horn &

McManus, 1992), and the finding that the ventricles of some schizophrenics appear to shrink substantially over time. If ventricles of some schizophrenics do enlarge over time, the change may not be etiologically significant (i.e., symptoms may predate morphological changes) nor diagnostically significant (i.e., morphological changes may not correlate with neuropsychological or cognitive changes).

Anatomical resilience: Relevance of the neuropil.

There appears to be a great deal of evidence that both genetic and experiential processes influence brain development. When brain morphological differences are found between a group diagnosed with a mental disorder and a control group, questions pertaining to etiology and permanence come to the fore. Etiologically, a difference in morphology may indicate that the mental illness is the result of pathological brain development (Casanova, 1997; Feinberg, 1983; Keshavan, Anderson, & Pettegrew, 1994). This pathological development may be determined either genetically or experientially, or caused by the interaction of genetics and experience. In other words, interactions between the individual and the environment (within a genetic context) that produce mental disorders may cause morphological changes through consistent patterns of neurophysiological activity. Studies showing morphological changes after the onset of mental disorders (e.g., Rapoport et al., 1997) substantiate this possibility that experience leads to changes in brain morphology. Alternatively, the morphological difference between a psychiatric group and a control group may be epiphenomenal or a non-causal "marker." For instance, lateral ventricular volume differences between schizophrenics and normals appear to be small overall, requiring large sample sizes to demonstrate the

difference, and showing a great deal of variation within groups and poor specificity to schizophrenia. In addition, morphological differences have not been shown to be etiologically or clinically significant for schizophrenia (Chua & McKenna, 1995; Stevens, 1997) or for obsessive-compulsive disorder (Robinson et al., 1995); although at least one study has reported a correlation between ventricular size and degree of psychomotor retardation in depression (Schlegel et al., 1989).

Studies of differences in brain morphology show a lack of diagnostic specificity and consistency. In addition, there is also some confusion about the resilience or plasticity of brain morphology. Some theorists hypothesize that mental disorders such as schizophrenia may cause a brain disabling or aging phenomenon (e.g., Pettegrew et al., 1991), or that a genetic defect creates abnormal anatomical development (e.g., Feinberg, 1983; Keshavan, Anderson, & Pettegrew, 1994). Yet, other evidence shows that whatever morphological change may occur along with a mental disturbance may be corrected endogenously when symptoms change, either through a biochemical compensatory process for the changed anatomy (Drevets et al., 1997) or through an anatomical reversal (Pfefferbaum et al., 1995), or possibly both. To the extent that such a corrective physiological process accompanies a psychotherapeutic experience, the special status of pharmacological agents in the treatment of disordered brain function is preempted. Several studies have demonstrated that schizophrenia is reversible without medication (Ciompi et al., 1992; Cullberg & Levander, 1991; Karon & VandenBos, 1994; Levander & Cullberg, 1993), and that between one-half and two-thirds of schizophrenics eventually achieve either full recovery or at least significant improvement when studied longitudinally (Harding, Zubin, & Strauss, 1987). Whether these improvements are

correlated with morphological changes would indicate to what extent the study of morphological correlates is relevant to our understanding of prognosis.

Drevets et al. (1997) demonstrated that the subgenual prefrontal cortex (SPFC) gray matter volume was significantly and substantially reduced in both unipolar depressed and bipolar patients relative to normals. However, by using high-resolution PET imaging, the researchers found that the medication-free bipolar patients who were in a manic phase had significantly greater SPFC metabolic activity than did normal controls or depressed patients in either the unipolar or bipolar groups. Although depression was associated with reduced SPFC metabolism and volume, the metabolic activity was mood-state dependent, and the reduced volume difference in the bipolar group was compensated by greater metabolic activity when in the manic phase. Thus, the impact of a morphological difference, however related to symptomatology, may be superceded by an experience-dependent biochemical process that reduces the relevance of any morphological difference.

A morphological change following the successful treatment of alcoholism may be an example of anatomical resilience. While there is some evidence that chronic alcoholism is associated with increased CSF volume and decreased gray matter volume (Jernigan et al., 1991; Pfefferbaum et al., 1997), there is also evidence that recovery from alcoholism results in a reversal of these effects. Pfefferbaum et al. (1995) obtained MRI data on a group of chronic alcoholic men to determine the effects of sobriety on brain volume changes. By studying abstainers and relapsers at different time points, and comparing them to a control group, they found that ventricular volumes significantly decreased in the abstainers relative to the relapsers and controls after 21 days of sobriety,

and there was a trend for increase of anterior cortical gray matter volume for the abstainers. Also, “greater volume abnormality at entry into the study was associated with greater improvement with abstinence” within this time frame (p. 1182). With 2 to 7 months of sobriety, there was a significant reduction in third ventricle volume so that it was not significantly different than the volume in the control group. The reduction in third ventricle volume was associated with improved performance on cognitive tests. The authors noted that ventricular enlargement could result either from cell loss, cell shrinkage, or cell compression. They hypothesized that “recuperation of brain tissue volume is evidence that the adverse effects of alcoholism do not result solely in neuronal atrophy (i.e., cell loss)” (p. 1189); but if partly so, may be compensated by axonal rearborization and dendritic regrowth.

Research on schizophrenia-related morphology yields other evidence in support of Pfefferbaum et al.’s (1995) hypothesis that brain volume changes are not due to cell death, but to reversible processes in the neuropil. Whereas Lim et al. (1996) found cortical gray matter volume deficits and lateral ventricular enlargement in a group of first-episode schizophrenics, they did not determine whether these differences were due to cell loss, or some other process. Goldmann-Rakic & Selemon (1997) reported that reduced cortical volume was associated with increased neuronal density. They hypothesized that the morphological abnormalities found in some schizophrenics were not due to neuronal cell-death, but were due to a change in the neuropil. In accord with this hypothesis, Weinberger (1997) reported no evidence of neuronal loss over time in people diagnosed with schizophrenia. Similarly, Keshavan, Anderson, & Pettegrew (1994) reviewed the literature to find evidence for Feinberg’s (1983) hypothesis that

schizophrenia is due to excessive synaptic “pruning” in the prefrontal cortex. They cited several studies demonstrating increased pyramidal cell densities that may have been due to loss of surrounding neuropil (that might also lead to increased CSF volume). Because the growth of axons and dendrites, blood flow, and other processes in the neuropil may be stimulated by new experiences, changes in the neuropil may not necessarily result in a permanent, totally irreversible “brain-aging” decline. The evidence of experiential and anatomical resiliency suggests that researchers should not assume that either a functional or anatomical difference between controls and psychiatric patients indicates a permanent “hard-wiring” deficit or disability.

In sum, morphological markers have not been shown to be necessary, sufficient, sensitive, or specific markers for diagnosis or prognosis of either mental disorders or mental health. Instead, behaviors or experiences that meet criteria for psychiatric disorders overlap and are inconsistent in their physiological expression. Regardless of any such correlations, physiological activity, per se, does not indicate a disease process; and studies that have focused on anatomical and functional differences between normal controls and psychiatric patients have demonstrated that different mental processes can result in, as well as from, changes in physiology. The experimental designs of such studies may lead to an appearance of cause-effect relationships between physiological processes and mental processes that may misrepresent a mutually determined or simultaneous physical and mental expression. As physiological processes, all experiences and behaviors are generated through the expression of gene products and processes. However, like morphology studies, genetic research has been limited by methodological and empirical shortcomings. In addition, conceptual and logical problems have prevented

the formation of coherent, testable hypotheses about the relationship between genetic processes and mental disorders.

