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LEAD ARTICLE

BIOLOGICAL PSYCHIATRY: A PRACTICE IN SEARCH OF A SCIENCE

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ABSTRACT: The rise of the biological causation model in the past thirty years is traced to psychiatry's efforts to regain lost status and to protect itself from intrusions by non-medical practitioners, as well as to the pharmaceutical industry's drive for profits. Evidence in support of the model, including studies of identical twins and of brain structure and function, are less revealing than was earlier thought, due to problems in methodology and interpretation. Organized psychiatry, when challenged in 2003, was unable to provide compelling evidence for biological causation of most mental and behavioral disorders. A paradigm shift away from biological causation and toward environmental causation is called for.

KEYWORDS: biological causation; pharmaceutical industry; organized psychiatry; efficacy of psychotropic medications; identical twins; brain imaging; paradigm

The term "biological psychiatry" describes a phenomenon of increasing visibility in both the professional and popular cultures in the past thirty years. It reflects growing acceptance of the notion that chemical imbalances, genetic defects and related biological phenomena cause disorders such as schizophrenia, depression, anxiety, substance abuse, and attention deficit hyperactivity disorder (ADHD). As biological causation has gained attention, acceptance of environmental causation has necessarily declined, and psychotropic medications have become the treatment of choice for mental and behavioral disorders (Antonuccio, Danton & DeNelsky, 1995).

However, an examination of the contributing variables, not all of which are empirical, suggests that the research in support of biological causation is weaker than one would expect, given its increased acceptance over the past three decades. Similarly, there are reasons to think that the claims of drug effectiveness are at times overstated (Glenmullen, 2002; Hubbard & Wald, 1997; Valenstein, 1998).

PSYCHIATRY'S ANXIOUS YEARS

To understand the rise of biological psychiatry's influence, it is necessary to examine the changing public face of psychiatry over the past few decades. "Psychiatry's

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Anxious Years” was the title of an early 1980s *New York Times* article (Nelson, 1982) that described an evident crisis in psychiatry, and psychiatry’s reaction to that crisis. The percentage of medical school graduates opting for careers in psychiatry had dropped by more than half from 1970 to 1980, from 11% to 5%. The *Times* article listed several reasons why decreasing numbers of young physicians had opted for careers in psychiatry. The reasons included the relatively low pay of psychiatrists and increasing interest in family practice. There were additional reasons that foreshadowed a return to an increased emphasis upon the connection between biology and behavior. First, many medical school graduates had developed the perception that psychiatrists had become “dinosaurs,” mired in pits of psychoanalytic confusion. Also, young physicians were not buying into fringe treatments such as primal scream therapy and nude encounter groups that had arisen within the mental health arena during the 1960s. The *Times* article described the efforts of organized psychiatry to reverse the trend by doing two things. It held recruitment strategy conferences such as one in San Antonio in the late 1970s, and it began to emphasize science, or what passed for science—to advocate a return to biological explanations of mental illness (Nelson, 1982).

As psychiatry was returning to biological causation, another concern emerged. Movement into the treatment field by non-physicians such as clinical psychologists, clinical social workers, psychiatric nurses, counselors and others was escalating. As the 1980s, 1990s and early years of the new century played out, the battles over Medicare reimbursement, hospital privileges and prescription privileges were joined. Those disputes continue today (APA Deplores, 2004). The related professions have gradually gained ground. By the early 1990s psychologists had won the right to treat Medicare patients without physician supervision (Buie, 1990). The military’s successful effort to train psychologists to safely prescribe psychotropic medications has boosted state legislation of the same kind. In response to one such effort, a news release from the American Psychiatric Association was headlined “APA deplors Louisiana Governor’s decision to sign psychologist’s prescribing bill” (APA Deplores, 2004). On November 5, 2004, the American Psychiatric Association’s Board of Trustees announced creation of a task force to review the psychology prescription issue and to put “an end to psychologists’ bid to win prescription privileges throughout the United States” (Psychiatry names, 2004). Despite the efforts of organized psychiatry, psychology and related disciplines continue to gain ground in the prescription privileges debate (Bradshaw, 2004).

Attacks upon related professions by organized psychiatry are not new. Such criticisms frequently have appeared in highly visible sources, and have tended to advise psychiatrists to turn to biological causation theory. Seldom mentioned is the fact that there exists minimal research evidence to demonstrate that, for example, most cases of depression are caused by a chemical imbalance. More than two decades ago an article in *Hospital and Community Psychiatry* (Bursten, 1981) stated, in part, that “medicalization” of disorders is useful “to rally the troops...to thwart the attackers...Economics demands that we be medical...we use the term to rout the enemy within.” The same year, readers of the *American Journal of Psychiatry* were urged to “...speak with a united voice not

only to secure support but to buttress (psychiatry's) position against the numerous other mental health professionals seeking patients and prestige" (Havens, 1981). The call for defense of psychiatry's turf was clear, and the rhetoric continued through the 1980s.

