DEPRESSION, THE USE OF FLUOXETINE [PROZAC] AND THERAPY

Running Head: Depression, Prozac and Therapy

David Johnston

ABSTRACT

In this paper I examine two causal explanations for depression, the psychological and the biochemical. I argue for a holistic Jungian depth perspective that may, at times, allow for the wise use of antidepressant medications. I differentiate between pathological depression, where antidepressants may be therapeutically advisable, and transformative depression, where antidepressants may, at times, be helpful although in the long run their use is detrimental to in-depth healing. I also explore the nature and therapeutic effectiveness of fluoxetine [Prozac], a potent and highly selective serotonin re-uptake blocker. According to medical literature it has proven itself to be effective in alleviating depression, while causing relatively few side effects.

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Introduction

Depression is a widespread illness in both North America and Europe. The lifetime risk for adult females to suffer from a depression range from an estimated 20% to 26% of the population, while far adult males it is estimated at 8% to 12% (Boyd and Weissman, as reported in Montgomery, 1988). Those currently suffering this disorder are estimated at 4.5% to 9.3% of the adult female population and 2.3% to 3.2% of the adult male population (DSMIII-R). The disease is generally considered to be 2.7 times more common for women than men, although recent evidence suggests that it is more common with men than has traditionally believed to be the case (Van Wyck et al, as reported in Calabrese and Markowitz, 1991). The elderly, a segment of the population that is growing twice as fast as the general population, suffers from depression four times more frequently than the population at large (Butley, as reported in Feighner, et al, 1988).

As this illness is frequently accompanied by feelings of worthlessness and helplessness, and comes with a high mortality rate, there is cause for concern. Indeed, according to Goodwin et al (as reported in Calabrese and Markovitz, 1991*),* some 15% of patients with depression succeed in committing suicide. For those over 85 years of age, suicide is four times greater than for the general population (Lehman, as reported in Feighner, et al).

With these sobering facts as background I now briefly explore the nature of therapy for people suffering from depression. First, I note the symptoms of major depression and briefly account for its etiology. Secondly, I examine three different approaches to therapy for people with depression, a) one based on the medical model, b) another based on a narrowly defined Jungian depth approach and, 3) a third position based on a Jungian oriented holistic approach, which attempts a reconciliation of the first two models. Finally, I study the choice of an antidepressant medication, specifically fluoxetine, as an aid to therapy, for people who suffer from this illness.

Major Depression, Symptoms and Cause

According to the DSMIII-R, major depression is either recurrent or comes in a single episode, with a severity that is mild, moderate or severe; with or without psychotic features. Although there are other forms of depression, major depression is the most prevalent one and its definition of depression usually prevails in antidepressant medication clinical trials. Symptoms include: depressed mood, loss of interest or pleasure, significant weight loss, insomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, diminished ability to think or concentrate, indecisiveness, and recurrent thoughts of death, suicidal ideation or specific plans for suicide. For purposes of this paper, there are potentially two principal causes of depression, biological and psychological or psycho-spiritual. There are other causes, for example: situational, socioeconomic, environmental and seasonal, but the limited scope of this paper does not permit me to examine them as well. First, I examine biological causes of depression.

Biological Causes of Depression

Studies indicate that recurrent major depression generally has a genetic base. First degree relatives of people suffering from unipolar major depression have a two to three times greater risk of developing a major depression themselves than the general population (Goldman, 1988). From this perspective, depression has a biological cause. In fact, there are presently three dominant theories on the biochemical cause of depression (Brasfield, 1991).

The first is known as the biogenic-amine theory, which assumes that depression is caused by a deficiency in norepinephrine (NE) and/or serotonin (5HT) at the post-synaptic receptors. As a result, there is an apparent faulty transmission of nerve impulses within the central nervous system (CNS), specifically in the limbic system and the diancephalon. A second theory is known as the cholinergic theory that assumes that depression is due to hypercholinergic activity. A third, more recent theory, assumes depression is the result of an increase in amine-receptor sensitivities involving super-sensitive beta-adrenergic receptors.

Biologically, therefore, depression seems to be the result of a complex interaction of several biochemical factors. Both the therapeutic effects and side effects of different antidepressant medications can be understood in light of these different theories and assumptions. I will go into these phenomena in more detail later with regards to fluoxetine, which was developed on the assumptions of the biogenic-amine theory.