Current Research Methodology Has Been Insufficient to Measure Genetic Effects

Heritability estimates are influenced by environmental factors.

In studies of genetic and environmental influences on mental disorders, the resemblance between parents and offspring is the phenomenon to be explained, not evidence of genetic transmission (Lewontin, 1991). The study of genetic factors in the etiology of mental disorders has produced conflicting and inconsistent results and is beset by a number of conceptual and methodological problems. Inconsistencies in diagnostic procedures, ad hoc inclusion of "spectrum" disorders, shared-environment factors, and hypothesized genetic heterogeneity have precluded construct validity and consistency between studies of schizophrenia (Kendler & Diehl, 1993; Kringlen, 1993; Murray & Harvey, 1989; Portin & Alanen, 1997; Prescott & Gottesman, 1993), as well as bipolar disorder (Ewald, Mors, Flint, Eiberg, & Kruse, 1994; MacKinnon, McMahon, Simpson, McInnis, & DePaulo, 1997), and attention deficit hyperactivity disorder (ADHD; Goodman & Stevenson, 1989; Sherman, McGue, & Iacono, 1997). For example, Sherman et al.'s (1997) large study of twin concordance for ADHD showed that genetic influence was determined by informant source. Mothers' ratings yielded a monozygotic (MZ) concordance of 0.67 and a dizygotic (DZ) concordance of 0.0. Teachers' ratings yielded a monozygotic concordance of 0.53 and a dizygotic concordance of 0.37. In addition, behavioral ratings fluctuated dramatically based on setting. Sherman et al. reported that their finding of a mother-rated dizygotic concordance of zero was at odds

with the findings of another study, but suggested that the incongruity "may reflect nothing more than statistical imprecision due to limited sample size" (p. 534) although the sample size for Sherman et al.'s study was 388 children. Sherman et al. also reported that the "consistently larger monozygotic than dizygotic concordance rates indicate the importance of genes in the expression of the ADHD syndrome" (p. 534). Yet, the heritability formula:

heritability = 2((MZ intraclass correlation) – (DZ intraclass correlation))

indicates nothing about genes, only something about relative behavioral similarities that are the object of correlation (R.C. Lewontin, personal communication, March 25, 1998). Thus, Sherman et al.'s inference is circular: it explains the behavioral similarity of monozygotic twins in terms of the genetic causes they seek to determine in the first place.

Goodman & Stevenson's (1989) twin study of hyperactivity took into account that some monozygotic twins go unrecognized as such by parents, and are raised as if they were dizygotic. In an effort to disentangle true genetic effects from expectancy effects, the experimenters conducted zygosity tests and found that the degree of behavioral similarity (measured by intraclass correlation) rated by parents and teachers varied dramatically based on whether parents thought their monozygotic twins were dizygotic or monozygotic (range = 0.42-0.71). In addition, the mothers' behavioral ratings yielded such high correlations for both recognized and unrecognized monozygotic twins and such low correlations for dizygotic twins that the heritability estimate for inattentiveness and hyperactivity, based on mothers' ratings, exceeded 100%, with common environmental effects being less than zero.

The concept of heritability for psychological symptoms must be understood as an inference affected by changes in the environment. Heritability is a formula that is influenced directly by social and cultural variance, rather than being a pure measure of genetic effect (Bouchard, Lykken, McGue, Segal, & Tellegen, 1990; Lewontin, 1991). Psychological difficulties, as biological processes, are influenced by genetic factors. However, the expression of these difficulties may be more varied and susceptible to change than the concept of a heritability estimate might make it appear.

Familial aggregation estimates vary widely between studies.

Another difficulty in determining genetic influence is demonstrated by the wide range of concordance rates reported for mental disorders such as schizophrenia. In a review of familial aggregation studies of schizophrenia, Portin & Alanen (1997) found concordance rates between 15 and 58% for monozygotic twins, and between 4 and 27% for dizygotic twins. Two studies of the offspring of discordant monozygotic twins have yielded opposite results for prevalence in their offspring: one found no difference in prevalence between offspring of “ill” and “well” twins; the other found a trend for a difference (17.9% of the offspring of symptomatic twins were ill versus 4.4% of the offspring of the asymptomatic twins). Portin & Alanen (1997) found that concordance of ordinary siblings is lower (3-14%) than that of dizygotic twins (8-26%) although both share the same proportion of genetic material as their symptomatic siblings. De Domenico et al. (1995) found that the range of concordance in first-degree relatives among studies ranged from 5.6% (for parents of schizophrenics) to 12.8 and 46.3% (for children of one or two schizophrenic parents, respectively). In another review, Kendler &

Diehl (1993) found that in family studies with Ns Δ 18, the morbid risk for first-degree relatives of schizophrenics was between 3.7-6.5%, whereas the morbid risk in first-degree relatives of normal controls was between 0.2-1.1%. In contrast to the population concordance rate between 15-58% for monozygotic twins, a set of monozygotic triplets showed a 100% concordance between them, all with onsets within 8 months of one another (H←rnryd, J¬nsson, Greitz, Nyman, & Sedvall, 1995). Sherrington et al. (1988) reported a linkage analysis in seven extended British and Icelandic families, none of which contained monozygotic twins. In one family, neither father nor mother had schizophrenia spectrum disorders (SSDs), but 7 of 10 children (70%) did. In two other families, 4 of 7 offspring (57%) had SSDs (each family had one SSD parent). In another family, 4 of 9 offspring (44%) had SSDs (parents did not have SSDs). In yet another family, 2 of 4 children (50%) had SSDs (parents did not have SSDs). These rates are substantially higher than the range that is generally reported in the literature for concordance of first-degree relatives. de Marchi (1991) cited results from the Finnish Adoptive Family Study of Schizophrenia (Tienari et al., 1987) in which the authors found that a healthy adopting family was a protective factor for the index-group children with schizophrenic biological mothers, and that having severely disturbed but nonschizophrenic parents did not adequately protect the control-group children against severe psychological symptoms. In the healthy adopting families

> None [of the index or control group children] was psychotic, and only 4 per cent of the index adoptees and only 2 per cent of the control adoptees had serious but non-psychotic disorders. When the rearing family was severely dysfunctional, 55 per cent of the index and 30 per cent of the control adoptees were abnormal (with psychosis, borderline syndrome or severe personality disorders). (di Marchi, 1991, p. 453)

In a 10-year update of the Finnish adoption study, Wahlberg (1997) found that index offspring (with schizophrenic mothers), who were raised by adoptive parents with low communication deviance, exhibited an even lower proportion of thought disordered responses to a Rorschach stimulus than did control offspring raised by adoptive parents with similarly low communication deviance. Only when the communication deviance of adoptive parents was high did the index offspring have a greater proportion of thought-disordered responses than their control group counterparts. Such a wide and inconsistent range of values of concordance and aggregation among these studies indicates that environmental effects profoundly influence any genetic contribution, and that whatever genetic effects may influence schizophrenic processes must in any case be heterogeneous, expressed through multiple genetic effects.

Adoption studies allow the environmental influence of biological relatives.