In 1988 Paul Fink, then President-elect of the American Psychiatric Association, stated that psychologists and other non-psychiatrists, "...don't have the training to make the initial evaluation and diagnosis...(and) are not trained to understand the nuances of the mind..." (Wyatt, 2003). Elsewhere that year Melvin Sabshin, then Medical Director of the American Psychiatric Association, in testimony before the New York State Legislature, warned legislators of "The grave risks to health care...of psychologists' self-serving claimed advantages for their clients..." Sabshin asked, "Do the substantial and inevitable risks to the quality of patient and medical care in hospitals outweigh the dubious, purported benefits associated with hospital privileges for these non-physician practitioners?" (Wyatt, 2003).

Psychiatry's efforts to stem the twin tides of reduced interest among medical school graduates and intrusion by non-physicians paralleled the rise of biochemical and genetic explanations of abnormal behavior. Though often only weakly supported by research evidence, medicalization of depression, anxiety and other disorders rapidly advanced in the professional and popular cultures. By the late 1990s and early years of the new century, biological causation had gained a great deal of ground with professionals, and with the public.

Claims that are published in respected sources and are then consumed by the professional community may find their way to the popular media where they influence public perceptions. For example, a 2002 article in *People* magazine described the extreme discomfort around others that has plagued Miami Dolphins' star running back Ricky Williams. The article characterized Williams' social anxiety disorder as a "...depression-like chemical imbalance that affects roughly three million Americans..." (Tresnioweski, Rozsa & Brass, 2002). However, to date there is no credible research to prove that social anxiety disorder is caused by a chemical imbalance. The *People* article typifies the present strength of the biological causation model in the popular culture. It is unfortunate that misinformation is routinely purveyed to the public. Equally unfortunate is that such statements are typically put forth as absolute fact, minus significant critical analysis. However, recently several scholars have begun to question the trend toward medicalization of disorders (Midkiff & Wyatt, 2005; Wong, 2005).

PHARMACEUTICAL COMPANY FINANCIAL INTERESTS

The suggestion that our biology is the source of disorders such as schizophrenia, depression, anxiety, addiction, and numerous childhood disorders is heavily promoted by the pharmaceutical industry. Biological causation suggests biological treatment, rather than behavioral intervention. Study after study shows that in the past thirty years the sales of psychotropic drugs have increased dramatically. Between 1985-1994 doctor visits at which psychotropic drugs were prescribed increased 20%. The prescription of stimulants tripled, and prescription of mood elevators doubled, to more than 20 million, during

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roughly the same time frame (Pincus, Tanielian, Marcus, Olfson, Zarin, & Thompson, 1998).

To achieve increased sales, the marketing practices of the pharmaceutical industry, including the marketing of psychotropic drugs, have mushroomed. The industry spent \$19 billion on advertising in the United States alone in 2001. It has more lobbyists than members of Congress, and it spent over \$200 million on lobbying and campaign contributions in 1999-2000, the largest amount of any industry (Antonuccio, Danton & McClanahan, 2003).

The Center for Public Integrity reported that since 1998 the drug industry has lobbied congress on more than 1,400 bills and spent \$759 million on lobbying, while employing 805 former federal officials as lobbyists. Within that group of lobbyists, more than fifty were former members of the U.S. House of Representatives, and a dozen were former senators (Ismail, 2005). Drug manufacturers flood physicians with free samples, free books, free videos, free continuing education programs (typically touting the company's drugs), and more. For example, at the 2003 meeting of the American Psychiatric Association in San Francisco, Pfizer (maker of anti-depressants Zoloft and Sinequan) supported four continuing education symposia involving twenty presenters. Each symposium included dinner for those in the audience. At the Pfizer display booth copies of widely sold books *The Memory Bible* (Small, 2003) and *The Quiet Room* (Schiller & Bennett, 1996) were distributed—with the books' authors present to provide autographs.

Since 1995 the drug industry has engaged in aggressive television, newspaper and other direct-to-consumer advertising (Antonuccio, Danton & McClanahan, 2003). Advertisements often tout biological causation, and frequently do so in absolute terms. For example, a 1996 newspaper advertisement for the Wyeth company's anti-depressant Effexor stated, "Depression is a medical condition with proven treatment alternatives available." Contrary to the advertisement's claim, there is minimal empirical evidence to establish that more than a small minority of cases of unipolar depression (by far the most frequently diagnosed type) may be attributable to biological causes (Antonuccio, Danton & DeNelsky, 1995). Rather, it is likely that most such cases are due to factors such as inadequately learned coping skills or, for those with good coping skills, overwhelming stress.

Drug company advertising of mood and nerve medicines to physicians, including family doctors, pediatricians and others not trained to practice psychiatry, has increased as well. In 1990 the journal *Pediatrics* (Lucey, 2003) contained seven full-page advertisements for stimulant medications used to treat ADHD. By 1995 that number had risen to twelve, and by 2000 to fifteen (Wyatt, 2003). Medco Health Solutions Inc., the nation's largest prescription benefit manager, reported a 49% rise in the use of ADHD drugs by children under five between 2001-2004, and a 23% increase in overall usage by children. The nearly 50% increase with children under five translated to a 369% increase in spending, in part because of the popularity of longer-acting versions of the medicines (Johnson, 2004).

