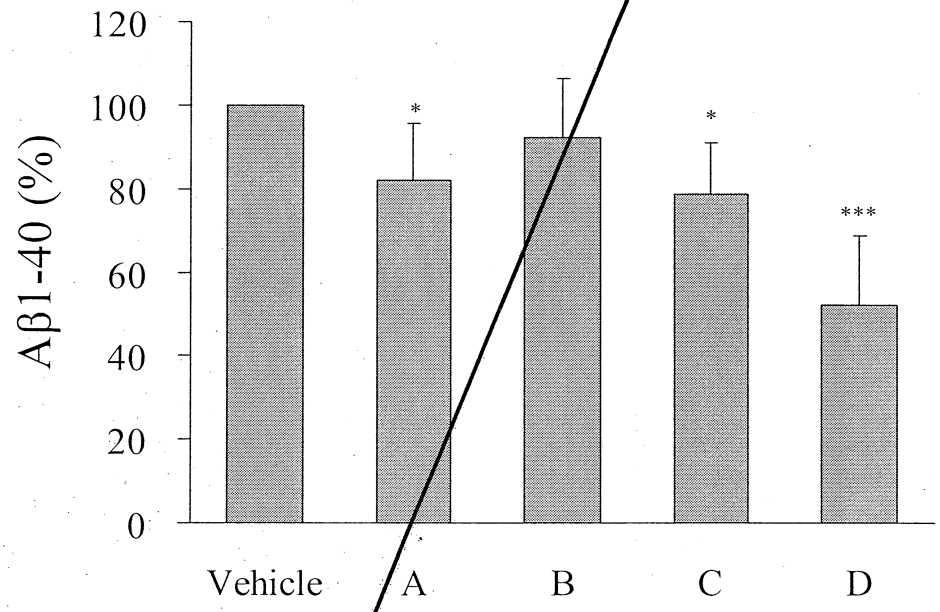


Fig. 1

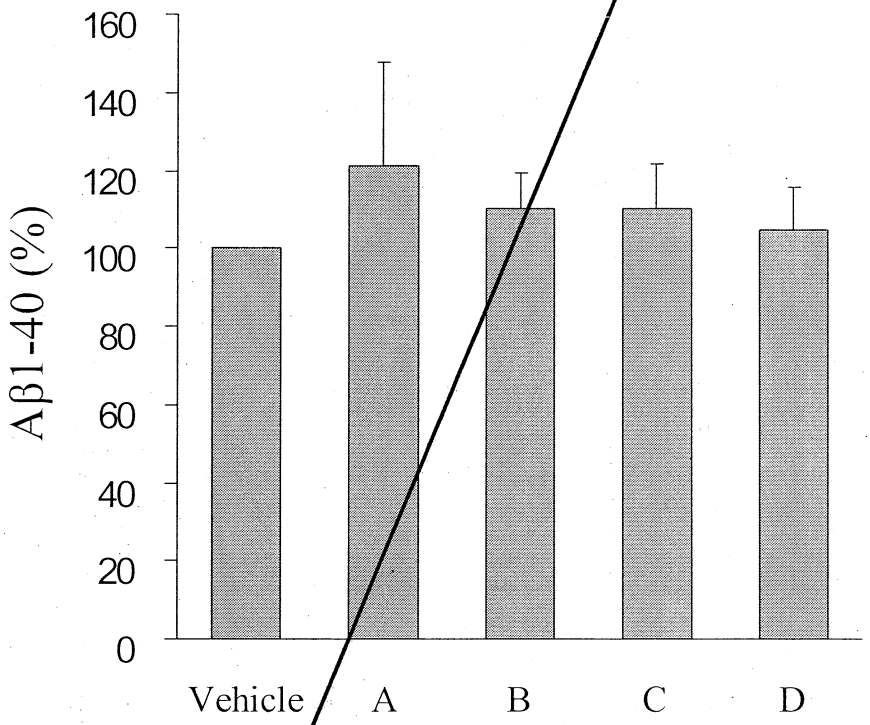


Fig. 2

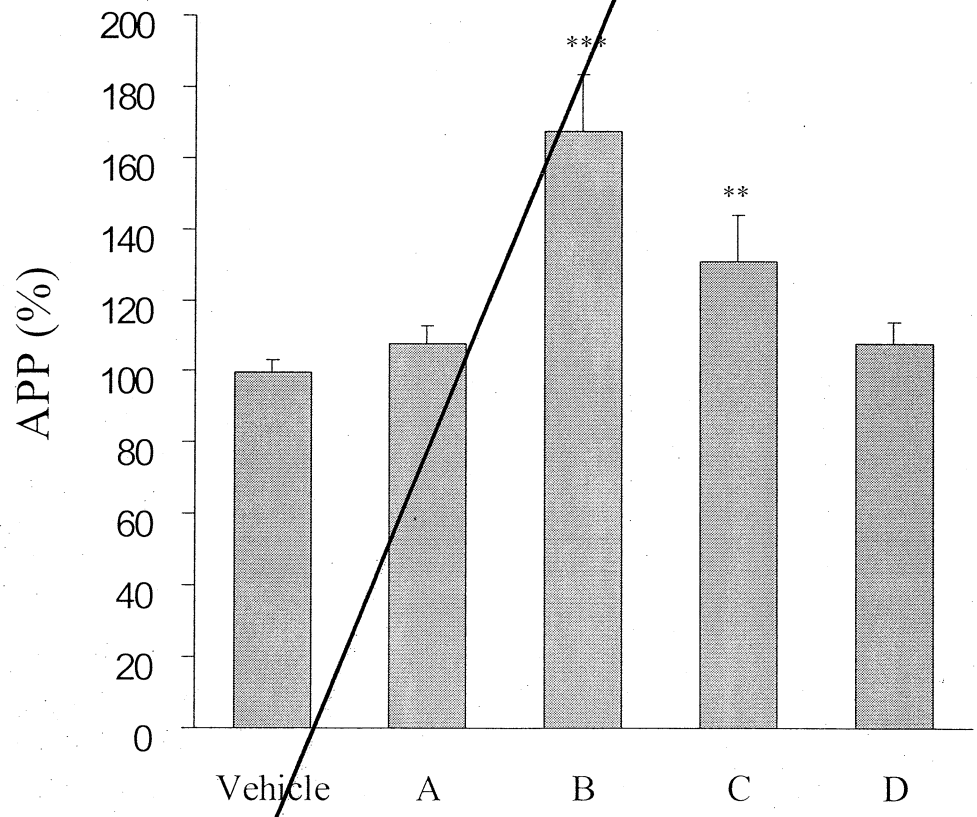


Fig. 3

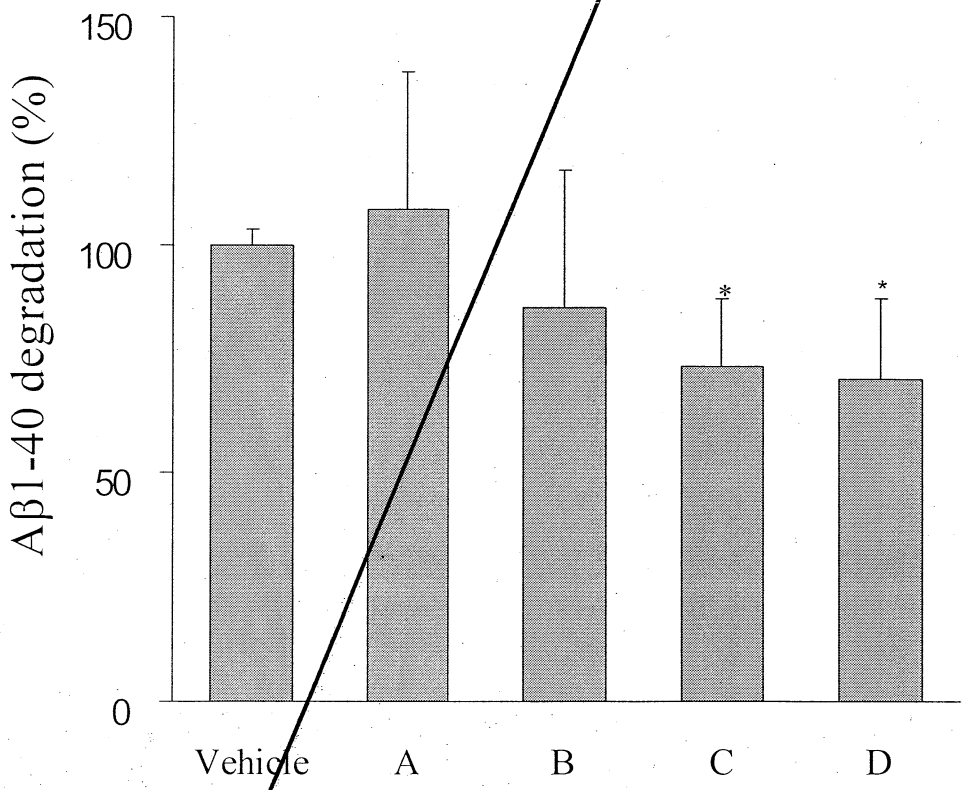


Fig. 4

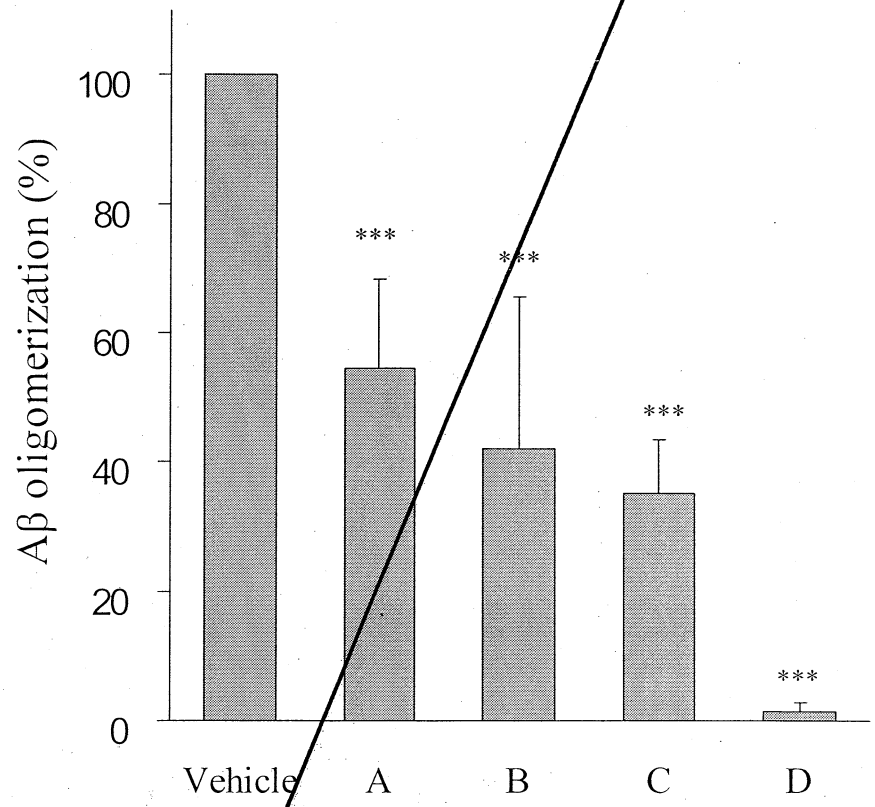


Fig. 5

