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## Omega-3 and Bipolar Disorder

,\_ In May 1999, my colleagues and I published the first scientifically rigorous clinical trial of omega-3 fatty acids in psychiatry. In this four-month study, we observed that omega-3 fatty acids from fish oil improved and stabilized mood in a group of thirty patients with bipolar disorder, when compared to a matched group of bipolar patients who received a placebo. Finding safer and more effective treatments for my patients and the millions of other people with the fascinating and potentially deadly illness known as bipolar disorder (or manic-depressive illness) was the inspiration for the discovery.

### What Is Bipolar Disorder?

Bipolar disorder, also known as manic-depressive illness, is a common and sometimes lethal medical condition. Patients with bipolar disorder suffer from mania, a dangerous elevation of mood into euphoria and irritability, combined with high energy, impulsive and sometimes dangerous behaviors, and a constellation of other symptoms. These patients also often suffer from recurrent bouts of major depression of the sort described in the previous chapter.

### DSM-IV Criteria for Bipolar Disorder

#### I. Manic Episode

- A. A distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least one week (or any duration if hospitalization is necessary).
- B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:
  1. inflated self-esteem or grandiosity
  2. decreased need for sleep (e.g., feels rested after only three hours of sleep)
  3. more talkative than usual or pressure to keep talking
  4. flight of ideas or subjective experience that thoughts are racing
  5. distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
  6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
  7. excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)
- C. The symptoms do not meet criteria for a mixed episode.

D. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

E. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

Note: Manic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of bipolar I disorder.

## II. Hypomanic Episode

A. A distinct period of persistently elevated, expansive, or irritable mood, lasting at least four days that is clearly different from the usual nondepressed mood.

B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

1. inflated self-esteem or grandiosity
2. decreased need for sleep (e.g., feels rested after only three hours of sleep)
3. more talkative than usual or pressure to keep talking
4. flight of ideas or subjective experience that thoughts are racing
5. distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
6. increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation
7. excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments)

C. The episode is associated with an unequivocal change in functioning that is uncharacteristic of the person when not symptomatic.

D. The disturbance in mood and the change in functioning are observable by others.

E. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalization, and there are no psychotic features.

F. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

Note: Hypomanic-like episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of bipolar II disorder.

## III. Mixed Episode

A. The criteria are met both for a manic episode and for a major depressive episode (see Chapter 6) (except for duration) nearly every day during at least a one-week period.

B. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

C. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication, or other treatment) or a general medical condition (e.g., hyperthyroidism).

Note: Mixed episodes that are clearly caused by somatic antidepressant treatment (e.g., medication, electroconvulsive therapy, light therapy) should not count toward a diagnosis of bipolar I disorder.

In the full-blown disorder, periods of suicidal depression may alternate with episodes of mania, including euphoria, irritability, increased energy, decreased need for sleep, and racing thoughts accompanied by impulsive behaviors and grandiose ideas. Symptoms associated with anxiety disorders and even schizophrenia, including hallucinations and delusions, may occur during different phases of the illness. In short, bipolar disorder is a serious, disabling, and sometimes life-threatening brain illness that can include a variety of psychiatric symptoms.

## Current Treatments for Bipolar Disorder

The long-term treatment of patients with bipolar disorder relies on the so-called mood stabilizers, such as lithium and valproate. These often produce dramatically good results long term and have doubtless saved thousands of lives. However, in certain patients, serious side effects, the continuation of psychiatric symptoms despite the drugs, and refusal to take their medications were frequent results. This disappointing outcome of the medication treatment is frequently encountered in teaching hospitals like McLean and Brigham and Women's, where many of the patients have severe or treatment-resistant conditions.

Who could blame these people, and those who treat them medically, for being disappointed? As pointed out earlier, lithium has several disadvantages. Many patients who use it experience troublesome weight gain as well as tremors, excessive urination, drowsiness, and acne. A small percentage of its users are likely to develop thyroid and kidney problems. To many of the gifted people who are among its users, its most serious disadvantage is the decrease it brings about in creative energy. Lithium may keep manias within check, but it also flattens emotions. Moreover, many patients require combinations of several mood stabilizers simultaneously to control recurrent manias or depressions, and such combinations increase the risk of drug interactions and harmful side effects.

The search for a cure for bipolar disorder is as old as psychiatry, but it was not until 1949 that a series of accidents ushered in the first real pharmacological hope. Back then, John Cade, a thirty-seven-year-old psychiatrist and superintendent of the Repatriation Mental Hospital in Bundoora, Australia, speculated that mania was caused by a toxic substance manufactured in the body. To find it, he collected urine from his manic patients and, working in the hospital's abandoned pantry, injected it into the bellies of guinea pigs. When the guinea pigs all died, Cade decided to dilute the urine to reduce the toxic uric acid content, and try again. Reckoning (mistakenly) that adding the element lithium would aid in dissolving the uric acid, he tested lithium itself on the guinea pigs. Guinea pigs are known for their dramatic startle reaction when placed on their backs, but Cade's lithium-treated guinea pigs were remarkably placid.

Acting on a hunch, Cade decided to try lithium therapy on his patients, including ten with mania, six with schizophrenia, and three diagnosed with psychotic depression. The lithium did nothing for the depressed patients, but it calmed the schizophrenic patients—and its impact on those with mania was dramatic. All ten showed significant improvement, and five were able to leave the hospital pronounced well.