The impact of direct-to-consumer advertising was demonstrated in a study published in the *Journal of the American Medical Association* (Kravitz, Epstein, Feldman, Franz, Azari, Wilkes, Hinton & Franks, 2005). In the study, 152 family doctors and internists were visited unannounced 298 times by “patients”—actors trained to present with symptoms of either major depressive disorder or adjustment disorder with depressed mood. At some visits the patients mentioned the anti-depressant Paxil, adding that they had seen an advertisement for the drug on television, and they asked the doctor whether it might be of help. At other visits the patients told the doctors they had seen an ad for anti-depressant medication, but they mentioned no specific drug. At still other visits the patients made no reference to medication. Of the 51 visits in which Paxil was mentioned by those with major depressive symptoms, 14 visits (27.4%) resulted in prescription of that drug. By contrast, of the 50 visits in which there was general reference to “medication,” only once (2.0%) was Paxil prescribed. When patients made no mention of medication, Paxil was prescribed twice (4.2%). Findings were similar when patients presented with symptoms of adjustment disorder.

The financial interests of the pharmaceutical industry have dovetailed with the guild interests of organized psychiatry. Both have much to gain by promoting the biological causation model of mental and behavioral disorders. By 2003 the drug industry was underwriting 70% of all clinical drug trials in the United States and there were accusations that negative studies were being terminated prior to publication (Antonuccio, Danton & McClanahan, 2003). All of this was paying off for the pharmaceutical industry. By 2001-2002 three psychotropic medications (Zyprexa, Zoloft and Paxil) were among the top ten revenue producing prescription drugs in the United States. They accounted for over \$7.5 billion in sales. Each showed greater than 10% sales growth from 2001-2002. (Vaczek, 2003).

In 2003, reporters for the Knight-Ridder News Service launched an investigation of a practice known as off-label prescribing (Young & Adams, 2003). Off-label is a term used when a doctor prescribes medication for a specific disorder or disease for which that drug has not been FDA approved. Although doctors may legally prescribe off-label, it is *illegal* for drug companies to promote the practice. Frequently they do so anyway. “By offering specialty drugs to non-specialists, sending salesmen to doctors’ offices and medical conventions, and touting their drugs’ benefits on the slimmest of evidence, pharmaceutical companies have sent off-label retail sales soaring” (Young & Adams, 2003). The investigation found that about 60% of anti-psychotic medication prescriptions were off-label, prescribed for disorders such as Alzheimer’s, ADHD, insomnia and autism. For antidepressants, not including the SSRI’s (selective serotonin re-uptake inhibitors), about 40% of prescriptions were off-label.

The Knight-Ridder investigation disclosed that between 1994-2003 the number of pharmaceutical sales representatives more than doubled to 94,000 (it has since topped 100,000), about one salesperson for every seven practicing physicians in the United States. From 1996-2002 the value of free drug samples given to physicians increased more than 140%, to \$11.9 billion. The investigative reporters concluded in part, “Promoting the growth (in off-label prescribing) is a symbiotic relationship between

physicians and drug makers in which sales representatives routinely target doctors untrained in the basics of drug therapy....”

Shifting trends in pharmaceutical industry jobs reflect the findings of the Knight-Ridder investigation. According to Boston University’s Health Reform Program, which obtained its data from the website of the drug manufacturer’s lobby group Pharmaceutical Research and Manufacturers of America (PhRMA), from 1995-2000 the number of drug industry jobs in research and development fell 2%, while the number of jobs in marketing those drugs rose 59%, to nearly double those in R & D (Sagar & Socolar, 2001).

While the drug industry has aggressively engaged both physicians and the public in order to maximize sales, safety of medications of all kinds is an ongoing concern. There are suggestions that the pharmaceutical industry exerts undue influence over the Food and Drug Administration, and that the agency is weak in carrying out one of its major functions—protecting the public from harmful drug side-effects. Merck pulled its arthritis pain-killer Vioxx from the market on September 30, 2004. FDA researcher David Graham testified to congress that his superiors at the FDA had tried to block publication of his research on the drug. Graham had discovered that Vioxx is associated with increased risk of strokes and heart attacks. Graham said he was subjected to an environment where he was “ostracized” and “subjected to veiled threats” and “intimidation” by superiors who suggested that he water down his findings (Rubin, 2004). Later the FDA’s advisory committee voted 17-15 that, for some patients, Vioxx’s benefits outweighed its risks. It was then disclosed that the majority of panel members voting *for* Vioxx had received speaker’s honoraria, consulting fees or research money from Merck, the company which manufactures the drug. Similar disclosures were brought to light regarding painkillers Bextra and Celebrex, and their maker Pfizer (Rubin, 2005).

In November, 2004, Bristol-Myers Squibb agreed to pay \$70 million to settle a class-action lawsuit with over two thousand users of its anti-depressant Serzone. While the company continues to assert that the drug is safe, the lawsuit claimed that the drug increases the likelihood of liver failure. Although the FDA had earlier required the company to put a “black-box warning” on the drug’s packaging, that warning came about only after more than a hundred of the drug’s users had reportedly developed serious liver disorders. The company stopped selling Serzone prior to settlement of the lawsuit (Coleman, 2004). Thus, with drug industry practices coming under increasing scrutiny, it is not surprising that the industry’s impact upon the mental health field has garnered attention as well.

Biological causation is the theoretical mortar that has cemented the marriage between psychiatry and the pharmaceutical industry. However, research in support of biological causation of mental disorders, and its counterpart, biological treatment, appears to be less compelling than we are often led to believe. The two primary lines of this research are family studies, especially studies of identical twins, and research into the brain’s chemistry and functioning.

