


**An Analysis of the Anti-Depressant
Prozac**

A Senior Studies Report

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**John Hughes Curry, Jr.
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Saint Meinrad College11
St. Meinrad, Indiana**



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Abstract

This analysis of Prozac, a selected serotonin reuptake inhibitor, will begin with a short summary of the major groups of antidepressants. The main points covered during this summary will be to uncover when they were first introduced to the general public, how the public has reacted to them, and an update on the drug's success.

The most important point to understand about the S.S.R.I.s is how they function. The antidepressant Prozac makes its impact on the serotonin level within the neurons. How this function happens will be explained. While on the drug, a counselor will maintain a weekly checkup for the first four to six weeks. This will be necessary to prevent from any reactions which may harm the patient.

After studying the performance of Prozac for the past eleven months, I trust my analysis will be reliable. Bringing this paper to a close will be a diagram of the primary function of Prozac. The producers of Prozac, Eli Lilly, couldn't explain how the reuptake inhibition occurs. This proves that the knowledge dealing with the human brain, although it has come a far way, is still far from being completed.

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I. Introduction

In the December of 1987, Eli Lilly--a pharmaceutical company based in Indianapolis--released the antidepressant fluoxetine hydrochloride, the generic name for Prozac. The antidepressant Prozac, a selected serotonin reuptake inhibitor (S.S.R.I.), has a much smaller, less oppressive list of side-effects than the other major antidepressants. Because of this, a majority of the psychiatrists have flocked to Prozac, prescribing it at such a rate that Prozac has acquired more prescriptions per year than all of the other antidepressants combined.

Unfortunately, along with the fame and fortune Eli Lilly has experienced with Prozac, there have been some hard times as well. Through comparison with other antidepressants, a proper analysis should prove, or disprove, if Prozac can rightfully be accused of the charges brought against it and its supplier, Eli Lilly & Company. Another goal for this thesis is to show the many efficiencies which coincide with Prozac.

The main sources used were the books *Listening to Prozac*, by Dr. Peter Kramer, M.D., *Talking Back to Prozac*, by Dr. Peter Breggin, M.D., and *Prozac: Questions and Answers for Patients, Family, and Physicians*, by Dr. Ronald R. Fieve, M.D. An interesting note in regards to Dr. Peter Breggin, considering he has been very negative on antidepressants and the methods used by many psychiatrists, is that he was linked with the Church of Scientology,

a cult which shall appear later in the paper. Another interesting point on Dr. Breggin is that he isn't even a psychiatrist, although he seems very comfortable in claiming Prozac's infidelity. He was consistent in his negative comments of the harm this antidepressant can do to the human body. But Dr. Breggin didn't limit his attacks on Prozac. He has written another book, *Toxicity*, in which he tried to prove his theory that chemicals don't have a part in the field of psychology. The direction taken by Dr. Fieve, who was paid by Eli Lilly to write his book, was to answer some of the most common questions about Prozac. Dr. Kramer was very thorough in regards to seeing Prozac for what it really is: a respectable antidepressant that isn't without its share of faults.

There were a few other sources used for writing this paper, such as articles in newspapers and magazines. But this paper may not have been possible if it wasn't for the information sent to me by Eli Lilly. These articles and documents gave a good overview of the effects Prozac has had on the public, both negative and positive. Some of the points made were very controversial, making it difficult at times to decide who may have the more biased approach. Over the past nine months, an array of questions have arisen. In order to get these questions answered, letters were sent to several psychiatrists. All of the letters had the same questions and every one was answered similarly to the statements sent to me by Eli Lilly & Company, proving that they are trustworthy in regards to the responses received.

