Prevention of age associated excitotoxicity of glutamate in brain by multivitamin containing vitamin B6 and vitamin B12 and folic acid

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Glutamate (Glu) is known as an excitatory amino acid neurotransmitter which interacts with N-methyl-D-aspartate (NMDA) receptors for basal excitatory synaptic transmission. Neurophysiological studies indicated that Glu causes many forms of synaptic plasticity such as long-term ostentation and depression, which are thought to influence learning and memory. However, excessive levels of extracellular Glu in the nervous system are excitotoxic and lead to neuronal death and several neurodegenerative processes. Several lines of evidence suggested that increased extracellular Glu, can give rise to many potentially damaging mechanisms which may be pathologically important. While there is little doubt that the high level of Glu is neurotoxic, diminutive evidence points towards the enzymatic control of Glu metabolisms of the brain. Since multivitamin B supplementation has been recommended as adjunctive treatment in Alzheimer's disease, this study was undertaken to investigate the efficacy of vitamins B6, vitamin B12 and folic acid on the activities of GS, GAD, GOT and GPT in aging rat brain. Male Wistar rats (3 and 30 months old) were used. The animals were injected with vitamins B6, vitamin B12 and folic acid (10mg/Kg/day) for 30 days and the day after last injection the animals were killed by decapitation after a mild anesthesia. Forebrains were removed and homogenized in phosphate buffer. The activities of the enzymes were measured in the supernatant. The first part of this in vivo study sought to measure the specific activities of GS, GAD, GPT and GOT in the brain as a function of the age of the rats. The enzyme activities in aged rat brain were considerably lower compared to young animals. Vitamin B6 induced activation of GAD, GOT and GPT in both ages, but, the differences were more pronounced in aged animals. Vitamin B12 and folic acid stimulate the activity of GS in both young and old animals, but had lintel effects on GAD, GOT and GPT of both ages. These results are consisted with the effect of the biologically active form of vitamin B_6, pyridoxal 5- phosphate, which acts as the cofactor for the activity of GAD, GOT and GPT. Folic acid and vitamin B12 have fundamental roles in brain function at all ages, especially the conversion of homocysteine to methionine, which is essential for neuronal nucleotide synthesis. However, the higher rate of activation of the enzymes in the brain of aged animals might be resulted from either; lower availability of the vitamins in aged animals, or; the lower affinity of the enzymes for the vitamin metabolites, due to the posttranslational modifications of the enzyme proteins as consequences of aging. It is concluded that Glu metabolism might be considered as a therapeutic target for prevention of neurodegenerative disorders and age related symptoms.

Key words; Aging, Excitatory amino acids, Glutamate, Multivitamin B, Neurotransmitter