Counteracting Pb2+ Induced Neurodegeneration: A Chemical and Genetic Approach towards Enhanced Synaptic Plasticity

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The neurotrophin BDNF has been shown to engage in retrograde signaling and interneuronal transport, causing increased synaptic transmission and neurogenesis, respectively. It was hypothesized that Pb2+ exposure causes neurodegeneration by lowering BDNF levels and transport. Thus, improving BDNF levels and transport would counteract Pb2+ induced neurodegeneration. To increase BDNF levels, Pb2+ exposed Drosophila were treated with curcumin, and dissected to isolate their neuromuscular junctions. Fluorescent indicators FRET, FM 1-43 dye, and FURA-2 dye were used to analyze levels of cAMP, presynaptic vesicle rate, and Ca2+ influx respectively. To increase neurotrophin transport, a knockout of FOS-1 was induced in Pb2+ exposed C. elegans with GFP-tagged motor neurons, and were then observed with a Zeiss-Axiovert fluorescent microscope and analyzed using ImageJ to quantify neurogenesis. Locomotion and lifespan were also analyzed in both flies and worms. The results suggest that curcumin caused an increase in Ca2+ influx, vesicle rate, and locomotion, but not in cAMP or lifespan. Knockout of FOS-1 increased neuronal growth (GFP) and lifespan, but not locomotion. This suggested that improving BDNF levels and transport was effective in counteracting neurodegeneration, thus indicating that Pb2+ causes neurodegeneration largely through its detrimental effects on BDNF. Furthermore, a third pathway involving acetylcholine was impaired, suggesting additional consequences of Pb2+ exposure. It was therefore determined that the inhibition of BDNF by Pb2+ significantly deteriorates motor functions, synaptic functions and lifespan, proposing this pathway as a suitable target when counteracting Pb2+ neurodegeneration.

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