

# THE RELATIONSHIP BETWEEN VITAMIN D DEFICIENCY WITH DEPRESSION AND ADDICTION: REVIEW ARTICLE

*Ahed J Al Khatib*

*Wafa Samih Rawashdeh*

Jordan University of Science and Technology

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## Abstract

The present review article brings current understanding of the relationship between vitamin D, depression and addiction. An overview of vitamin D was introduced. Depression was described in details. Addiction was also reviewed in details. Although the relationship between vitamin D and depression is controversial, but it seems that a minimal concentration of vitamin D is required to overcome depression. Taken together, this study collected appropriate literature to cover various parts of the topics.

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**Keywords:** Depression, addiction, vitamin D

## Vitamin D Overview

There are two forms including vitamin D2 (ergocalciferol), which is derived from plants and often added to foods, on the other vitamin D3 (cholecalciferol) is synthesized from 7-dehydrocholesterol in the skin (Ross et al., 2010). Various studies have indicated that D2 and D3 to be functionally equivalent, and the difference is that vitamin D2 is less stable than D3, at least in animal studies (Ross et al., 2010).

Once in the circulation, either form of vitamin D is hydroxylated to 25(OH) D in the liver and then by 1-alpha-hydroxylase in the kidney, which results in 1,25(OH)2D, known as calcitriol. Unlike 25(OH)D levels that vary markedly depending on dietary intake and sun exposure, 1,25(OH)2D levels are tightly regulated (Ross et al., 2010).

Vitamin D deficiency has prevalence rate from one third to one half of adults (Hoogendijk et al., 2008). The deficiency of vitamin D has been traditionally linked to musculoskeletal disorders and then the situation has been expanded to be included in optimal functioning of many body organs and tissues (DeLuca , 2004; Holick, 2004) .

## **Vitamin D deficiency and Depression**

The relationship between vitamin D and depression has been investigated in several studies. Wilkins et al (2006) examined a group of elderly subjects and found mean Vitamin D levels of 18.6 nM/L, with 58% of subjects being frankly deficient, defined as a level below 20 nM/L. furthermore, low vitamin D was robustly associated with the presence of mood disorder (odds ratio 11.7, 95% CI 2.0–66.9). In his study, Armstrong et al (2006) found that Vitamin D deficiency to be associated with depression and anxiety in a cohort of individuals with fibromyalgia. Schneider et al (2000) found lower levels of 25-hydroxyvitamin D<sub>3</sub> and 1,25-dihydroxyvitamin D in patients with schizophrenia (N = 34), depression (N = 25) and alcoholism (N = 30) compared to healthy controls (N = 31). In another study, Gloth et al (1999) conducted a study and randomized eight subjects with seasonal affective disorder to receive 100,000 IU of vitamin D and seven subjects to receive phototherapy. Results indicated that vitamin D, but not phototherapy was associated with improvement in depression measures.

## **Depression**

Depression, as defined by Salmans and Sandra (1997), is a condition or state characterized by low mood and aversion to activity that can affect a person's thoughts, behavior, feelings and sense of well-being.

There are many depressive feeling including sadness, anxious, , empty, hopeless, worried, helpless, worthless, guilty, irritable, hurt, or restless. Furthermore, depressed people may lose interest in activities that once were pleasurable, loss of appetite or overeating, have problems concentrating, remembering details, or making decisions, and may contemplate, attempt, or commit suicide. Insomnia, excessive sleeping, fatigue, loss of energy, or aches, pains, or digestive problems may also be present (NIMH, 2012). Depressed mood is not always due to psychiatric diseases. It may also be a normal reaction to certain life events, a symptom of some medical conditions, or a side effect of some drugs or medical treatments. Depressed mood is also a primary or associated feature of certain psychiatric syndromes such as clinical depression (NIMH, 2012)..

## **Causes of depression**

### **Life events**

Life events and changes that may lead to depressed mood include childbirth, menopause, financial difficulties, job problems, a medical diagnosis (cancer, HIV, etc.), bullying, loss of a loved one, natural disasters, social isolation, relationship troubles, jealousy, separation, and catastrophic injury (Schmidt and Peter, 2005; Rashid and Heider, 2008).

