

The Effect of Enhanced Levels of Zinc on Spatial Memory and Brain Function in Rats

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Introduction

Zinc is the fourth most abundant metal in the brain and has high levels in the hippocampus. It is found in over 200 enzymes, including the anti-oxidant superoxide dismutase (SOD). Previous research has documented the adverse effects of zinc deficiency; however, little research has examined the possible adverse effects of high levels of zinc. This is important as levels of zinc in natural water systems are continuing to rise, while levels of other metals such as lead, have fallen significantly.

Prior studies in our lab examined the levels of zinc in brain tissue of rats exposed to augmented levels of zinc in their drinking water (10 ppm ZnCO₃) and found elevated concentrations of zinc in the hippocampus and adjacent cortex and deficits in spatial memory. To further explore the relationship between zinc levels and hippocampal function, we assessed the effects of higher levels of zinc intake on SOD levels and spatial memory. We report here the results of administering 20 and 40 ppm of ZnCO₃. Both levels of zinc produced impairment in spatial memory in 9-month-old rats, as measured in the Morris water maze.

Methods

Zinc Concentrations

30 male and 30 female Sprague-Dawley rats were raised on drinking water containing enhanced levels of zinc. Exposure was both pre-and post-natal. 20 ppm ZnCO₃ and 40 ppm ZnCO₃ were used at a pH of ~ 7.3.

Behavioral Testing

Rats were tested in the Morris Water Maze at 9 months of age. There were 2 trials per day for 8 days. Each trial lasted for a maximum of 120 seconds with a 45 second inter-trial rest period. Observers were blind to the subject's condition.

Comparison of Male and Female
Control v. 20ppm

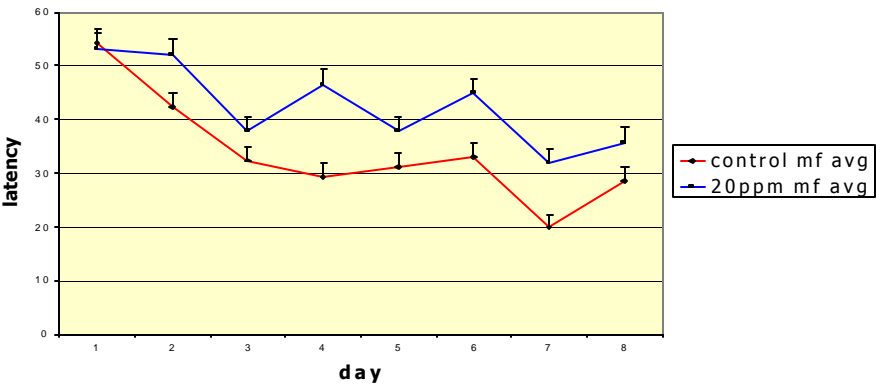


Figure 2. Trials A and B,
Controls

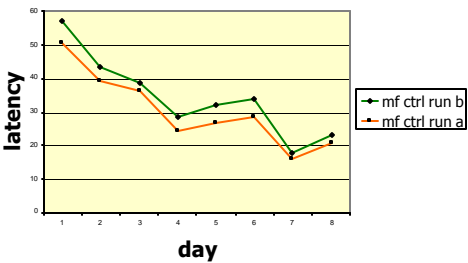


Figure 3. Trials A and B,
20ppm ZnCO3

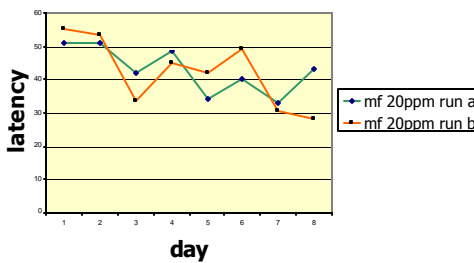
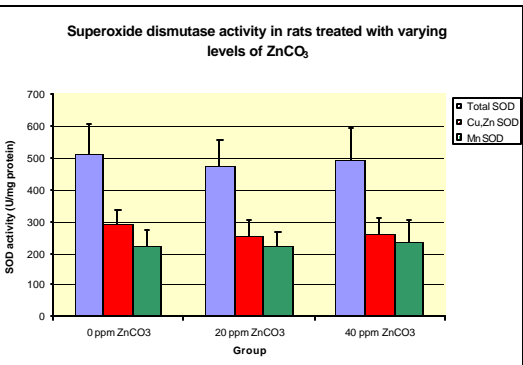
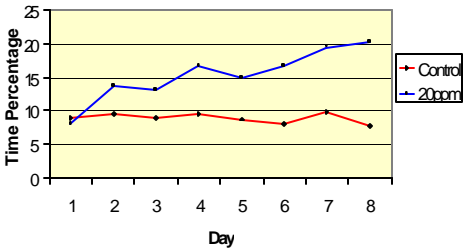


Figure 4. Percentage of Time in Thigmotaxic
Movement



SOD activity was determined by a competitive spectrophotometric assay that used xanthine and xanthine oxidase to generate the SOD radical and the tetrazolium salt WST-1 to detect SOD formation (Peskin & Winterbourne, 2000). One unit of SOD was inhibited WST-1 reduction by 50%, as determined by detection at 450 nm. Cu, Zn and Mn SODs were distinguished in a separate reaction by the addition of 5 mM KCN, which selectively inhibits Cu, Zn SOD.

Results

The overall analysis showed no significant difference between the 20 and 40 groups. Here we focus on a comparison of the control (0) and 20 ppm groups. We hypothesized that the latency of the 20 ppm group would be significantly slower than the control group. Independent-sample t-tests on the daily means showed that from day 2 through 8, the 20 ppm group were significantly slower than the controls, $t_{(df=12)} = 2.75$, $p < .02$ (see figs. 1, 2 & 3). There was a greater difference for the males $t_{(df=12)} = 3.600$, $p < .004$.

The 20ppm animals showed significantly greater thigmotaxis than the controls, $t_{(df=14)} = 4.59$, $p < .001$, with the thigmotaxis increasing over time for the 20ppm group (see fig. 4).

Ongoing analysis of the SOD levels (see fig. 5) show the Cu, Zn SOD was greatest in the control rats. There was a tendency for it to exceed that in both Zn groups ($t(19) = .$, $p < .06$). There were 7 controls and 14 Zn animals.

Conclusion

Rats exposed to excess levels of zinc in their drinking water have a deficit in spatial memory as revealed by a slower latency in the Morris water maze. We have previously discovered excess levels of zinc in the hippocampus and adjacent cortex following exposure to zinc-enhanced drinking water using synchrotron X-ray analysis. These findings may have important implications for humans, as the levels of zinc rise in our drinking water. SOD analyses are ongoing. Additional studies will investigate whether zinc collects in other areas of the brain, at what ages, and what the behavioral effects might be.