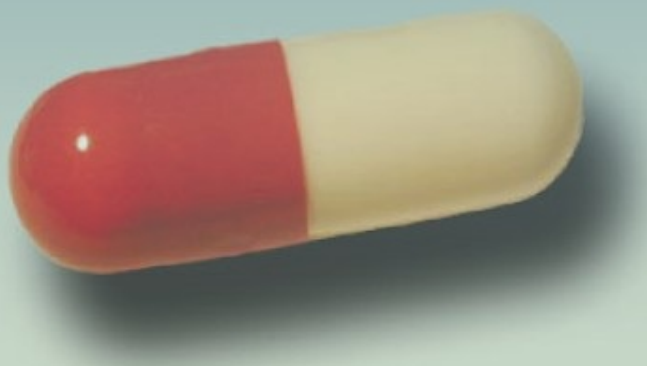
THE BRAVE NEW WORLD OF ANTIDEPRESSANTS

No Need to Grieve



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Abstract:

Today's prevailing model of depression is that it results from an imbalance of the neurotransmitters serotonin, nor epinephrine, and dopamine. This paper presents an alternative model, that is, that depression is best viewed as a pathologic form of grief response. This conceptual shift not only has a profound implications for research and clinical practice, but has ethical implications as well.

Grief has evolved in Homo sapiens because of its importance to the maintenance of close attachments. From a physiological as well as psychological standpoint, grief is indistinguishable from depression. In fact, it is common for antidepressants to be prescribed following the loss of a close friend or relative. Antidepressants likely make such loss less painful. At the same time, it is likely that they alter the nature of close relationships.

This paper briefly reviews the evolution of grief and its probable survival value, laboratory models of depression used in the development of antidepressants, the effect of antidepressants on grief in primates, and the variables that affect the course of grief and depression. This forms the basis for the hypothesis that depression is best conceptualized as a pathology of the grief response.

A shift in the prevailing viewpoint from the neural chemical imbalance theory to seeing depression as a pathologic grief response will open new avenues of research. One of the most important of these would be exploring the effect that antidepressant usage has on close interpersonal relationships. Outcome research based on the imbalance theory narrowly focuses on changes in depressive symptoms such as those defined by the Hamilton Depression Scale. Outcomes of interest are improvement in symptoms such as: sleep disorder, anorexia, and lethargy. However, while the individual may show fewer symptoms of depression, little is known about the effect of

antidepressants on close interpersonal relationships. It is hypothesized that they remain diminished-often crippled.

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Today's prevailing model of depression is that it results from an imbalance of the neurotransmitters serotonin, nor epinephrine, and dopamine. This paper presents an alternative model, that is, that depression is best viewed as a pathologic form of grief response. This conceptual shift not only has a profound implications for research and clinical practice, but has ethical implications as well.

In Aldous Huxley's book *Brave New World*, Benito encourages his friend Bernard to take the drug:

> "But, I say," he went on, "you do look glum! What you need is a gramme of soma." Diving into his right-hand trouser-pocket, Benito produced a phial. "One cubic centimeter cures ten gloomy" (Huxley, 1932, 1946)

Science-fiction writers have predicted many of sciences greatest developments. Huxley in *Brave New World* (1932) anticipated

the development of antidepressants.

A number of years ago our family was staying at a motel. My bored four-year-old was entertaining himself by bouncing on the bed. Before discipline took hold he flew sideways hitting the wall causing his neck to hyperextend to one side. He immediately began to cry holding his neck. While the injury did not seem serious, necks are not to be fooled with, so we took him into the emergency room. After an examination, including x-ray, he was diagnosed with a soft tissue injury. The altruistic doctor feeling sympathetic to his pain gave him acetaminophen with codeine and suggested a repeat dose in several hours if he again became uncomfortable. About an hour later after returning to the motel he was feeling better, and began to jump on the bed again. Parental discipline was sufficient to stop this behavior, but we regretted giving him the medicine since feedback on the consequences of his behavior, that is the pain, was no longer educating him. Suffice it to say no repeat dose was given.

