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A review of selected neurochemical and cognitive hypotheses of depression

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Abstract

According to the American Psychiatric Association (1980), the characteristic traits of depression are quite well established. Symptoms include dysphoric mood, insomnia, psychomotor agitation or retardation, loss of interest or pleasure in usual activities, loss of energy and fatigue, feelings of worthlessness, diminished ability to think or concentrate, and thoughts of death or suicidal ideation/attempt. Depressed persons also have been characterized as self-deprecating and unrealistically pessimistic as well as suffering from distorted cognitive processes (Coyne & Gotlib, 1983). The only essential criterion for a diagnosis of major depression is that the syndrome be present for at least two weeks (Willner, 1985).

A REVIEW OF SELECTED NEUROCHEMICAL AND COGNITIVE HYPOTHESES OF DEPRESSION

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According to the American Psychiatric Association (1980), the characteristic traits of depression are quite well established. Symptoms include dysphoric mood, insomnia, psychomotor agitation or retardation, loss of interest or pleasure in usual activities, loss of energy and fatigue, feelings of worthlessness, diminished ability to think or concentrate, and thoughts of death or suicidal ideation/attempt. Depressed persons also have been characterized as self-deprecating and unrealistically pessimistic as well as suffering from distorted cognitive processes (Coyne & Gotlib, 1983). The only essential criterion for a diagnosis of major depression is that the syndrome be present for at least two weeks (Willner, 1985).

Each year between four and eight percent of the population experience clinical depression (Klerman, Weissman, Rounsaville & Chevron, 1984). In the United States alone there are between twelve and twenty-five million depressed people. Approximately eight to eleven percent of men and eighteen to twenty-three percent of women will be clinically depressed at least once in their lifetime (Weissman & Myers, 1978). Because it is so widespread, depression has been called the common cold of psychopathology (Chute, 1982).

To establish a cause or causes of depression is a complex matter. Beck and Harrison (1982) have indicated that it may

be counterproductive to speak of the cause of depression, since there appear to be a multitude of possible predisposing factors for depression. Dimsdale (1982) suggested that one of the difficulties in studying depression is lack of an accurate definition of depression. "A diagnosis of depression," states Dimsdale (1982), "conveys little more information than a diagnosis of fever" (p. 105).

For this reason, researchers of the etiology of depression have spoken of hypotheses (Jimerson, 1984; Stahl, 1984) and predisposing influences (Abramson, Seligman & Teasdale, 1978; Anisman & Zacharko, 1982; Sedvall, 1981). There have been no prospective studies done that have reliably predicted depression (Beck & Harrison, 1982). Neither has there been a physiological change discovered which invariably precedes a depression (Rowe, 1983).

The purpose of this paper is to review two of the major hypothetical models related to etiology of depression. In the first model, the neurochemical, a physiological explanation is made for depression. The emphasis here is on biochemical changes that occur in the brain itself when a person is depressed. Within a second broad area, the cognitive model, the focus will be on how a certain style of thinking relates to depression. Again, the brain is the focus of attention, but as the center of logic and emotion as opposed to a

physical organ. This review will be limited to these two broad paradigms with three specific theories because of the rich supply of research data and because these theories together have formed the basis for a significant percentage of the current clinical treatment of patients with depressive symptoms.

Neurochemical Hypotheses of Depression

Within the central nervous system (e.g., brain and spinal cord), messages pass from one nerve cell to another in an efficient manner when certain chemical conditions are met. Important chemicals, called neurotransmitters, must be present in prescribed concentrations in the narrow space between nerve cells called the synapse. Small knob-like structures at the end of the nerve cell make contact with this synaptic space. On the surface of these knobs are tiny areas known as receptor sites which are designed to send and receive nerve impulses. In the depressed individual measurable changes occur in the neurotransmitter levels and in the ability of the receptor sites to process messages.

Research dealing with the physiology of the human brain and its relationship to depression is necessarily limited because it is not ethically possible to accomplish experimentation with human brain tissue in live subjects. Therefore, physiologists have taken a different tact and have

been able to develop neurochemical hypotheses of depression through studies of laboratory animals (Kraemer, 1982) and suicide victims (Anisman & Zacharko, 1982). Studies with depressed humans have centered on the quantitative analysis of neurotransmitter byproducts in urine (Jimerson, 1984), along with analysis of other human cells such as erythrocytes (Goekoop, Wisse, Van Brussel, Van Kempen & Spies, 1984) and platelets (Coursey, Buchsbaum & Murphy, 1982) that serve as models for events in the brain. A final avenue of study on humans centered on the effects of antidepressant drugs on behavior and mood as associated with measurable changes in neurotransmitter levels in the central nervous system (Charney, Menkes & Heninger, 1981; Harper, Rodwell & Mayes, 1977).

The following sections will focus on the relatively new neurotransmitter hypothesis of depression along with the even more recent hypothesis that is emerging from studies of neurotransmitter receptors.

