INTERVENTION INSIGHTS

Vitamin D: is it relevant to psychiatry?

A wide array of factors contribute to the generation and progression of psychiatric disorders. Many of these are well known, and individually they contribute a small share of the variance of the aetiology. A key issue is if a factor is modifiable, although risk factors such as prior trauma and genetics are major contributors to the variance, they are not easily reversed. Pragmatically, those factors that are potentially reversible are more relevant as intervention targets; at a population level, a small proportion of variance translates to a significant number of cases. Vitamin D may be such a factor.

Vitamin D is the only vitamin that is widely deficient in Western populations (1,2). It is unique in requiring ultraviolet light for synthesis, with low levels being found in only a few foods (3). Although, it is now not uncommon to find foods fortified with vitamin D. There is a notable seasonal variation in levels of serum 25-hydroxyvitamin D [(25-OHD), the major circulating form], corresponding with ambient daylight (2,4). In an epidemiological study of women, the prevalence of deficiency measured at the strictest cut-off for low serum 25-OHD (<28 nmol/l) was 7.2%, while 30% had insufficient levels (<30 nmol/l). This was most marked in the elderly with 53% above the age of 80 having vitamin D insufficiency (2). Even higher rates of vitamin D insufficiency are seen in cohorts of psychiatric patients. In one study, 58% had levels considered insufficient and 11% were moderately deficient (5).

An association between Vitamin D deficiency and low mood in the elderly has been documented (odds ratio 11.7, 95% CI 2.04–66.86) (6). In a cohort of people with fibromyalgia, vitamin D deficiency was associated with both depression and anxiety (7). A similar pattern was seen in patients with schizophrenia, depression and alcoholism compared to healthy controls (8). In people with secondary hyperparathyroidism, low serum 25-OHD was associated with higher depression scores (9). Vitamin D may be a mediator of the relationship between the well-described seasonal change in photoperiod and seasonality of mood. A reduction in the photoperiod, and thus capacity to synthesise vitamin D may be a critical factor in seasonal depression (10).

Vitamin D is relevant to other psychiatric disorders, particularly schizophrenia. Findings from epidemiological studies that support this linkage include higher rates of schizophrenia among offspring of mothers giving birth in winter, higher rates of schizophrenia in dark-skinned migrants to cold climates, higher rates of schizophrenia births in urban compared to rural settings and the reported link between prenatal famine and schizophrenia (11). Maternal deficiency in the prenatal period is consequently thought to be a vulnerability factor. Supporting this notion, a study of vitamin D supplementation in 9114 participants, administered during the first year of life was associated with a reduced risk of schizophrenia in men (12).

Neurodevelopmental studies shed some light on the possible underlying mechanisms. The vitamin D receptor is present in a variety of brain regions, including those intimately implicated in psychopathology, including the hippocampus, and the white matter of the striatum and corpus callosum (13). Maternal vitamin D3 deficiency in rats led to an abnormal brain shape in pups, who also had an increased number of mitotic cells, lower levels of nerve growth factor, reduced glial cell line-derived neurotrophic factor and reduced low-affinity neurotrophin receptor compared with controls (14). Vitamin D is neuroprotective, playing a key role in hippocampal cell survival. Vitamin D is important in cellular homeostasis, having a role in calcium buffering mechanisms, the regulation of calcium ion channels, activation of protein kinase C and mitogen-activated protein kinase pathways. These effects suggest that vitamin D modulates neuronal excitability and other electrophysiological phenomena (15). Vitamin D3 interacts with glucocorticoids in the hippocampus, which is relevant to disorders with dysregulated glucocorticoid signalling such as depression (16). Vitamin D is a critical co-factor for glutathione synthesis. Glutathione is the brain's key free radical scavenger, and oxidative stress is increased in major psychiatric disorders such as schizophrenia, depression and bipolar disorder (17). Vitamin D also influences nerve growth factor, thyroid hormone, testosterone, and the neurotransmitters acetylcholine and serotonin, all of which are implicated in depression.

In order to clarify the role of the vitamin D receptor, knockout mice that do not express the receptor have been developed. These mice display an interesting phenotype. They are less active, more anxious and have poorer swimming ability than their wild type littermate controls. This phenomenology is relevant as it overlaps substantially with the phenomenology observed in the typical animal models of depression (18). In addition there are changes in behavioural models of anxiety (19). This adds weight to the idea that vitamin D has behaviourally relevant brain functions.

A few intervention studies have been published. In a small group of patients with seasonal affective disorder, depression

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improved in those who received 100 000 IU of vitamin D, but not the group which received phototherapy (20). Improved positive affect and reduced negative affect have been reported after the administration of vitamin D3 in late winter (21). In contrast, a moderate dose (800 IU daily) supplementation of vitamin D in a cohort of elderly women in winter was not associated with clinical benefit (22).

These data suggest that vitamin D may have an important role in many psychiatric disorders. High rates of insufficiency in clinical samples suggest that monitoring vitamin D should be part of the routine laboratory screening investigations in psychiatric cohorts. There is also a high rate of comorbidity between osteoporosis and psychiatric disorders, particularly depression (23). The role of vitamin D in bone (3,4) suggests that monitoring levels may have additional value in these core comorbidities. The value of supplementation for core psychopathology requires further study; however, vitamin D has known benefits in bone and general health, and supplementation in individuals who have insufficient levels of vitamin D is merited.

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