Pain has evolved because it provides valuable feedback

necessary for the survival of Homo sapiens.

> "In a crowd," he grumbled. "As usual." He remained obstinately gloomy the whole afternoon; wouldn't talk to Lenina's friends (of whom they met dozens in the ice-cream soma bar between the wrestling bouts); and in spite of his misery absolutely refused to take the half-gramme raspberry sundae which she pressed upon him. "I'd rather be myself," he said. "Myself and nasty. Not somebody else, however jolly." …
>
> "Now don't lose your temper," she said. "Remember, one cubic centimeter cures ten gloomy sentiments." …
>
> "A gramme is always better than a damn," she concluded with dignity, and drank the sundae herself. (Huxley, 1932, 1946)

Grieving and depressed people often are angry or irritable, feel a drag on others and often isolate themselves. They frequently make those around them feel uncomfortable. There becomes a strong motivation to seek a quick fix.

A while ago a family practice resident and I saw a 37-year-old maintenance worker requesting antidepressants. He said that his coworkers pushed him to seek antidepressant medication since at work he was crying all the time. His history revealed he had most vegetative signs of depression as well as

dysphoria, difficulties concentrating and guilt. He was asked if there were any recent changes in his life. He responded that a couple months previously his wife asked for a divorce. She found out that he had been having an affair. His girlfriend, following this, pushed him to make a commitment to her since he always promised that if he ever could leave his wife he would move-in with her. He was now uncomfortable making this commitment so she broke off the relationship. He then said that his teenage daughter was at the juvenile detention center and would be delayed in getting out until she had a stable home situation. He was feeling guilt about this as well. He said all this made him depressed and in need of antidepressant medication.

My response was that his unhappiness was telling him changes are necessary. Better treatment might be to work on change and when he felt better he would know that the changes were working.

Many clinicians might disagree with my therapeutic plan. They would say I was making a value judgment and punishing

him for what I perceived as misbehavior, that the goal of doctors should be to help him relieve psychic pain or they might say he would have more energy for change if he felt better.

Charles Darwin however may have applauded my response. While he had a keen awareness of the pain of "low spirits," he also viewed its connection to the evolutionary process of natural selection as a trait that aided in the survival of humans. In 1872 he wrote,

> "After the mind has suffered from an acute paroxysm of grief, and the cause still continues, we fall into a state of low spirits; or we may be utterly cast down and dejected. Prolonged bodily pain, if not amounting to an agony, generally leads to the same state of mind. If we expect to suffer, we are anxious; if we have no hope of relief, we despair.
>
> Persons suffering from excessive grief often seek relief by violent and almost frantic movements, as described in a former chapter; but when their suffering is somewhat mitigated, yet prolonged, they no longer wish for action, but remain motionless and passive, or may occasionally rock themselves to and fro. The circulation becomes languid; the face pale; the muscles flaccid; the eyelids droop; the head hangs on the contracted chest; the lips, cheeks, and lower jaw all sink downwards from their own weight… The corners of the mouth are drawn downwards, which is so universally recognized as a sign of being out of spirits, that it is almost proverbial" (Darwin, 1965)

Darwin's description of "being out of spirits" is almost interchangeable with modern-day description of grief and depression. Darwin points out that the behavior and body language of grief is universal and highly evolved and therefore must have resulted from considerable survival advantage in the environment of evolutionary adaptation [EEA]. Today no one questions Darwin’s observation that the grief response is universal. Darwin's hypothesis that the grief response evolved because of its survival benefit gets further support from modern animal and human research.

Harlow (1974) in his experiments was able to produce grief/depressive symptoms in young monkeys and their mothers. Depression in the monkeys occurred either after frequent separations or a more singular longer separation and if prolonged was often maintained even when the monkeys were reunited with their mothers and normal social circumstances. Harlow and his associates found that if the separation went beyond a certain point in the baby monkeys, sequelae appear

permanent. For example females had attenuated attachments to their own offspring when they became parents. Harlow did demonstrate that some of the symptoms could be reversed with the introduction of what he called “therapist monkeys." Therapist monkeys would attempt to socially engage repeatedly with the depressed monkey even though they did not receive any reciprocal social reinforcement for a long time. Finally the depressed monkeys would begin to engage socially and their grief/depressive symptoms would remit.