Neurotransmitter Hypothesis of Depression

The notion that depressive illness was associated with deficient levels of neurotransmitters in the brain began to surface 30 years ago (Jimerson, 1984). Reserpine, an antihypertensive and antipsychotic drug, was found to produce serious depressive side effects on patients (Julien, 1985).

Investigations revealed that reserpine reduced concentrations of the neurotransmitters norepinephrine, serotonin or dopamine. Subsequent to the above research Jimerson (1984) reported that a group of drugs which became known as tricyclic antidepressants and another class of drugs known as monoamine oxidase (MAO) inhibitors alleviated depressive symptoms. The specific action of the tricyclic antidepressant drugs, according to Winokur (1981), was to block the re-uptake of neurotransmitters released in the synapse between nerve cells thus enhancing its availability to perform its designated function by allowing for transfer of chemical messages across the synaptic space. The MAO inhibitors had antidepressant qualities because they retarded an enzyme called monoamine oxidase from converting serotonin (a neurotransmitter) into a useless acid (Harper, Rodwell & Mayes, 1977).

Variances in levels of a fourth neurotransmitter, acetylcholine, were also reported in patients with depressive disorder (Mathew, Ho, Khan, Perales, Weinman & Claghorn, 1982). Now the number of known neurotransmitters has increased from four to more than twenty making the study of chemical neurotransmission even more complex (Stahl, 1984).

In addition, Sedvall (1981) found that in families with a history of psychiatric disorder there was a higher standard deviation of concentrations of neurotransmitter byproducts in

the urine. Thus, genetic factors have also been linked to dysfunctions associated with neurotransmitters.

Neurotransmitter Receptor Hypothesis of Depression

As investigations of affective disorders have progressed, a number of serious questions about the neurotransmitter hypothesis have been put forward. Stahl (1984) summarized these questions as follows: 1) Why don't the tricyclics and MAO inhibitors work more rapidly? They bring the neurotransmitter levels up to adequate concentrations within hours and yet in clinical settings patients don't begin to respond with mood improvements for days or weeks. 2) Why are newer categories of drugs effective as antidepressants since they don't block re-uptake of neurotransmitters as do the tricyclics or block enzymatic action as do the MAO inhibitors? and 3) Why isn't cocaine an effective antidepressant since it is known to also block re-uptake of the neurotransmitters as do the tricyclic antidepressants?

These questions have led researchers to shift their focus from the neurotransmitters to the neuron receptors themselves (Charney, et al., 1981). Receptors, which are located on the presynaptic and post synaptic knobs of neurons of the brain are defined as specific molecules on the synaptic membrane capable of recognizing and selectively binding with certain chemicals (Andreoli, Hoffman & Fanestil, 1980). They are

identified by the neurotransmitter with which they bind, for example, as a serotonin receptor or a norepinephrine receptor (Davison & Neale, 1986). Neurotransmitter receptors have been likened to a lock to which the transmitter is the key (Willner, 1985).

Charney, Heninger and Sternberg (1984) suggested that the true mechanism of action of not only tricyclic antidepressants and MAO inhibitors, but also of electroconvulsive shock and the atypical antidepressants referred to above, was modulation of receptor sensitivity. This was supported by the fact that the biochemical effects on the receptors was found to be equal in length of time to noticeable changes in mood in depressed patients (Stahl, 1984). Thus this newly emerging hypothesis centered on receptor abnormalities in depression.

Charney, et al. (1981) have delineated the specific impacts on abnormal receptors by tricyclic antidepressants and MAO inhibitors. They included a desensitization of receptor response to norepinephrine and, in long term treatment, a decrease in density of receptors. They further concluded that receptor alterations were induced selectively, depending on the class of antidepressant treatment used.

Since the relationship of neurotransmitters and receptors to depression is such a new field of study, one expects an abundance of data in the years ahead. One researcher

commented that "at the rate things are going, the autoreceptor hypothesis too many be dead before the ink is dry" (Kalat, 1982, p. 109). Most would probably agree, however, with Dimsdale (1982) that in "one way or another, depression must be neurochemically expressed" (p. 105).

A Cognitive Hypothesis of Depression

To merely understand that neurochemical changes in the brain are related to depression is to fall far short of understanding depression. Willner (1985) warned of the faultiness of assuming that depression can be understood in biochemical terms alone when he said, "It is not immediately apparent how including any number of chemicals in a comprehensive biochemical formulation would help us to understand why it is that a depressed patient feels worthless or tries to commit suicide" (p. 18). In attempting to construct a psychobiological explanation of depression Willner (1985) suggested that investigators and practitioners must lessen the gap between the physiological and the cognitive (information processing) phenomena. In this section the cognitive mechanisms of depression will be reviewed.

Rowe (1983) quotes the Greek philosopher, Epictatus, as saying, "It is not things in themselves which trouble us, but the opinions we have about these things," (p. 15). According to Rowe (1983), our interpretation of life events is clearly

associated with the depression "we create for ourselves" (p. 13).