Traumatizing events that took place in childhood can cause depression. Although childhood trauma and particularly child sex abuse is not always a factor of adulthood depression, it may create psychological pathways that can lead to depression. Research has been done in this field to demonstrate the chemical involvements explaining this phenomenon (Jonathan, 2003; Christine et al., 2008). According to the study of Pillemer et al (2010), one of the risk factors for depression is unequal treatment of parents.

### **Medical treatments**

It has been noted that there are certain medications that have the ability to induce depressed mood in a significant number of patients including interferon therapy for hepatitis C (Ehret and Sobieraj, 2014).

### **Non-psychiatric illnesses**

Depressed mood has been shown to be caused by a number of infectious diseases, neurological conditions (Murray, Buttner, Price, 2012) and physiological problems including hypoandrogenism (in men), Addison's disease, Lyme disease, multiple sclerosis, chronic pain, stroke (Saravane et al., 2009), diabetes (Rustad, Musselman, Nemeroff, 2011), cancer, sleep apnea, and disturbed circadian rhythm (Fitzgerald and Rodin, 2012).

### **Psychiatric syndromes**

A group of psychiatric syndromes are known to attribute to depressed mood as a main symptom and include major depressive disorder (MDD; commonly called major depression or clinical depression) in which a person has at least two weeks of depressed mood or a loss of interest or pleasure in nearly all activities; and dysthymia, a state of chronic depressed mood, the symptoms of which do not meet the severity of a major depressive episode. Another mood disorder, bipolar disorder, features one or more episodes of abnormally elevated mood, cognition and energy levels, but may also involve one or more depressive episodes (American Psychiatric Association, 2000; Gabbard and Glen, 2005; Vieweg et al., 2006). It is worth mentioning that if the course of depressive episodes follows a seasonal pattern, the disorder (major depressive disorder, bipolar disorder, etc.) may be described as a seasonal affective disorder.

### **Assessment**

Depression or the severity of its symptoms can be measured through certain tools for assessment including the Beck Depression Inventory and Children's Depression Inventory test for depression and/or depressive symptoms (Kovacs, 1992).

## **Treatment**

In general, depressed mood may not need professional treatment since it may reflect a normal reaction to certain life events, a symptom of some medical conditions, or a side effect of some drugs or medical treatments. In case there is a prolonged depressed mood, particularly in combination with other symptoms, which may lead to a diagnosis of a psychiatric or medical condition so that patients can benefit from treatment (Cheog, 2014).

According to a study of Khan et al (2012), it is important to reach an accurate diagnosis of major depressive disorder to initiate the treatment. Furthermore, Craft and Perna (2004) reported that moderate levels of physical activity can treat depression by increasing the levels of endorphins and the neurotransmitters serotonin, dopamine, and norepinephrine. Furthermore, it has been indicated that exercise improves the health of individuals while building new relationships with others and bolstering the sense of community that comes with exercising as a group (Skrinar et al., 1992; Pelham and Campagna, 1993). The authors have also expressed their observations in which group activities can reduce depression by increasing depressed individuals' ability to interact with others. Exercise has also been found to increase individuals' self-confidence by encouraging social skills that people with depression often lack and interrupts the cycle of isolation from the general population that can further increase depression. Exercise has another advantage in which it fosters non-demanding behaviors while allowing people to socialize and identify themselves as part of the general population (Skrinar et al., 1992; Pelham and Campagna, 1993).

Depression can also be treated through lifestyle strategies that may improve depressed mood include wake therapy, light therapy, eating a healthy diet, meditation, exercise, and smoking cessation (Praschak-Rieder et al., 1999; Even et al., 2008; Madhav et al., 2014; Taylor et al., 2014).

## **Social**

According to Podgornik (2012), women are generally more likely to have depression which is plausible to due to gender roles and norms associated with those roles. Women are expected and required to care for family and friends, but they lack strong, stable supportive relationships and accordingly they are more susceptible to depressive symptoms.