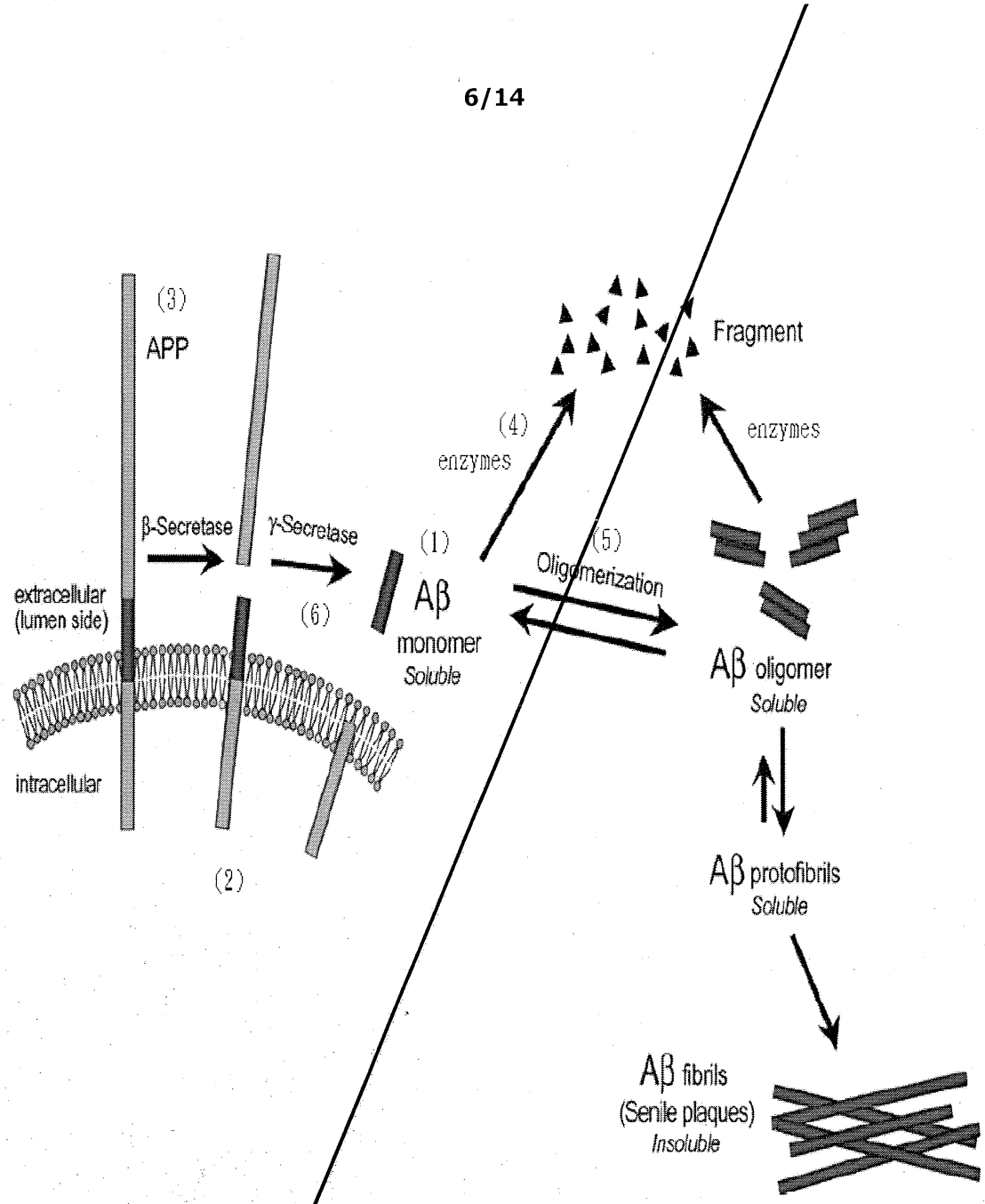

(3)
APP
β-Secretase
γ-Secretase
extracellular
(lumen side)
intracellular
(2)
(6)
(1)
Aβ
monomer
Soluble
(4)
enzymes
Fragment
enzymes
(5)
Oligomerization
Aβ oligomer
Soluble
Aβ protofibrils
Soluble
Aβ fibrils
(Senile plaques)
Insoluble