Concerning the role of cognition in depression Coyne and Gotlib (1983) declared that two major theoretical positions existed. Those two positions included Beck's model of depression, which deals with cognitive distortions arising from early traumatic experiences such as parental loss or peer group rejection, and the revised learned-helplessness (e.g., attributional style) model of Abramson, Seligman and Teasdale. Accordingly, the largest proportion of studies have fallen into these two positions. The purpose of the following section is to review the reformulated hypothesis of attributional style.

Hypothesis of Attributional Style in Relationship to Depression

Studies by experimental psychologists have shown that when laboratory animals were exposed to factors that were perceived as uncontrollable in their environment, such as shock or noise, they developed motivational, cognitive and emotional deficits (Seligman & Beagley, 1975). This phenomenon became known as learned-helplessness, and it has constituted a major theory of depression (Willner, 1985). Abramson, et al. (1978), who had earlier been proponents of the learned-helplessness theory, later acknowledged that their

theory was incomplete in describing depression in humans. They argued that humans, unlike rats and dogs, asked why they were helpless. Thus people attempted to attribute cause to their helplessness and their failure. Furthermore, depressed people had a certain attributional style.

Abramson, et al. (1978) suggested in their reformulated hypothesis that people's beliefs about causality relate to three dimensions. The first dimension is labeled internal-external. To attribute cause to internal factors is to hold that outcomes are more or less likely to happen to self than relevant others. Self-esteem deficits occur with this style. To attribute cause to external factors is to believe that outcomes are as likely to happen to relevant others as to self. The second dimension is described as global-specific. To think globally is to imply that one's helplessness will occur across situations whereas to think specifially leads one to feel that one's helplessness is limited to an original situation. The third dimension is called stable-unstable. To attribute cause to stable factors is to feel that outcomes are related to long-lived or recurrent factors. In contrast, to attribute cause to unstable factors is to believe that outcomes are related to short-lived or intermittent factors. The depressed individual thinks in an internal-global-stable style. Abramson, et al.

(1978) illustrated this by the hopeful, but depressed, graduate student who failed the math portion of the GRE exam. His conclusion was "I lack intelligence" implying "I am always stupid in every area of my life." The undepressed student can attribute cause in other ways. "I am not good in math but am in other areas" (specific) or "This is an unfair math test" (external) or finally, "Today I was exhausted, I will do better next time" (unstable).

The existence of a causal relationship between the style in which one attributes blame for negative events and depression remains in question. The attributional hypothesis clearly rests on the notion that the "style emerges irrespective of the event" (Cochran & Hammen, 1985, p. 1569). Said another way, "bad events are likely to result in depression when they are explained by internal, stable and global causes " (Peterson, Bettes & Seligman, 1985, p. 379).

Williams (1985) acknowledged the correlation of attribution to depressed mood but felt the model failed to establish the primacy of one factor over another. Harvey (1981) felt that the attributional style theory was insufficient in that it did not take into consideration controllable life events as a source of stress. He cited Beck's findings that depressed students felt greater responsibility than did non-depressed ones. It is true that

Abramson et al. (1978) were continuing to formulate their theory around the sense of helplessness in the subject.

The reformulated learned-helplessness hypothesis was defended in a study of 227 college students given the Attributional Style Questionnaire before a mid-term examination (Metalsky, Abramson, Seligman, Semmal & Peterson, 1982). In that study the subjects established their own standards of success and failure on the examination. Following completion of the exam the mood of those students who received a grade with which they were unhappy correlated positively with the previously assessed attributional style. Metalsky, et al. (1982) further defined the reformulated hypothesis as being a "diathesis-stress" model where one's style of thinking was the "diathesis" and where the negative life event was the "stress."

In a later study (Peterson et al., 1985) 66 college students (31 male and 35 female) wrote essays describing the two worst events that had occurred to them during the preceding year. Again, it was found that certain unsolicited attributional styles of thinking correlated positively with results in the Beck Depression Inventory. The authors, however, acknowledged that whereas the attributional model was based on the premise of cause and effect, these results were merely correlational.

It seems that the best that can be done with the theory in question is to continue to adapt its clinical application so as to make it as effective as possible in the treatment of depressed persons. Perhaps to establish anything more solid than a correlational relationship will not be possible.

Conclusion

This review has emphasized that depression has both physiological and psychological components. Although theorists in both camps have been unable to establish a cause for this syndrome, some have acknowledged that answers will come clearer as the brain-mind gap is closed (Willner, 1985).

Meanwhile, mental health practitioners must get on with the task of helping those members of the population that are depressed and suffering from a problem that, in its severe form, has been poignantly described as "a living hell" (Willner, 1985, p. 35). It is in this arena of treatment that the professionals' personal bias for one hypothesis or another is of practical importance. Some would agree with Winokur (1984) that pharmacotherapy is the preferred treatment of depression. Rowe (1983) contends that anti-depressant drugs have their place for short term relief but that the business of changing the depressed persons opinions and interpretations of the world around them is the more efficacious method for obtaining longer-term healing.

Perhaps with the large amounts of research being done in regard to depression, the wise approach would be to not polarize in allegiance to one hypothesis or another. Continuing review of all related literature will allow for more effective treatment plans to be created. Certainly a synthesis of these two approaches into a psychobiological one will be most useful.

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