The Psychological Dimension of Depression

I now examine psychological aspects of depression from a perspective based on Jungian depth-psychology, which is my own orientation to therapy. Although Jung himself did not extensively develop his thinking on the nature of depression, one can discern essentially two kinds of depression in his writings, a transformative depression and a pathological depression (Steinberg, 1990). In either case the libido or life energy is withdrawn from the ego and directed towards the unconscious. In the case of transformative depression, the unconscious or underlying creative matrix provides the ego with ingredients for a transformed adaptive response to external circumstances (Exhibit). In order for this to happen, individuals need to turn inwards to enter into the dark feelings attending the depression and not to deny or escape them in any way. In the case of pathological depression, in contrast, rather than a potentially creative inward flow of energy, there is, according to Steinberg, regression and degeneration.

For Jung (as reported in Steinberg, 1990), depression is a forced introversion of libido. In the case of transformative depression, which is not in any way pathological, there is potentially a creative regeneration from the Self and a transformed adaptive extraversion. For pathological depression, the energy does not flow inwards to the Self but to destructive inner constructs, perhaps inner parental ideals or conflicted orientations to which the individual submits, reinforcing depressive behavior.

Contemporary Jungian therapist, Warren Steinberg (1990), argues that people who suffer from a depressive disorder have learned very early in life to gain support and

nurturing through depressive behavior. He observes that these people generally experience love and then have it withdrawn. Self assertion of being is also frowned upon while pleasing others, they learn, brings the desired acceptance and, along with that, depression.

Therapy for the Depressed Patient

Given the fact that there are two major causal explanations for depression, biochemical and psychological, what is the optimal approach to therapy for the depressed patient? I discuss a Jungian approach, one based on the medical model, and then a Jungian holistic approach that attempts to find some reconciliation between the first two ways of doing therapy.

Jungian Depth-Therapy

From a strictly Jungian depth-psychological perspective, there is a need to distinguish between a non-pathological potentially transformative depression and one that is pathological and possibly based on a genetic defect (Steinberg, 1990). In the former case, therapy is prospective and involves insight into the meaning of dreams and possibly the use of a form of meditation that Jung called active imagination, which involves active participation of the ego. In this case, the patient is essentially required to sink into the depression in order to emerge with new creative life enhancing insights. In the case of pathological depression, in contrast, before prospective oriented therapy can ensue, there is first a need for a reductive approach to therapy to uncover personal and family psychodynamics that caused the long-term depression in the first place.

Steinberg (1990) warns against supporting pathological depression-related behavior including a dependent and submissive attitude to the therapist, which he sees as a reinforcing replay of the original parental situation. In this light, the administration of antidepressant medication can be experienced as supporting this original neurotic situation. What is needed instead is encouragement for individuals to gradually learn to respond to their own feelings and to reject self-criticism and the need to please others, along with the realization of a healthy extraversion. In short, in this view, clients are seen as needing to develop genuine self-assertion of being that comes with a positive and creative introversion.

Therapy based on the Medical Model

In sharp contrast to the depth-psychological perspective, therapy based on the medical model relies on a biochemical explanation for the cause of depression and the use of antidepressant medication. Calabrese and Markovitz, (1991) argue that in addition to the actual administration of drugs, therapy ideally involves an educational process. Based on their experience they have found that clients respond more compliantly should that be the case. They believe that patients need to be taught the following:

- that depression is a treatable illness that involves the “limbic system,” a part of the brain that governs mood: that depression is a genetically based biologic disease,
- that depression is not a sign of character weakness, and
- that antidepressant medication does not cause pharmacological dependency. They also need to be told, they believe, that people with at least moderately severe

depressions benefit from antidepressant medication, and that frequently psychotherapy can be a helpful adjunct.

Within the limits of the medical model such advice and education process makes good sense. It differs widely from the Jungian depth perspective, however, which is more interested in the psychodynamics underlying the depression itself and healing at that level. From this point of view medication, even along with therapy, limits the amount of psychological transformation that is possible as too many feelings are repressed by the drug and, along with that, at least to some degree, the motive for change has been repressed. This, at any rate, is my concern. If there is any truth about the vital, that is to say the life dimension of being itself, it is that learning comes through actual life experience and self-reflection on that experience, and not just mental realization. Most of my analysands who are on an antidepressant medication inform me that, although they can function better, it puts them in a kind of bubble with a less immediate relationship to their emotions than previously was the case. One woman, who came off her antidepressant after being on it for seven years, exclaimed to me that she didn't know what to do with all the emotions that were now being thrust up into consciousness.

Although there may be little pharmacological dependency, there is a real danger of the patient becoming psychologically dependent on the medication. I have often observed that people using anti-depressant medication are reluctant to give it up. Unfortunately medical practitioners often encourage them to continue using the medication, holding fast to their assumption that depression is primarily due to a bio-chemical imbalance. In

fact, my personal experience with the medical profession is that they are generally reluctant to co-operate with a therapist who holds different views on the etiology of depression than they do. Some, I have been informed by my clients, have actually actively discouraged them from participating in Jungian styled therapy, while encouraging the use of antidepressant medication.