Fig. 6

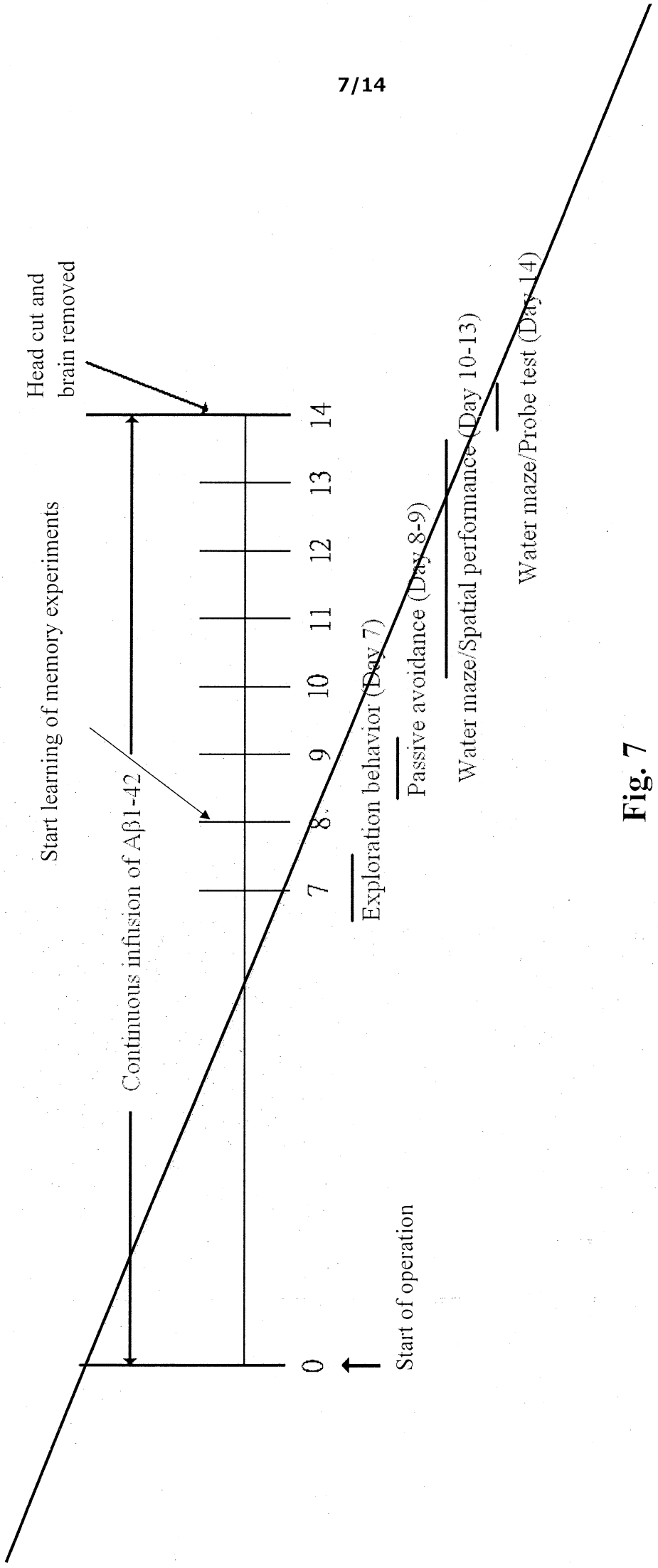

Head cut and brain removed
Start learning of memory experiments
Continuous infusion of Aβ1-42
0
7
8
9
10
11
12
13
14
Start of operation
Exploration behavior (Day 7)
Passive avoidance (Day 8-9)
Water maze/Spatial performance (Day 10-13)
Water maze/Probe test (Day 14)

Fig. 7

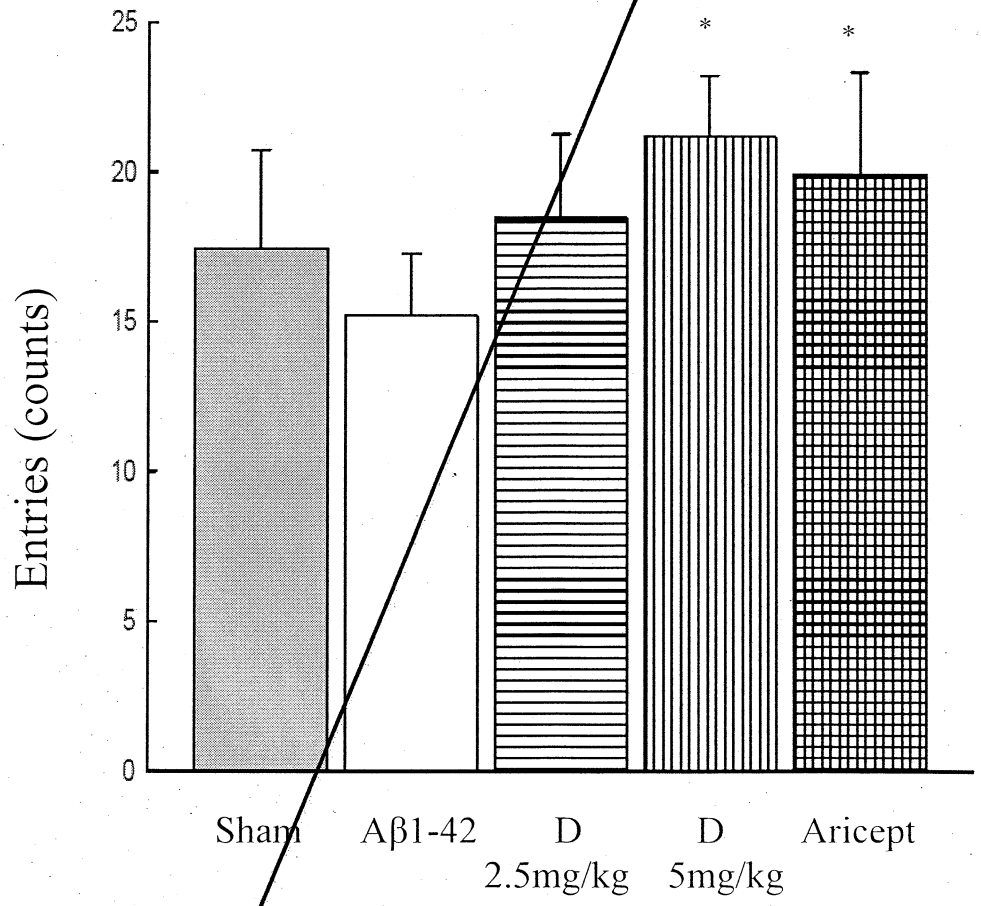

25
20
15
10
5
0
Entries (counts)
*
*
Sham
Aβ1-42
D
2.5mg/kg
D
5mg/kg
Aricept

Fig. 8

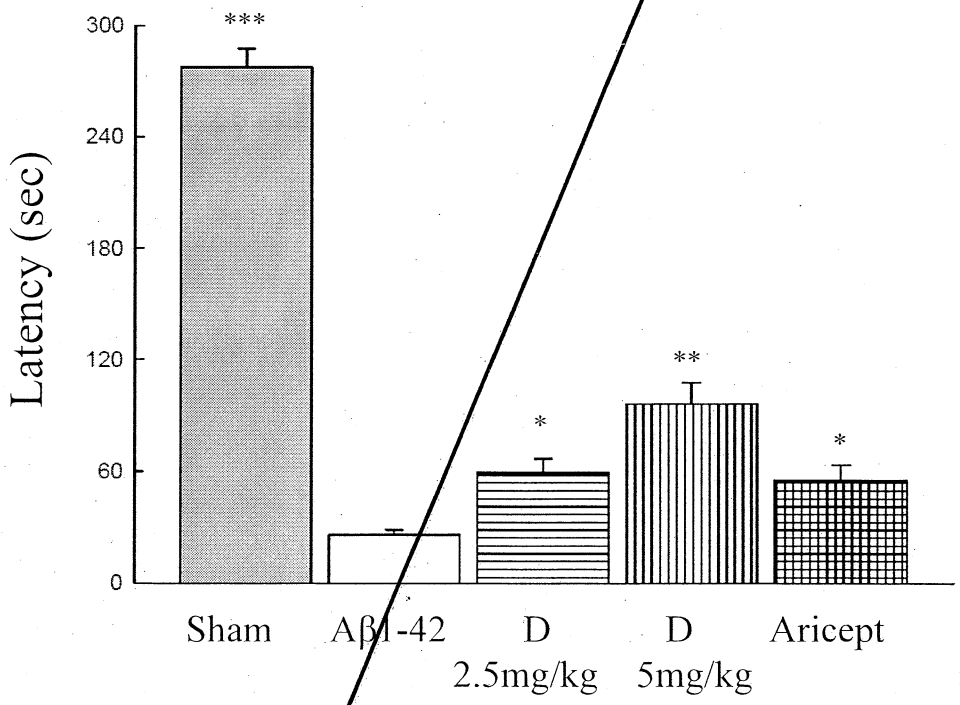

Latency (sec)
300
240
180
120
60
0
***
*
**
*
Sham
Aβ1-42
D 2.5mg/kg
D 5mg/kg
Aricept

Fig. 9

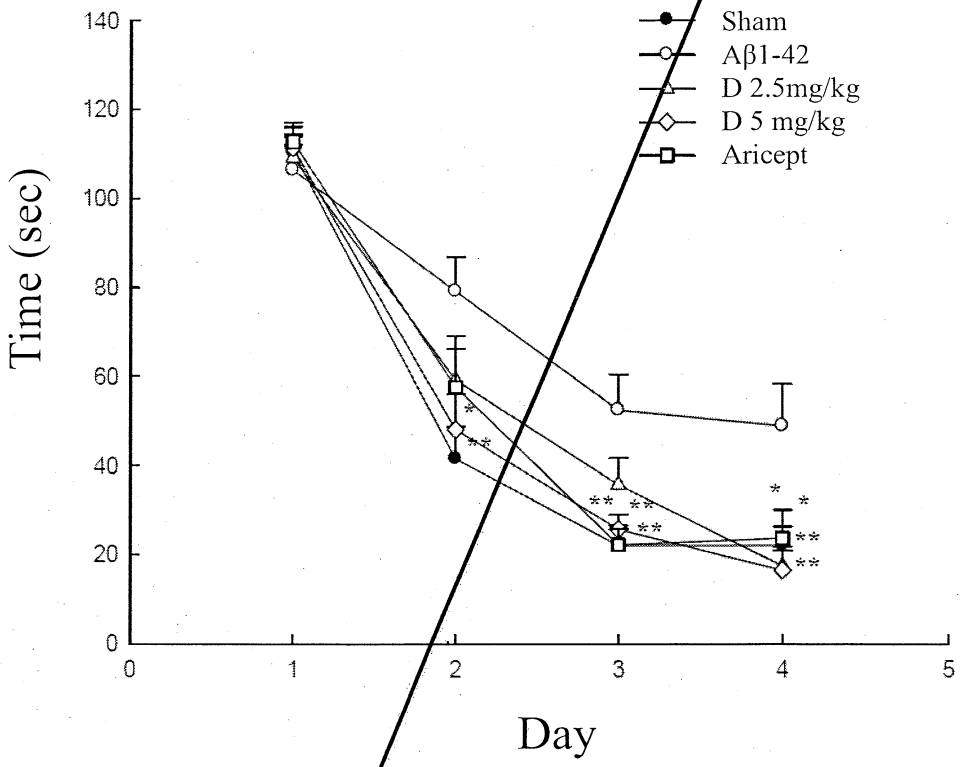

Sham
Aβ1-42
D 2.5mg/kg
D 5 mg/kg
Aricept
Time (sec)
Day
0
20
40
60
80
100
120
140
0
1
2
3
4
5