II. Analysis of Antidepressants

The first antidepressant, Iproniazid, was introduced to the public in 1958. The antidepressants affect the mind by working on the neurotransmitters serotonin, norepinephrin, and dopamine. If these neurotransmitters flow through the neurons at an excessive rate, the person will react in a manic frame of mind. But if there are too few neurotransmitters, also known as amines, depression will set in. Iproniazid affected the norepinephrin and serotonin levels in such a way that it worked like an "upper," or a psychic energizer. This drug seemed to work wonders with depression, but iproniazid was initially designed for people suffering from tuberculosis. (Kornetsky: pp.103-104)

A recipient of the prescription drug iproniazid would feel less fatigued and experience an elevated mood. The altered mood would lead to a change in behavior and there would be an increase in physical activity. Iproniazid was identified as a monoamine-oxidase inhibitor (MAOI). Monoamine oxidase creates a block against the amines in the presynaptic neurons. If the level of these amines can be elevated, as they will if the MAOIs were not blocking them, then serotonin and norepinephrin levels will rise. The elevation will minimize the level of depression. Unfortunately, the MAOIs were proven to be toxic if taken at the same time as other medications or foods that are high in amine levels. This prompted the discontinuation of this antidepressant, keeping it off the counter and only available to patients in the hospital who could

have their food and medication carefully monitored. (Kornetsky: pp.104-107)

Iproniazid appeared to function appropriately, but it was flawed. By fooling a man's brain, this drug was doing the same job as the oriental stimulant, opium. A non-stimulating drug would have to be created. Dr. Kuhn, the man who designed Imipramine, worked with doctors who studied the effect antihistamines had on schizophrenics. In the September of 1957, Kuhn made an antihistamine capable of sedating normal people while it relieved the brain from depression. The "mood pill" imipramine can help a person become less concerned with what ailed them mentally. (Kramer: pp.52-56)

Imipramine, a tricyclic antidepressant (TCA), works the same as the MAOIs with the dopamine, norepinephrine, and serotonin levels. The negative side-effects between the TCAs and the MAOIs explains why the S.S.R.I.s have been so successful. The TCAs can be lethal if taken in excess. Because of this it might not be used for the right purpose in the hands of a patient suffering from major-depression. (Stokes: pg.218)

Bryan Molloy, a chemist from Scotland, knew changes needed to be made to improve antidepressants. He began his research for designing an antidepressant without devastating side-effects. Molloy joined forces with Ray Fuller and David Wong, all of whom worked with Eli Lilly & Co. of Indianapolis. The first step was to run experiments in the laboratory with non-stimulating agents.

They followed the “bind and grind” method introduced by Dr. Solomon Snyder of the Johns Hopkins University. They took the brains of lab rats, ground them in a meat grinder, and tested many different chemical compounds on them, hoping to find one which could get a response from the serotonin level. This response was discovered with the compound fluoxetine oxulate, a compound later simplified as fluoxetine hydrochloride; better known as Prozac. (Kramer: pp.60-62)

The antidepressant fluoxetine hydrochloride was first introduced by the trio--Wong, Fuller, and Molloy--in the June of 1974. Prozac wasn't released to the public for thirteen years. During this time extensive testing was done to prove Prozac clean and effective. There were 3,300 people who took the medication during this time, half of whom took placebos. In 1987, Eli Lilly was granted permission by the Food and Drug Administration (FDA) to introduce their new antidepressant to the public. (Stokes: pg.218)

The MAOI iproniazid was known as the “mood pill”. Prozac had been dubbed the “personality pill.” The effect the drug has on the brain seems to alter a person's personality, making them into what may appear to be a different person. But what is happening when Prozac is successful is an elevation of the self-esteem. When the self-esteem is low, a person will feel the lows known as depression. With a higher self-esteem, a person will be capable of achieving more. (Toufexis: pp.61-62)

A fine example of the effects of Prozac would be a study done by Michael McGuire, a sociobiologist, and his colleagues on a troop of vervet monkeys. The vervet monkeys live in a hierarchical system, very similar to what is seen in many cultures in the human lifestyle. For the test, they secluded two monkeys of the troop, the dominant monkey and one from the bottom of the hierarchical order. While in seclusion they injected the weaker of the two with Prozac for four-weeks. After the drug took effect, he was returned to the troop. He became the dominant member of the troop within a week. The original dominant monkey was returned to the troop and he regained his status. But the monkey who was the least dominant did not return to his previous status. He maintained a certain amount of dignity, even after the Prozac was discontinued, and was capable of accomplishing more than ever. (Kramer: pp.212-214)

