

Psychopharmacology: A Means to Treat Depression

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Abstract This literature review will examine antidepressants as a treatment of depression. The aim of this article is to also discuss the uses of various pharmaceutical treatments that may not typically be used to treat depression. The review will describe how antidepressants influence the chemical structure of the brain to alleviate depression, their overall effects on the individual, and an analysis of their effectiveness as a treatment. There are several types of antidepressant medications prescribed to patients; this article evaluates the four categories these drugs belong to. The four categories of antidepressant medications are: monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and selective serotonin-norepinephrine reuptake inhibitors (SSNRIs). In conclusion, by understanding the brain and the effects depression has on it, medical practitioners and prescribing psychologists can better treat their clients with contemporary and alternative treatments.

Keywords Depression, Antidepressants, Treatment, Neurotransmitters

1. Introduction

The study and application of psychopharmacology finds its roots in the work of psychiatry. In psychiatry's early development, there was an overwhelming belief that there was a biological cause for all mental illness that exist. However, while there were developments by Kraepelin and other theorists, there was no clear method of treatment that could be used in practice. The systemic approach was focused on a biological approach in which the search to find the cause of pathology was paramount to the researchers of that time. In the late 1800's, there was a discovery that propelled the study of biological psychiatry to a new place of knowledge, it was the discovery that mental illness could be caused by different types of bacteria. While the wheels of the movement were slow, and at some point didn't move at all, this discovery laid the groundwork for understanding other causes of mental illness and helped to develop medical treatments. Kraepelin, a prominent force in the field of psychiatry, recommended several different pharmaceutical drugs that he used in his own practice. For clients with agitation, he prescribed and recommended Opium, Morphine, Scopolamine, and Hashish. To put clients to sleep, he prescribed and recommended Chloral Hydrate, Ether, Alcohol, Chloroform and Bromides.

With the stagnation in medical research to effectively treat mental illness, I can agree that psychiatry was given a better opportunity to be more receptive and allowed for the development of different approaches based upon their

influences, such as Freud. However, biological psychiatry began to take off in the 1950's and this allowed for the discovery of new pharmaceutical treatments that included psychotropic drugs like Thorazine, Thofranil, Benzodiazepine, and Librium that were aimed at causing a calming effect for those with schizophrenia or bipolar illness. As the studies of psychotropic drugs and genetics were underway, so was the change in opinion of how to treat mental illness, and I believe this debate still is being argued today. There are those that believe the best way to help someone with a mental illness is to develop a psychotherapeutic treatment plan and to carry it out as its theoretical framework would dictate; while there are those that argue no matter how much therapy some clients are given, they are going to need medication, creating two schools of thought that in many programs still exists today. However, I do believe we have evolved to understand that there are benefits for the use of both treatments when working with clients. Those who were pro-psychotherapy for treatment argued that due to the complexity of human cognition and behavior that only psychotherapy could reach the deep psyche of a person. It was also believed that because therapy is aimed at helping a person grow and become autonomous, drugs could only inhibit that necessary development. Those in this camp also believed that drugs could lead to a chemical dependency while causing unnecessary side effects that do little to actually help a person manage the illness. In the pro-medication camp, the belief was that medication is necessary and the ability to monitor the type of medication and the dosage made it controllable and manageable. Medications were believed to make it possible to not rely on the skills of a

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therapist to cause relief or change, but that medications do their jobs on time, every time, regardless of who is administering them. Symptoms are quickly abated and the time it takes to see changes and results with medications does not take any real growth or autonomy. Studies on stress show that it can lead to physiological changes that lead to illness. This sparked interest in the psychological – biological interactions and how they play an integral part in the daily living of those with mental illness as its “never a question of all or none” [1]. The use of PET and SPECT scanning along with new innovative technology allowed for a better understanding of the different structures of the body/brain relationship and how to better treat those with such illness. Studies on the cellular level opened up the door of information on neurobiology, and since the human brain “contains approximately 100 billion nerve cells,” there was a lot of information to obtain and generalize to other clients [1]. The structure of a neuron contains the cell body, dendrites, the axon and the terminals; this was important to know at that time because it helped illuminate how information was transmitted throughout the brain. Why is this so important? Well, the way the medications are used to help those with mental illness has much to do with the effects of receptor binding in the brain as well as what chemicals are inhibited upon uptake. Many disorders are seen and manifested due to neurotransmitter degradations by enzymes, the use of different drugs “either facilitate or inhibit the release of neurotransmitters” or marked changes in second messengers can cause pathological manifestations [1]. Other structures of the brain may be affected such as the hypothalamus, the limbic system, the cortex, the prefrontal cortex, and the diencephalon. Stressors in life can also be the cause of mental illness and the physiological manifestation of that illness. When a stressor presents itself, the body on a cortical or subcortical level begins to evaluate and interpret the stressor to determine the next action. Once this is determined, an emotional response is elicited, and this causes different receptors in the brain to release chemicals to aid in the fight or flight response. Abnormalities in neurobiology may not always immediately cause a clear manifestation of a psychological disorder; however, as previously stated a stressor if presented long enough can actually cause changes in the structures of the brain. Events such as brain damage due to over-exposure to cortisol levels in the brain can cause pathology as well as trauma, brain tumors or other diseases that can travel to the brain and cause mental illness. While it is important to understand some of the basic concepts that have established the field of pharmacology, the therapist does not have to become an expert in that field; however he or she needs to be able to identify the different functions and use of the drugs. There are two broad categories derived from the study of drugs, which is defined as “any substance that brings about a change in biologic function through its chemical actions” [1]. These two processes for which can be seen as categorical functions of drugs are

