In ME/CFS, [hypomethylation](<http://dx.doi.org/10.4172/2155-9899.1000228>), which is greatly affected by the vitamins B12 and folate, is seen in a majority of certain immune cells. The low B12 and homocysteine levels correlated significantly with ratings of [mental fatigue](<https://www.ncbi.nlm.nih.gov/pubmed/25902009>).

It is strongly recommended that people in this group take an [oral folic acid](<https://www.ncbi.nlm.nih.gov/pubmed/25902009)> supplement on a daily basis to provide blood saturations high enough to be a remedy for good and safe relief in CFS patients. However,

opioid analgesics and other drugs that have to be demethylated as part of their metabolism cause worse MTHRF function.

ME and FM are unexplained disorders with molecular and immunological abnormalities. In ME patients, hypomethylation is seen in a majority of certain immune cells [http://dx.doi.org/10.4172/2155-9899.1000228] and of DNA in genes associated with immune cell regulation [https://www.ncbi.nlm.nih.gov/pubmed/25111603/]. Although the reason for such hypomethylation can only be speculated upon, for the time being, it is interesting that the combined action of the vitamins B12 and folate (Fig 1) play a fundamental role in providing methyl groups to hundreds of substrates in various elementary cell processes. Yet another and recently revealed role of vitamin B12 is related to detoxification, by having substantial antioxidant properties [https://www.ncbi.nlm.nih.gov/pubmed/19409980/–https://www.ncbi.nlm.nih.gov/pubmed/19799418/].

The CSF-B12 level appeared to be generally low, and CSF-homocysteine and CSF-B12 levels correlated significantly with ratings of mental fatigue. The results suggested a blockage of B12 transport over the blood brain barrier.