Antioxidant Treatment Prevents the Increased Acetylcholinesterase Activity and Memory Impairment in an Animal Model of Maple Syrup Urine Disease

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Introduction: Maple syrup urine disease (MSUD) is an inherited aminoacidopathy resulting from dysfunction of the branched-chain keto acid dehydrogenase complex, leading to accumulation of the branched-chain amino acids (BCAA) leucine, isoleucine and valine. Objectives: Considering that the neurotoxic mechanisms in MSUD are not completely understood, we aimed to assess the acetylcholinesterase activity and behavioral impairment of rats subjected to chronic administration of a pool of BCAA, treated or not with antioxidants N-acetylcysteine and deferoxamine. Methods: Wistar rats (7 days) received a pool of BCAA containing leucine, isoleucine and valine, or saline (control group) twice a day for 21 days. The animals were also supplemented with N-Acetylcysteine (20mg/kg) twice a day and deferoxamine (20mg/kg) every two days. Twelve hours after the last administration the rats were killed by decapitation, the brain was removed and cerebral cortex, hippocampus and striatum were isolated and acetylcholinesterase activity was measured. At the same time, the rats were subjected to behavioral tests. Results: Our results showed that chronic administration BCAA increase AChE activity in any of the structures studied; and cause long-term memory impairment in the inhibitory avoidance (a type of single-trial that aversively motivated conditioning) and CMIA tasks, whereas we found no alterations in CMIA retention memory. Additionally, the co-administration of N-Acetylcysteine plus deferoxamine prevents increased acetylcholinesterase activity and the behavioral alterations. Conclusion: Thus, we suggest that the impairment of cognition provoked by BCAA may be caused by cholinergic synapses dysfunction, possibly by association between free radicals/oxidative damage and cognitive impairment.

Word Keys: Maple syrup urine disease; antioxidant treatment; cognitive impairment; acetylcholinesterase activity

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