## **Addiction**

Addiction can be defined as the continued repetition of a behavior despite adverse consequences, or a neurological impairment leading to such behaviors (Angres and Bettinardi-Angres, 2008; American Society for Addiction Medicine, 2012 ).

Addictions are widely classified and can include drug abuse, exercise addiction, food addiction, computer addiction and gambling. Classic characteristics of addiction include impaired control over substances or behavior, preoccupation with substance or behavior, continued use despite consequences, and denial (Morse and Flavin, 1992). Habits and patterns associated with addiction are typically characterized by immediate satisfaction (short-term reward), coupled with delayed deleterious effects (long-term costs) (Marlatt et al., 1998).

According to Torres and Horowitz (1999), physiological dependence occurs when the body has to adjust to the substance by incorporating the substance into its "normal" functioning. This state creates the conditions of tolerance and withdrawal. Tolerance is the process by which the body continually adapts to the substance and requires increasingly larger amounts to achieve the original effects. Withdrawal refers to physical and psychological symptoms experienced when reducing or discontinuing a substance that the body has become dependent on. Symptoms of withdrawal generally include but are not limited to anxiety, irritability, intense cravings for the substance, nausea, hallucinations, headaches, cold sweats, and tremors.

### **Biological mechanisms explaining addiction**

Various studies agree about the biological mechanisms are present beyond addiction. It has been indicated that many variables are present, but researchers expressed variations about among which are the primary contributing factors. There has been a debate in which the biological "nature" of individual innate qualities can be in relation for many decisions and actions, such as a family history in which genetics, DNA, and other mental disorders remain latent for generations and then are triggered (Tsuang et al., 1998).

The risk of a future addictive disorder has been suggested to greatly increase if an individual gets exposed to repeated stress or engages in drug abuse during adolescence due to it being a critical neuro-developmental stage which is sensitive to such experiences or insults. The reason that stress and substance abuse during adolescence increases the risk of addiction is due to the changes it does to the brain (Crews and Vetreno, 2011).

It has been shown that Several brain regions are also involved in the biological mechanisms of addiction. Most notably, the release of dopamine into the nucleus accumbens, which is triggered by a wide variety of drugs in a wide variety of ways, plays a role in the reinforcing qualities of stimuli (Salamone, 1992). It has been suggested to have a role for dopamine because its secretion is also characteristic of natural reinforcing stimuli such as food, water, and sex. Accordingly, it's evident that the addictive nature of drug

involves processes that capture these mechanisms. Furthermore, it has been found that this process begins in the limbic dopaminergic system and subsequently modifies other parts of the brain that receive input from the affected neurons. Among these areas is the ventral tegmental area (Kauer and Malenka, 2007).

Belin and Everitt (2008) clarified some biological mechanisms including the insertion of extra  $\alpha$ -Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors into the postsynaptic membrane of the DA neurons. Studies conducted in mice indicate that exposure to cocaine for two weeks can cause long-term changes in the ventral tegmental area. They also found that the pleasurable effects of the drug reinforce the behaviors associated with acquiring and ingesting the drug until they become a habit. Early on, this process takes place largely in the ventral striatum, specifically in the nucleus accumbens but eventually, these changes primarily involve the dorsal striatum. Further studies suggest that the neuronal modifications involved in addiction follow a dorsally cascading sequence of reciprocal connections between the two aforementioned areas.

Various studies have targeted the changes that happen in the nucleus accumbens and in the dorsal striatum including alterations in the dopamine receptors on the neurons which send axons to other areas. Dopamine D1 receptors were found to increase which, in turn, results in excitation and facilitation of behavior. On the other hand, dopamine D2 receptors were found to lessen, resulting in inhibited and suppressed behavior. It has been found that certain drug use has the ability to affect acetylcholinergic interneurons which, though few in number, exert their influence on medium spiny neurons in the nucleus accumbens (Witten, Lin, Brodsky, 2010). In conclusion, the release of dopamine in the nucleus accumbens results in the early stages of drug addiction. It has been shown that subsequent impairments in regions such as the dorsal striatum attribute to the formation of actual drug-taking habitual behaviors. According to this context, it is possible to explain why drug addicts are prompted to obtain the drug and consume it when environmental cues associated with drug-taking are present but become withdrawn and sad when participating in drug-free activity (Volkow, Wang, Fowler, 2011).