pharmacodynamics and pharmacokinetics. Pharmacodynamics is basically the “drugs effect on the body,” while pharmacokinetics is basically “the body’s effect on the drug” [1]. Drug interaction is a major factor when clients are being prescribed medications for different pathologies. The prescribing psychologist or psychiatrist needs to ensure that when they are prescribing medications, that they consider how the drugs will interact with each other to ensure this does not cause any undue harm since the “absorption, distributions, metabolism and excretion is potentially affected by the presence of administered medications” [1]. This is significant because there are many clients that have comorbid conditions that require medications that affect different parts of the brain. And in order for the medications to take affect, they must enter the bloodstream, yet they will also affect receptors in a certain way to either increase or inhibit re-uptake of certain chemicals in the brain. For each psychopharmaceutical drug, there is a specific task that the receptor is supposed to complete in order to treat the psychological disorder appropriately. Some of the actions are to activate the receptor while others are to block the receptor. Yet if the desired effect is to be anti-depressing, the adverse and unwanted effect could be an increase in anxiety or increase heart rate or blood pressure. This happens because at this time there is no drug that can specifically target the receptor without affecting other parts of the body. Fortunately, research in this area is in progression and better drugs are being formulated.

2. Not Just Mood

Depression is something millions of Americans frequently deal with on a daily basis that has an enormous impact on their everyday life. Depression is commonly known as a chemical imbalance in the brain that affects a person physically, mentally and emotionally [2]. There are several different types of depression that affect people, they are, Dysthymia, Bipolar disorder or manic-depressive illness, and Major depression. All of these illnesses affect individuals similarly, but the difference is in the severity and length, yet all can be treated effectively with antidepressant medications. In an article called *The Influence of Sad Mood on Cognition*, the influences of an individual’s mood on how they think and function while depressed was examined. In this article, there is an established idea, that how we feel can affect the way we think, behave, and ultimately perceive the world. Researchers Chepenik, Cornew and Farah [3], have suggested that there is a difference in the cognitive ability in individuals with depression compared to those who don’t. Depressed individuals have “impaired...working memory and cognitive control” (p.805), meaning they think slower, forget things or simply have trouble remembering, as well as other cognitive functions. Through various tasks, the authors hypothesized that there would be an “extreme” difference

between those with a happy mood and those with a sad mood. Though the results didn't exactly support their hypothesis, the study was beneficial to research. The authors continued to discuss that this study is evident that being sad is not what affects the cognitive abilities of a depressed person, it's the depression itself, and sadness is one of its effects. So simply trying to get a depressed person in a better mood doesn't change the fact that the person is depressed, nor does it eliminate the other effects of the "depression disease" (p.810).

3. Depression

Author Barry Jacobs [4] discusses the history of depression, the previous beliefs about its causes and current treatments that use the brain to correct the imbalance. He describes how clinical depression is no longer looked at with the same stigmas that it previously was associated with. *Depression: The brain finally gets into the act*, suggests that clinical depression is a disease that affects many people, whether acute or chronic. By utilizing different factors of the brain, and new discoveries such as neuroplasticity (changes in the brain) and neurogenesis (new neurons), scientists have developed medications that prevent depression [4].