Fig.10

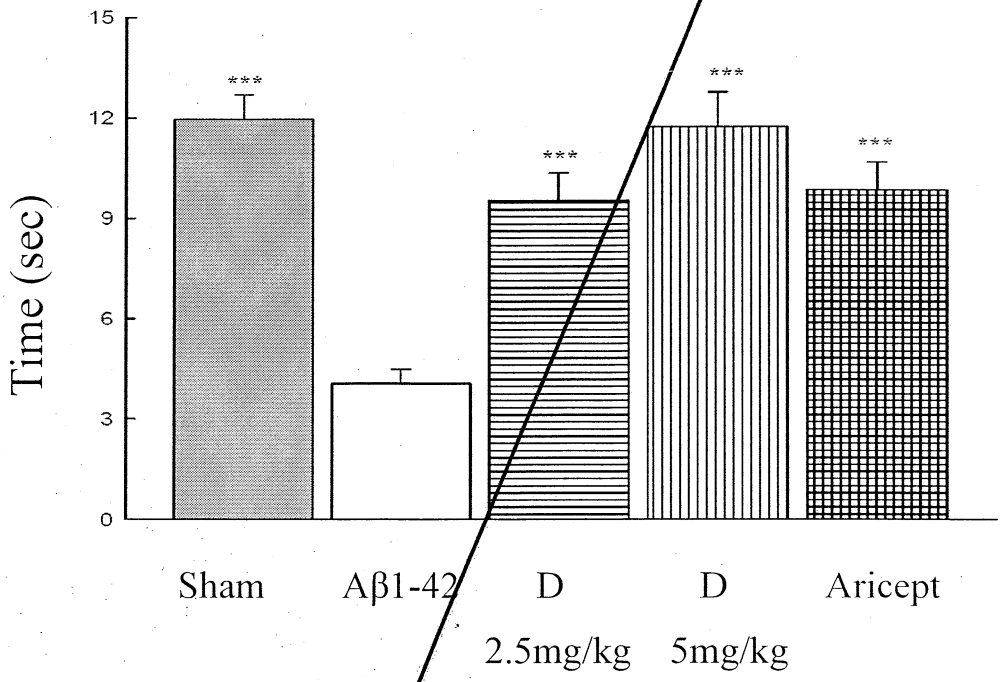
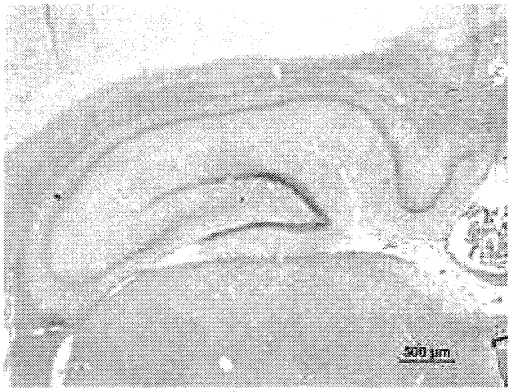
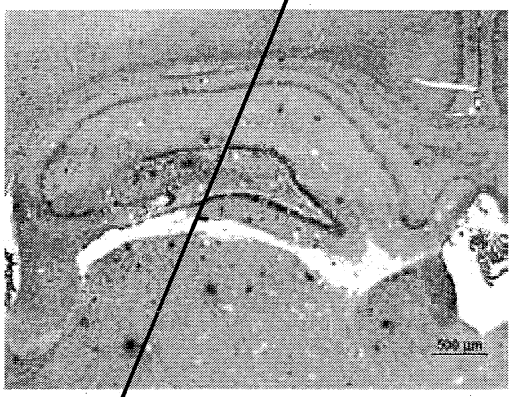