IDENTICAL TWIN STUDIES

For many years the biological causation model has been bolstered by results of studies of families, especially by similarities in identical twins. Identical (one-egg) twins have identical genetic structure. When identical twins were studied and found concordant for (when both developed) schizophrenia, anxiety disorders, substance abuse, chronic depression or other disorders at rates above that of the general population, it was thought that we had uncovered powerful evidence that genetic factors are causal. Other researchers, thinking more critically, correctly surmised that such a conclusion was unwarranted. That was because environmental factors (growing up in the same dysfunctional home, for example) could not be ruled out as having caused the disorder. For example, if one or both parents had been abusive or had been maladjusted in any significant way, the home environment, rather than genes, might have been to blame. There was no way to separate environmental variables from genetic variables. Thus, researchers began to search for pairs of identical twins who had been separated soon after their births and reared in different environments. Then any concordance for a mental disorder could be attributed to genes. At least that was what behavioral scientists believed.

Researchers found that identical twins' concordance for various disorders was indeed greater than population base rates, even if reared apart. For example, although the population base rate for schizophrenia is generally said to be about 1%, the concordance rates for schizophrenia in identical twins who have been separated soon after birth and reared apart are typically presented, by authors of widely adopted textbooks, to be anywhere from 15% to about 40%, depending upon the study (e.g., Comer, 2005; Sarason & Sarason, 2002). Similar results are reported for other disorders. Such studies have long been cited as providing powerful proof of genetic contributions to schizophrenia and other mental disorders (Owen & O'Donovan, 2002).

Along the way, at least a few researchers had suspected that there were methodological difficulties with the identical twin research (Farber, 1981; Watson, 1981; Wyatt, 1993). The integrity of the studies rested upon an important assumption--that when identical twins were reared apart, they necessarily had been reared in differing environments. We now know the assumption was wrong.

Identical twins, even if reared apart, are alike in both physical appearance and rate of maturation, factors that exert powerful influence upon one's adjustment.

Given adequate nutrition, identical twins will both be handsome, homely or average looking. Their worlds, even when far apart geographically, will tend to treat them similarly based on their looks, and in ways that are known to contribute to mood and overall adjustment. For example, a substantial body of research has documented that attractive people tend to be treated better than unattractive people. Attractive people receive more liking and desire for contact by others than do unattractive individuals (Walster, Aronson, Abrahams, & Rottman, 1966). Others express a greater desire to date them, and others evaluate attractive people more positively as prospective spouses (Bynne, Ervin & Lamberth, 1970). Compared to unattractive people, good-looking

individuals even get better grades on essays when the same essay is graded by two professors who have been shown photos of attractive and unattractive “authors” (Landy & Sigall, 1974). Researchers who have hitched their conceptual wagons to the twin study star have seldom considered that unattractive twins likely are at increased risk for depression, and perhaps other disorders, based on the ways that their environments treat them, rather than on their genes.

Physical attractiveness is not the only source of environmental influence at work in shaping the adjustment of children, including that of identical twins. Rate of maturation also undercuts the assumption that identical twins, even those who were separated soon after birth, necessarily have been raised in quite different environments. Identical twins are likely to reach puberty at the same rate. Whether that development is early, at the average age, or late has much to do with how young people feel about themselves and how others respond to them. For example, early maturing girls tend to be below average in popularity, withdrawn, lacking in self-confidence, psychologically more stressed and they generally hold fewer leadership positions than their later-maturing peers (Ge, Conger & Elder, 1996; Graber, Lewinson, Seeley & Brooks-Gunn, 1997; Jones & Mussen, 1958). Also, they are more involved in behaviors such as getting drunk and participating in early sexual activity and, on average, they achieve less well in school (Caspi, Lynam, Moffitt & Silva, 1993; Dick, Rose, Viken & Kaprio, 2000). It would be disingenuous to assert that the day-to-day feedback that adolescent girls receive regarding their attractiveness and maturation is unrelated to contemporary or later problems in adjustment, such as depression.

For boys the maturation trends are globally similar, though different in specifics. With boys, early maturation is better than late maturation, at least superficially. Early maturing boys are seen as relaxed and independent, and get more leadership positions in school. Late maturing boys are viewed by others as anxious, too talkative and are seen as seeking too much attention (Brooks-Gunn, 1988; Clausen, 1975; Jones, 1965; Mussen & Jones, 1957). Interestingly, early maturing boys report greater psychological stress than do their later maturing peers (Ge, Conger & Elder, 2001), contrary to how they are seen by others. Identical twins mature at the same rate, even if reared apart, and as a result live in worlds that treat them similarly in ways that have implications for adjustment, including the development of mental and behavioral disorders.

Thus, environments bombard children with identifiable and differential classes of feedback based upon the youngsters’ levels of physical attractiveness and rates of maturation. Twin researchers have generally failed to account for this body of developmental psychology research.

There are other reasons to doubt researchers’ long-held assumption that identical twins who were separated soon after birth were necessarily reared in substantially different environments. One issue is the reported ages at which the twins in the studies were separated. One of the leading researchers in twin similarities reported that he had studied 315 pairs of identical twins who had been reared apart “since age ten” (Lykken, McGue, Tellegen & Bouchard, 1992). Unaccounted for is a flood of environmental water that has gone over the life experience dam, prior to age ten.