According to a study of Tarter et al (2003), regarding to initial use and drug addiction, different factors can play a role in determining one's predisposition. Furthermore, the prefrontal cortex, which has bearing on judgement, risk taking, and impulse control, may be complicit in explaining why adolescents are more prone to drug-taking behavior. In fact, some studies have demonstrated that children, as young as ten to twelve years old, who score lowest on measures of behavioral inhibition displayed the highest risks of developing substance addiction.

## **The Relationship between Vitamin D and Depressive Disorders**

As previously mentioned, the seasonal changes of vitamin D and the numerous CNS actions of calcitriol make vitamin D a key player to explain seasonal mental health problems.

Several studies across literature have investigated the relationship between SAD and phototherapy and raised the question of light wavelength and the proposed role of vitamin D. The studies reached to conclusions that UV light does not have that efficacy in addition to the noninvolvement of vitamin D (Oren, Schulkin, Rosenthal, 1994; Lee et al., 1997). According to this context, phototherapy research worked to filter UV light away and because the patients may be fully covered which leads to formation of negligible amounts of vitamin D (Partonen et al., 1996).

Lansdowne and Provost (1998) conducted a double-blind study and found that vitamin D<sub>3</sub> led to a more positive mood in healthy individuals during winter. In another study by Gloth 3<sup>rd</sup>, Aalam, and Hollis (1999) in which the authors compared vitamin D and light therapy, the results showed that among 15 SAD patients, 100,000 IU of vitamin D was more effective than 3 weeks of light therapy. The reduction of depression was explained by increasing of 25-OHD. These findings were on line with another study conducted by Shipowick et al (2009) who studied six patients, treated in winter with vitamin D 5000 IE/day. The results showed that among the 6 patients, 3 patient reached a final vitamin D level above 100 nmol/l responded while the others did not. The results of other two larger studies did not prove the efficacy of vitamin D, and this is expected to be resulted from using lower doses of vitamin D (400–800 IE/day). Accordingly, it is plausible to think that participants were unlikely to reach the necessary blood levels (Harris and Dawson-Hughes, 1993; Dumville et al., 2006). Two European studies proved the relation between lower levels of vitamin D and depressed mood irrespective of season (Jorde et al., 2006). On the other hand, a study on Chinese population did not support the relationship between vitamin D and depression (Pan et al., 200).

The results of 4 clinical studies on patients diagnostic with psychiatric diseases, including major depression indicated that vitamin D levels in general were lower than control groups with similar range (mean/median 40–50 nmol/l) for depressed patients (Berk et al., 2007, 2008; Schneider et al., 2007; Humble, Gustafsson, Bejero, 2010).

Taken together, the previous findings gave a support, but did not confirm the hypothesis that low availability of vitamin D could cause a substantial proportion of depressive disorders.