A Reconciling Jungian Holistic Approach.

James Hall (1983), a medical doctor and Jungian analyst, takes a position that tries to reconcile both the medical approach and a narrowly defined Jungian depth perspective. Although he takes an essentially depth perspective using dreams and insight therapy, he does not hesitate to use medication when he believes it is warranted, including for people suffering from depression. He argues that the purpose is to move the ego from a hopeless, unmotivated state of mind to one where individuals are able to work on themselves and gain from therapeutic insight.

Hall (1983) stays in the Jungian tradition, however, in that he contends that dreams can serve as guide posts to when medication should be administered or not. In his view, dreams that show the dream ego as being aggressively attacked or when they directly refer to the original conflict that caused the depression in the first place are examples of when medication is warranted. When dreams return to normal, which the therapist can determine from experience with the client, he believes, medication can be dispensed with. In the long run the depth perspective prevails and the client is weaned away from reliance on medication, with the emergence of a healthy self-assertion of being.

Hall's position is holistic in that it allows for both a biochemical explanation and a Jungian oriented psychodynamic one. Moreover, It allows for potential psychological transformation away from the depression. Nonetheless, it requires a sensitive and astute practitioner to know when medication is called for and when it gets in the way of genuine therapy. The dream ego, for instance, can be attacked in a dream without indicating the need for an antidepressant. In addition, for psychotherapists who cannot prescribe or dispense drugs, it is helpful to have a harmonious working relationship with the prescribing psychiatrist or medical doctor. Finally, there may well be some people who will never be interested or motivated to do anything but use antidepressant medication as a cure, perhaps along with some supportive psychotherapy. With this in mind, I now examine the nature and use of fluoxetine, a widely prescribed antidepressant medication, marketed with the brand name Prozac.

Fluoxetine [Prozac]: Its Biochemical Nature and Effectiveness as an Antidepressant Medication

With a reported 650,000 prescriptions per month in the United States in 1990, fluoxetine is one of the most widely distributed antidepressant medications on the market today (Soringen, et al, as reported in Levinson et al, 1991). In my own general psychotherapeutic practice, I meet more clients on fluoxetine than on any other antidepressant, indeed on any other medication. For this reason I have chosen to briefly examine its biochemical functioning, its comparative therapeutic effectiveness and other factors that directly relate to its use in therapy.

There has long been research involving the implications of serotonin (5HT) in depression and other psychiatric conditions (Lopez-Ibor, JR, 1988). Fluoxetine, along with its demethylated metabolite, norfluoxetine, is a highly potent and selective serotonin re-uptake blocker, with little affinity for muscarinic, cholinergic, histaminic, dopaminergic and noradrenergic ($_{a1}$ and $_{a2}$) neuron receptors (Stark et al, as reported in Cooper, 1988). In addition, its potency at blocking re-u-ptake is relatively greater than its potency in blocking both ($5HT_1$) and ($5HT_2$) receptors, suggesting that the net effect is to significantly increase serotoninergic transmission (Richelson, 1988).

The development of fluoxetine was based on the biogenic-amine theory discussed above. The increased transmission of serotonin is undoubtedly the reason for fluoxetine's effectiveness in alleviating depression. Indeed, in several standard controlled and administered trials, and now clinical experience, this compound has proven itself to be at least equally effective as any of the conventional tricyclics in treating major depression and significantly more effective than placebo. Specifically, from my reading, compared to imipramine (Stark and Eardison, 1985, Reimherr et al, 1984, Bremner, 1984, Cohn and Wilcox, 1985) and amitryptline (Feighner, 1985, Chouinard, 1985, Fawcett, et al. 1989) fluoxetine has proven itself to be equally as effective in alleviating depressive symptoms for adult patients. Moreover, from my research, there is no significant difference between fluoxetine and doxepin in alleviating major depression in geriatric patients (Feighner and Cohn, 1985, Brymer and Winagrad, 1992). Finally, in both efficacy and activating sedating effects in agitated and retarded

depression, there appears to be no significant substantial difference between fluoxetine and imipramine according to Beasley, et al (1991).

If the effectiveness of alleviating depressive symptoms is not significantly different, then other factors become important in the selection of an antidepressant medication. These include side effects, safety and adverse effects, dosage rates and patient compliance. To begin with, fluoxetine was developed with the expectation of having few side effects, given its high selectivity as a serotonin re-uptake blocker and its low affinity for other neural receptors, as indicated above (Richelson, 1988). This contrasts with other antidepressants that have been on the market for a longer time, including the tricyclics.