Goodall(1986) studying chimpanzees in natural field settings observed evidence of mothers and their offspring highly distressed at separations. In the case of death offspring or mother showed clear symptoms of grief/depression.

Human studies of maternal-child separations have shown similar results. Bowlby (1951, 1953) and Spitz(1945, 1955) as early as the 1950s reported on studies of separations of human children from their mothers. Spitz studied parent-child separations as a result of the child being hospitalized. Bowlby

during World War II studied parent- child separations as a result of the child being placed outside of London to avoid the bombings. The studies showed that babies have profound reactions similar to the primate separation responses, which can have lasting effects such as a propensity to develop depressive symptoms later in life as well as problems of later attachment.

As a result of these and many other studies, it is generally concluded by evolutionary psychologists and ethologists that the grief response initially evolved to promote close ties between mother and child, an obvious survival necessity in our EEA.

The grief response in humans has evolved to include more broadly the loss of family relations and close associates. An explanation for this can be found in Homo sapiens' evolutionary history.

Climatic change led to a widespread increase in savanna replacing the arboreal environment of our primate chimpanzee like ancestors. Those primates who could adapt to the savanna

would survive. Two critical factors pressured the natural selection process. The need to replace the primarily vegetarian diet with one more reliant on animal nutrients and the ability to survive predation without resorting to climbing trees that became less available. This led to dramatic evolutionary change such as bipedal locomotion, greater hand dexterity, upright posture, development of a much larger brain, language, and more complex social structure. More specifically related to the evolution of grief, changes in social structure were required by the human predecessor to remain viable in the new environment.

Our arboreal ancestors likely lived like chimpanzees today in groups of 60 or more. Hunting and scavenging on the savanna requires the population to spread out, so small group living was advantageous. Hunting and gathering groups for the most part are made up of two to four generations of closely related members. The grief response likely evolved to support the maintenance of this social construct, a significant survival

advantage. For example, in the EEA if a young male impregnated a female and comfortably left her group, the group would be more vulnerable to predation and likely have less hunting success. The progeny of this male would therefore be less likely to survive and propagate. If however the young father to be, upon leaving the group experienced grief, which motivated him to return to the group, the family would be strengthened and his chromosomes more likely would be passed on.

There is widespread research on the expanded role of grief responses in humans. Parkes(1972) and Marris(1974) were among the first to research grief beyond mother-child relations. They began by studying widowers. Marris conducted a very interesting study of African villagers who were forced to move to public housing in the city. He found many of these people who lived for generations in small kin based villages on having to move to more modern and seemingly pleasant accommodations in the city, responded by becoming highly grieved by the loss of their close associates in the village. This study and many more

like it show the influence of the grief response.

We can see an example of the way grief may prevent future separations by observing the termination of a romance. The painful end of a romance motivates one to carefully choose future attachments to avoid the repeated pain. Thus, the grief experience strengthens future attachments.

In the present medical culture, molecular based theories have become more prestigious than any others including evolutionary and ecological. In this setting, the most popular explanation of the etiology of depression is chemical imbalance, ignoring any association with grief. Yet the animals used in research studies of depression are not usually made depressed by chemicals (although this is possible) or genetic alteration but by behavioral interventions. Specifically the rodents used for research are made to exhibit symptoms of depression by subjecting them to random noxious stimuli such as electric shocks (Willner 1992, 2002). Primates can be made to exhibit depression in a similar way in what is referred to as learned

helplessness but more often they are made depressed by separations (Rosenblum 1987, Willner 1984). Once depressed, pharmaceutical company researchers then use their drugs to ameliorate the symptoms of depression (Willner, 1995).