When compared to other antidepressants, the S.S.R.I.s appear to be clean. The side-effect profile of Prozac is quite minimal. They will effect the user, but they are preferable to the pain of depression. The common side-effects are nausea, nervousness, insomnia, anxiety, tremors, headaches, drowsiness, diarrhea, dizziness, sweating, sedation, vision disturbance, and dry mouth. The most common of these side-effects, nausea, is present in only four-percent of the patients prescribed Prozac. The side-effects diminish once the body learns to accept the foreign body which is being administered. There has been

only one documented overdose which proved to be fatal due to Prozac. The patient died after taking seven-thousand milligrams of the medication: 350 of the 20 milligram pills. This would seem very unlikely because a monthly prescription would only contain thirty pills to hold a person over for a month. (Stokes: pg.231)

Looking at Prozac's side-effects and comparing them to the side-effects of the MAOIs and the TCAs would explain once more why the S.S.R.I.s have become more popular. The MAOIs (e.g. Marplan, Nardil, and Parnate), are prescribed only when the other antidepressants have failed. The severity of the MAOIs side-effects go so far as causing death. The adverse effects of the MAOIs include high blood-pressure, fever, convulsions, insomnia, and the possibility of heart-attacks if the wrong foods are eaten with the medication. The TCA's side-effects include weight-gain, drowsiness, and dry mouth. Another consequence of these drugs is the possibility of an overdose. (Stokes: pg.219)

III. Recipients of the S.S.R.I., Prozac

Tests have proven Prozac capable of helping people who are suffering from anxiety, compulsiveness, melancholic temperament, borderline personalities, and social inhibition. Although Prozac does show its effectiveness against these many different symptoms, the Food and Drug Administration will not allow prescriptions to be filled for everyone. (Stokes: pg.223) Most of the people prescribed to Prozac are suffering from depression--approximately sixty-six percent--the other one-third are suffering

from bulimia or obsessive-compulsive disorders. (Fieve: pg.53)

In order to have a clear understanding of how Prozac works, it is best to get a clear view of who is taking the drug, how it affects them, and why they are taking it. Depression is more complex than it may appear. People may say they are depressed when they are merely feeling upset. The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* labels four different types of depression: major depression, dysthymia, manic-depressive disorder (bipolar I), and manic-depressive disorder (bipolar II).

When a person is suffering from major depression, certain symptoms will arise that will occur during the episode. These episodes will last at least two weeks and occur randomly, meaning that some people may experience the imbalance of major depression either once in their life, or perhaps in continuous stages for their entire life. The symptoms include, as mentioned in the *DSM-IV*:

- a sad, empty feeling, giving a loss of interest in life.
- an inability to find pleasurable activities and enjoyment.
- lack of energy.
- anxiety.
- trouble of either sleeping or excessive lack of sleeping.
- feelings of hopelessness, helplessness, guilt, and worthlessness.
- trouble concentrating and making decisions.
- feelings of agitation.
- frequent thoughts of death.

Looking over all of the symptoms, it is hard to believe they could all fit under the one disorder of major depression. Couldn't there be some difficulty helping people showing different symptoms? Dr. Ronald Fieve mentioned the different phases of depression. There is the acute phase, the middle phase, and the maintenance phase.

The acute phase starts when the patient realizes help is needed and seeks help by contacting a counselor. The counselor will respond by finding the cause of the problem. If the patient is suffering from major depression, the counselor will either suggest an antidepressant, begin psychotherapy, or, if the counselor prefers, both. (Fieve: pg.147)

The middle phase, also known as the continuation phase, is the time when the patient and the psychiatrist will review the effects of the therapy. Even if the depression appears to have diminished, it is best to continue the medication in fear of the depression returning. Many psychiatrists feel that it would be best for the patients if they make appointments for psychotherapy during the first two to three months in order to be certain the medication is working properly. (Fieve: pp.146-148)

The final phase, maintenance, is the period when the patient returns on a regular basis to be updated. While taking a medication, a person will develop a tolerance, so a larger dose will be needed to maintain effectiveness. (Fieve: pg.148)