Fig. 11

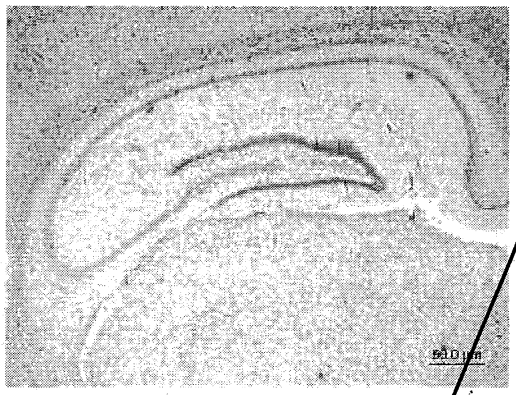
(A) Sham



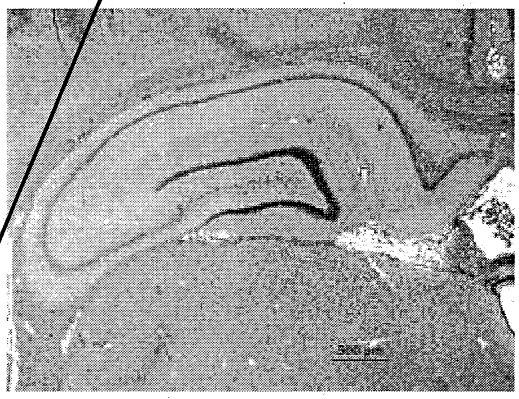
(B) Aβ1-42



(C) D 2.5 mg/kg



(D) D 5 mg/kg



(E) Aricept

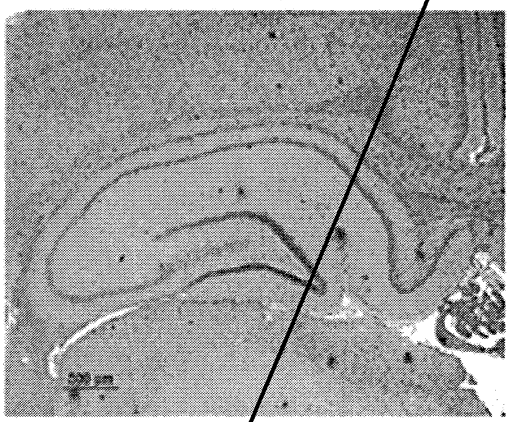


Fig. 12A-E

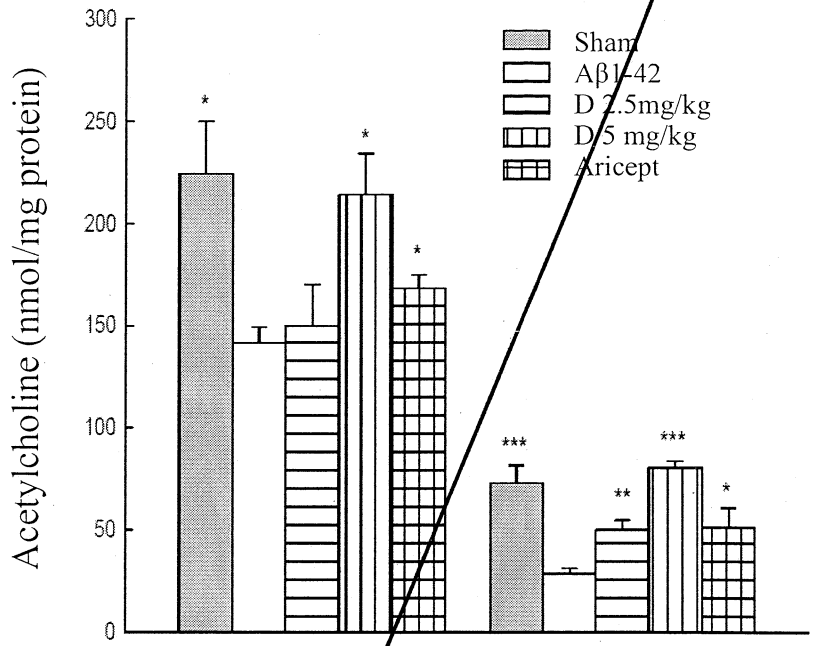


Fig. 13A

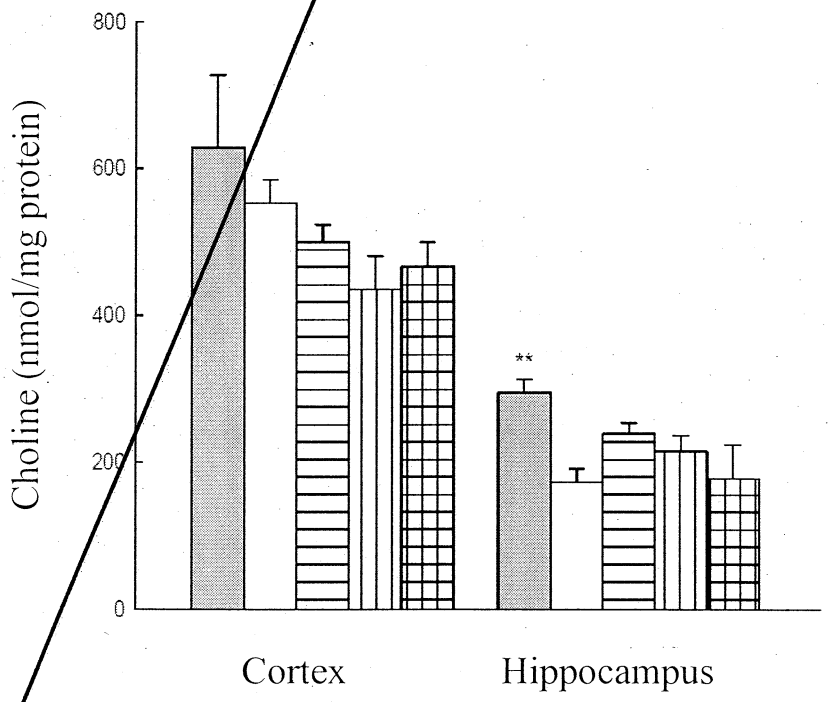


Fig.13B

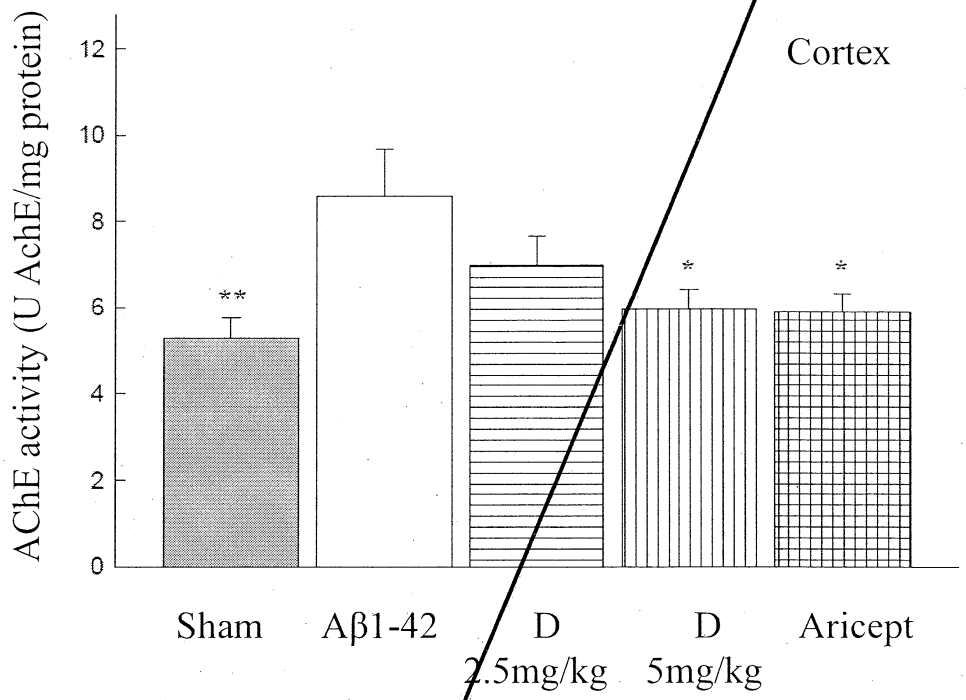


Fig. 14A

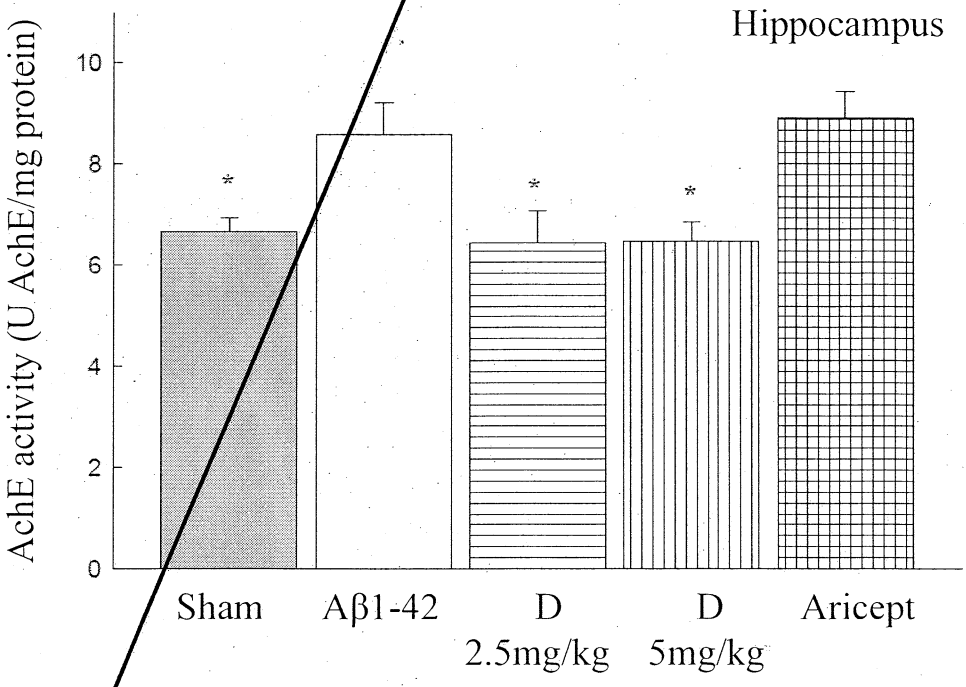