In a chilling study which further demonstrated the close association between separation and depression, primates were pretreated with antidepressants and then when later exposed to separation were "protected" from the grief/depression response (Hrdina, 1979). That is, those who were pretreated with antidepressants would not respond with grief/depressive symptoms when removed from their close associates.

Modern researchers, as stated, have defined depression as a result of pathological neural activity primarily in the limbic system. This has led to a widely used explanation of depression promoted by pharmaceutical companies that depression is "caused" by a chemical imbalance. This conclusion is drawn from research that shows a correlation between low levels of serotonin, norepinephrine and dopamine sensitive

neuroreceptor activity and depressive symptoms.

However correlation is not the same as etiology (Harris, 1989). These research results could mean depression is caused by neural pathophysiology as many researchers conclude. However this can also be explained as the evolutionary neural manifestation in the limbic system to separation, that is, grief response on the neural level. In fact no one has ever been able to detect neuropathic differences between grief and depression.

Nesse (2000) takes up the evolutionary benefits of "low mood" and depression. While he points out that grief may be an evolutionary factor in mood, he quickly dismisses it. He states "however it remains to be determined whether grief is merely a design constraint or an adaptation in its own right." (p. 16) His dismissal of the pain of grief benefiting humanity appears a result of his emphasis on individual needs influencing evolutionary vector. The study of evolution has recently been strongly influenced by concepts from sociobiology which emphasized the importance of needs of the breeding population

(gene pool) as primary in understanding evolutionary direction as opposed to individual needs.

Glass (2005) in an editorial commenting on non-pharmacological treatment of grief says that although DSM-IV diagnosis does not adequately distinguish between grief and depression he believes this dichotomy important. However he then touches on the difficulties in distinguishing between complicated grief, depression and normal grief.

Studies from an evolutionary perspective such as those described by Marris call into question whether or not creating such artificial dichotomies is in fact meaningful.

Differential responses to loss are to be expected. Studies of variables affecting the experience of loss show several significant factors and there may be others not yet studied. For example, some may experience grief/depression in response to moderately stressful loss like a move to a new city or graduation from college, while others may require extraordinary loss to set

off a grief/depression response such as the death of a spouse. Some may recover in a few months while others may take a year. These differences may be mediated by physiological factors such as degree of neurotransmitter reactivity. Perhaps this explains why genetic studies have shown that some individuals are more prone to depression. However, they may also be mediated by psychosocial factors such as coping mechanisms. Past experience no doubt plays a role in the degree of response to loss as well. Traumatic early loss experiences in monkeys have shown permanent indications of neuropathic changes (Gilmer & McKinney, 2003; Clarke, Ebert, Schmidt, McKinney & Kraemer, 1999; Kaufman, Plotsky, Nemeroff, & Charney, 2000; Kraemer, Ebert, Schmidt, & McKinney, 1989). As stated, studies have shown that early losses in humans make them more susceptible to pathological response to loss later in life. This likely is not just an alteration in neural transmitter activity but also an alteration in how one interprets their loss. If symptoms are seen as overwhelming in early life they are more likely to be seen that way later. Cognitive-behavioral therapists refer to this as

catastrophizing (Persons, Davidson, & Topkins, 2001). Lack of social support also has been shown to contribute to the likelihood that grief will turn into long-term depression (Bowlby, 1980). Those who as a result of a tragic event become withdrawn and inactive are more likely to develop long-term depression. This no doubt reflects both reinforced behavior as well as behavior which has been role modeled. Those with good social support have less depression probably because they are less likely to become isolated. Finally, depressed behavior itself can be reinforced when significant others pay attention to an adequate degree only when they exhibit depressed behavior.

To say then that depression is caused by a chemical imbalance is like saying a heart attack is caused by a thrombolytic event. While this may be true, it is only a half-truth. It ignores many proceeding physiological and behavioral contributing events. Given this, it should be no surprise that medication and psychotherapy treatments have been shown to be effective in the treatment of depression (Butler et al, 2004).