Complicating the interpretation of genetics studies of identical twins reared apart and of adopted offspring is the high average age of separation from biological mothers in these studies. Human adoption studies rarely follow a “separated at birth” paradigm, and often have a substantial delay between birth and adoption that may allow for a high degree of environmental, attachment effects to be exerted upon the neonate before it is raised by its adoptive family. The largest study of adopted-away offspring of schizophrenia and control mothers, The Finnish Adoptive Family Study of Schizophrenia, had a mean age of placement of 15 months (median=11), with an upper cutoff of 48 months (Wahlberg, 1997). The twins in the Minnesota Study of Twins Reared Apart (Bouchard, Lykken, McGue, Segal, & Tellegen, 1990) spent a mean of 5.1

months together (range = 0-48.7 months) prior to separation from each other. The time at separation from mother was not reported, but it can be assumed that they were not adopted until this point. In an early study of adopted children of schizophrenic mothers, the children were separated from their hospitalized mothers within several days of birth. However, many were discharged to the care of family members (Heston, 1966). Another study of the genetic effects of schizophrenic parents on adopted away children had a sample with a range of separation age between 5 days and 48 months, and a median of 5.9 months (Rosenthal, Wender, Kety, Welner, & Schulsinger, 1971). Adoption studies such as these that presumably measure genetic effects do not control for the powerful environmental influence of early attachment relationships with biological relatives, or of the loss of such relationships upon adoption. Research on early attachment behaviors between mothers and infants raises questions about whether the early interactions between schizophrenic biological mothers and their offspring, before adoption, may have significantly contributed to the risk that the Finnish and Minnesota investigators attribute to a genetic effect. Likewise, it is unclear to what extent biological relatives who raised the children played a role in the Heston (1966) study.

The falsifiability problem.

Popper (1963) regarded falsifiability as one of the cornerstones of a scientific discipline. He argued that scientific propositions must be made in a way that can be tested. If the conditions of a proposition make it impossible to find the proposition false, the proposition is not relevant to the practice of a science that concerns itself with testing the truth-value of hypotheses with evidence. To the extent that a hypothesis is expressed

in terms that can be disproved with evidence, the hypothesis is falsifiable and scientific. The issue of falsifiability is directly relevant to genetic hypotheses about mental disorders.

Researchers using genetic linkage analysis to identify DNA loci associated with schizophrenia and bipolar disorder have found evidence for significant linkage in families. However, all attempts to replicate these studies have been unsuccessful (GW-NIMH, 1997), and in some cases, the inclusion of a much broader range of diagnoses, rather than schizophrenia or schizophrenia spectrum disorders, has actually increased statistical significance (Sherrington et al., 1988). The problem of nonreplication in genetics studies has been explained in two ways: lack of diagnostic agreement, and genetic heterogeneity (de Marchi, 1991). Both of these explanations prevent the falsifiability of hypotheses. Modrow (1992) has pointed out that in an effort to ameliorate the problem of nonreplication, and increase construct validity and falsifiability, researchers and theorists often have split mental disorder constructs, such as schizophrenia, into diagnostic subtypes or clusters such as:

process/reactive

positive/negative

genetic/sporadic

altered morphology/no altered morphology

early onset/late onset

episodic/continuous

episodic with interepisode remission/without interepisode remission,

paranoid/catatonic/hebephrenic

paranoid/catatonic/disorganized/undifferentiated

Weinberger et al. (1990) questioned the validity of diagnostic subtyping:

> While this subtyping may have descriptive and occasionally prognostic value and may also rescue research data that are otherwise not significant, the implicit assumption that the illness is etiologically or pathophysiologically heterogeneous is pure speculation. (p. 548)

Subtyping has been used extensively, but it has not fixed the nonreplication problem, or "rescued research data that are otherwise not significant." The symptomatology of the endogenous depression subtype, for example, has had some limited success being linked with greater symptom relapse and cortisol non-suppression after challenge with dexamethasone (Charles, Schittecatte, Rush, Panzer, & Wilmotte, 1989; Frank, Kupfer, Hamer, Grochocinski, & McEachran, 1992; Thompson, Rubin, & McCracken, 1992). Yet, this finding is inconsistent, and the validity of the "endogenous/reactive" depression subtypes has been challenged by contradictory evidence (Bron & Lehmann, 1990; Brown, Harris, & Hepworth, 1994; D'haenen, De Weert, & Feyaerts, 1990; Halbreich et al., 1989; MʃIler, Hofschuster, Ackenheil, Mempel, & Eckstein, 1993; Parker, Hadzi-Pavlovic, & Boyce, 1989; Reno & Halaris, 1990; Tandon et al., 1991; Thase, Simons, Cahalane, & McGeary, 1991).

The validity of diagnostic categories and subtypes has been challenged by many authors. One of the more prominent debates about such behavioral "phenotypes" is focused on the concept of endogenous depression. Frank, Anderson, Reynolds III, Ritenour, & Kupfer (1994) remarked that

> Despite the advances in biological and psychosocial assessment methods, reliable distinction between depressed patients with endogenous presentations or melancholic symptom features and those with nonendogenous presentations has remained elusive. (p. 519)

Conde-L∧pez, Roig, Fern↔ndez, Regatero, & de la Torre (1995) summarized that

> The concept of endogenous depression has become one of the everlasting troubles of Psychiatry. Along this century, no clinical definition has been mostly accepted and no conceptual consensus has been reached. (p. 5)

One study of melancholic/endogenous depression, as the subtype with "a biological rather than an environmental etiology" (Peselow et al., 1992, p. 1324) found that 23% of their subjects had a complete or partial response after one week of placebo treatment. Despite this nonconfirming finding, the authors concluded that "patients with DSM-III melancholia may be *unresponsive* to nonsomatic treatments" (p. 1324, italics added), a conclusion clearly falsified by their own data. The study methodology of "washing out" the placebo responders from the original sample may have facilitated this conclusion. In addition, there is some evidence that dexamethasone non-suppression of cortisol is ameliorated by clinical response, whether from drug or ECT treatments (Bielski et al., 1990; Varma, Trivedi, Anand, Gulam, & Lal, 1989). This indicates that the subtype of endogenous depression may not be a stable trait variable, but a simply a state-dependent collection of symptoms.

Zimmerman, Coryell, & Black (1993) found systematic biases in the application of diagnostic criteria within three different major study centers of depression. Although the centers used the same diagnostic criteria (RDC and DSM-III), and reliability coefficients were very good within each research center, there were significant between-center differences due to different interpretations of patients' responses. A study of depressed patients in the United Arab Emirates found that endogenous depression as delineated by western criteria was not likely to manifest due to cultural differences in emotional expression (Hamdi, Amin, & Abou-Saleh, 1997). Wood, Moore, Harrington,

& Jayson (1996) found only a quantitative, not qualitative, basis for a distinction between endogenous and nonendogenous depression in an adolescent sample. Problems with content validity and diagnostic reliability occur for other psychiatric diagnoses as well (di Marchi, 1991; Sarbin, 1997). In a review of heredity-environment studies of schizophrenia and affective disorders, Kringlen (1993) stated that the main problem in psychiatric diagnosis is validity rather than reliability:

> Our classification of mental disorders is without strong scientific evidence, although it is more or less agreed on by the psychiatric establishment. Thus the whole problem of phenotype is debatable. Without an improved phenotype, linkage studies are not likely to succeed. (p. 79)

Without valid behavioral or experiential phenotypes, the failed attempt to replicate a study can be attributed to the testing of a different phenotype. Efforts to increase the construct validity of mental disorders have not been particularly successful, preventing the falsifiability of hypotheses.