Additionally, family adoption practices and adoption agency practices further muddy the genetic/environmental causation waters, when twin studies are looked at closely. Reviews of a number of studies (Farber, 1991; Wyatt, 1993) revealed that frequently the “separated” twins had been reared in the same extended family. Similarly, when adoption is handled by an adoption agency, a biological parent often insists that the infant be placed in a home similar to that of the biological parents with regard to religion, ethnicity, socioeconomic status and population density (urban/rural setting). All are variables that are known to correlate with various mental and behavioral disorders. When separation of twins is not done soon after birth, and when adoption involves intentional placement of the twins into similar environments, it becomes difficult or impossible to separate genetic contributions from environmental contributions, when one attempts to tease out the causes of later mental or behavioral disorders.

Physical attractiveness, rate of maturation, age of separation, and family and agency adoption practices have typically been unaccounted for by researchers whose studies show up to 40% concordance for mental disorders in identical twins who were reared apart. Yet, cultural factors are powerful and often unyielding. Identical twins reared “apart” are actually exposed to daily streams of similar environmental pressures—influences that may well account for the reported levels of concordance for emotional and behavioral disorders. Given all of this, it is reasonable to conclude that genetic and environmental influences have been hopelessly confounded in the identical twins studies.

It is likely that identical twin studies have done little more than confuse our understanding of mental and behavioral disorders. In that respect there are similarities to other misuses of genetic studies. At times other genetic studies have played unwarranted roles in a number of social and political struggles. For example, alleged biologically based IQ differences between races have been used to deny economic justice to African Americans. Male domination over women has been justified on the basis of flawed genetic studies as well. These issues will not be explored here. Extensive reviews are available elsewhere (Lewontin, 1992; Lewinton, Rose & Kamin, 1984).

STUDIES OF BRAIN STRUCTURE AND FUNCTION

Apart from the identical twin studies, another line of research has at times been touted as yielding convincing evidence of biological causation of behavioral disorders. There are two primary threads to this line of research. The first is done on autopsy and involves microscopic analyses of the cellular structure of the brain tissue of individuals who had suffered mental disorders while living. These studies tend to consistently show differential cell structure for those who were schizophrenic, depressed, etc., vis-à-vis those who had suffered no disorder. Hypothetically, a typical study might show that 60% of schizophrenics’ brains had contained excess amounts of the neurotransmitter dopamine-4, while only 10% of the brains of normals had contained excess amounts of the chemical. At first blush this would seem to provide compelling evidence that, for many schizophrenics, excess dopamine-4 had played a major causal role in their disorder.

However, there is another interpretation of those data, one that weakens any inferred causal connection between the neurotransmitter and schizophrenia. Examination of the absolute numbers reflected by the above percentages, 60% and 10%, provides a less compelling picture. If one considers the adult (because schizophrenia is seldom diagnosed in children) population of the United States to be roughly 200 million, then there are about 2 million schizophrenics in the country (based on the commonly accepted notion that about 1% of the population is schizophrenic). If 60% of them have excess levels of dopamine-4, then it follows that about 1.2 million American schizophrenics have excess amounts of the chemical in their brains. Then, not counting the 2 million who are schizophrenic, there remain roughly 198 million American adults who are not schizophrenic, 19.8 million (10%) of whom have excess dopamine-4. In this scenario the non-schizophrenics outnumber the schizophrenics more than sixteen to one. It is difficult to argue that an elevated neurotransmitter level is causal for a specific disorder when that elevation is much more frequently found in individuals who *never* suffered from the disorder. However, researchers tend to report percentages, minus extrapolated references to the population numbers that follow logically from those percentages.

Apart from the autopsy studies, brain-imaging research has focused on the living. Those studies employ technologies such as PET scans and fMRI. Frequently they reveal interesting differences between the brains of the disordered and the brains of those with no mental or behavioral disorder. Even so, it is not possible to infer either environmental or biological causation from such studies. In part, that is because the direction of the causality remains unknown.

Although it is tempting to conclude that a given mental disorder resulted from an identified abnormality in brain structure or function, evidence from studies of both sub-humans and humans makes clear that the disorder may have come before the brain abnormality. Valenstein (1998) reviewed a number of studies in which the brains of lower species were subjected to various stressors. He concluded, "The now overwhelming evidence that experience can alter neuronal structure and function should make it clear that it is dangerous to assume that any anatomical or physiological characteristic found in brains of people with mental disorders was the cause of that disorder" (p. 128). A study at UCLA focused upon brain functioning with obsessive-compulsive disorder (OCD). Continuous monitoring of brain activity in the patients as they received either medication or behavioral therapy showed that both treatments modified brain activity (and overt functioning) equally well (Friedman, 2002).