## References:

- A. Pan, L. Lu, O.H. Franco, Z. Yu, H. Li, X. Lin (2009). Association between depressive symptoms and 25-hydroxyvitamin D in middle-aged and elderly Chinese, *J. Affect. Disord.* 118, 240–243.
- A.T. Lansdowne, S.C. Provost (1998). Vitamin D3 enhances mood in healthy subjects during winter, *Psychopharmacology (Berl.)* 135, 319–323.
- Aging* 3, 5–7
- American Psychiatric Association (2000). *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision: DSM-IV-TR.* Washington, DC: American Psychiatric Publishing, Inc. ISBN0-89042-025-4.
- American Society for Addiction Medicine (2012., <http://www.asam.org/for-the-public/definition-of-addiction>).
- Angres DH, Bettinardi-Angres K (2008). The disease of addiction: origins, treatment, and recovery. *Dis Mon* 54 (10): 696–721.
- Armstrong DJ, Meenagh GK, Bickle I, Lee AS (2006). Curran ES, Finch MB. Vitamin D deficiency is associated with anxiety and depression in fibromyalgia. *Clin Rheumatol* 26(4):551-4.
- B. Schneider, B. Weber, A. Frensch, J. Stein, J. Fritz (2000). Vitamin D in schizophrenia, major depression and alcoholism, *J. Neural Transm.* 107, 839–842.
- Belin, D.; B.J. Everitt (2008). Cocaine Seeking habits depend upon dopamine-dependent serial connectivity linking the ventral with the dorsal striatum. *Neuron*, (57): 432–441.
- C.D. Shipowick, C.B. Moore, C. Corbett, R. Bindler (2009). Vitamin D and depressive symptoms in women during the winter: a pilot study, *Appl. Nurs. Res.* 22, 221–225.
- Cheog J et al. for PsychCentral.com. Frequently Asked Questions About Depression. [http://psychcentral.com/library/depression\\_faq.htm](http://psychcentral.com/library/depression_faq.htm). Retrieved on 27/6/2014.
- Christine Heim; D. Jeffrey Newport; Tanja Mletzko; Andrew H. Miller; Charles B. Nemeroff (2008). The link between childhood trauma and depression: Insights from HPA axis studies in humans *Psychoneuroendocrinology* 33 (6): 693–710.
- Craft LL, Perna FM (2004). The benefits of exercise for the clinically depressed. *Prim Care Companion J Clin Psychiatry* 6:104–111.
- Crews, FT.; Vetreno, RP. (2011). Addiction, adolescence, and innate immune gene induction. *Front Psychiatry* 2: 19. doi:10.3389/fpsyt.2011.00019. PMID 2162983.
- D.A. Oren, J. Schulkin, N.E. Rosenthal (1994). 1,25 (OH)<sub>2</sub> vitamin D3 levels in seasonal affective disorder: effects of light, *Psychopharmacology (Berl.)* 116, 515–516.

- DeLuca H (2004). Overview of general physiologic features and functions of vitamin D. *Am J Clin Nutr*, 80 (6, Suppl):1689S-96S.
- Ehret M, Sobieraj DM (2014). Prevention of interferon-alpha-associated depression with antidepressant medications in patients with hepatitis C virus: a systematic review and meta-analysis. *Int. J. Clin. Pract.* 68 (2): 255–61.
- Even, C; Schröder CM; Friedman S; Rouillon F (2008). Efficacy of light therapy in nonseasonal depression: a systematic review. *J Affect Disord*: 11–23.
- F.M. Gloth 3rd, W. Alam, B. Hollis (1999). Vitamin D vs. broad spectrum phototherapy in the treatment of seasonal affective disorder, *J. Nutr. Health*.
- Gabbard, Glen O (2005). *Treatment of Psychiatric Disorders 2* (3rd ed.). Washington, DC: American Psychiatric Publishing. p. 1296.
- Gloth 3rd FM, Alam W, Hollis B (1999). Vitamin D vs broad spectrum phototherapy in the treatment of seasonal affective disorder. *J Nutr Health Aging*, 3(1):5–7.
- Holick MF (2004). Sunlight and vitamin D for bone health and prevention of autoimmune disease, cancers, and cardiovascular disease. *Am J Clin Nutr*, 80(6, Suppl):1678S-88S.
- Hoogendijk WJG, Lips P, Dik MG, et al (2008). Depression is associated with decreased 25-hydroxyvitamin D and increased parathyroid hormone levels in older adults. *Arch Gen Psychiatry*, 65:508-12.
- J.C. Dumville, J.N. Miles, J. Porthouse, S. Cockayne, L. Saxon, C. King (2006). Can vitamin D supplementation prevent winter-time blues? A randomised trial among older women, *J. Nutr. Health Aging* 10, 151–153.
- Jonathan Hill (2003). Childhood trauma and depression *Current Opinion in Psychiatry* 16 (1): 3–6.
- Kauer, J.A.; R.C. Malenka (2007). Synaptic plasticity and addiction. *Nature Reviews Neuroscience* (8): 844–858.
- Khan, Arif; James Faucett; Pesach Lichtenberg; Irving Kirsch; Walter A. Brown (2012). A Systematic Review of Comparative Efficacy of Treatments and Controls for Depression. *PLoS ONE* 7 (7): e41778. doi:10.1371/journal.pone.0041778. PMC 3408478. PMID 22860015.
- Kovacs, M. (1992). *Children's Depression Inventory*. North Tonawanda, NY: Multi-Health Systems, Inc.
- Li, M; Fitzgerald, P; Rodin, G (2012). Evidence-based treatment of depression in patients with cancer. *Journal of clinical oncology: official journal of the American Society of Clinical Oncology* 30 (11): 1187–96.
- M. Berk, F.N. Jacka, L.J. Williams, F. Ng, S. Dodd, J.A. Pasco (2008). Is this D vitamin to worry about? Vitamin D insufficiency in an inpatient sample, *Aust. NZ J. Psychiatry* 42, 874–878.