While a lack of diagnostic agreement may prevent replication of biopsychiatric findings (Zimmerman, Coryell, & Black, 1990), the genetic heterogeneity hypothesis asserts that the lack of diagnostic agreement and lack of study replication may be due to genetic differences between the participants in different studies. Genetic heterogeneity refers to a phenotype that is "the result of the action of two or more different genes in different families," with the result that "analyzing families of both types together in a linkage analysis confounds the analysis" (MacKinnon, McMahon, Simpson, McInnis, & DePaulo, 1997, p. 94). For example, MacKinnon et al. (1997) found that "inheritance patterns in bipolar disorder suggest complex mechanisms of transmission. . . and raise suspicions of genetic heterogeneity; i.e., causation by different genes in different families" (p. 90). In their study, they found that 57 families with high rates of bipolar

disorder also tended to have bipolar individuals who were comorbid for panic disorder. They hypothesized that this comorbidity of panic disorder was a marker for a different genetic linkage than families without the comorbidity. Ewald, Mors, Flint, Eiberg, & Kruse (1994) conducted a study of genetic markers for bipolar disorder, and found that

> "DBH was excluded as a major gene causing manic depressive illness in one large family, assuming dominant mode of transmission. The extended sib-pair analyses yielded no evidence of linkage. (p. 181)

Nevertheless, Ewald et al. stated that "the major problem in the search for psychiatric disease genes may be misclassification of phenotypes at the diagnostic level" (p. 181). They concluded that like previous studies with nonreplicated findings that were "most likely due to chance findings, though they might be caused by genetic heterogeneity" (p. 177),

> Linkage between manic depressive illness and the DBH locus has been excluded in several families, [but] *the possibility exists that DBH is a susceptibility locus for manic depressive illness*. (p. 181, italics added)

Sherman et al.'s (1997) study of twin concordance for ADHD in 287 pairs of twins called into question the relative validity of teachers' and parents' ratings. In addition to arguing for more "rigorous and consistent operational definitions of ADHD," the authors also stated that "it is possible that mothers and teachers are actually rating different phenotypes" in the same children, and that "even larger samples would permit genetic contributions to ADHD to be separately evaluated in pervasive and situational subtypes" (p. 535). In other words, the anomalous findings led the authors to hypothesize that either the different raters were rating different phenotypes of the same underlying genotype, or possibly that genetic heterogeneity was responsible for the different phenotypes so that phenotypic subtyping might be necessary to increase diagnostic

validity (hence reliability). Kendler & Diehl (1993) remarked that "an accurate definition of the affected phenotype is crucial in any genetic investigation" (p. 266). Nevertheless, the difficulty of this task in psychiatric classifications is pervasive. Weinberger (1997) reported that while "a number of studies have been unable to replicate the genetic linkage findings; this failure may be due to differences in the pedigrees or the use of different genetic markers located on the same chromosome" (p. 22). Regions-of-interest on chromosomes often contain hundreds of genes, any of which might presumably combine to increase the risk of a "fringe" psychiatric disorder in the offspring of schizophrenics (Sherrington et al., 1988; Weinberger, 1997). The lack of diagnostic specificity and the presumed polygenic properties of mental disorders make for scientific "shifting sands" that may allow for the falsification of specific hypotheses; but lead to a continual production of post-hoc explanations rather than a scientific test of the general premise (Meehl, 1991). The scientific doctrine of falsifiability requires a hypothesis of genetic effects to be constructed as refutable. However, as with a lack of diagnostic agreement, the genetic heterogeneity hypothesis makes falsifiability impossible because the overarching hypothesis of genetic effect is untestable except through narrowly defined parameters. For example,

> Cases classified as nonfamilial could have genetic loading due to polygenic inheritance, lack of penetrance of major genes, recessive genes, and quality of data regarding diagnoses in relatives, including difficulty in identifying spectrum cases, sibship size differences, and relatives not having passed through the age of risk. (Schwartzkopf et al., 1991, p. 57)

While other authors (e.g., Sherrington et al., 1988) cite familial phenotypic expression as evidence for genetic loading, these authors point out that the lack of

familial expression does not falsify the genetic hypothesis. Similarly, in the recent study of monozygotic triplets concordant for schizophrenia, the authors conclude

> The reported absence of psychiatric disease in the parental and grandparental generations gave no indication for a fully penetrant dominant genetic transmission as an etiological mechanism. However, this does not rule out other ways of genetic transmission. (H←rnryd et al., 1995, p. 6)

De Domenico et al. (1995) state that

> Most of the data are consistent with a genetic component in the causation of schizophrenia, even if none of the studies allows to define the mode of inheritance, the exact definition of the phenotype and the relationship between the hereditary substrate and the physiopathology of the disease. . . The existence of a genetic predisposition to schizophrenia [is presumable], but only the interaction between genetically determined traits and biological and environmental concomitant factors allows the disease [to become] clinically manifest. (p. 135)

Adding to the conceptual confusion of genetic influence is the idea that common medical diseases, although often multifactorial, are not necessarily so for each individual case: “In coronary artery disease, some cases are a direct consequence of the mendelian inheritance of the gene for familial hypercholesterolemia, while others are almost entirely dependent on hazardous behaviors” (Murray & Harvey, 1989, p. 526). Likewise, in some individuals, schizophrenia may be largely determined by environmental influences, while in others, the disorder might be caused more by genetic factors (de Marchi, 1991; Kendler & Diehl, 1993; Murray, Reveley, & McGuffin, 1986).

In addition to genetic heterogeneity, other similar concepts complicate the issue of genetic influence on mental disorders (Prescott & Gottesman, 1993). For example, the concept of phenotypic heterogeneity allows for multiple “spectrum” disorders with one underlying genotype. Etiological heterogeneity allows for a common phenotype produced by a variety of different gene-environment interactions. Phenocopies refer to phenotypes

generated solely by environmental effects that are indistinguishable from genotypically produced phenotypes.

The limitations of diagnostic or phenotypic validity combined with the possibility of multiple or even infinite varieties of environment-genetic influences on psychiatric symptoms may continue to make study replication difficult or impossible. While the hypothesis that there is some genetic influence on the incidence of mental disorder is reasonable, it also appears to be unfalsifiable in the face of numerous nonreplications. In addition, there is growing evidence that this method of research may not be useful at this time, given not only the problems of phenotypic classification, but also the lack of generalizability of genetic findings to different samples with similar phenotypes, possibly due to genetic heterogeneity.

Without a valid and reliable way to measure genetic effects on mental phenomena, we may turn to a more basic point: to the extent that psychological disturbances are a product of both genetic and environmental influences, it must be remembered that genetic and environmental factors do not act independently of each other. Statistical models that separate these factors do so artifactually, not actually. The variability of results in the literature have prevented the formulation of a coherent model for a genetic transmission of the prototypical mental disorder, schizophrenia, without casting doubt on the validity of the major hypothesis of genetic transmission. The ability of the major hypothesis to resist falsification despite the consistent falsification of its specific cases, undermines the scientific standing of the genetic hypothesis (Meehl, 1991). While there can be no doubt that for some individuals, schizophrenia, like many other psychological problems and strengths, may derive in part from genetic processes

transmitted in pedigrees, the complexity of gene-environment interactions may prevent the possibility of conducting clinically useful research that generates replicable, generalizable findings about mental disorders.

