L-DOPA TREATMENT REDUCES PLASMA CONCENTRATIONS OF PYRIDOXAL PHOSPHATE (VITAMIN B6) AND DECREASES BRAIN SEROTONIN METABOLISM IN THE MOUSE: IMPLICATIONS FOR VITAMIN B6 DEPENDENT ENZYMES

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Introduction: L-dopa therapy, alone or in combination with a peripheral amino acid decarboxylase (AADC) inhibitor still remains the first-line treatment for Parkinson's Disease (PD). While the benefits of L-dopa therapy are clear it may be associated with toxic effects including the interaction of L-dopa with pyridoxal phosphate (PLP), a cofactor for a number of enzymes including AADC. This interaction results in a complex Schiff base formation and inactivation of both L-dopa and PLP.

Aims: To study the effect of L-dopa on blood PLP levels and brain dopamine and serotonin metabolism.

Method: In an acute treatment study 2 doses of L-dopa (100mg/kg, i.p) were given in combination with benzerazide (10mg/kg) at 45 minute interval and C57BL/6 mice were sacrificed 30 minutes after the last dose. Blood was analyzed for PLP and regional brain tissue for monoamine neurotransmitters.

Results: Blood PLP levels decreased from 486 ± 129 (n=6, mean ± SD, nmol/L) in the saline group to 20 ± 14 (n=6) in the L-dopa group. As expected dopamine was elevated (415%) in the striatum after L-dopa treatment. However, 5HT was significantly decreased in the frontal cortex (-63%), cortex (-65%), midbrain (-57%) and cerebellum (-51%) but not in the striatum.

Conclusions: Since the synthesis of 5-HT is dependent on the activity of AADC, a PLP dependent enzyme, these results suggest that the deficiency of PLP induced by L-dopa can adversely affect AADC enzyme activity. These findings have implications for the activity of other PLP dependent enzymes that may be influenced by L-dopa treatment.