- M. Berk, K.M. Sanders, J.A. Pasco, F.N. Jacka, L.J. Williams, A.L. Hayles, S. Dodd (2007). Vitamin D deficiency may play a role in depression, *Med. Hypotheses* 69, 1316–1319.
- M.B. Humble, S. Gustafsson, S. Bejerot (2010). Low serum levels of 25-hydroxyvitamin D (25-OHD) among psychiatric out-patients in Sweden: relations with season, age, ethnic origin and psychiatric diagnosis, *J. Steroid Biochem. Mol. Biol.* 121, 467–470.
- Madhav, Goyal; Sonal Singh, Erica M. S. Sibinga, Neda F. Gould, Anastasia Rowland-Seymour, Ritu Sharma, Zackary Berger, Dana Sleicher, David D. Maron, Hasan M. Shihab, Padmini D. Ranasinghe, Shauna Linn, Shonali Saha, Eric B. Bass, Jennifer A. Haythornthwaite (2014). "Meditation Programs for Psychological Stress and Well-being". *JAMA Intern Med* 174 (3): 357–68. doi:10.1001/jamainternmed, 13018. PMID 24395196.
- Marlatt GA, Baer JS, Donovan DM, Kivlahan DR (1988). Addictive behaviors: etiology and treatment. *Annu Rev Psychol* 39: 223–52.
- Morse RM, Flavin DK (1992). "The definition of alcoholism. The Joint Committee of the National Council on Alcoholism and Drug Dependence and the American Society of Addiction Medicine to Study the Definition and Criteria for the Diagnosis of Alcoholism". *JAMA* 268 (8): 1012–4.
- Murray ED, Buttner N, Price BH (2012). Depression and Psychosis in Neurological Practice. In: *Neurology in Clinical Practice*, 6th Edition. Bradley WG, Daroff RB, Fenichel GM, Jankovic J (eds.) Butterworth Heinemann.
- NIMH · Depression". [nimh.nih.gov](http://nimh.nih.gov). Retrieved 15 October 2012.
- Pelham, Campagna (1993). The effects of exercise therapy on clients in a psychiatric rehabilitation program. *Psychosocial rehabilitation Journal*, 16(4) 75-84.
- Pillemer, Karl; Suitor, J. Jill; Pardo, Seth; Henderson Jr, Charles (2010). Mothers' Differentiation and Depressive Symptoms Among Adult Children". *Journal of Marriage and Family* 72 (2): 333–345.
- Podgornik, N (2012). Depression - a sociocultural way of manifesting women's psychological crises, *Anthropological notebooks*, 18 (2): 55-67.
- Praschak-Rieder, N; Willeit M; Neumeister A; Hilger E; Kasper S (1999). Therapeutic sleep deprivation and phototherapy". *Wien Med Wochenschr*: 520–524.
- R. Jorde, K. Waterloo, F. Saleh, E. Haug, J. Svartberg (2006). Neuropsychological function in relation to serum parathyroid hormone and serum 25- hydroxyvitamin D levels. The Tromsø study, *J. Neurol.* 253, 464–470.
- Rashid, T., Heider, I. (2008). Life Events and Depression. *Annals of Punjab Medical College* 2 (1). Retrieved 15 October 2012.