Research on the concomitance of psychological and physiological process has shown that not only are there biochemical processes that correlate with experience, but that changing one's mental state affects one's physiology. Early developmental experiences exert powerful effects on neural development, but the effects of later experiences on brain function may have been underemphasized in favor of biopsychiatric interpretations of behavior rather than behavioral interpretations of biochemical process. Genetic, morphological, and functional data pertaining to mental disorders are inconsistent and suffer from problems related to the validity of phenotypes and nonfalsifiability. Little can be made of any physical or genetic causal hypotheses of mental disorders because of the severity of conceptual shortcomings and the lack of adequate replication. Furthermore, effective treatment (whether psychological or pharmacological) does not appear to be predicted by any biological or genetic marker in any consistent fashion. Thus, the physiological expression of mental disorders does not appear to be a necessary or sufficient condition for pharmacological treatment on the basis of a unique etiology or pathophysiology separate from "psychogenic" disorders; and in addition, interpersonal psychological treatments exert their effects through a physiological, biochemical process. Biopsychiatric research conceptualizes mental disorders through the entity metaphor of physical illness or disease, and much empirical research has been done on physiological states of the brain that accompany mental disorders. However, this research has demonstrated that mental processes are not simply

emergent products of physiology, but that mental processes changed by life experiences are concomitant with physiological change. The evidence implies that mental disorders, like all mental processes, are biologically expressed, and that mental and physiological change coincide regardless of which is experimentally manipulated. The use of terms such as “biological basis,” “brain disorder,” and “chemical imbalance,” implies a physiological prime mover and a biopsychiatric strategy for treatment. Neither of these implications are supported empirically.

CHAPTER 4: Research and Treatment Considerations

> Many scientific theories have, for long periods of time, stood the test of experience until they had to be discarded owing to man's decision, not merely to make other experiments, but to have different experiences.
>
> –*Heller*

The biopsychiatric ontology, that mental or emotional disturbance is caused by physiological dysfunction, is based on scientific evidence that mental processes are in constant conjunction with physiological processes. This link between mental and biological events can be verified to some degree through experiments on brain physiology; but this correlation does not mean that problematic mental processes are caused by brain disease. A biological study of mental disorder does not mean that mental disorder is, in essence, a biological phenomenon. Likewise, a psychodynamic study of mental process does not mean that mental processes are caused by psychodynamics. The epistemology one chooses in learning about mental disorders does not determine the underlying nature of mental disorders. The medical illness or disease metaphor of mental disorders can be understood as one epistemology or strategy for understanding the mechanisms of mental function. The metaphor does not establish the ontological basis of mental disorders. Thus, when the National Alliance for the Mentally Ill uses the slogan, "Open your mind, mental illnesses are brain disorders," and states that "nine out of 10 insurance policies treat the brain differently from the heart," NAMI is using the biopsychiatric ontology that psychological problems are essentially medical illnesses to

promote biopsychiatric research, and to gain support for mental health insurance parity (NAMI, 1997b).

Epistemology versus Ontology: Implications for Treatment

The danger in confusing an epistemology of mental disorder with the ontology of mental disorder is that as an ontology, the biopsychiatric perspective gains preeminent status in public policy decisions, personal treatment decisions, and the economic status of mental health practitioners. While the biopsychiatric epistemology of mental disorder focuses on certain physiological processes that sometime, though not consistently, accompany mental phenomena, this epistemology has not yet determined the cause of either the physiology or psychology of such phenomena. The inference that biochemical processes cause mental disorders is an ontological view of mind-brain interaction that the empirical evidence does not support at this time. The evidence indicates that brain function is dynamic and plastic, profoundly influenced by a person's experiences and behaviors. A metaphor of physical illness for mental disorders misrepresents the extent to which intentionality and novel social interactions influence the function and structure of the brain, and the whole person.

Informed consent for treatment depends on an accurate depiction of the range of research evidence pertaining to the question, "What is mental disorder?" Informed consent should include alternative epistemologies even when they are outside of the clinician's theoretical framework, insurance carriers' conceptualizations, or the popular view. Standards of care developed by associations of practitioner-scientists that are based on guild-friendly epistemologies also must include adequate references to competing

hypotheses and evidence. The evidence for a physical cause of severe mental disorders is unsupported at present, and should be presented as such to the media and lay public.

Training programs for mental health providers, educators, and researchers, should include coursework that teaches the critical examination of the epistemologies of mental health and illness. Psychology, social work, and psychiatry programs that focus on the dissemination of research and knowledge to the exclusion of critical analysis and discussion prevent students from developing the basic tools required to make informed use of that knowledge. The trend in psychology toward "integrationism" of approaches must be done based not only on the research that different schools of treatment develop, but also through an improved understanding of the assumptions that frame the research questions. Courses in the philosophy of science, and the critique of empirical research may best address these issues. Teaching scientists and practitioners to be more critical consumers of research, and to examine the broader assumptions that guide their work, will increase dialogue between modes of treatment, and create more thoughtful integrations of the wisdom collected in different epistemologies. In turn, this may allow clients to make better-informed decisions about their options for getting help. Specific to the issues presented in this paper, practitioners should not tell clients with serious mental disturbances that their problems are biologically based or the result of a chemical imbalance. Such information is not only inaccurate, given the empirical evidence, but may be unethical if clients are adversely affected by the (untested) assertion by a clinician that they are physically disabled, and if clients are misled to believe that their problems, because they are physiological, require a pharmacological treatment.

Public policy.

While new state and federal mental health parity laws (which equalize insurance coverage for mental and medical benefits) may provide better insurance coverage for specified psychiatric symptoms, the development of these laws does not address the problem of "medically necessary" provisions that may limit decision-making policies to biopsychiatric, medical interventions. For example, the CEO of the National Mental Health Association stated in a newsletter that

> "Biological brain diseases" normally [are] defined to encompass schizophrenia, schizoaffective disorder, major depressive disorder, bipolar disorder, paranoia and other psychotic disorders, obsessive-compulsive disorder, panic disorder and autism. . . . Some proponents of a "restrictive parity" emphasize that the designated mental illnesses have a biological origin. This distinguishes them from mental or emotional problems resulting from the environment or difficult life circumstances. . . . [However,] biomedical and behavioral research conducted by the National Institute of Mental Health continues to reveal that increasing numbers of mental disorders have a biological or genetic origin. For example, attention deficit and hyperactivity disorder has been shown to have a biological cause, and ADHD can often be effectively controlled by psychotropic medications; however, this disorder is not often included on the list of brain diseases. (Faenza & Guida, 1996)

Policy decisions about insurance coverage and treatment decisions may be based on this kind of erroneous inference about research, driven by the biopsychiatric ontology.

Economic factors.

The conversion of the biopsychiatric epistemology into an ontology of mental disorders may also be influenced by economic incentives to researchers from pharmaceutical companies, such as the honoraria and consulting fees that these companies pay to biopsychiatric researchers and psychiatric journal editors who oversee the publication of research trials. The conflicts of interest that have arisen between

conducting or reviewing research on drug effects and receiving money from drug companies whose products are being evaluated has been extensively documented by Breggin (1991). For example, the *Archives of General Psychiatry* published a research article about the effectiveness of Xanax→ for panic disorder while the editor-in-chief, Daniel X. Freedman, was a paid consultant to Upjohn, the company that manufactures Xanax→. The research study was controversial because of the way the findings were depicted in the abstract. The abstract discussed the significant difference between Xanax→ and placebo at 4 weeks, but did not mention that at 8 weeks, there were few differences between Xanax→ and placebo effectiveness, and significant side effects and withdrawal effects for the Xanax→ (Pecknold et al., 1988). A contingent of researchers wrote a letter to the Archives criticizing the report, and after the publication of the letter was delayed, the first author accused Freedman of obstructing the publication of the letter and editing out central points in the final version (Breggin, 1991). Through advertising, pharmaceutical companies also provide the funding that allows psychiatric journals to be published. It is possible that conflicts of interest such as these may hinder the accommodation of biopsychiatric theory to the disconfirming data that the epistemology has actually yielded. Such financial arrangements may be antithetical to the preferred scientific stance of attempting to accept or reject the null hypothesis.

