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Axonal Loss and Mitochondria Damage in Mice Brain after Tryptamine Treating

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Tryptamine is a monoamine alkaloid found in human, plants, fungi, and animals. It is a decarboxylated analogue of an essential amino acid, tryptophan. It was believed to play a role as a neuromodulator or neurotransmitter [1]. As it was shown in the past decade tryptamine may easily cross a brain-blood barrier [2]. In this study we developed metabolic model of neurodegeneration using tryptamine-mice. Balb/c male mice were injected with various doses of tryptamine (hydrochloride form). Changes in mouse brain were analyzed in ~a month after beginning of treatment. No toxic effect of the dozes 1-500 μg tryptamine was detectable within ~48 hours after each injection in each mouse. To the end of experiments the tryptamine-mice were in good health and visibly gained more weight than the control mice. Brains were isolated from three control mice injected with placebo and three tryptamine-treated mice. The hippocampal areas were cut out from the paraffinized blocks, and the ultrathin sections were examined in Morgagni 268 electron microscope at 80 kV. Micrographs were taken at 45,000 and 90,000 and lower magnification and analyzed using the program ImageJ [3].

We analyzed ultrastructure and myelination of axons and the structure of mitochondria in axons and supporting cells in hippocampus of tryptamine-treated and control mice. We identified axonal defects in hippocampus of tryptamine-mouse (Fig.1). Treatment by tryptamine leads to severe axonal defects characterizing by appearance of membrane vesicles and accumulation of abnormal amounts of helical filaments, amyloid and organelles. The mean diameter of axons was larger in tryptamine-mice (TAB. 1), suggesting axonal swellings. The uneven thickness of the myelin in tryptamine-treated mice may indicate the beginning of myelin breakdown (Fig.1B and TAB.1). Moreover, the tryptamine-mouse had a lower density of hippocampal total (somatic and axonal) mitochondria, many of which have degenerated and included twisted fibrils. The mitochondria cristae became twisted (Fig 2B) and rapidly broken. This is in agreement with recent findings of other investigators [4].

The abnormal fission and fusion resulted in formation of mitochondrial clusters in axons of tryptamine-mouse brain. Tangles of helical filaments were observed in the cytoplasm of neuronal cells suggesting that augmented amounts of tryptamine may damage neurons [5]. Thus, tryptamine has been implicated as a causative agent in neurodegeneration resembling progressive neurological and neurodegenerative human diseases.

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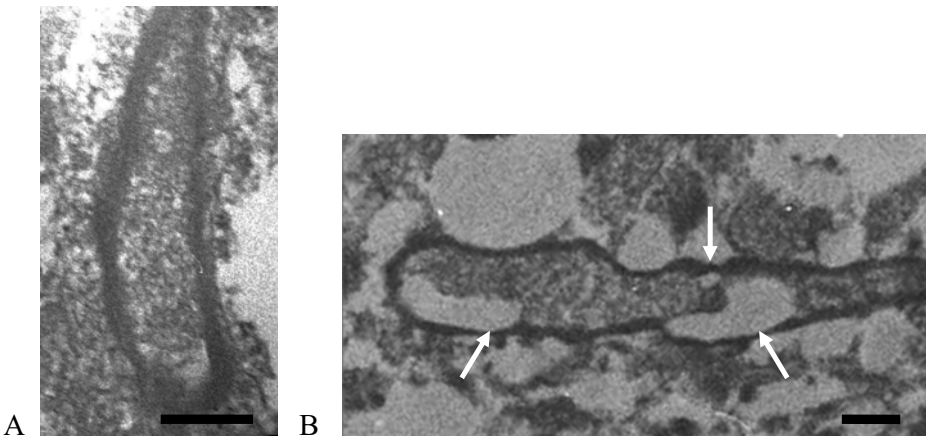

FIG.1 Comparison of the myelinated axon sizes in brain of control (A) and tryptamine treated (B) mice. White arrows are pointing to the myelin defects. Bar – 0.3 um

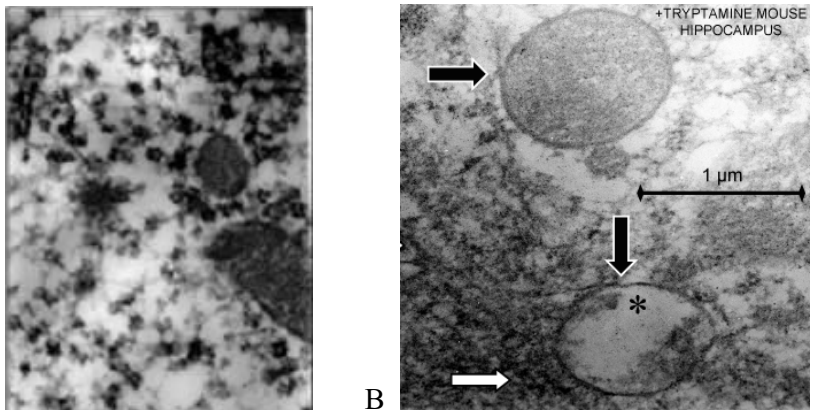

FIG. 2 Mitochondria in control (A) hippocampus; Mitochonrial damage after tryptamine treatment (B): loss of of cristae (black arrows) and NFT amyloid tangles (white arrow).

TABLE 1. Organelle's sizes in control and tryptamine treated mice brain

Organelle	Diameter (um) of myelinated axons	Thickness (nm) of myelin	Density of mitochondria /100 (um^2)
Control	1.89±0.51	61.5±5.8	50
Tryptamine treated	4.56±0.9	68.3±44.3	20

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