- Ross AC, Taylor LC, Yaktine LA, and Heather B. Del Valle (eds) (2010). Committee to Review Dietary Reference Intakes for Vitamin D and Calcium. Washington, DC, Institute of Medicine.
- Rustad, JK; Musselman, DL; Nemeroff, CB (2011). The relationship of depression and diabetes: Pathophysiological and treatment implications. *Psychoneuroendocrinology* 36 (9): 1276–86.
- S. Harris, B. Dawson-Hughes (1993). Seasonal mood changes in 250 normal women, *Psychiatry Res.* 49, 77–87.
- Salamone, J.D. (1992). Complex motor and sensorimotor function of striatal and accumbens dopamine: Involvement in instrumental behavior processes. *Psychopharmacology*, (107): 160–174.
- Salmans, Sandra (1997). *Depression: Questions You Have – Answers You Need*. People's Medical Society. ISBN 978-1-882606-14-6.
- Saravane, D; Feve, B; Frances, Y; Corruble, E; Lancon, C; Chanson, P; Maison, P; Terra, JL et al. (2009). Drawing up guidelines for the attendance of physical health of patients with severe mental illness. *L'Encephale* 35 (4): 330–9.
- Schmidt, Peter (2005). Mood, Depression, and Reproductive Hormones in the Menopausal Transition. *The American Journal of Medicine*. 118 (12): 54–8.
- Schneider B, Weber B, Frensch A, Stein J, Fritz J (2000). Vitamin D in schizophrenia, major depression and alcoholism. *J Neural Trans*, 107(7):839–42.
- Skrinar et al (1992). Fitness: a viable adjunct to treatment for young adults with psychiatric disabilities. *Psychosocial Rehabilitation Journal*, 15(3):20–28.
- T. Partonen, O. Vakkuri, C. Lamberg-Allardt, J. Lönnqvist (1996). Effects of bright light on sleepiness, melatonin, and 25-hydroxyvitamin D(3) in winter seasonal affective disorder, *Biol. Psychiatry* 39, 865–872.
- T.M. Lee, C.C. Chan, J.G. Paterson, H.L. Janzen, C.A. Blashko (1997). Spectral properties of phototherapy for seasonal affective disorder: a meta-analysis, *Acta Psychiatr. Scand.* 96, 117–121.
- Tarter, R. E.; L. Kirisci; A. Mezzich; J. R. Cornelius (2003). Neurobehavioral disinhibition in childhood predicts early age at onset of substance use disorder. *American Journal of Psychiatry* (160): 1078–1085.
- Taylor, Gemma; Ann McNeill; Alan Girling; Amanda Farley; Nicola Lindson-Hawley; Paul Aveyard (2014). Change in mental health after smoking cessation: systematic review and meta-analysis. *BMJ* 348: g1151. doi:10.1136/bmj.g1151. PMC 3923980. PMID 24524926.
- Torres G, Horowitz JM (1999). Drugs of abuse and brain gene expression. *Psychosom Med* 61 (5): 630–50.

Tsuang, M. T.; M. J. Lyons; J. M. Meyer; T. Doyle (1998). Co-occurrence of abuse of different drugs in men: The role of drug-specific and shared vulnerabilities. *Archives of General Psychiatry*, (55): 967–972.

Vieweg, W. V.; Fernandez, D. A.; Beatty-Brooks, M; Hetteema, J. M.; Pandurangi, A. K.; Pandurangi, Anand K. (2006). "Posttraumatic Stress Disorder: Clinical Features, Pathophysiology, and Treatment". *Am. J. Med.* 119 (5): 383–90.

Volkow, N. D.; G.-J Wang; J. S. Fowler (2011). Addiction: Beyond dopamine reward circuitry. *Proceedings of the National Academy of Science* (108): 15037–15042.

Wilkins CH, Sheline YI, Roe CM, Birge SJ, Morris JC (2006). Vitamin D deficiency is associated with low mood and worse cognitive performance in older adults. *Am J Geriatr Psychiatry*, 14(12):1032–40.

Witten, I; S.-C. Lin; M Brodsky (2010). Cholinergic interneurons control local circuit activity and cocaine conditioning. *Science* (330): 1677–1681.