A deeper look into the brain revealed that factors outside of serotonin suppression caused depression. Jacobs explains how researchers now speculate that the birth and death of neurons in the brain may play a vital role in the operations of the hippocampus. With this in mind, he suggests that the use of stem-cell research may be helpful in replacing damaged or lost neurons, allowing for a healthier hippocampus and an overall reduction in depression. Zhang, Hauser, Conty, Emrich, and Dietrich [5] used a battery of tests to identify if having a history of mental illness, especially depression, in the family would make that individual more likely to suffer from that illness. By using technology to track changes in the brain while engaging in a specific activity, the researchers were able to conclude that having a decreased P3b amplitude, "[a possible] vulnerability marker for the development of depression" [5], may indicate the possibility of becoming clinically depressed. The results in this study indicated that individuals with a history of depression were more likely to have lower P3b amplitude, thus supporting the idea that they were at a higher risk for depression compared to those who had no such known history.

Overall, the results of the study were favorable to its purpose. Though not all of the results produced a comprehensible way of predicting possible future episodes, it does provide a clear pathway for future research to follow. This information would definitely be beneficial to researchers and scientists that study depression. Instead of treating the disorder after it manifests, detecting and preventing its occurrence would clearly have profound benefits. Assuming this is possible, current research may benefit from investigating this possibility. Of course, it has

been suggested that this wouldn't be something drug companies would be interested in.

4. Antidepressants

Four major types of antidepressant drugs commonly prescribed are, monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and selective serotonin-norepinephrine reuptake inhibitors (SSNRIs). MAOIs. Monoamine oxidase inhibitors were the "first class of antidepressants developed" (p.49) [6]. This works by inhibiting and preventing the breakdown of monoamine neurotransmitters. Depending on the exact type of MAOI's, it either inhibits the breakdown of serotonin, dopamine and norepinephrine, or better known as noradrenaline, which is considered the chemical cause of depression in the brain. The process is that by inhibiting the breakdown of the chemicals in the brain, this will allow more neurotransmitters to be available to "stimulate the [central nervous system]" which in turn alleviates depression (p.49) [6]. TCAs. Similarly to MAOIs, this drug inhibits the re-uptake of the neurotransmitters, norepinephrine and serotonin. Re-uptake is the process of recycling and releasing of a neurotransmitter. Tricyclic antidepressants cause more norepinephrine and serotonin neurotransmitters to be available at the synapse in the brain where they are transmitted throughout the brain and body. For years Tricyclic antidepressants were the "first line of treatment for depression". Though the chemical process takes effect immediately, the actual alleviation of the symptoms of depression may not be felt by the patient for 3 to 4 weeks after the beginning of the treatment [6]. SSRIs. Selective serotonin reuptake inhibitors do just as the name implies. It selectively inhibits the re-uptake of serotonin in the brain. SSRIs are the most commonly known prescribed drug to treat depressed patients. These along with SSNRIs are known as at the "top of the line" treatments for depression. By selectively blocking the uptake of serotonin, the remaining serotonin, "act as a CNS [central nervous system] stimulant for an extended period" (p.50) [6]. For the general public, common prescriptions of this type of drug include Prozac and Zoloft, which are frequently advertised on TV. The alleviation of depressive symptoms is almost immediately felt by patients taking SSRIs.

SNRIs. Almost identical to SSRIs, Serotonin-norepinephrine reuptake inhibitors also inhibit the re-uptake of serotonin as well as norepinephrine. Norepinephrine is a stress hormone, and by inhibiting its neurotransmitter re-uptake, stimulation of the CNS occurs, which increases brain activity. This increase in brain activity is believed to be the main contributor to the change in sad mood and irritability, which are the most common symptoms of depression. A common prescription of this drug is Cymbalta [7].

5. Dosage

If a psychiatrist gives an antidepressant medication to an individual he or she believes to be depressed, and there are no improvements, what is he or she to do? This is essentially the question asked and answered in a study by Adli, Baethge, Heinz, Langlitz, & Bauer [8]. The authors summarized an enormous amount of studies to determine if increasing the dosage of a “non-responsive individual” (p.396), would actually increase the likelihood of improvement. Three types of antidepressant drugs were examined, monoamine oxidase inhibitors (MAOIs), tricyclic or tetracyclic antidepressants (TCAs), and selective serotonin reuptake inhibitors (SSRIs). Overall, it was found that TCAs may be the only antidepressant that may be beneficial in higher dosages. Of the other drugs studied, either higher dosages were ineffective, or the adverse side effects were so strong they overpowered the alleviation of depression [8].

