

Vitamin D and Depression

Is psychiatry that branch of medicine that can explain everything but predict nothing? No group of scientists is working harder to change that definition than those at the National Institute of Mental Health (NIMH).

Among the scientists at NIMH are many of the most famous names in psychiatry and some of my personal heroes. They know that nothing could be a crueler message than to tell those suffering from major depression that physiological amounts of vitamin D will cure it. Premature claims for a variety of nonprescription supplements have given suffering millions hopes that were soon dashed on the rocks of scientific reality. Even the supplements that may help such as [SAmE](#), omega-3/omega-6 intake ratios, or lowering homocysteine with adequate methylating B vitamins/[TMG](#) are not cure-alls.

Perhaps raising false hopes of curing an illness as devastating as major depression is not as serious as some of psychiatry's past crimes, such as telling mothers of schizophrenics that they caused their child's illness or using false recovered memories of sexual abuse to the destroy innocent families. That said, we must not raise false hopes. Nevertheless, what do we know about major depression and vitamin D?

Bright Light

We know that 15 years ago, Professor Walter E. Stumpf of the University of North Carolina, one of the great pioneers in vitamin D research, predicted a substantial role for both bright light and vitamin D in psychiatry. [Stumpf WE, Privette THLight, vitamin D and psychiatry. Role of 1,25 dihydroxyvitamin D3 \(soltriol\) in etiology and therapy of seasonal affective disorder and other mental processes.Psychopharmacology \(Berl\). 1989;97\(3\):285-94.](#)

Bright light in the visible spectrum (without any vitamin D producing [UVB](#)) clearly improves mood, although it is hard to conduct good studies due to the lack of a control condition. So the question is: does vitamin D have an effect on mood that differs from, or is complimentary to, the effect of bright light?

Seasonal Affective Disorder

Harris and Dawson-Hughes found 400 [IU](#) of [ergocalciferol](#) (vitamin D2) did not help the seasonal mood swings of 125 Boston women compared to placebo. [Harris S, Dawson-Hughes BSeasonal mood changes in 250 normal women.Psychiatry Res. 1993 Oct;49\(1\):77-87.](#) Such mood swings can be severe and are related to season, latitude and sun exposure. The authors did not obtain [25\(OH\)D levels](#) but we now know 400 IU of ergocalciferol is close to a homeopathic dose of vitamin D. We also know ergocalciferol is a significantly less potent form of vitamin D than is the naturally occurring vitamin D3, [cholecalciferol](#). One of the authors, Professor Dawson-Hughes, will be the first one to tell you 400 IU of ergocalciferol is an inadequate dose of vitamin D.

If you are thinking that Oren, Schulkin and Rosenthal have already shown that vitamin D has nothing to do with seasonal affective disorder, I am sorry to tell you they measured the wrong vitamin D metabolite, 1,25(OH)2D3 ([calcitriol](#)), which can be high, low, or normal in almost any condition. [Oren DA, Schulkin J, Rosenthal NE1,25\(OH\)2 vitamin D3 levels in seasonal affective disorder: effects of light.Psychopharmacology \(Berl\). 1994 Dec;116\(4\):515-6.](#) The only lab test that should be used to measure vitamin D stores, [vitamin D deficiency](#) and vitamin D adequacy is 25(OH)D, which they did not measure.

In a 1998 controlled experiment, Australian researchers found that cholecalciferol (400 and 800 IU), significantly enhanced positive affect when given to healthy individuals. Forty-four subjects were given 400 IU cholecalciferol, 800 IU cholecalciferol, or placebo for 5 days during late winter in a random double-blind study.

Results on a self-report measure showed that vitamin D3 enhanced positive affect a full standard deviation and there was some evidence of a reduction in negative affect. The authors concluded: "vitamin D3 deficiency provides a compelling and parsimonious explanation for seasonal variations in mood." [Lansdowne AT, Provost SC Vitamin D3 enhances mood in healthy subjects during winter. Psychopharmacology \(Berl\). 1998 Feb;135\(4\):319–23.](#)

In 1999, in an even more interesting study, the vitamin D scientist, [Bruce Hollis](#), teamed up with Michael Gloth and Wasif Alam to find that 100,000 IU of vitamin D given as a one time oral dose improved depression scales better than light therapy in a small group of patients with seasonal affective disorder. [Gloth FM 3rd, Alam W, Hollis B Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder. J Nutr Health Aging. 1999;3\(1\):5–7.](#) All subjects in the vitamin D group improved in all measures and, more importantly, improvement in [25\(OH\)D levels](#) levels was significantly associated with the degree of improvement.

