ZINC ACCUMULATION IN THE MIDBRAIN FOLLOWING METHAMPHETAMINE EXPOSURE AS A POTENTIAL BIOMARKER FOR NEURODEGENERATION

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Introduction

Illicit use of methamphetamine (METH) is a rising concern due to the well-established link between METH intoxication and neuron death. Many studies have suggested that the death of these neurons is in part due to an overzealous response of the immune system following METH exposure. Notably, excessive buildup of zinc, a common co-factor of the immune system, has also been implicated in many neurodegenerative disorders.

Hypothesis

Neuron death following METH exposure is due to the accumulation of zinc in the brain from over activation of the immune system.

Methods (cont’d)

Total Reflection X-Ray Fluorescence:

Methods

Day 1:
- Weigh mice
- Injections:
  - METH (5mg/kg)
  - Saline (0.9% NaCl)

Day 2-9:
- Weigh mice
- Injections:
- Final injection
- Harvest tissues:
  - Midbrain
  - Striatum

Day 10:
- Weigh mice
- Final injection
- Harvest tissues:
  - Midbrain
- Striatum

Tissues were sonicated and analyzed for elemental content via Total Reflection X-Ray Fluorescence and CuZn superoxide dismutase activity.

Results (cont’d)

Figure 3. Relative levels of CuZn Superoxide Dismutase in the midbrain of C56BL/6 mice following 10 days of METH (n=3) or Saline (n=3) treatment. Inhibition rate is reported following colorimetric methodologies. A) Total protein concentrations were standardized at 20 μg of protein per sample. Data are expressed as means±SE; two sample t-test; p<0.05 vs. saline. B) Protein concentration-dependent responses of CuZn Superoxide Dismutase activity. Data are expressed as means±SE; two-way ANOVA.

Future Directions

- Analyze genes of interest relating to inflammation and neurodegeneration, including nitric oxide synthase (eNOS/nNOS).
- Continue our search for alternate sources of zinc, including brain specific zinc transporters (MT3).

Summary and Conclusions

- An increase in zinc deposition was observed in the midbrain of METH treated mice compared to saline.
- While zinc is an important co-factor for superoxide dismutase, this enzymatic activity does not appear to be the source of zinc deposition following METH treatment.
- Although we do not have a known mechanism, we have established that METH exposure leads to zinc accumulation in the midbrain.

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