Metal and Hyperglyecmia-induced Neurotoxicity using a Caenorhabditis elegans RAGE Model

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Diabetes is a metabolic disease impacting more than 400 million adults worldwide. Most of the major complications associated with diabetes are caused by hyperglycemia. Under hyperglycemic conditions, advanced glycation endproducts (AGE) can develop, causing neurodegeneration. The receptor for advanced glycation end products (RAGE) can bind and facilitate development of AGEs, potentially worsening the diabetogenic effects. Metals play key roles in diabetes: manganese can influence blood sugar regulation and cadmium can negatively affect the cardiovascular system. C. elegans with human RAGE were recently developed to facilitate neurotoxicity experimentation through targeted green-fluorescent protein (GFP) neurotransmitter pathways. In the presence of RAGE, the neurotoxic effects of AGEs and metals will be increased. C. elegans were exposed to hyperglycemic conditions resembling diabetic patients and metal toxicity. Dopamine and serotonin neurotransmitter fluorescence were evaluated post treatment using fluorescence microscopy and Fiji software. The neurotoxic effects of AGEs and manganese in dopaminergic and serotonergic pathways were enhanced by RAGE. Further investigation into RAGE in the C. elegans model seems profitable and likely to improve the understanding of the effects of ligand-receptor interaction with broad implications for diabetes and neurodegenerative diseases.

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