German authors found healthy controls had an average serum 25(OH)D of 46 ng/L while depressed subjects had 37 ng/L. [Schneider B, Weber B, Frensch A, Stein J, Fritz J Vitamin D in schizophrenia, major depression and alcoholism. J Neural Transm. 2000;107\(7\):839–42.](#) Finnish authors found no seasonal differences between seasonal affective disorder patients and normal controls but also found no seasonal variations in 25(OH)D levels in the same patients. [Partonen T, Vakkuri O, Lamberg-Allardt C, Lonnqvist J Effects of bright light on sleepiness, melatonin, and 25-hydroxyvitamin D\(3\) in winter seasonal affective disorder. Biol Psychiatry. 1996 May 15;39\(10\):865–72.](#) Most recently, a direct correlation was found between 25(OH)D levels and mental health scores in a group of healthy, elderly adults—although 1,000 IU of cholecalciferol did not improve mental health scores of these highly-functional subjects. [Kenny AM, Biskup B, Robbins B, Marcella G, Burlison JA Effects of vitamin D supplementation on strength, physical function, and health perception in older, community-dwelling men. J Am Geriatr Soc. 2003 Dec;51\(12\):1762–7.](#)

Reduced Sunlight, Increasing Depression

To further strengthen the case that [vitamin D deficiency](#) causes some cases of depression, evidence should exist that the incidence of depression has increased over the last century. During that time, humans have reduced their sunlight exposure via urbanization (tall buildings and pollution reduce [UVB](#)), industrialization (working inside reduces UVB exposure), cars (glass totally blocks UVB), clothes (even light clothing blocks UVB), sunblock and misguided medical advice to never let sunlight strike you unprotected skin.

All these factors contribute to reduce circulating [25\(OH\)D levels](#). Klerman and Weissman's claim that major depression has increased dramatically over the last 80 years is one of the most famous (and controversial) findings in modern psychiatry. [Klerman GL, Weissman MM Increasing rates of depression. JAMA. 1989 Apr 21;261\(15\):2229–35.](#) Something called recall bias (a type of selective remembering) may explain some of the reported increase, but does it explain it all?

To learn more about increasing rates of mental illness over the last 2.5 centuries I recommend the incredible book, [The Invisible Plague: The Rise Of Mental Illness From 1750 To The Present](#), by E. Fuller Torrey—the scientist the Washington Post called "the most famous psychiatrist in America."

Which Came First?

Is depression associated with other conditions thought to be associated with vitamin D deficiency, such as heart disease, diabetes, hypertension, rheumatoid arthritis, cancer, or osteoporosis? [Zittermann A Vitamin D in preventive medicine: are we ignoring the evidence? Br J Nutr. 2003 May;89\(5\):552–72.](#) For example, there is a strong association between heart disease and depression, and countless theories to explain it. The obvious one—that heart disease would cause anyone to get depressed—is incorrect.

You see, depression often precedes the heart disease, suggesting a third factor causes both. Moreover, if depression were associated with heart disease, one would expect excess unexplained mortality in major depression, which is a well-established finding. [Rugulies R Depression as a predictor for coronary heart disease. a review and meta-analysis. Am J Prev Med. 2002 Jul;23\(1\):51–61. Cuijpers P, Smit F Excess mortality in depression: a meta-analysis of community studies. J Affect Disord. 2002 Dec;72\(3\):227–36.](#)

Remember that association does not mean causation. If A is associated with B, then A could cause B, B could cause A, or a third factor(s), C, could cause both A and B. Therefore, if heart disease is associated with depression then the possibilities are depression caused the heart disease, heart disease caused the depression, or an unknown factor(s), perhaps vitamin D deficiency, caused some portion of both the depression and the heart disease. "Perhaps" being the key word. Remember, most of the serious errors in psychiatry (and medicine) are made when associations are confused with causation; or when subsequence is confused with consequence.

Deficiency Diseases and Depression

What about other diseases associated with vitamin D deficiency? What explains the significant association between depression and diabetes, [Musselman DL, Betan E, Larsen H, Phillips LS Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. Biol Psychiatry. 2003 Aug 1;54\(3\):317–29.](#) hypertension, [Scherrer JF, Xian H, Buchholz KK, Eisen SA, Lyons MJ, Goldberg J, Tsuang M, True WRA twin study of depression symptoms, hypertension, and heart disease in middle-aged men. Psychosom Med. 2003 Jul–Aug;65\(4\):548–57.](#) rheumatoid arthritis, [Abdel-Nasser AM, Abd El-Azim S, Taal E, El-Badawy SA, Rasker JJ, Valkenburg HA Depression and depressive symptoms in rheumatoid arthritis patients: an analysis of their occurrence and determinants. Br J Rheumatol. 1998 Apr;37\(4\):391–7.](#) cancer, [Benedito Monleon MC, Lopez Andreu JA, Serra Estelles I, Harto Castano M, Gisbert Aguilar J, Mulas Delgado F, Ferris I Tortajada J Psychological sequelae in longterm cancer survivors. An Esp Pediatr. 2000 Dec;53\(6\):553–60.](#) advanced cancer, [Smith EM, Gomm SA, Dickens CMA Assessing the independent contribution to quality of life from anxiety and depression in patients with advanced cancer. Palliat Med. 2003 Sep;17\(6\):509–13.](#) pancreatic cancer, [Carney CP, Jones L, Woolson RF, Noyes R Jr, Doebbeling BN Relationship between depression and pancreatic cancer in the general population. Psychosom Med. 2003 Sep–Oct;65\(5\):884–8.](#) and decreased bone mineral density in women? [Yazici KM, Akinçi A, Sutcu A, Ozcakar L Bone mineral density in premenopausal women with major depressive disorder. Psychiatry Res. 2003 Mar 25;117\(3\):271–5.](#) [Coelho R, Silva C, Maia A, Prata J, Barros HB Bone mineral density and depression: a community study in women. J Psychosom Res. 1999 Jan;46\(1\):29–35.](#) [Michelson D, Stratakis C, Hill L, Reynolds J, Galliven E, Chrousos G, Gold P Bone mineral density in women with depression. N Engl J Med. 1996 Oct 17;335\(16\):1176–81.](#)