A married 40-year-old father of two, a very successful businessman, feels unfulfilled and decides to go to graduate school 300 miles away, returning home only on weekends. Soon after the separation began he felt lethargic, but after six months, the student developed depressive symptoms, and felt like dropping out. After telling his spouse his feelings, she knowing for a long time he wanted to return to school and how much all had sacrificed for it, she felt this must be an illness and encouraged him to see a doctor. The patient expected his wife to feel bad about the separation like he felt and when she encouraged him to stay in school, he felt worse. He agreed he must be sick. The doctor upon seeing him elicits positive responses to questions regarding symptoms of depression. The physician does not consider asking about recent changes in his life. Such questions are simply not considered relevant to his treatment since the doctor "knows" that the symptoms are caused by a chemical imbalance. The physician prescribes antidepressants. The antidepressants relieve the vegetative symptoms although the feelings of unhappiness when he is away

from home remain. Within a few weeks his score on one of the popular depression scales falls below the depression threshold. If he were in a study on medication effectiveness for depression, he would be considered significantly "improved" even if he had remaining anhedonia.

Why has the "neurotransmitter imbalance" explanation which leads to antidepressant treatment become so popular in today's society? How depression is defined by one's social group and culture determines to a large extent who is seen as responsible for causing the depression and also who is responsible for treatment. This no doubt has what might be considered an unconscious but powerful effect on how depression is defined in our culture today.

> "By this time the soma had begun to work. Eyes shone, cheeks were flushed, the inner light of universal benevolence broke out on every face in happy, friendly smiles. Even Bernard felt himself a little melted. When Morgana Rothschild turned and beamed at him, he did his best to beam back." (Huxley, 1932, 1946)

In Western Culture for many centuries depression was

commonly defined as God's punishment or God's way of challenging a person. Prayer by the individual and the congregation was seen as the healing process. In the early twentieth century, Western Culture's emphasis on personal responsibility led depression to be viewed as a person's own making. From this outlook a depressed person was defined as a "crybaby" and told to take responsibility for their actions. For much of the 20th century, psychoanalysis had the most powerful influence on how depression was defined. It was defined as a result of an internal conflict related to early experiences mainly with parents. Although recent events were considered possible triggers to this reaction, the underlying problem was considered the internal conflict. The responsible party in most situations was seen as one's parents. Improvement was seen as a co-responsibility of the patient and psychoanalyst by developing insight. In today's cultural environment depression is most commonly defined as a neural transmitter imbalance. The doctor is responsible for cure. Each of these explanations reflects the culture's world view and within it, how needs are met for the

patient, their significant others, as well as the doctor.

In the case of the 40-year-old student described, one can see important needs getting met by this explanation. It relieves all parties involved of responsibility and requires no one to change beyond taking a pill.

> "She continued in another tone, "why don't you take soma when you have these dreadful ideas of yours. You'd forget all about them. And instead of feeling miserable, you'd be jolly. So jolly," she repeated and smiled, for all the puzzled anxiety in her eyes, with what was meant to be an inviting and voluptuous cajolery (Huxley, 1932, 1946).

Modern culture, often promoted by medicine, has created an atmosphere where patients believe pain is always bad and can always be cured without the patient's active effort. This has come to include the pain of depression.

The use of antidepressants has skyrocketed since the development of fluoxetine and other antidepressants with more acceptable side effect profiles than tricyclics. The notion that pharmaceuticals can treat depressive symptoms with few side

effects makes for few disincentives for their use and no one has to work for change. Why should anyone have to experience psychic pain if a simple medication can relieve it? And more effective pharmaceuticals with fewer side effects may be on the horizon. In the present reality there is a lot of pressure placed on doctors to prescribe antidepressants for painful grief reactions/depression.

This is far from the first time a culture has been markedly altered by drug usage. Alcohol, peyote, opium, coca, cannabis, yopo, to name a few have significantly changed their culture by fulfilling some needs of large segments (but in some instances a minority) of the populous. Today we can ignore the effects of antidepressants on our culture or make a conscious decision about whether we want this impact on our culture.