Fig. 14B

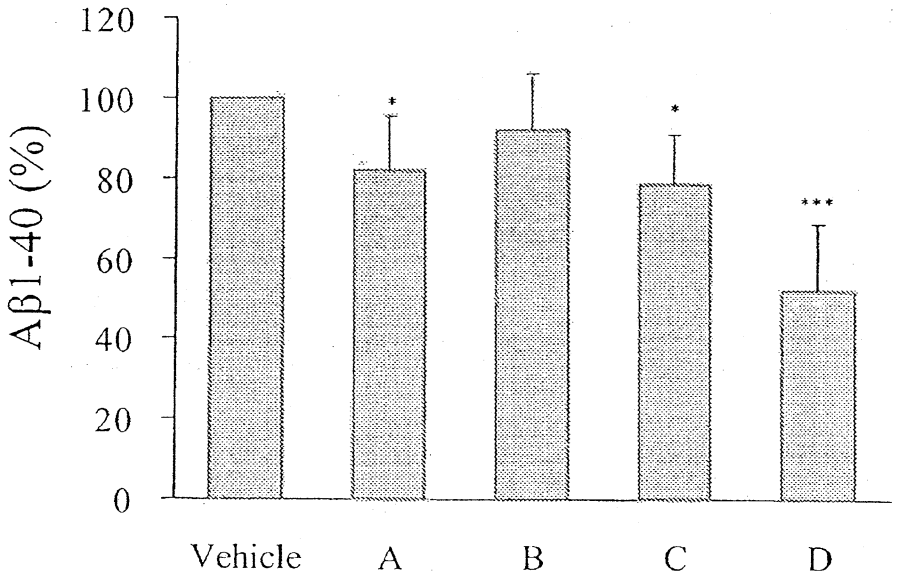


Fig. 1

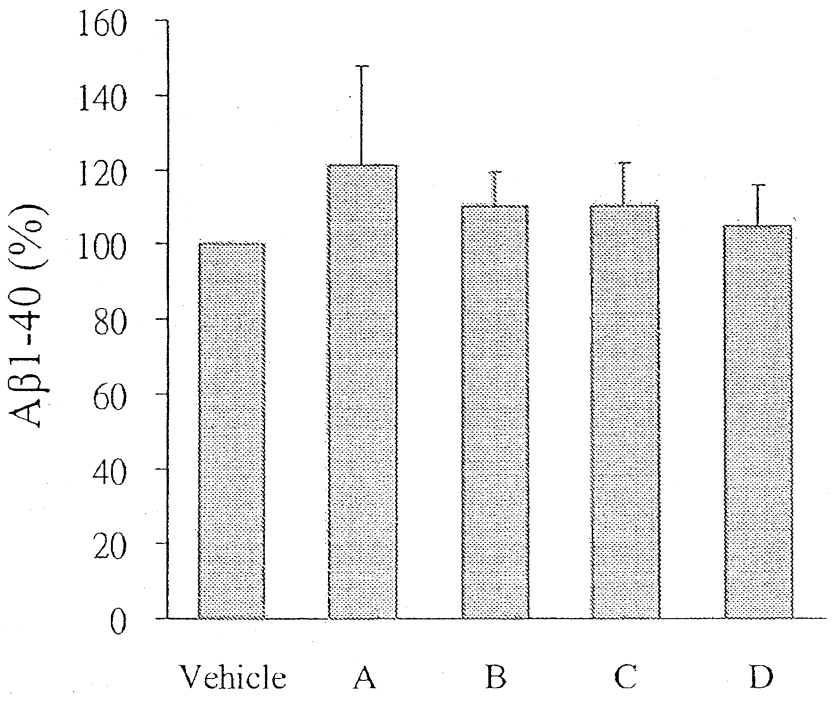


Fig. 2

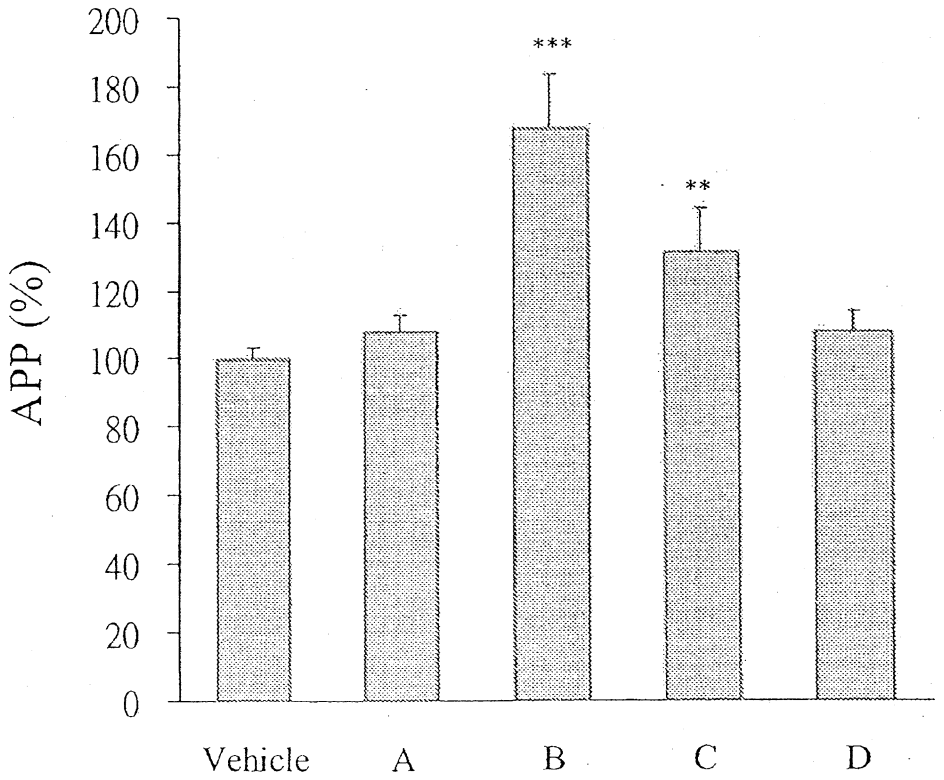


Fig. 3

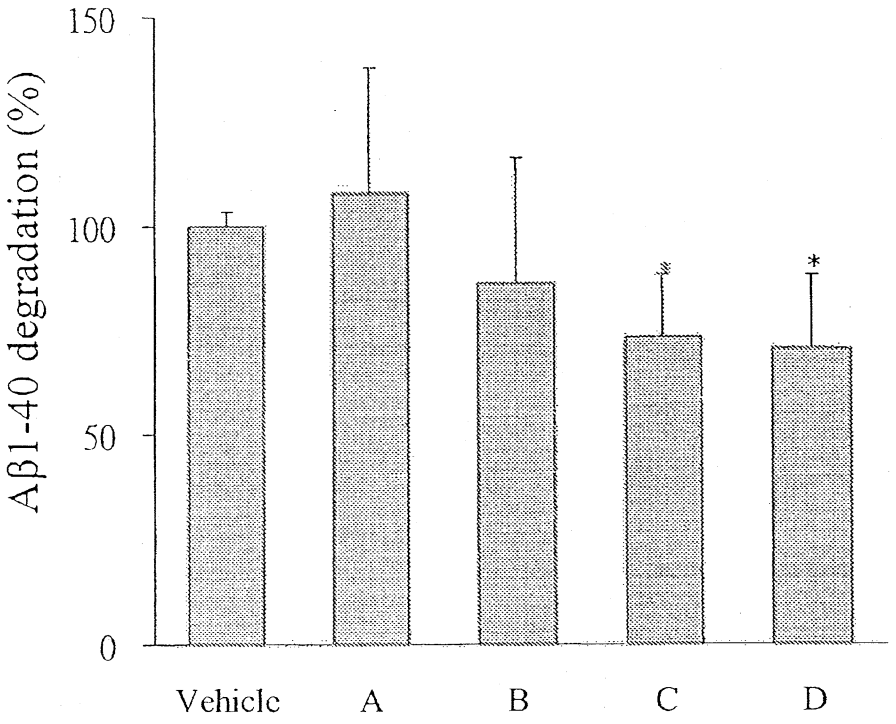


Fig. 4

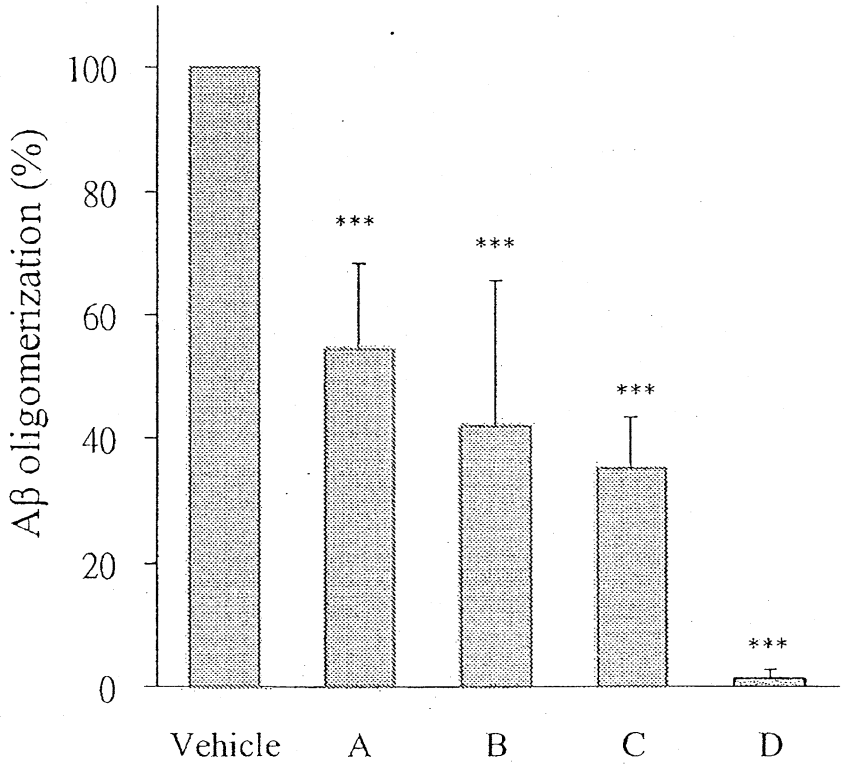


Fig. 5

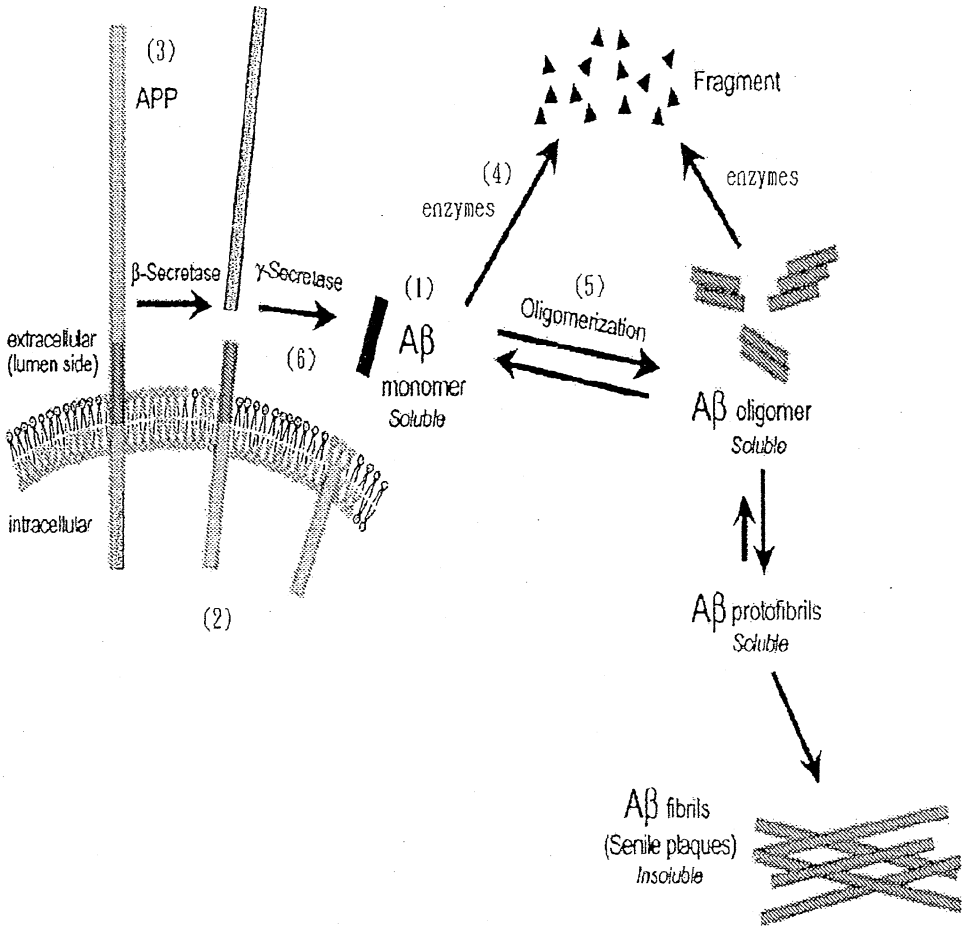

(3)
APP
β-Secretase
γ-Secretase
(1)
Aβ
monomer
Soluble
(2)
(4)
enzymes
Fragment