Practitioners' behaviors and their ontology of mental disorders also may be influenced by the changing economics of mental health care. According to Mu™oz et al. (1994), recent guidelines in the treatment of depression in primary care, published by the Agency for Health Care Policy and Research (AHCPR),

> clearly suggest that primary care physicians initiate treatment with most patients and refer to a mental health specialist only in the event of [pharmacotherapy]

> nonresponse or complications. Such a recommendation amounts to a virtual single option strategy, which may not be sound national health policy. (p. 47)

Krupnick et al. (1996) noted that the guidelines specify referring to a mental health specialist only after two unsuccessful antidepressant trials by the primary care doctor. *Psychotherapy Finances* (Ridgewood Financial Institute, 1997), a monthly publication about market trends in the helping professions, recently noted in an annual survey that

> More therapists than ever are reporting that managed care is squeezing down hard on their private practices. All five therapy professions surveyed say that managed care has reduced their income in the past year. They all agree that the companies cut their patient loads over that period and, *except for psychiatrists*, they report a trend to an increasing number of disallowed claims. (p. 7, italics added)

While it may be in the professional interests of psychiatrists and psychologists to promote their respective epistemologies of mental disorder, it must be remembered that these approaches are strategic rather than ontological. The question of how best to help people with mental disorders must be understood as separate from the epistemological framework of how one studies mental disorder phenomena. Congruence between a particular epistemology and its corresponding treatment does not ensure treatment success. Thus, informed consent requires informing clients of the strategy used, without implying that it uniquely addresses the source of the problem.

Although the evidence indicates that mental processes correspond to changes in brain activity, it is also the case that psychological experiences exert an effect on biochemistry and genetic function (e.g., Baxter et al., 1992; Fawzy et al., 1993; Galvin et al., 1991; Higley, Suomi, & Linnoila, 1991; Maier, Watkins, & Fleshner, 1994; Miller, 1994; Pardo, Pardo, & Raichle, 1993; Perry, Pollard, Blakely, Baker, & Vigilante, 1995; Post, 1992; Schiffer, Teicher, & Papanicolaou, 1995; Teshima, Sogawa, Mizobe, Kuroki,

& Tetsuya, 1991; van der Kolk, 1988). With increasingly powerful brain imaging techniques it may be possible to observe physical functional correlates to many kinds of mental processes, but it is important not to confuse biochemical correlation with biochemical cause. A mental process that is undesirable is not a brain disease simply by virtue of being physically expressed or present in family members. From current empirical evidence, it may be said that mental disorders cause biochemical imbalances as easily as it is said that biochemical imbalances cause mental disorders. Yet, neither view appears to be an adequate description of what mental disorders are. A more heuristic model may be that within a context of genetic sensitivity to environmental influences, one's life experiences, especially very early developmental experiences, affect brain development and psychological function in both a biochemical and psychosocial context. Changes in one's experiences and behaviors, whether detrimental or life enhancing, are concomitant with changes in mental function that are expressed physiologically.

The biopsychiatric epistemology of mental disorders has yielded evidence that is in conflict with a physical cause model. On the one hand, measurable differences in brain function or anatomy do not necessarily precede or even accompany symptomatology. On the other hand, damaging experiences affect psychophysiology, and effective psychotherapy affects both symptomatology and brain physiology without pharmacological intervention. The term "brain disease" is meant to discriminate between biologically caused and "life-circumstance" caused mental disorders (Faenza & Guida, 1996). Yet, empirical evidence indicates that this distinction is not valid because life circumstances are both biochemical and psychological experiences. Neither symptom idiopathy nor physiological correlates of mental disturbance are sufficient conditions to

establish a biological or endogenous cause of the disturbance. Genes, while playing an important influential role in physical and behavioral development, are activated by different environmental circumstances. The role they play in the formation of mental disorders is little understood, highly variable, and in some cases appears to be both preventable and reversible. The validity of the biopsychiatric ontology of mental disorders is disconfirmed by the data yielded by the biopsychiatric epistemology. There are important implications of this disconfirmation for the treatment of mental disorders.

Treating Mental Disorders with Drugs: Methodological Controversies and Pitfalls

Effectiveness of drugs versus psychotherapy.

A number of meta-analyses in the past 20 years have shown psychotherapy to be effective versus placebo treatments for depression, with dose-response curves showing greater effectiveness with a year of treatment (although most treatment protocols last fewer than 6 months), and few significant differences between therapeutic modalities and levels of training (Jacobson & Christensen, 1996). Studies comparing the effectiveness of psychotherapy and drugs often use treatments of short duration, and rely on brief manualized therapies such as cognitive-behavioral and interpersonal therapy (DiMascio et al., 1979; Elkin, Gibbons, Shea, & Shaw, 1996; Elkin et al., 1989). Some studies indicate that individual therapist characteristics and strength of therapeutic alliance (from the client's point of view) may be better predictors of response than specific therapies are for schizophrenia (Cullberg & Levander, 1991) and depression (Krupnick et al., 1996). In Krupnick et al.'s (1996) analysis of the NIMH Treatment of Depression Collaborative Research Program results, the authors found that therapeutic alliance had a significant

effect on outcome for all conditions, including two different psychotherapies, drug treatment with clinical management, and placebo treatment with clinical management. The authors suggested that alliance with a therapist might be a common factor of effective treatment, regardless of modality. Studies that do not measure or control for this factor may be committing a Type II error, and also may be over-estimating the specific pharmacological effect in drug-treatment groups.

Several studies have shown that the effectiveness of drug treatment for depression may be significantly overestimated or nonsignificant when adequate control procedures are used. For example, two methodological problems in placebo studies may exaggerate the differences between active drugs and placebo treatments. The two problems are the "placebo washout" methodology, and the use of placebos without side effect profiles. In the placebo washout technique, all potential subjects are given placebo treatments, usually for about one week. After this period, the placebo responders are dropped from the protocol. This technique accentuates and confounds the difference between the active drug and placebo groups by systematically reducing the placebo's effect on mood during the main trial (Breggin, 1994). Since placebo effects are sometimes found to be not significantly different from drug effects (Breggin, 1994; Greenberg, Bornstein, Greenberg, & Fisher, 1992; Simons, Murphy, Levine, & Wetzel, 1986), the systematic removal of placebo responders biases these studies toward demonstrating significant differences between placebo and drug.