PET scan and fMRI studies frequently show that chronically mentally disordered individuals have enlarged ventricles or unusual protein levels in the brain, or differential brain metabolism compared to the brains of those who suffer no mental disorder (Wyatt, 2003). But causality cannot be determined based upon such brain differences. Did these brain abnormalities cause the individuals' mental disorders? Or did years of suffering from a disorder cause changes in their brains? The latter question is not as quirky as it may seem. Valenstein (1998) presented the case of the Dexamethasone Suppression Test (DST) as an example that had misled the clinical and scientific communities. Dexamethasone is a synthetic hormone that functions somewhat like the hormone

cortisol, a hormone that has been shown to be elevated in depressed individuals. It was found that upon receiving an injection of DST, the cortisol levels of depressed individuals were suppressed for a significantly shorter period than were the cortisol levels in individuals who were not depressed. As a result, by the 1980s the DST was thought to have detected a biological marker for depression. However, subsequent research showed that the DST had not revealed a brain abnormality that caused depression. Rather, the test reflected the loss of appetite and lowered food intake of most depressed individuals (Mullen, Linsell & Parker, 1986).

We know that depressed individuals tend to sleep and eat poorly, and they often get less physical and mental exercise than do non-depressed individuals. Years of living a depressed lifestyle may change one's physiology. The depressed person's health may change in overt ways as he becomes lethargic and loses muscle tone. There also may be unobserved changes in brain physiology and chemistry that result from failure to maintain a stimulating routine of enjoyable, productive activity. In fact, it would be quite surprising if there were not at least some identifiable internal changes, including changes in the brain, that occur in individuals who live specific lifestyles. The chronically anxious person may ultimately undergo changes in his gastrointestinal tract, as excess stomach acid causes an ulcer. Brain changes likely take place at the same time. Both the G-I tract changes and the brain changes may be the results of stress, rather than causes of stress-related mental disorders.

When one looks beyond difficulties in determining the direction of causality, one finds philosophical and methodological problems in brain imaging studies. Chief among them is the difficulty in defining hypothetical underlying mental processes. Added to the disagreement as to what constitutes the components of human thought is the questionable assumption of localization of mental processes. The brain is highly complex, its regions are interconnected at microscopic levels. The fundamental idea that brain imaging techniques can localize any cognitive or emotional process to a single area of the brain is questionable (Faux, 2002; Uttal, 2004; Uttal, 2001).

Among the methodological and interpretative problems in PET and fMRI studies is the subtraction method of data collection. The method involves the collection of baseline brain images as a subject completes a task not involving a specific cognitive process. Then that cognitive process is added to the task. Differences in the sets of images are observed across many subjects. The averages of these differences are said to localize the regions that account for the cognitive process under study. However, the subtraction method rests on several questionable assumptions including that a single brain operation is at work for a given mental process, and that neurological importance applies only to the rather large brain areas that have been "localized" (Faux, 2002). One may question, as well, the practical usefulness of average differences in brain functioning.

Moreover, there have been highly inconsistent findings across studies of brain imaging. For example, a review (Cabeza & Nyberg, 1997) of 73 PET studies showed that across only five studies that used the same task (in an effort to localize "attention"), twenty areas of the brain were found to be involved. The fundamental assumption that cognitive processes can be localized may itself be wrong (Uttal, 2001).

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One researcher summarized the reliance upon brain imaging saying, “What is clear is that there has been a rather reckless community decision to commit an inordinate portion of psychology’s limited resources to this one research program” (Uttal, 2004). As with the studies of identical twins, studies done on autopsy and studies using imaging are able to provide little evidence that mental disorders have their genesis in our biology.

A CHALLENGE TO BIOLOGICAL PSYCHIATRY

On July 28, 2003 an organization called Mind Freedom issued a challenge to three high profile proponents of the theory that our biology causes mental disorders (Mind Freedom, 2003). Mind Freedom is a loose-knit federation comprised mainly of professionals and former patients. They believe that claims of biological causation have gone too far and are hurting patients. The group also disputes many of the claims of effectiveness of psychotropic medications.

The three organizations that were challenged by Mind Freedom were the American Psychiatric Association (APA), The National Alliance for the Mentally Ill (NAMI), and the Office of the Surgeon General of the United States (OSG). Mind Freedom challenged the three to produce any scientifically valid evidence to show that schizophrenia, depression or other mental disorders (apart from the obvious such as Down’s syndrome, autism, and those that are clearly brought on by identifiable tumors, infection, etc.) are biologically based. Mind Freedom also challenged the three groups to prove that there is any physical diagnostic test which can reliably distinguish those so diagnosed from “normals.” Next, Mind Freedom asked for any evidence that would demonstrate the existence of a chemically balanced “normal” personality against which a neurochemical “imbalance” may be compared. Finally, Mind Freedom asked APA, NAMI and the OSG to produce scientific evidence that any psychotropic medication can correct a “chemical imbalance” or decrease the likelihood of violence or suicide.

Mind Freedom’s challenge drew a response from James H. Scully, Jr., MD, Medical Director of the American Psychiatric Association. In a letter dated August 12, 2003, Scully affirmed psychiatry’s support of biological causation: “The answers to your questions are widely available in the scientific literature and have been for years...” Scully wrote. He advised Mind Freedom to see five sources. The five included a report by the Surgeon General; the third edition of the *Introductory Textbook of Psychiatry* (Andreason & Black, 2001); the fourth edition of the *Textbook of Clinical Psychiatry* (Hales & Yudofsky, 2003); or any recent issues of either the *American Journal of Psychiatry* (Andreasen, 2003) or the *Archives of General Psychiatry* (Barchas, 2003).

