

Effects of dietary enhancement of iron on APP2576 mice assessed through novel object recognition.

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Introduction

Iron is found in amyloid plaques (Lovell et al., 1998) and iron in drinking water increases levels of iron in amyloid-β plaques, perhaps accelerating formation of plaques in the brain (Linkous et al., 2004). Amyloid plaques first appear in the temporal lobes and hippocampus, an important brain area for learning and memory. Clark et al. (2000) reported that lesions of the hippocampus impair performance on tasks of visual recognition memory (in VPC task, similar to NOR). The novel object recognition task is one of the few tests available for assessing declarative memory in animals. Wild type mice will choose a novel, unfamiliar object given the capability to distinguish between objects with which they have or have not had previous experiences. The present study examined novel object recognition as an assessment for changes in cognitive deficits due to consumption of enhanced levels of iron in the drinking water in Tg2576 mice.

Methods

Tg2576 (n=16) and Wt2576 (n=18) mice consumed either iron (II) nitrate (Fe(NO₃)₂, 10ppm) or lab tap water pre- and post-natally. Mice and objects were counterbalanced and were assessed through the novel object recognition test (CleverSys, Reston, VA) at 12 months of age. Mice were habituated for five days with varying paradigms: during day 1 all cage mates were placed in the box at the same time for 7 minutes; during days 2, 3, and 5 individual mice were placed in the box for 6 minutes; and during day 4 mice were first exposed to a standard object for 6 minutes. After habituation, the NOR test consisted of an initial trial where the mice were first exposed to a standard object which was present in all future trials. This initial trial was followed by three other trials at 1 hour, 24 hours, and 72 hours where the mice were exposed to their standard object and a novel object, which was different in each trial. Each trial lasted 5 minutes.



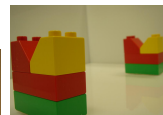
Egg/Block



NOR box set-up with a standard and a novel object



Lightbulb



Lego



Trophy

References and Acknowledgements

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Results

Figure 1: Difference scores for sniffing duration on the novel and standard objects. Figure 2: Mean sniffing on standard and novel objects. A significant effect due to genotype (F(1,29)=5.299, p=.029) was seen, even though significance due to water was not found. All groups, with the exception of the transgenic lab group, sniffed at the novel object for a longer duration than the standard, exhibiting novel object recognition. At 1 hour a significant effect between genotype was found (F(1,32)=4.187, p<.05).

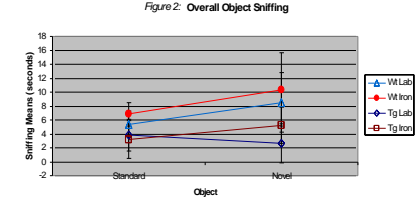
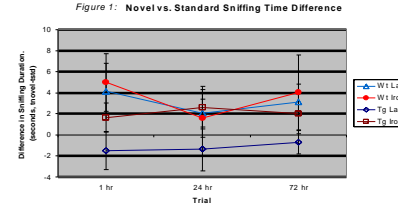


Figure 3: Sniffing means for Tg and Wt mice on standard and novel objects. Figure 4: Sniffing means for lab and iron water on standard and novel objects. A significant effect was found for object sniffing preference (F(1,30)=8.583, p<.01). The interaction of genotype and object also produced a significant effect (F(1,30)=4.966, p=.034). This can be seen due to Wt mice sniffing longer on the novel objects than Tg animals.

Figure	Data Point	Mean	SD	N
3	Wt Std Obj	6.12	5.08	18
3	Wt Nov Obj	9.45	6.86	18
3	Tg Std Obj	3.50	3.27	16
3	Tg Nov Obj	3.96	2.999	16
4	Lab Std Obj	4.61	3.72	18
4	Lab Nov Obj	5.58	4.87	18
4	Iron Std Obj	5.01	5.27	16
4	Iron Nov Obj	7.82	7.06	16

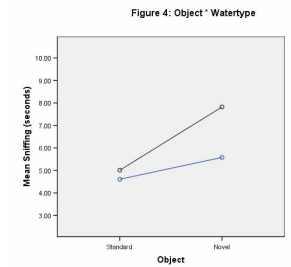
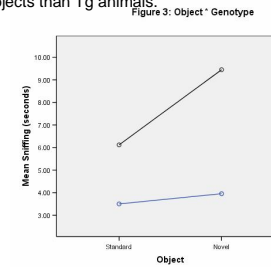
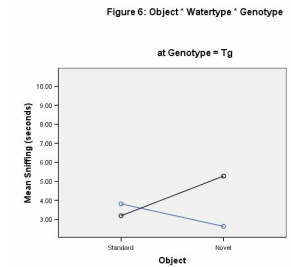
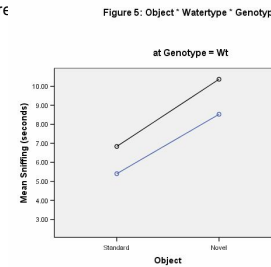


Figure 5: Sniffing means for Wt mice on lab and iron water. Figure 6: Sniffing means for Tg mice on lab and iron water. Wt iron and lab water mice show almost parallel levels of sniffing with Wt iron mice sniffing longer on both the sta over a standard object while Tg lab water mice show no such pre

Figure	Data Point	Mean	SD	N
5	Lab Std Obj	5.40	3.48	9
5	Lab Nov Obj	8.53	5.10	9
5	Iron Std Obj	6.84	6.45	9
5	Iron Nov Obj	10.37	8.49	9
6	Lab Std Obj	3.82	3.99	9
6	Lab Nov Obj	2.63	2.20	9
6	Iron Std Obj	3.19	2.29	7
6	Iron Nov Obj	5.28	3.82	7



Conclusions

Wt2576 mice showed significantly more novel object recognition than Tg2576 mice.

Tg2576 mice sniffed less overall on objects, both standard and novel, than Wt2576 mice.

An effect due to water type was not seen. Iron mice sniffed more on a novel over a standard object than did lab water mice within respective genotypes. However, Tg lab water mice sniffed for a shorter duration on the novel than the standard object, which was the opposite of all other groups.

Tg mice raised on iron water showed preference for the novel object, in contrast to Tg mice raised on lab water, suggesting that iron enhances novel object recognition in Tg mice. Thompson et al. (2006) showed impairment in Morris Water Maze performance in Tg mice raised on iron, indicating that iron decreases spatial memory performance. These data indicate that Tg mice raised on iron exhibit task specific effects on cognitive performance as a consequence of the different effect of iron on different brain regions.