The problem with using placebos without side effects is that blind conditions are not maintained and expectancy effects are not controlled. Side effects from active psychotropic medications are common, and these effects may act as expectancy cues that

are not present in sugar-pill placebo conditions. Some depression researchers have included enhanced or “active” placebos in their study designs that have mild sedative and anticholinergic effects, so as to provide a better simulation of active medication (Antonuccio, Danton, & DeNelsky, 1995; Simons et al., 1986). These active placebo protocols suggest that the differential effects of antidepressants from placebos disappear under such control conditions (Greenberg, Bornstein, Greenberg, & Fisher, 1992). Murphy, Simons, Wetzel, & Lustman (1984) found that in a cognitive therapy versus medication versus active placebo trial for moderately to severely depressed patients, the differences between drug and placebo were not significant, and that psychotherapy, antidepressants, and active placebos were equally effective after 12 weeks of treatment. Simons et al. (1986) found that at one-year follow-up, patients in the Murphy et al. (1984) study who had recovered at termination were less likely to relapse if they had received cognitive therapy, regardless of whether they had also received the drug treatment. Patients were more likely to relapse if they had received the drug treatment, regardless of whether they had also received therapy. The gradual tapering from the tricyclic antidepressants after termination may have contributed to a greater rate of relapse for those subjects, but this was not the case for the subjects who had terminated therapy.

While the NIMH Treatment of Depression Collaborative Research Program found a mildly superior effect for imipramine versus the therapy treatments for the severely depressed patients in the sample, the study lasted only 16 weeks, and follow-up data revealed that none of the treatments were particularly effective versus the inactive placebo (Elkin et al., 1989, 1996). There appear to be numerous unresolved debates about

research methodology in the study of drug versus therapy treatments for depression (Antonuccio, Danton, & DeNelsky, 1995; Elkin et al., 1996; Jacobson & Hollon, 1996a, 1996b; Klein, 1996; Medawar, 1997); and this debate has extended to panic disorder (Klerman et al., 1989; Marks et al., 1989; McNally, 1996), bipolar disorder (Suppes, Baldessarini, Faedda, Tondo, & Tohen, 1993) and schizophrenia (Karon & VandenBos, 1994; Meltzer, 1989; Olson, Bornstein, Schwartzkopf, & Nasrallah, 1992; Viguera, Baldessarini, Hegarty, van Kammen, & Tohen, 1997).

As evidence for greater effectiveness of psychotherapy than neuroleptics for schizophrenia, Karon & VandenBos (1994) cite the results of the Michigan State Psychotherapy project, conducted in the late 1960s with a group of severely and chronically schizophrenic patients. The study randomly divided patients into a psychotherapy-only group, psychotherapy with adjunctive medication group (50-200 mg. of chlorpromazine), and standard hospitalization with medication group (approximately 400 mg. of chlorpromazine). The two psychotherapy groups were further subdivided into experienced therapist and inexperienced trainee subgroups. Therapy recipients had an average 70 sessions over a 20-month period (an average of less than one session per week). Outcome measures were taken at 6, 12, and 20 months, and at 2-year follow-up. The researchers found that at 12 months, the pooled psychotherapy patients were hospitalized for a significantly shorter length of time, exhibited significantly less thought disorder on the Feldman-Drasgow Visual-Verbal Test (VVT), and performed significantly better in a blind diagnostic interview than the medication group. At 20 months,

> On five of the eight measures, psychoanalytic psychotherapy for schizophrenic patients made an appreciable difference as compared to medications alone. The

> psychotherapy patients spent less time in the hospital, showed better overall functioning, and less thought disorder than those patients receiving "routine" treatment. (Karon & VandenBos, 1994, p. 431)

When therapist experience was taken into account, therapy patients did significantly better than medication "controls" on all measures, but "on *no* criterion [did] the patients of inexperienced therapists do worse that those patients treated by medication alone" (p. 433, italics in original). Patients receiving therapy but no medication had lower thought disorder scores on the VVT than did patients receiving both therapy and medication (who, in turn, had lower scores than did patients receiving only medication).

At the 2-year follow-up, patients treated with medication alone spent an average of 99.8 days hospitalized between the study termination and follow-up assessment. Patients treated with a combination of therapy and medication spent an average of 78.5 days hospitalized. Patients treated with psychotherapy alone spent an average of 27.2 days hospitalized. Patients of experienced therapists continued to do better than patients of inexperienced therapists. While 67% of medication-only patients were not rehospitalized during the follow-up period, 57% of the patients of inexperienced therapists and 86% of the patients of experienced therapists stayed out of the hospital. In addition, therapy patients continued to exhibit significantly fewer thought disordered responses, measured by the VVT, than the medication-only group. Karon & VandenBos (1994) state that these findings echo those obtained by study projects in Massachussetts and Wisconsin, that found reduced rehospitalization rates for patients treated with psychotherapy only versus patients treated with more traditional regimes of hospitalization and medication. While the Michigan State project does not provide evidence that schizophrenic patients were "cured" by psychotherapeutic treatments, it

does indicate that chronic, severe schizophrenic symptoms can be treated effectively (as measured by several objective criteria) by well-trained psychotherapists, and without medication, in comparison with traditional pharmacological treatments or a combination of drugs and therapy. In addition, the decreased rate of hospitalization and rehospitalization for the therapy recipients in the Michigan, Massachusetts, and Wisconsin studies has consequences for cost-reduction efforts by insurance companies and private-pay individuals that might offset costs or produce savings from the use of psychotherapy rather than medication.

In order to obtain a more accurate representation of treatment effects, double-blind crossover studies should refrain from using the placebo washout design; and studies comparing drug treatments with psychotherapy and placebo treatments should use placebos that have side effects equivalent in degree to the active drugs. In addition, the effect of therapeutic alliance should be measured, and longer treatment trials that reflect the response curve of psychotherapy should be used. Melzer (1989) has argued that in the treatment of schizophrenia, a delayed response to clozapine is common, sometimes requiring 3 to 12 months to show an effect. He suggests that “a trial of clozapine should last 9 months or longer if one wishes to identify the majority of possible responders” (p. 672). Possibly, both psychotherapy and drug treatment protocols suffer from being too brief (Consumers Union, 1995). Longer treatment trials especially require adequate placebos to control for spontaneous remission or transient improvement. In addition to longer treatment trials, drug and therapy treatment groups should be tapered in parallel, and adequate follow-up protocols of at least one year should be used, to indicate comparative relapse and recurrence rates. These methodological changes should improve

our understanding of what factors lead to lasting clinical improvement for individuals. Currently, drug-versus-therapy treatment studies indicate that biologically based treatments might not be superior whether used alone or in addition to psychologically based treatments. Improving research methodology should clarify this question. Nevertheless, the notion that severe mental disorders are biochemically based, thus best treated biochemically (or in combination with psychotherapy) remains questionable on both counts.

Relapse as an iatrogenic effect of drug therapies.

Several studies have found that withdrawal or relatively fast tapering from psychotropic drugs leads to rebound, relapse, and other withdrawal effects. This has been reported for benzodiazepines (Medewar, 1997; Pecknold, Swinson, Kuch, & Lewis, 1988), lithium (Suppes et al., 1993), neuroleptics (Suppes et al., 1993; Viguera et al., 1997), and antidepressants (Breggin, 1994; Marks, 1986; Medewar, 1997). In addition, abrupt withdrawal from cognitive behavioral therapy also has been associated with high relapse rates compared to more gradual tapering (Thase, Bowler, & Harden, 1991). The contemporary view that medications be used for maintenance treatment may partly derive from past findings that stopping medications leads to a return of symptoms. However, recent studies that substantially lengthen the tapering period have demonstrated that drug-free patients have a reduced risk of relapse or recurrence, and that abrupt discontinuation leads to a greater risk of symptoms than no treatment at all (Suppes et al., 1993; Viguera et al., 1997). For example, Viguera et al. (1997) conducted a meta-analysis of neuroleptic treatment studies and found that the probability of relapsing within six months was 32.5%

for gradually withdrawn subjects versus 64.9% for abruptly withdrawn patients. No comparison data for subjects who continued neuroleptic treatment were reported. A study by Green et al. (cited in Suppes et al., 1997) found that after six months, the recurrence rate for rapidly withdrawn neuroleptics was 50%, but only 7.7% of the schizophrenic patients had a recurrence within six months if they were gradually withdrawn. Patients who continued neuroleptic treatment, on the other hand, had a recurrence rate of 11%.

