Biofactor deficiency: increased risk of depression?

Depression represents a significant health and economic burden worldwide. In addition to classical treatment methods such as psychotherapy and anti-depressants, patients with depression should also pay attention to an adequate supply of the biofactors vitamin B₁₂, magnesium, vitamin D and zinc.

Avoiding vitamin B₁₂ deficiency in depression

In addition to the known deficiency symptoms of pernicious anaemia and neurological diseases, vitamin B_{12} deficiency can lead to a wide variety of non-specific complaints such as reduced performance levels, drive disorders, mood swings, as well as sleep and concentration disorders – or even burnout syndrome and depression.

"In affected patients, the vitamin B₁₂ status should therefore also be kept under review in addition to treatment with anti-depressants and psychotherapy. About 30% of people suffering from depression have been found to have a lowered vitamin B₁₂ blood level," warned Prof. Hans-Georg Classen, Chairman of the Society for Biofactors (GfB).

An increased risk of developing depression is observed among senior citizens with vitamin B_{12} deficiency in particular.¹ And according to the result of the Augsburg KORA-Age study, around one third of people over 65 years of age are affected by an undersupply of vitamin B_{12} . With increasing age, the risk continues to rise: among 85 to 93-year-olds it is $37.6\%.^2$

What role does hyperhomocysteinaemia play?

The biofactor vitamin B_{12} – in combination with folic acid and vitamin B₆ – is known to be involved in the homocysteine metabolism, while the toxic amino acid homocysteine is in turn under discussion as one of the risk factors in the development of depression.³ Even though the study situation is still inconsistent, there are increasing indications however that it is not the connection between hyperhomocysteinaemia and vitamin B₁₂ deficiency that is causal in the development of depression. For example, one investigation did indeed show that hyperhomocysteinaemia, vitamin B₁₂ deficiency and, to a lesser extent, folate deficiency are all associated with depressive disorders. However, the association was significantly reduced for folate deficiency and hyperhomocysteinaemia after adjustment for functional disorders and cardiovascular diseases, whereas this was independent with respect to vitamin B₁₂. Therefore, the authors of the study assume that vitamin B₁₂ deficiency is the primary cause and not a factor in the development of depression due to its correlation with homocysteine levels.¹

Another study investigating hyperhomocysteinaemia, vitamin B₁₂ and folate deficiency showed even clearer results: Neither the serum homocysteine level, nor the prevalence of folate deficiency was associated with the depression status. However, the depressed subjects, especially those with severe depression, had a significantly higher level



of methylmalonic acid – a marker for intracellular vitamin B₁₂ deficiency in serum – and a lower vitamin B₁₂ level in the serum than the nondepressed subjects. Metabolically significant vitamin B₁₂ deficiency was present in 14.9% of the 478 non-depressed subjects, in 17% of the 100 mildly depressed subjects and in 27% of the 122 severely depressed subjects. After adjusting for socio-demographic characteristics and health status, the subjects with vitamin B₁₂ deficiency were 2.05 times more likely to be severely depressed than non-deficient subjects.⁴

Vitamin B₁₂ supplements helpful for depression?

A recent review from 2020^5 analysed numerous studies with respect to the potential benefit of vitamin B₁₂ supplementation for depression. Based on the results of the studies examined, it was concluded that early supplementation with the biofactor vitamin B₁₂ – the daily doses were between 500 and 1,000 µg – can delay the onset of depression and improve the effect of anti-depressants. The last statement was also confirmed in other studies: Vitamin B₁₂ supplements enable depressed patients to respond better to anti-depressants such as selective serotonin re-uptake inhibitors:⁶

What role does the biofactor magnesium play in depression?

Magnesium deficiency can impair resistance to stress and promote physical and mental exhaustion or even the development of depression.

"The stress-shielding effect of magnesium has been known since the 1970s," emphasises Prof. Classen. It resulted from a dampening of the pituitary-adrenal axis, which was over-activated under the influence of stress.⁷ "Magnesium also received particular interest as a natural antagonist of the NMDA (N-methyl-D-aspartate) receptor," according to the magnesium researcher Classen. This receptor, which is found above all in the central nervous system, was also inhibited by drugs used in psychiatry. As a result, magnesium was increasingly used in the treatment of sleep onset⁸ and sleep maintenance disorders and as co-medication for depression, especially in cases of proven magnesium deficiency.^{9,10}

Consideration of the biofactor status in depression

The biofactor vitamin D is also under discussion as a therapeutic option in the treatment of depression, although controlled clinical studies have so far produced contradictory results. Although a recent analysis in 2020 of a total of 61 publications was able to confirm the connection between vitamin D and depression, the evidence for universal supplementation would not yet be sufficient.¹¹ Various studies also point to a correlation between zinc deficiency and depression, whereby the severity of the depression correlates with the level of the zinc deficiency.¹²

In summary, this article shows that – even if the study situation is not always consistent – attention should be paid to an adequate supply of the biofactors vitamin B₁₂, magnesium, vitamin D and zinc in the treatment of depression, in addition to classical methods.



Further information on the biofactors referred to here, as well as others, can be found here.

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