

Key Points

1. Depression is a common occurrence associated with chronic pain
2. Existing antidepressant drugs work by altering levels of neurotransmitters, such as serotonin, and have significant side effects
3. Some researchers believe that the fluidity of cell membranes in the brain might be linked to mood disorders like depression
4. Study examined the effects of two natural substances versus existing drugs on rats
5. Found that both uridine and omega-3 fatty acid acted as antidepressants
6. When used in combination, less of each was required
7. How they work is not yet known
8. Omega-3 is found in fish, especially oily ones
9. Uridine is found naturally in many foods in small amounts; there is currently no uridine supplement

Definitions

antidepressants - medications used to treat depression

citalopram - antidepressant drug, also known as Celexa

depression - mental illness involving strong and prolonged feelings of sadness, despair, and discouragement

desipramine - antidepressant drug

fluidity - the property of flowing easily

fluoxetine - antidepressant drug, also known as Prozac

lipid - a fatty substance

membrane - flexible layer surrounding a cell; regulates the movement of molecules across its

Fish Oil & Food May Help Fight Depression

Depression often walks hand in hand with chronic pain, spinning pain sufferers into a downward spiral which can be difficult to come out of. Current antidepressants, like Prozac, work by changing the levels of certain neurotransmitters in the brain, such as serotonin. Researchers believe that these neurotransmitters are responsible for mood control, and that low serotonin levels lead to depression. However, this is just a theory, and the neurobiology of depression is not yet well understood. In addition, current antidepressant drugs have significant side effects and drawbacks.

Recently, some researchers have begun focusing on other mechanisms which might affect people's moods. Specifically, some scientists are focusing on the membranes of brain cells. The membrane is like an outer covering to a cell and controls what can pass into and out of that cell. Cell membranes are largely made up of phospholipids, a type of fatty substance. There is growing evidence that the production of these phospholipids, and the fluidity of brain cell membranes (meaning how much like a fluid they are) may affect a variety of activities in the brain, such as how easily neurotransmitters are exchanged, and how well mitochondria - the energy producing part of a cell - operate. This in turn has led some to suspect that the cell membranes may be important in causing, and treating, mood disorders.

If this is true, then substances which affect phospholipid levels and the membranes of brain cells may be effective in treating mood problems like depression. Indeed, there is some indirect evidence for this already. Populations of people whose diet includes a lot of fish tend to have lower rates of major depression. Fish contain high concentrations of omega-3 fatty acid, which is believed to make brain cell membranes more fluid. In addition, studies have shown an association between depression symptoms and low levels of omega-3 fatty acids in people's blood.

Given this recent evidence, Dr. William Carlezon, at the Department of Psychiatry of Harvard Medical School and McLean Hospital, and several of his colleagues decided to examine whether omega-3 fatty acids and uridine (a naturally occurring substance which is also thought to play an important role in cell membranes) had antidepressant effects in rats. They published their results in the February 15th, 2005 issue of the journal *Biological Psychiatry*.

In order to test the substances, the researchers used a well known - and validated - model for depression in rats, known as the Forced Swim Test. Basically, rats are placed in water from which they can not escape. The rats will essentially swim for a period of time in an effort to get out of the water, but once they realize they can't get out, they only do what is necessary to stay afloat. When the rats are retested 24 hours later, they become immobile more quickly. When common antidepressants are given to the rats between the tests, they again try to escape for a longer period of time. This effect has shown to be correlated with antidepressant effects in people.

To test the uridine, a group of rats were injected with three different dosage levels between the two tests. To test the omega-3, a different group of rats were fed a special diet for 3, 10, or 30 days before the test. In addition, the researchers tested three existing antidepressants citalopram, desipramine, and fluoxetine.

The team found that both uridine and omega-3 showed antidepressant effects similar to the existing drugs (see Table 1). This was determined by measuring how long the rats swam in an attempt to escape before giving up, and also by recording the rats activity every 5 seconds and classifying it as swimming, climbing, diving, or immobile.

Table 1
Antidepressant Effect Seen In Rats At Different Dosages

	72 mg/kg 3 days	130 mg/kg 10 days	239mg/kg 30 days
Uridine	No	Yes	Yes
Omega-3	No	No	Yes

Note: Uridine was administered at three different dose levels; Omega-3 was given for 3 different time periods

Source: Carlezon WA Jr, Mague SD, Parow AM, Stoll AL, Cohen BM, Renshaw PF Antidepressant-like effects of uridine and omega-3 fatty acids are potentiated by combined treatment in rats. *Biol Psychiatry*. 2005 Feb 15;57(4):343-50.

boundary

mitochondria - part of a cell that produces energy

neuron - a nerve cell

neurotransmitter - a chemical which carries a signal, or message, from one neuron to another

norepinephrine - neurotransmitter which plays several roles and is involved in the stress response and mood disorders

omega 3 fatty acid - type of fatty acid found in fish oil, thought to have beneficial effects

phospholipid - a fat which contains phosphorus; make up a large part of the membranes of cells

serotonin - neurotransmitter which plays many roles and is involved in mood, appetite, aggression, body temperature and sleep

uridine - a naturally occurring substance found in many foods and is an important component in breastmilk

The uridine was effective at the two higher dose levels, and the omega-3 was effective only when it had been in the diet for 30 days. The lowest dose of uridine and the 3 and 10 day diets did not significantly alter the rats behavior.

Next, the researchers wanted to see how the two substances worked together, so they gave yet another group of rats levels of uridine and omega-3 which by themselves were too low to do anything. However, they found that in combination, even the low doses of the two substances had an antidepressant effect.

Although much more research is required to uncover how these natural substances work, Dr. Carlezon, in media interviews, has said that he believes they affect the mitochondria of the brain cells in a positive way; essentially enabling them to produce more energy.

As stated previously, omega-3 fatty acid can be found in fish, especially oily ones like salmon. Unfortunately, uridine, while present in low levels in many foods, is not found in high levels in any particular food, and there is not yet a uridine supplement on the market. Interestingly, uridine is a key component of breast milk, so maybe that's why babies are so happy after they nurse.

Editor's Note: *It should be pointed out that the scientists disclosed that one of the study authors has written a book about omega-3 and has a financial stake in a company which sells an omega-3 product. However, neither this author, nor the company in question, contributed financially to the study.*

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