Suppes et al. (1993) reviewed lithium treatment studies and found that at an average follow-up interval of 16.8 months, the recurrence risk was 79.5% for placebo groups and 31.6% for lithium groups. However, when rate of discontinuation was studied, 68% of abruptly withdrawn lithium patients had a recurrence within 12 months, but only 20% of gradually withdrawn patients had a recurrence. The rate of recurrence for bipolar patients who were lithium-free for 12 months compares favorably to rate of recurrence for the group that continued lithium treatment at a mean of 16.8 months (20% and 31.6%, respectively).

The Cross-National Collaborative Panic Study was a multinational, multicenter study of alprazolam (Xanax™) treatment of panic disorder and agoraphobia. The researchers found that although there was some differential effect for alprazolam at four weeks (and a large initial dropout rate in the placebo group), the placebo group's response was strong, and at 8 weeks not significantly different from alprazolam on many of the measures (Marks et al., 1989). In addition, the alprazolam group had a complete relapse after discontinuation at eight weeks, with 27% of patients having a rebound of panic attack frequency that was at least double their baseline levels, and 30% having a withdrawal syndrome lasting at least two weeks. Four alprazolam-treated patients could

not be tapered off the medication because of “the severity of the discontinuation symptoms” (Pecknold et al., 1988, p. 431). The researchers recommended a prolonged tapering period to combat this problem (tapering lasted four weeks in the study), although they did not report any evidence to support the effectiveness of this technique (Pecknold et al., 1988).

Both tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) have been found to produce severe withdrawal responses upon abrupt discontinuation that, as with other drugs, sometimes leads to reinstatement of the drug (Medawar, 1997). For example, in a survey of 192 doctors in Britain, the Committee on Safety of Medicines, Medicines Control Agency, found that the severity of withdrawal reactions from paroxetine (Paxil→, an SSRI) was “moderately severe” to “severe” in 79% of cases (Medawar, 1997). Patients who cease taking psychotropic medications clearly should be withdrawn very gradually from these drugs. In addition, the inference that relapse is an indication that the patient should remain on the drug is not borne out by several studies comparing gradual withdrawal versus continuation on medications. These studies indicate that the withdrawal and relapse phenomena upon abrupt discontinuation of medications might be an iatrogenic effect rather than a sign that the patient continues to have “underlying” symptoms.

Conclusion

Empirical evidence indicates that the choice of using drugs for the treatment of psychological problems should not be based on an assumption that the essential problem is a biochemical imbalance or a brain disease that, as such, is best treated chemically.

While drugs either alone or in combination with psychotherapy may produce substantially positive effects for certain individuals, placebos and therapy alone are often found to be just as effective. When either drugs or therapy work for an individual, there may be some measurable shift in brain physiology that accompanies the changes in affect, cognition, and behavior. On the other hand, there may not be such a physiological shift. For example, the use of medications may affect release of neurotransmitters without any clinical change, or clinical response may take a number of weeks or months to occur (Medawar, 1997; Meltzer, 1989). The ultimate measure of treatment efficacy for mental disorders is not a biological change, but a psychological change. Rather than describing mental disorders as biochemical imbalances caused by genetic diseases, it may be more empirically and ethically sound to conceptualize mental disorders as experiences that result from a combination of genetic, developmental, and experiential factors that may be examined and treated from a number of different perspectives. People who seek help for these problems should be educated about the variety of alternative treatments, all of which are effective for some people (including placebo and no treatment), and they should be given the choice of treatment that fits best for them.

A recent study of prescribing trends among psychiatrists and other physicians estimated that between 1985 and 1994, the number of psychotropic medication visits to psychiatrists almost doubled, increasing from 7.77 million to 15.09 million (Pincus et al., 1998). The number of visits to psychiatrists in which antidepressant drugs were prescribed increased from an average of 4.09 visits per week to 11.04 visits per week. The number of psychotropic medication visits by children to physicians more than tripled, and as a proportion of all medical visits, they more than doubled. These recent

trends in the biopsychiatric treatment of mental disorders reflect a growing social attitude that mental disorders should be treated pharmacologically. It is unclear to what extent this view is reinforced by the marketing of new drugs, and reports about the biological basis of mental disorders in the mass media. Nevertheless, the study authors point out that the increase in prescription of psychotropic medications may be due to the effects of such publicity both on patients seeking help, and on physicians who may alter their diagnoses in line with the availability of new drugs. The proportion of visits to psychiatrists that resulted in a diagnosis of depression rose from 35.8% in 1985, to 52.6% in 1994. The authors suggest that "Effective, well-tolerated medications might encourage psychiatrists to evaluate patients more carefully for depressive symptoms and recharacterize their condition" (Pincus et al., 1998, p. 530). Yet there is evidence that such drugs as fluoxetine and alprazolam, commonly regarded as both effective and well-tolerated, are not as comparatively effective or well-tolerated as they are reported to be (Breggin & Breggin, 1994; Marks et al., 1989; Medawar, 1997). By informing people that depression, schizophrenia, and other disorders are medical diseases, clinicians and researchers do not give adequate informed consent, and they influence their patients' attitudes and choices toward biochemically oriented treatments. Such limited information is based on an ontology of mental disorder that distorts the empirical evidence in the direction of a biopsychiatric *a priori*.

In the introduction to Foucault's *Mental Illness and Psychology*, Dreyfus states "Thus the therapeutic strategy for turning the ontological back into the epistemological ultimately must undermine the patient's sense of reality" (Foucault, 1987, p. xxi). Ontological assumptions about the nature of things provide a sense of security, but

prevent paradigmatic growth and change because these assumptions stand above the fray of scientific questioning. By transforming the biopsychiatric ontology back into an epistemology, questions may be asked and assumptions may be tested. Indeed, bringing the biopsychiatric ontology back in line with scientific evidence entails undermining the sense of reality that has been established in the Decade of the Brain—that mental illness is the result of a brain disease—and requires a new, more empirically grounded appraisal of the nature of mental illness. A paradigm shift for researchers and clinicians, like that for an individual, can not come without a sense of loss and resistance to an upheaval in one's understanding of the world. Yet, without a clarification between epistemology and ontology, biopsychiatric researchers will have to admit that like Melville's Captain Ahab, all their means are sane; their motives and objects mad (Scheff, 1975).

The search for biochemical processes coincident with mental disorders has taught us much about how the brain works. Now, it is important to include in our awareness that psychological experiences affect brain function as well. Biochemistry has become our modern *deus ex machina*, a construct devised to tie up the loose ends of the mind-brain split, and to neatly explain the cause of emotional and behavioral problems. We may find that our understanding of such problems would be improved by the consideration of a *deus in machina*, a conceptualization in which psychological experience and physiological process are echoes of the same unitary phenomenon still yet to be explained. We may need to broaden our search for and our inferences about causes of such phenomena, and this may also require an incorporation of factors such as culture, gender, race, economics, and politics. An openness to diverse epistemologies, and the

abandonment of a singular ontology of serious mental disorders is bound to lead to healthier, more complete, and more rigorous research models and treatments.

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