The manic-depressant disorders, bipolar I & II, experience

periods of major depression and mania. The bipolar I disorder will suffer extensive manic highs so hospitalization will be required. The second bipolar disorder will cause a milder state of mania, also known as hypomania, through which medication will be sufficient for treatment. Lithium has proven itself effective for the manic state, but has a very potent side-effect known as psychomotor retardation. Because of this, some psychiatrists may prescribe Prozac with lithium in regard to its less sedative side-effects. (Fankhauser: pg.1056)

IV. Prozac's Procedure on the Human Brain

The most puzzling question about Prozac relates to how it works. Antidepressants are effective because they work with the neurotransmitters of the brain. While the M.A.O.I.s and the T.C.A.s work with the serotonin, norepinephrin, and even the dopamine levels, the S.S.R.I.s only effect the serotonin level. The procedure followed in "inhibiting" the reuptake of serotonin takes place in the presynaptic neuron. The serotonin are jettisoned into the synaptic cleft, where they will enter the postsynaptic neuron through the receptors. Some of the serotonin will not be taken up by the receptors of the postsynaptic neuron, so the presynaptic neuron will "vacuum" the serotonin from the synaptic cleft and reemit them. (Breggin: pp.18-21) The S.S.R.I.s fulfill their function at the reuptake valve of the presynaptic neuron. The diagrams at the end of the report show how this process works.

The neurotransmitter serotonin can have a major role in

altering the behaviors of people. While researching the effects of deficient and excessive levels of serotonin, many similarities with the side-effects of Prozac became noticeable. When the serotonin level is either too high or low, the person effected will notice "a difference in sleep, appetite, energy, psychomotor function, mood, sexual activity, and cognitive function." (Wells and Hayes, pg.1066) All of these are listed as side-effects of Prozac, also.

There has been another connection made with the serotonin level and the negative effects of Prozac. The serotonin level will effect a person's impulse to commit suicide, act aggressively, and perform violent acts if not controlled properly. This would explain why it is very necessary to remain under close surveillance during the first six weeks this medication is taken. However, this doesn't prove that Prozac should be considered more threatening than the other antidepressants. They all have similar side-effects. But Prozac isn't lethal, if the one incident isn't considered when the man took nearly six months worth of Prozac capsules at one time. (Stokes: pg.231)

Autopsies have been made on people who had committed suicide. The serotonin levels in the postsynaptic neuron are consistently high. A conclusion made here is that, when the S.S.R.I.s are proceeding in the way expected, the reuptake is blocked. The reduction of the uptake is monitored in the postsynaptic neuron by the brain and a discharge of more serotonin will soon come in through the neurons. This excessive

amount of serotonin will cause a change in a person's personality.

The prescription level will become important. The average number of milligrams of Prozac prescribed is 20. The response to the antidepressant will be monitored during psychotherapy for 4-6 weeks. This is the amount of time it will take for the tolerance level to show. If there is no effect, the prescription would be increased. If the response is immoderate, then the prescription would be lowered.

According to statistics, one person in twenty is suffering from an acute depressive episode. This total includes all four forms of depression. The second depression listed, dysthymia, is similar to major depression, but not as severe. Although the symptoms may not be as severe, dysthymia is more persistent than the major depression. It has a chronic course, by definition, and will last at least two years before a diagnosis is made.

V. Accusations Made On Prozac

Several groups have tried to make a mockery of this antidepressant. The main opposition has been the Church of Scientology, a religious cult started in the '60s by L. Ron Hubbard, a science-fiction writer best known for his book, Dianetics. Known for their efforts against psychiatry, the Church of Scientology formed a particular social action group, called the Citizens Commission on Human Rights (C.C.H.R.). Their main goal is to draw people away from the psychiatrists, who they view as evil-doers putting false thoughts into the minds of their victims. They

believe the antidepressants, such as Prozac, are the weapons of the psychiatrists, used to brainwash their victims. (Behar: 32-35)

The attack the scientologists used on Eli Lilly was quite effective. Members of the congregation, who had taken Prozac, took Eli Lilly to court for damages. They also paid magazines to write aggressive articles on Prozac, making a vicious attempt to make the drug appear dangerous to the public. Due to the negative publicity from the C.C.H.R. in 1990, sales dropped twenty-percent. Eli Lilly reported a total loss of \$5.8 million. (Behar: 32-35)