enzymes
(5)
Oligomerization
(6)
extracellular
(lumen side)
intracellular
Aβ oligomer
Soluble
Aβ protofibrils
Soluble
Aβ fibrils
(Senile plaques)
Insoluble

Fig. 6

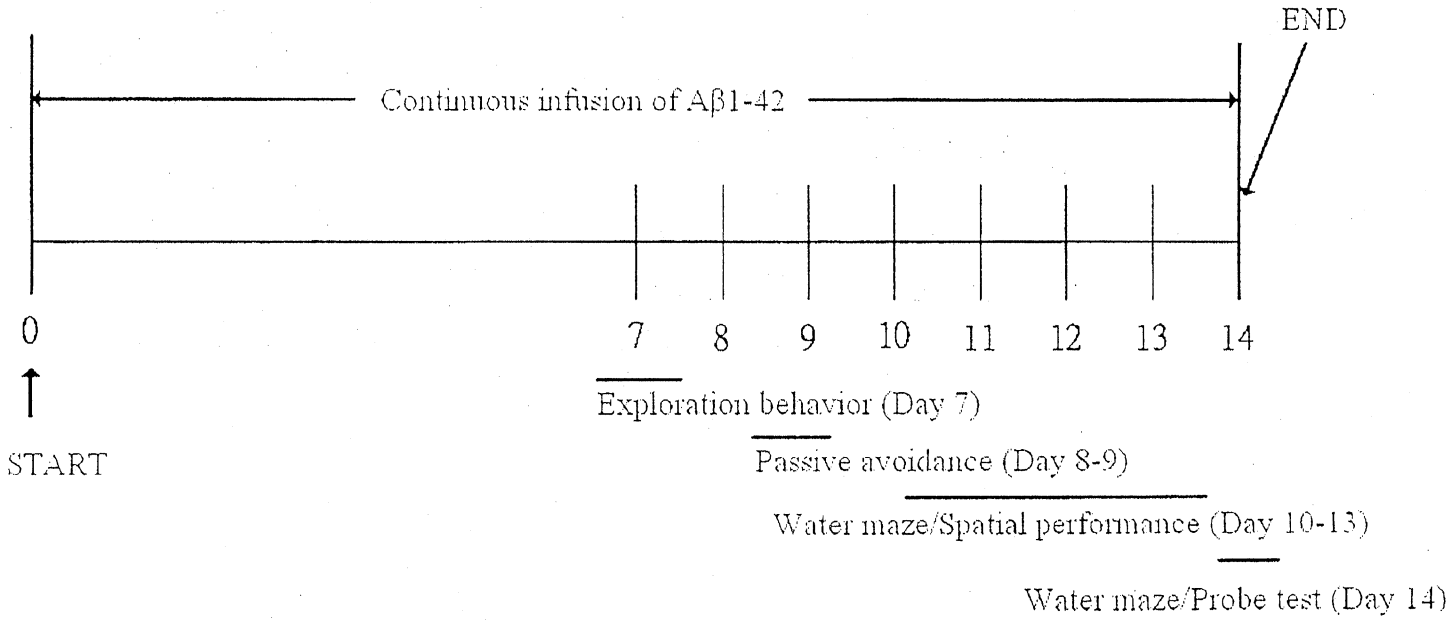

END
Continuous infusion of Aβ1-42
0
7
8
9
10
11
12
13
14
START
Exploration behavior (Day 7)
Passive avoidance (Day 8-9)
Water maze/Spatial performance (Day 10-13)
Water maze/Probe test (Day 14)