> "And that," put in the Director sententiously, "that is the secret of happiness and virtue—liking what you've got to do. All conditioning aims at that: making people like their inescapable social destiny." (Huxley, 1932, 1946)

In Brave New World, Huxley's totalitarian government uses

the antidepressant “soma” to dampen motivation to change, since unhappiness is the inherent motivation for change. Thus the government can easily maintain its authority. In our culture however the words of C.S. Lewis may be more relevant. “Of all tyrannies, a tyranny exercised for the good of its victims, may be the most oppressive. Those who torment us for our own good, will torment us without end, for they do so with the approval of their own conscience.”

Doctors today get pressure from patients, pharmaceutical companies, insurance companies, government payees and agencies, all for the quick fix. Doctors themselves want a simple, quick solution to patients’ problems. Antidepressants appear to fit the bill on all accounts.

> “Don’t you wish you were free, Lenina?”
>
> “I don’t know what you mean. I am free. Free to have the most wonderful times. Everybody’s happy nowadays.”
>
> He laughed, “Yes,” ‘Everybody’s happy nowadays.’ We begin giving the children that at five. But wouldn’t you like to be free to be happy in some other way, Lenina? In your own way, for example; not in everybody else’s way.” (Huxley, 1932, 1946)

Closely working extended family relationships are no longer an economic necessity for modern day survival. Yet we are left with evolved genomes that make the grief response remain a human reaction to separations. In our culture separations such as moves away from close associates are more common. Taking a simple pill to mask our innate reaction is much less painful, easier, and tempting. Yet in doing so we may loose something of what makes us human.

What does this conceptual shift mean for research on depression? A shift in the prevailing viewpoint from the neural chemical imbalance theory to seeing depression as a pathologic grief response will open new avenues of research. One of the most important of these would be exploring the effect that antidepressant usage has on close interpersonal relationships. Outcome research based on the imbalance theory narrowly focuses on changes in depressive symptoms such as those defined by the Hamilton Depression Scale. Outcomes of interest are symptoms such as: sleep disorder, anorexia, and lethargy.

However, while the individual may show fewer of these symptoms, little is known about the effect of antidepressants on close interpersonal relationships. It is hypothesized that they remain compromised-often crippled. And it is hypothesized they diminish motivation to work on interpersonal problems by attenuating the associated pain of depression.

Isolating the multiple variables affecting interpersonal relationships will no doubt make this research difficult. However the greater challenge to this research is securing funds. Nearly all research on depression is supported by pharmaceutical companies. Research on this hypothesis is not consistent with their best interests. Even NIMH studies on depression are carried out primarily by those also supported by these companies.

For many years Dr. Jones has taken care of Dan, a married 40-year-old physical therapist with two children. During this time Dan has had intermittent marital problems with associated dysphoric feelings. Occasionally they have flared up to the point

where marital separation has been considered. On each occasion marital counseling had helped the problems resolve acceptably for both partners. Especially motivating to the couple is the welfare of their children which both believe benefit from married parents. At an appointment with Dr. Jones several months ago, he said his marriage was again in trouble and wondered if depression was to blame rather than being the result of marital discord. Dan requested and was given antidepressants. Dr. Jones now observes that after antidepressant treatment for three months some depressive symptoms have improved, but also that he is apathetic about his marriage and does not have much motivation to work on it. They are talking of separation instead. Dr. Jones wonders if the lack of depressive symptoms, including the associated dysphoria, which he always noted in the past during marital problems, has led at least in part to this apathy. He wonders if continuing the medication is a good idea since it separates Dan from his feelings of pain about the marital separation, which may have motivated him in the past to seek resolution.

Despite Dr. Jones reservations in the present medical environment, considering the standard of care, the only response he could offer in this case is to discuss with Dan his concerns. The broader question of how this might affect our society requires an open discussion of the issues involved on a much broader scale.

> "Often in the past he had wondered what it would be like to be subjected (soma-less and with nothing but his own inward resources to rely on) to some great trial, some pain, some persecution; he had even longed for affliction." (Huxley, 1932, 1946)

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