Eli Lilly & Co. responded appropriately. Their lawyers publicly exposed the plot by the Church of Scientology. They degraded the scientologists by exposing their lies in popular magazines such as *Time*, *Newsweek*, and *U.S. News & World Report*. Before long the sales of Prozac were on the rise again. Eli Lilly sent memos out to psychiatrists, informing them that, if they would prescribe Prozac more often, they would supply attorneys for all subpoenas brought on them because of Prozac. Doctors began writing these prescriptions for Prozac on a whim. A reported 2.5 million prescriptions were written in the first year. During 1993, sales ran in excess of \$1.2 billion, over 900,000 prescriptions per month: equivalent to all of the other antidepressants combined (Styron: pp.18-20).

On September 14, 1989, Joseph Wesbecker, a man who had been prescribed Prozac on August 10, attacked his former place of employment, the Standard Gravure Printing Press of Louisville,

Kentucky. He entered the printing company, carrying an AK-47 automatic rifle, a Mac-10 sub-machine gun, a 9 mm. semi-automatic pistol, and a pump shotgun. There were approximately 1,400 rounds of ammunition in his backpack. He killed eight workers, wounded twelve, and then shot himself. With the ammunition he had, more harm could have been done.

(Willis: A1)

Wesbecker had been seeing a psychiatrist, Dr. Lee Coleman, M.D., at Our Lady of Peace Hospital since the April of 1984. The son and wife of Wesbecker noted that he had never acted in such a manner as he did when he began taking Prozac. "He just wasn't himself." But looking at the record of this man it would appear he was a madman. He had noted several times that he desired to kill his supervisor at Standard Gravure, and that was before Prozac had been introduced. (Schwartz: 64-66)

Everyone related to Joseph Wesbecker and the relatives of his victims are trying to sue Eli Lilly, but the lawyers of the pharmaceutical company are defending their company's reputation quite well. They are proving Wesbecker's unstable mental status was present before he began taking Prozac. They have plenty of evidence saying he wanted to assassinate his supervisor before he began therapy with the S.S.R.I.

There is proof that he was well prepared for the assault before August 10, the date when he was prescribed Prozac by Dr. Coleman. The receipts for the handguns and automatic rifles

Wesbecker purchased were on his desk and they were all dated August 26, 1988. He also had several newspaper articles taped on his walls, reporting the AK-47 assault made by a young man on a playground, filled with several hundred children, on January 18, 1989. It was reported that, earlier that year, Wesbecker had entered the Standard Gravure office carrying a pistol. He left without making any threats, so it was not looked on as an assault. (Willis: A1)

Considering Wesbecker had a desire to kill someone at his place of employment before he had been introduced to the new drug, it would seem likely that he was going to go through with this homicidal act without the added supplement of Prozac, which was discontinued two weeks after it was first prescribed in the beginning of August, two months before his attack. On October 5, 1994, five years later, the case concerning Joseph Wesbecker and his assault on the Standard Gravure has been reopened. This is giving Eli Lilly and Company a chance to prove Prozac to be a safe drug in regards to suicidal and homicidal ideation. Doctor W. Leigh Thompson, M.D., the chief scientific officer at Eli Lilly, is attempting to demonstrate that the suicidal and homicidal ideation in manic depressants is present before the drug is prescribed. (Scanlon: A10)

Studies shall continue on the connection between Prozac and suicide ideation because, as Dr. Thompson of Eli Lilly & Company said, "all things are possible." (Scanlon: A10) The relation is

possible due to akathisia, an inner sense of restlessness caused by being in a constant state of discontentedness. People have said that Prozac makes them "feel like they are ready to jump out of their skin." Due to this excessive feeling of anxiety, the patient may feel compelled to partake in violent actions, perhaps even commit suicide, in order to bring an end to the suffering caused by the restlessness. (Fava: pp.108-111)

Some patients who suffer from akathisia, and believe Prozac to be the cause, are likely to have the prescription discontinued. The claim has been made that if the prescription is brought to a halt, the akathisia and the suicidal or homicidal thoughts would subside. To gain a better understanding of why Prozac may induce akathisia, it would be important to understand what akathisia is. The extra-pyramidal motor system, composed of dopamine, acetylcholine, gamma amino butyric acid (GABA), and serotonin, seem to contradict one another in their process. This process induced extra-pyramidical symptoms (EPS), one of which is akathisia. According to statistics, the suicidal ideation level is less for Prozac patients than it is for the patients on TCAs, but this wasn't mentioned in five out of six of the reports which were received from the Journal of Clinical Psychology. Could this be another plot from the Church of Scientology? (Hamilton: pp.401-406)