Mind Freedom replied to Dr. Scully ten days later. The sources he had cited, Mind Freedom pointed out, provided little support for biological causation of mental disorders. For example, the Surgeon General’s report contains statements such as, “The precise causes (etiology) of mental disorders are not known” (p. 49). The *Textbook of Clinical Psychiatry* states, “Although reliable criteria have been constructed for many psychiatric disorders, validation of the diagnostic categories as specific entities has not been established” (p. 43). The *Introductory Textbook of Psychiatry* states, “Much of the current

investigative research in psychiatry is directed toward the goal of identifying the pathophysiology and etiology of major mental illnesses, but this goal has been achieved for only a few disorders (Alzheimer's disease, multi-infarct dementia, Huntington's disease, and substance induced syndromes such as amphetamine-related psychosis or Wernicke-Korsakoff syndrome)" (p. 23). Mind Freedom requested that Dr. Scully point specifically to any supporting research within the over 200 volumes of the journals he had cited.

The American Psychiatric Association responded again to Mind Freedom, this time with a position statement in which it held to the position that mental disorders are "neurobiological." The APA's statement asserts, in part, that there has been "...remarkable scientific and clinical progress (in the) understanding of disorders that afflict and are mediated by the brain..." However, no citations or references beyond those previously cited by Dr. Scully were listed. The APA's position statement was unsatisfying for another reason. It also said, in part, "...brain science has not advanced to the point where scientists or clinicians can point to readily discernible pathologic lesions or genetic abnormalities that in and of themselves serve as reliable or predictive biomarkers of a given mental disorder or mental disorders as a group..." (Mind Freedom, 2003).

A viable conclusion is that the American Psychiatric Association is engaged in self-serving advocacy of biological causation, and that it does so in the absence of conclusive scientific evidence. The psychiatric guild is evidently urging blind faith in the theory of biological causation, but is unable to produce the research evidence that would confirm it. As was written in *Hospital and Community Psychiatry* more than twenty years ago, "Medicalization is useful to rout the enemy...."

EFFICACY OF PSYCHOTROPIC MEDICATIONS

If organized psychiatry bases many of its assertions as much on faith as upon evidence, what of the claims of pharmaceutical companies that medications represent effective treatments for depression, anxiety, schizophrenia and other disorders? Increasingly, the effectiveness of psychotropic medications is being called into question (Friedman, 2004). Although testimonials and anecdotal reports are common, they do not substitute for double-blind, placebo-controlled studies.

When one looks at participants in such studies, it becomes evident that they often are not representative of typical patients. For example, it is routine that pregnant women, lactating women and women of childbearing years who are not using contraceptives are excluded from studies of new drugs (which is as it should be). Also generally excluded from the studies of drug efficacy are many other kinds of patients. They include those who suffer from any mental disorder other than that which the drug is designed to treat; patients with any serious medical illness; patients with significant lab test results; patients with EKG abnormalities; patients receiving anticoagulants; patients with positive drug screens; patients with suicidal ideas; and patients who have ever received cognitive behavioral therapy or electroconvulsive shock treatment. Once such patients are

eliminated, the remaining pool of potential drug study subjects is less than representative of the population that the drug eventually may be used to treat. Brown University's Mark Zimmerman noted with evident chagrin that 86% of the depressed patients he saw would have been excluded from studies of anti-depressants. Yet, he had prescribed the medications for 93% of them (Wyatt, 2003).

Another question is whether psychotropic medications actually live up to their advertised claims of effectiveness. One review of ninety-six antidepressant trials between 1976-1996 found that in 52% of the studies there was no difference between drug effect and placebo effect. The Eli Lilly Company had to run five studies of Prozac to obtain two (the FDA minimum for approval) that showed positive effects. Paxil and Zoloft required even more trials to get two that were positive (Kahn, Leventhal, Kahn & Brown, 2002). It would be irresponsible to argue that no one is helped by psychotropic medications. However, there is reason to conclude that the medications are less helpful than was previously thought.

Even when drug study results are positive, a routine methodology leaves interpretation in limbo. The procedure in question causes the research to be carried out in a way that boosts the likelihood that the drug will be found effective. Prior to the start of a drug study researchers actively attempt to cull from the subject pool all patients who might respond favorably to the placebo. Before placing patients into either the drug group or the placebo group, all are given the placebo and observed for up to three weeks. This is termed the placebo "run-in" or "wash-out" period. Those who improved while taking placebo are removed from the subject pool. They have no further participation in the study. Then the remaining subjects are divided into drug and placebo groups and the study is conducted. The practical result is that the deck is stacked to show that the drug is more effective than placebo. It is difficult to defend as suitable methodology, although it is done routinely by drug researchers.

Even so, the results of drug studies are frequently negative, or are only marginally positive. For example, a review was undertaken of thirty-eight studies of anti-depressants such as Prozac, Zoloft, Paxil, Serzone, Celexa and Effexor that had been done during 1987-1999. On the 50-point Hamilton Depression Scale the studies showed an average 10-point improvement in mood for patients who took the drugs, and an 8-point improvement for those who took a placebo (Kirsch, Moore, Scoboria & Nicholls, 2002). It is doubtful that the two-point average advantage for the drugs is meaningful in the real world in which patients function every day, or that the drugs would have had even that slight advantage over placebo had it not been for the wash-out methodology.