The expression, “you never can have too much” is clearly not the case in this study. This type of research has definitely been vital to medical health care providers and recipients of mental health care. The consuming public may assume that by taking more dosages of the medication that are prescribed, that they are in some way increasing their chances of improvement. Likewise, psychiatrists and other mental health care providers are discovering that just upping the dosage doesn’t necessarily do the job.

Tolerability. The adverse side effects of antidepressants are what the term tolerability refers to. In short, tolerability is the ability of the body to consume this drug without serious consequences. Newer drugs such as SSRIs and SNRIs have very few side effects compared to their older counterparts such as MAOIs and TCA’s. These drugs were known for having such adverse physical effect that patients refused to continue treatment.

6. Effectiveness

In a study by Joanna Moncrieff [9], it identified several reasons why she doesn’t believe that antidepressant drugs are really effective. Moncrieff takes on an offensive stance against the notion that depression can be treated or cured by taking the current antidepressant drugs in the pharmaceutical market today. Because of the many trials that confirm this idea are not published, as she reports, there isn’t much information for the public to investigate. In fact, she accuses some researchers of tampering with the results or reinterpreting the self-reports of the individuals to meet their clinical result needs [9]. Unfortunately, there is not a lot of evidence in her article to back up what she says. True, she may have gathered research from unpublished trials, but the fact of the matter is, independent research and evidence would hold for a stronger argument.

The author does give reasons why it is possible that some clinical trials may obtain significant results in their study. She states that antidepressant drugs have sedation similar

effects, and this is why people appear or think to have diminished depression. Joanna’s position is that there isn’t just one treatment that will be the all cure for individuals with depression, but that they may need different types of treatment. Though she doesn’t give any suggestions as to what these alternate solutions would be like, one would assume they would not include any antidepressant drugs.

Authors Adam, Kasper, Möller, and Singer [10], argue that using placebos in clinical trials to test the effectiveness of antidepressant drugs is needed to test reliability and false results. The authors state that as many as 50% of patients that were given placebos in their trial, with no real effectiveness, reported a change and, “showed substantial clinical improvement” (p.259) [10]. With these types of results, it would seem almost impossible to know if anyone is actually benefiting from taking antidepressant medications, or if they are improving just for the simple fact of thinking the medications will make them improve.

The reasons for these possible results are that the individuals listed above may suffer from brief or very short-term depression and this could be why such an improvement was possible. In addition to this idea, it’s also been suggested that possibly the way these individuals were informed and debriefed about the study, or simply being in the study could have affected their psychological awareness of their depression. Of all current depression research, this is where many of the studies are being driven to prove whether antidepressant drugs really alleviate depression, or if a sugar pill can do the same. Many of the issues with using placebo trials including determining if the patient is at any health risk. One of the issues presented is if outpatients or those who are not confined to the hospital should be part of the trials. The thought is that by including these individuals, it would allow a better generalization to the population.

7. Alternative Drug

Erick Check, author of *Comfortably Numb*, [11], explores the science and practical use of a controversial drug called ketamine. Due to the strong psycho-cognitive effects, so far this drug has only been used to sedate animals and young children, where the effects are not as strong. Yet researchers are looking into the fact that individuals who use this drug illegally, that also suffer from depression seem to have beneficial results. Check discusses how current treatments of depression work to influence certain chemicals in the brain and the patient will not feel the effects for weeks. Using ketamine, the effects are almost immediate, with a higher percentage of individuals reporting better mood. But looking back, what many other scientists are concerned with is the fact that this drug has similar “psychedelic” effect as cocaine and many other illegal drugs. One scientist actually describes the drug as briefly making people crazy [11].

As the pros and cons of the use of ketamine are argued, the undeniable fact is that the benefits for those with depression are astounding. Yet, what can’t be forgotten are the other

reality changing effects it has on the brain and on the individual's consciousness. Keeping its benefits as a primary goal, it is possible that scientist and researchers can develop a way to only utilize the medicinal effects of ketamine and discard any other negative or unwanted effects. If this were possible, this would mean a whole new outlook on life for those with depression.

8. Conclusions

Educating clients about their mental health is important and necessary to ensure a complete understanding of the bio-chemical treatment plan developed by the care provider. Clients need to be informed and be aware of both the benefits and the different potential risks that are associated with taking medications such as the side effects: dependency, withdrawal, overuse, tolerance and more. Also, there is a needed to remind clients that they will need to continue taking the medication until there is a receptor build up so that they can actually feel the effects of the medications. Mental Health Clinicians should continue to investigate other possible alternatives that can be utilized to successfully treat depression.

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