When a person is prescribed Prozac, the depression will have already made them feel as if though they had already failed

in some way. This feeling of failure would lead to hopelessness, a common precursor to suicide. Depression is a hard pain to deal with; and when a prescription is given to the sufferer, they will have some hope that the suffering will soon subside. Imagine the distress they must feel, then, if the drug doesn't cure the pain. The psychiatrist needs to make it perfectly clear that the antidepressants won't cure the patient overnight. Prozac usually takes four to six weeks before the drug can begin doing its job. If not made aware of this, the patient may begin to feel the hopelessness, questioning why this "wonder drug" doesn't work for him.

This drug would appear to be addictive due to the effect it has on the mind. It has the ability to relieve the person of a great deal of stress and making day-to-day life much more grandiose. But the officials at Eli Lilly have proven that addiction to Prozac is impossible. In a response from a letter sent to Dr. Robert Todd, M.D., of Louisville, this antidepressant isn't addictive because it works through the presynaptic neuron. Prozac doesn't provide pleasure. The individual taking the drug will be alleviated of the woes being felt due to depression. Consider a college student, preparing for a test or writing his senior thesis. There will be times when he might experience moments of anguish due to the pressure. If he makes the proper decision he will go to the counselor. A question that has come about during my studies of this drug has been in reference to what might happen if Prozac is

prescribed? While taking the medication for a couple of weeks he begins to feel more comfortable with his work. Will this mean that he might become satisfied with work that will be considered insufficient for his level of mentality, or will he be able to work harder with less stress on his shoulders?

There have been several patients who have experienced the success of this drug but have stopped taking it because it was “fooling with their mind” too much. A man with whom I spoke over the Summer had been taking Prozac for six weeks, but he stopped taking the medication because it had made him into a different person. His personality had changed for the better. But he was scared because this was totally foreign to him.

Other people with whom I spoke had also been taking Prozac, one for a total of five years, and they couldn't be happier with what the drug had done for them. They all realized depression had just about gotten the better part of them, so they had gone to a counselor and were later prescribed Prozac. Out of the three people who had told me of the good Prozac had done for them, two have gotten better jobs, leading to better lives. The other went on to living in the same lifestyle, but he went about living in a less depressed state of mind.

With all of this being true, the four people I was able to find who had been taking Prozac had all reacted to the drug in a positive manner. The one man stopped taking the medication, but that was only because of the overwhelming effect it had taken.

V. Closing Statements

Prozac is a very young drug, considering it has only been on the market for a little less than six years, so many may be scared to take the final step needed to escape from the confines of depression. Success has become possible for those who had lost hope. Without hope, people would not be able to set goals needed to live.

My overall opinion of Prozac should seem very explanatory in this paper. According to the statistics, reviews, and personal experiences that have been shared with me, this antidepressant should be considered reliable for the greater percentage of people who are prescribed to it. There will always be a certain number of people who will take Prozac and not respond favorably. This is true for all of the other antidepressants, so Prozac shouldn't be considered a failure because it wasn't able to help a small percentage, reportedly one to four percent. What should be considered in this case is the number of people who have responded favorably.

