Behavioral Studies on an Animal Model for Alzheimer's Disease

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INTRODUCTION

Genetic studies have clearly demonstrated that Apolipoprotein E (apoE) is a major risk factor for several neurodegenerative diseases like Alzheimer's Disease; however the mechanism of pathogenesis is unknown. ApoE is a lipid transporting protein. Previous studies from our laboratory have shown that apoE plays a vital role in nerve repair and remodeling. Since the olfactory system is in a continuous state of remodeling, the present study tested the hypothesis that apoE is required for normal functioning of the olfactory system. Olfactory behavior of wild type (WT) and apoE deficient (apoE KO) mice was assessed by using three standard olfactory tests: 1) the buried food pellet (BFP) test; 2) the odor choice (OC) test; and 3) the odor cued taste avoidance (OCTA) test. ApoE KO mice performed poorly in all the three tests as compared to WT mice, although they learned the tasks at a rate comparable to WT mice. ApoE KO mice had a significantly longer latency to find the buried pellet than WT mice. In the OC experiment, apoE KO mice did not differentiate water from an odorant solution. Furthermore, in the OCTA test the apoE KO mice were significantly less successful than WT mice at avoiding water containing an odorant and a bad tastant. These data demonstrate that apoE deficiency in apoE KO mice leads to a deficit in olfactory function, suggesting an important role for apoE in the olfactory system.

RESULTS

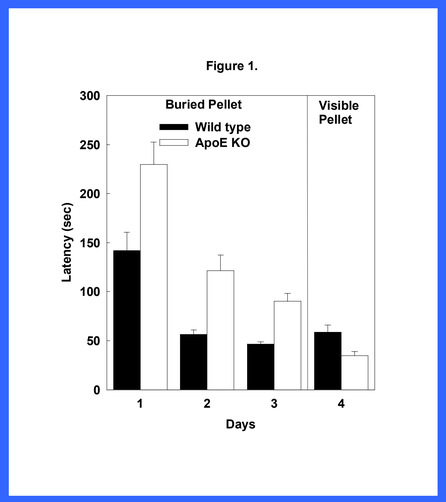

Figure 1. Performance of WT (n=28) and apoE KO (n=25) on buried and visible pellet tests. On each of the first 3 consecutive days, the latency for the mice to recover a buried food pellet was recorded. Latency declined significantly across days in both apoE KO and WT mice. However, latency of apoE KO mice was significantly higher than WT on all the three days. In visible pellet test latency to find a visible pellet was recorded (WT, n=9; apoE KO, n=9). In contrast to buried pellet test, apoE KO mice had significantly shorter latency to find the visible pellet as compared to WT mice. The results of the BFP test indicate that that apoE KO mice do not have a simple deficit in locomotor ability, appetitive behavior, or learning ability but rather a deficit in olfactory function .

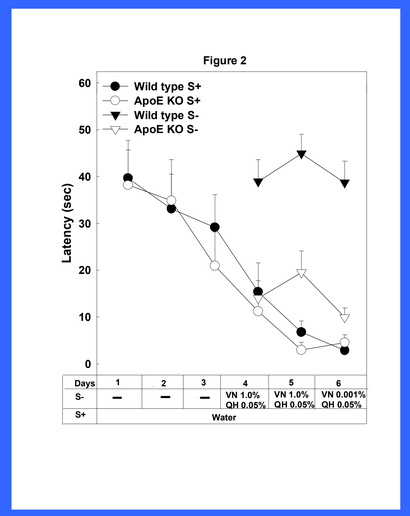

Figure 2. Performance of WT (n=8) and apoE KO (n=9) mice on the odor cued taste avoidance task. In the initial 3-days training period, with only S+ (water) used, there were no significant differences between apoE KO and WT in the daily latency value. However, latency of both WT and apoE KO mice significantly decreased across days. Also, during the 3-day testing period, the latencies to S+ of both WT and apoE KO mice decreased across days. In both the training and testing period, there were no significant differences between apoE KO and WT mice in their latencies to S+. However, apoE KO mice had significantly shorter latency to S- than WT mice. These results suggest that that mice from both genotypes did not differ in their ability to learn this task, thus differences in S- latencies is most likely due to a deficit in olfactory functioning in apoE KO mice.
VN, vanillin; QH, quinine monohydrochloride.

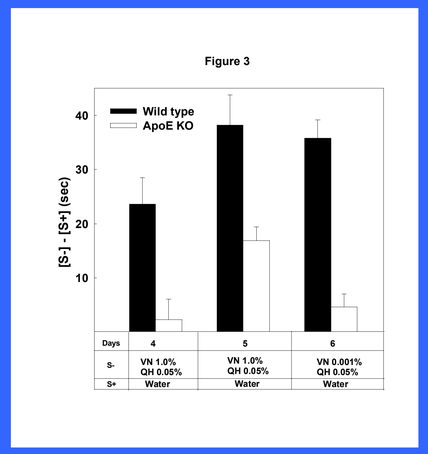

Figure 3. Mean treatment differences [(S- latency) – (S+ latency)] between WT (n=8) and apoE KO (n=9) mice in the odor cued taste avoidance task. Mean treatment differences were significantly lower in the apoE KO mice than WT on all the three testing days. Within genotypes, WT had significantly longer latencies to S- versus S+ on all days. In contrast, for apoE KO, latencies to S- were significantly greater than those to S+ only on day 5. These results suggest that apoE KO mice have some deficit in olfactory functioning.
VN, vanillin; QH,quinine monohydrochloride.

CONCLUSIONS

- ApoE KO mice did learn tests at a rate comparable to WT mice.
- ApoE KO mice had a significantly longer latency to find a buried food pellet than WT MICE.
- In OC experiment, apoE KO mice did not differentiate water from odorant solution.
- In OCTA test, apoE KO mice were significantly less successful than WT at avoiding an odorant with a bad tastant.
- ApoE KO mice performed poorly in all 3 olfactory tests as compared to WT mice.

SIGNIFICANCE

ApoE deficiency in apoE KO mice leads to a deficit in olfactory function, suggesting a vital role for apoE in the olfactory system. Further studies aimed at understanding the precise function of apoE in this model system may shed light on the mechanism whereby apoE is involved in neurodegenerative diseases.

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