The [abstract](#) of our favorite study showing the association between depression and bone mineral density concludes with the following sentence: "We postulate that there may be an unmeasured third factor, such as an endogenous steroid, that is responsible for both low [BMD](#) and depression." The paper says not a word about the steroid hormone, vitamin D.

Therefore, heart disease, hypertension, diabetes, rheumatoid arthritis, cancer and low bone mineral density are all associated with depression. One parsimonious explanation is that vitamin D deficiency causes some portion of all these illnesses. Remember, all these diseases are multifactorial, so we are only talking about the percentage of the illness possibly caused by vitamin D deficiency. See Zittermann for the best review of diseases associated with vitamin D deficiency. [Zittermann A Vitamin D in preventive medicine: are we ignoring the evidence? Br J Nutr. 2003 May;89\(5\):552–72.](#)

Does Vitamin D Affect The Brain?

Vitamin D rapidly increases the in-vitro genetic expression of tyrosine hydroxylase (the rate-limiting enzyme for the catecholamine biosynthesis) by threefold. [Puchacz E, Stumpf WE, Stachowiak EK, Stachowiak MK. Vitamin D increases expression of the tyrosine hydroxylase gene in adrenal medullary cells. Brain Res Mol Brain Res. 1996 Feb;36\(1\):193-6.](#)

Summer sunlight increases brain serotonin levels twice as much as winter sunlight, a finding compatible with both bright light in the visible spectrum and vitamin D affecting mood. [Lambert GW, Reid C, Kaye DM, Jennings GL, Esler M. Effect of sunlight and season on serotonin turnover in the brain. Lancet. 2002 Dec 7;360\(9348\):1840-2.](#)

Vitamin D is widely involved in brain function with nuclear receptors for vitamin D localized in neurons and glial cells. Genes encoding the enzymes involved in the metabolism of vitamin D are expressed in brain cells. The reported biological effects of vitamin D in the nervous system include the biosynthesis of neurotrophic factors, inhibition of the synthesis of inducible nitric oxide synthase and increased glutathione levels, suggesting a role for the hormone in brain detoxification pathways. [Garcion E, Wion-Barbot N, Montero-Menei CN, Berger F, Wion D. New clues about vitamin D functions in the nervous system. Trends Endocrinol Metab. 2002 Apr;13\(3\):100-5.](#)

Evidence suggests that vitamin D may help mood but that evidence is not conclusive. (Remember, the way our medical literature system works, scientists often do not publish negative studies). The two positive studies above used vitamin D to treat seasonal affective disorder, not major depression. We were unable to find any studies in the literature in which patients with depression were treated with enough natural sunlight, artificial sunlight or plain old cholecalciferol to raise their levels to 35 ng/mL or higher. We all know how we feel after a week at the beach, but is that bright light, vitamin D, or something else?

Evidence exists that major depression is associated with low vitamin D levels and that depression has increased in the last century as vitamin D levels have surely fallen. Evidence exists that depression is associated with heart disease, hypertension, diabetes, rheumatoid arthritis, cancer and low bone mineral density, all illnesses thought to be caused, in part, by vitamin D deficiency. Finally, vitamin D has profound effects on the brain including the neurotransmitters involved in major depression.

Further Research Needed

Therefore, vitamin D may help major depression. It is too early to say. To know for sure, patients with severe major depression would have to have baseline 25(OH)D blood levels, be treated with doses of vitamin D adequate to raise their levels to at least 35 ng/mL for several months and be compared to a normal control group treated with placebo. No one has ever published such a study.

However, it is not too early to heed the following advice: If you suffer from depression, get your 25(OH)D level checked and, if it is lower than 35 ng/mL (87 nM/L), you are vitamin D deficient and should begin [treatment](#). If you are not depressed, get your 25(OH)D level checked anyway. If it is lower than 35 ng/mL (87 nM/L), you are vitamin D deficient and should begin treatment.

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<http://www.vitamindcouncil.org/depression.shtml>