VI. Diagrams

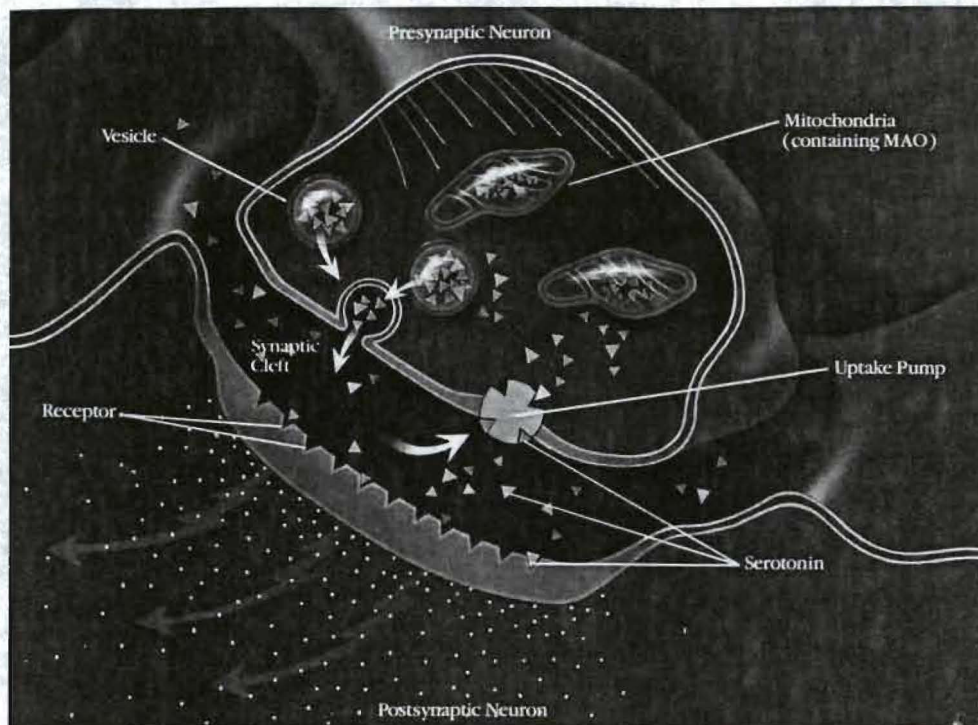


Figure 1. Normal Serotonergic Neurotransmission

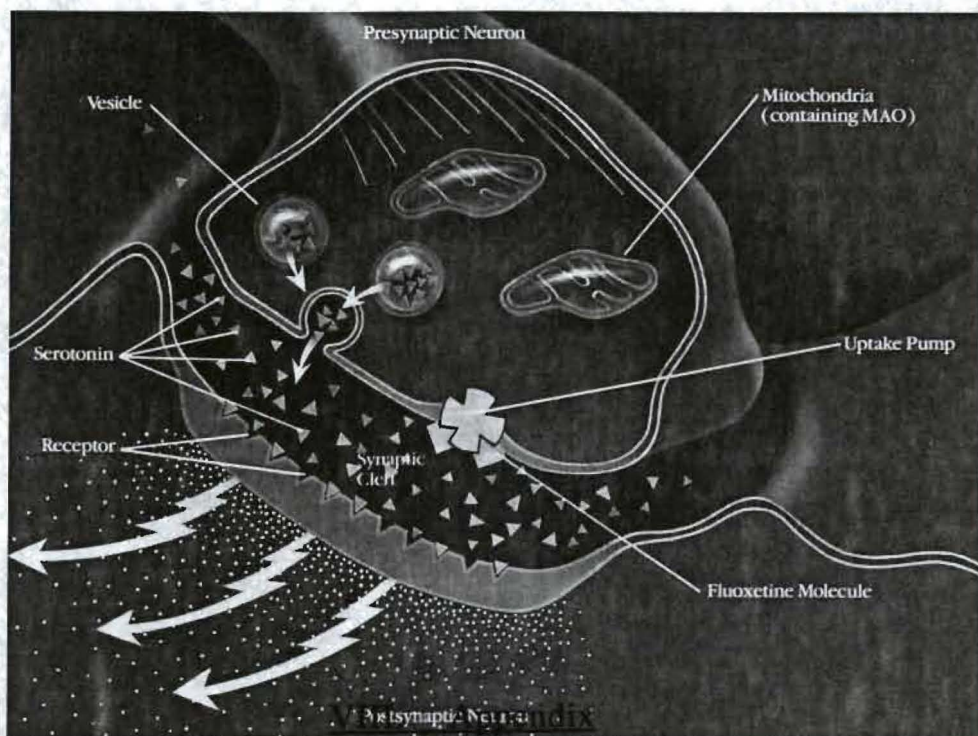


Figure 2. Effect of Fluoxetine on Serotonergic Neurotransmission

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