The pharmaceutical industry continues to aggressively market its psychotropic drugs. Since the mid-1990s it has doubled the number of its employees in marketing and advertising, while the number employed in research and development has dropped slightly. The former now outnumber the latter by about two to one (Sagar & Socolar, 2001). The industry has recently stepped up its efforts to target children. According to the pharmacy benefit management company Express Scripts, pre-schoolers are the fastest growing market segment for antidepressants. During 1998-2002 prescriptions of antidepressants for boys under age five increased 64%. For pre-school girls the increase

was 100% (Johnson, 2004). However, it has been known for some time that antidepressants often are not effective or are only marginally effective for children (Sommers-Flanagan & Sommers-Flanagan, 1996).

The absence of compelling results of drug trials may explain why drug companies now sometimes hire ghostwriters to author the studies they fund. Although the studies may be conducted by respected faculty members at highly visible universities, it is fairly common for ghostwriters far from the lab to write the published versions of the results. Ghostwriting has been especially noted to occur in psychiatry journals, and Pfizer pharmaceutical company employs a New York medical writing agency, according to a recent lawsuit disclosure (Barnett, 2003).

For the drug industry the economic stakes are so high that principles of good practice may at times be compromised. Recently drug giant Pfizer agreed to pay \$430 million to settle a fraud case involving its anti-epilepsy drug Neurontin. Pfizer had purchased Warner-Lambert, which had been illegally marketing the drug off-label (non-approved by the FDA) for psychiatric problems such as bipolar disorder and attention deficit hyperactivity disorder. Using the off-label marketing strategy, sales of the drug had escalated 2,700%, from \$97.5 million in 1995 to \$2.7 billion in 2003. Although evidently the illegal marketing practice stopped in 2000, and even though the penalty paid by Pfizer seems severe, the amount paid represents only about 15% of the gross sales of Neurontin in 2003 alone. While the *marketing* of Neurontin off-label has been stopped, it is still legal for doctors to prescribe it off-label, and the effects of the earlier illegal marketing evidently continue, as prescriptions written continue to spiral upward (Farrell, 2004).

TURF, MONEY AND POWER

It is not the purpose of this article to advocate for an exclusive environmentalism. As discussed in the opening section, there is no dispute that several mental and behavioral disorders are biologically caused, and that others may be the result of the interaction of biological and environmental variables. Rather, our view is consistent with that of Skinner's as articulated decades ago. He wrote that "...genetic sources sometimes become a kind of dumping ground: any aspect of behavior which at the moment escapes analysis in terms of contingencies of reinforcement is likely to be assigned to genetic endowment..." (Skinner, 1974). In fact, one of the foundational principles of the behavioral point of view is that we are genetically endowed with the capacity to change our behavior, based upon its consequences.

Nor is it our purpose here to claim that psychotropic medications are never of help. Certainly anti-anxiety medications usually bring about temporary relaxation. Anti-psychotic medications, if they do not cure psychosis, are at times able to render such disorders more tolerable to patients, and communities more tolerant toward patients. Although the evidence in support of anti-depressants and other psychotropic medications is weaker, surely they are beneficial at times.

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Our purpose here is to make clear that biological explanations have gone too far—well beyond the data. The pharmaceutical industry has made questionable claims of biological causation in order to build its profits. Other groups, though perhaps not as powerful as the drug industry, have done the same. Members of the American Psychiatric Association become the treaters of choice. Patient advocacy groups such as the National Alliance for the Mentally Ill (NAMI) and the National Alliance for Research on Schizophrenia and Depression (NARSAD) also push the biological causation perspective. Each receives substantial financial support from the drug industry and, in turn, each pushes the biological causation model with the Congress and the public. Literature from such groups often emphasizes medication as the preferred treatment (Wyatt, 2003).

The one-two efforts of organized psychiatry and the pharmaceutical industry have had enormous impact upon mental health care in America. Evident as well is that the claims by these two groups are symbiotic. Each supports the other in their quests for turf, money and power. Psychiatry and the pharmaceutical companies play upon the patient's desire to be told that his psychological disorder or adjustment difficulty is not his fault, is not due to a lack of will or character, but rather is due to his biological make-up. Some therapists now say that an initial major task of therapy is to undo the new patient's assumption that his or her difficulty is rooted in biology (Wyatt, 2003).

Patients are being shortchanged. One study showed that when genetic causation is assumed, patients indeed feel less responsible. However, they are also less likely to think they can improve with appropriate help. In addition, they are more likely to assume that others in the family will develop the same problem (Phelan, 2002). They may then become more likely to depend upon medications, less likely to seek therapy that might provide them with improved coping skills or other enduring changes.

It is time for a paradigm shift, away from extreme biological causation and toward an environmental causation model, one that recognizes that at least some disorders are biologically caused. We are not optimistic that our culture will change anytime soon. Our pessimism comes after careful examination of the rise of biological causation theory, a phenomenon that has come about as a direct result of the powerful influences of organized psychiatry and the pharmaceutical industry. Their impact is far-reaching, unyielding and seductive to the unwashed. Mental health treatment careens under the influence. Ironically, there could scarcely be better evidence of the environment's impact upon us.

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