Many clinical trials have confirmed expectations, indicating that, with fluxotine, there are significantly fewer side effects than with the trycyclics and the side effects are generally well tolerated. Specifically, compared with fluoxetine, patients who use doxepin have significantly more of the following side effects: dry mouth drowsiness sedation, constipation, and dizziness/lightheadedness (Feighner and Cohn, 1985). For those using amitriptyline, there is significantly more dry mouth, constipation, dizziness and drowsiness increased body weight and blurred vision (Shark and Hardison 1985). Likewise with imipramine there is significantly more constipation, dizziness, dry mouth and drowsiness (Chouinard, 1986). Those using fluoxetine, on the other hand, report significantly more nervousness, anxiety nausea, and weight loss (Shark and Hardison, 1985). Despite these side effects fluoxetine is generally tolerated somewhat better than any of the above tricyclics.

As many of the side effects of a medication are related to dosage size, the smaller the optimal dosage rates the better. In a fixed rate dosage clinical trial 20 mg per day of fluoxetine was found to be equally as effective as 40, 60 or 80 mg with fewer side effects (Fabre and Putman 1987 Wernicke et al, 1987). Indeed these are now trials that suggest that 5 mg of fluoxetine, administered on a daily basis may be effective (Wernicke, et al, 1989).

Several trials and clinical experience suggest that fluoxetine is a relatively safe drug (Cooper 1988), with a significant margin of safety over the tricyclics. In one study of 234 cases of acute fluoxetine overdose, it was determined that supportive care alone was the only required intervention (Borys et al, 1992). This does not mean to say that in some cases fluoxetine is not associated with adverse side effects. It is. For example, there are reported cases of side effects when fluoxetine interacts with other drugs (Ciraulo and Shader, 1990). In addition, there have been several cases that associate fluoxetine with increased suicide and suicidal ideation, although trials have not indicated that a significant increase in the risk of suicide is associated with this drug (Beasley, 1991).

An additional advantage of fluoxetine is the fact that it has a long half life compared to the tricyclics -- 2-3 days versus 10-14 hours (Calabrese, 1991). For this reason only one dose of fluoxetine needs to be administered per day in the morning. Ease of drug administration, along with significantly fewer side effects than more conventional

antidepressant medication, and equal effectiveness against depression, has led to physician's acceptance and general patient compliance.

The Need for Diagnostic Discernment

From a holistically oriented Jungian depth-psychological perspective, it is helpful to know about such medications and how they function. My general perception is that the medical profession, educated mainly with the medical model, is often far too quick to prescribe antidepressants such as fluoxetine. Nonetheless, the administration of antidepressants, specifically fluoxetine, can be a therapeutic aid in treating people with what Jung calls pathological depression, which may be based on a severe genetic defect.

Perhaps, today, this is usually diagnosed as recurrent major depression. There is a considerable amount of subjective bias in psychological diagnosis, however, and not everybody who is diagnosed with a recurrent major depression is pathologically depressed in the sense Jung means. For a single episode major depression and some cases of recurrent depression, for that matter, wise use of medication may help to overcome the bleakest periods and put sufferers in a state of mind that encourages them to carry on and try to come to terms with their problems. However, one needs to bear in mind that, from a Jungian depth perspective, it is therapeutically necessary for the client to eventually fully experience the depression in order to find a creative response. Indeed, I have observed that many people prefer to take an antidepressant and be carried above the problems of life rather than deal with them. A woman, for

example, recently told me that she liked the fact that all her negative self-talk vanished thanks to her medication. These comments notwithstanding, I am aware of several cases where individuals use an antidepressant on a regular basis and dreams are still pointing to a creative resolution on their life path. For transformative depression, however, ultimately the use of medication is detrimental. Above all, there is a need for diagnostic discernment.

Conclusion

Depression is a widespread illness in both the adult and geriatric populations. There are two divergent causal explanations for depression, one biologic and the other psychological. Those that support a biologic explanation usually encourage a therapeutic approach based on the administration of antidepressant medication along with supportive psychotherapy. One effective and successful antidepressant medication on the market today is fluoxetine [Prozac], a highly selective and potent serotonin re-uptake blocker, which has relatively few side effects.

Those that emphasize a psychological explanation recommend psychotherapy. From a narrowly defined Jungian depth-psychological perspective there is an attempt to uncover underlying psychodynamics and to encourage self-assertion of being, while shunning medication. From a more holistic Jungian perspective, there is a need to discern between pathological depression and transformative depression. Wise administration of medication can be therapeutically helpful although, at least in the case of transformative depression, dispensed with in the long run.

EXHIBIT

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