

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

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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.

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 D₃ 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 α -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 D₃ led to a more positive mood in healthy individuals during winter. In another study by Gloth 3rd, 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.

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