Fig. 7

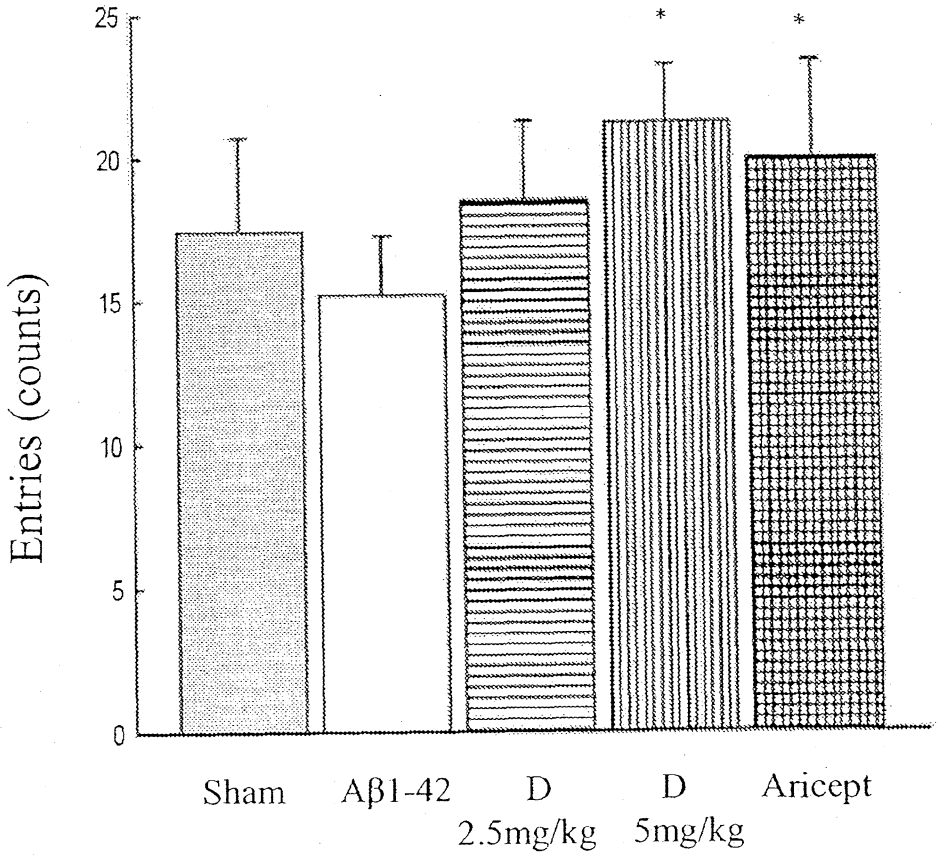

Entries (counts)
25
20
15
10
5
0
*
*
Sham
Aβ1-42
D 2.5mg/kg
D 5mg/kg
Aricept

Fig. 8

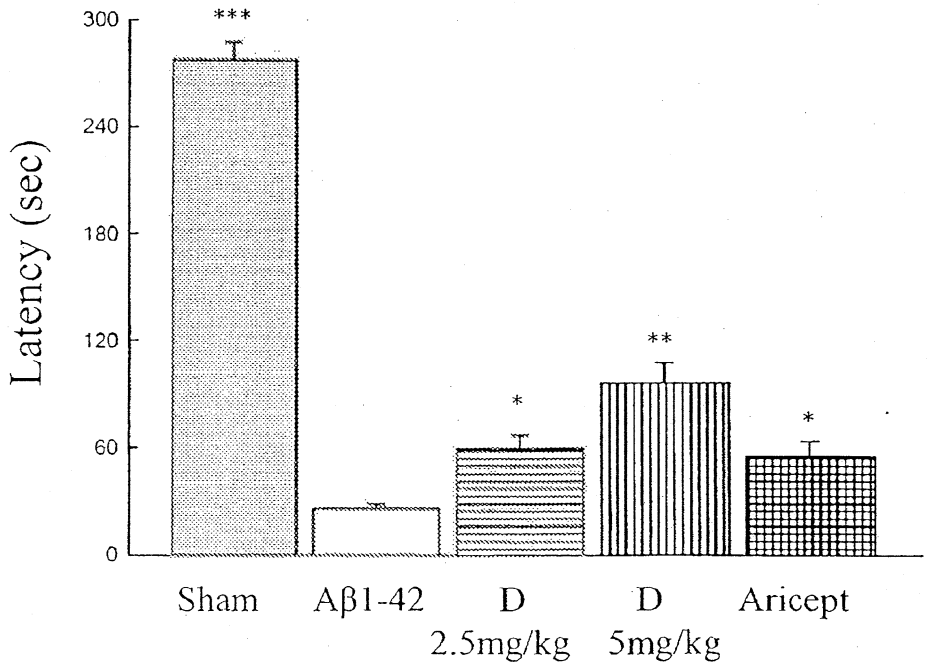

Latency (sec)
300
240
180
120
60
0
***
*
**
*
Sham
Aβ1-42
D
2.5mg/kg
D
5mg/kg
Aricept

Fig. 9

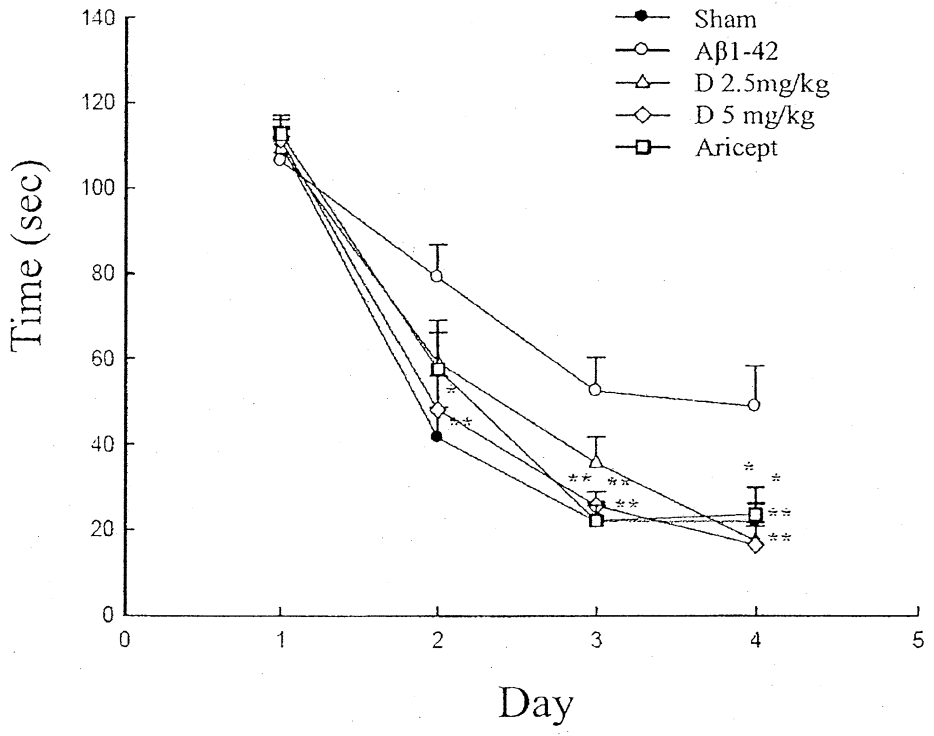

Sham
Aβ1-42
D 2.5mg/kg
D 5 mg/kg
Aricept
Time (sec)
Day
140
120
100
80
60
40
20
0
0
1
2
3
4
5

Fig.10

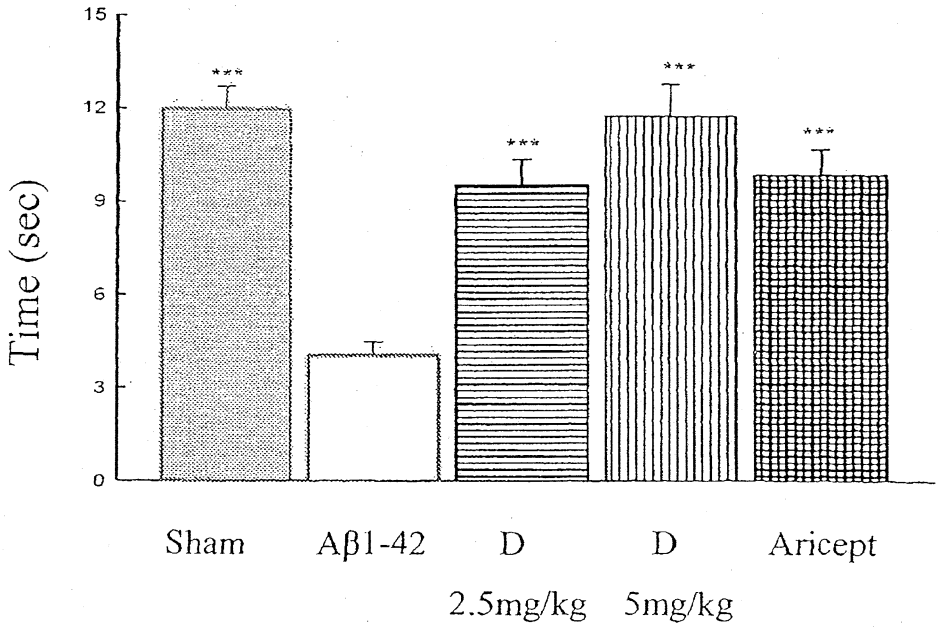
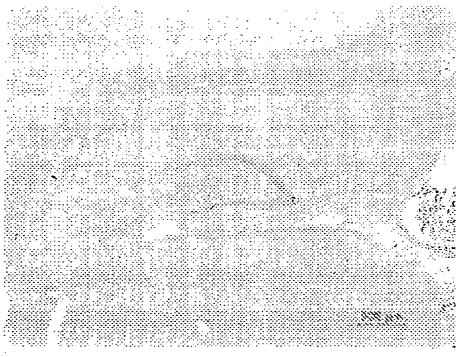
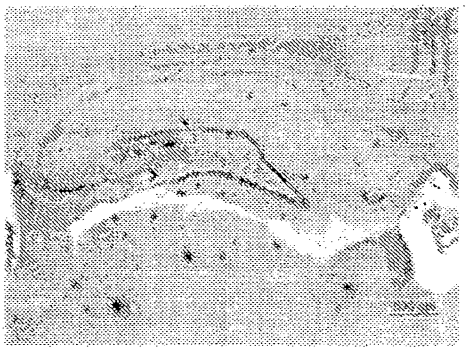


Fig. 11

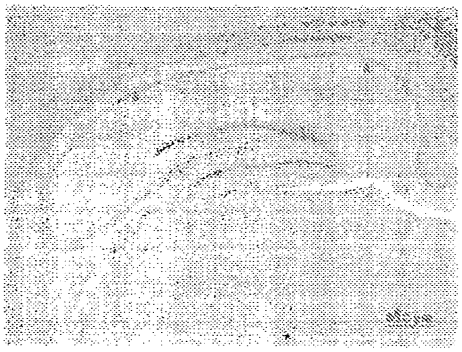
(A) Sham



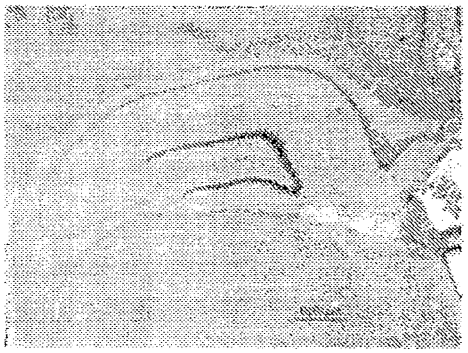
(B) Aβ1-42



(C) D 2.5 mg/kg



(D) D 5 mg/kg



(E) Aricept

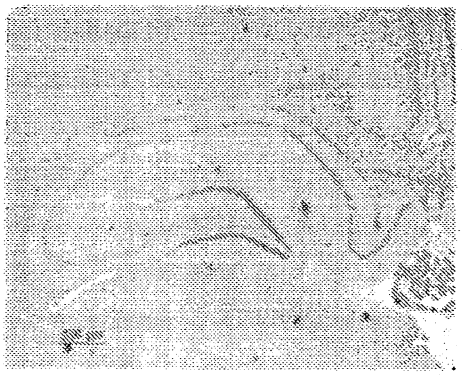


Fig. 12A-E

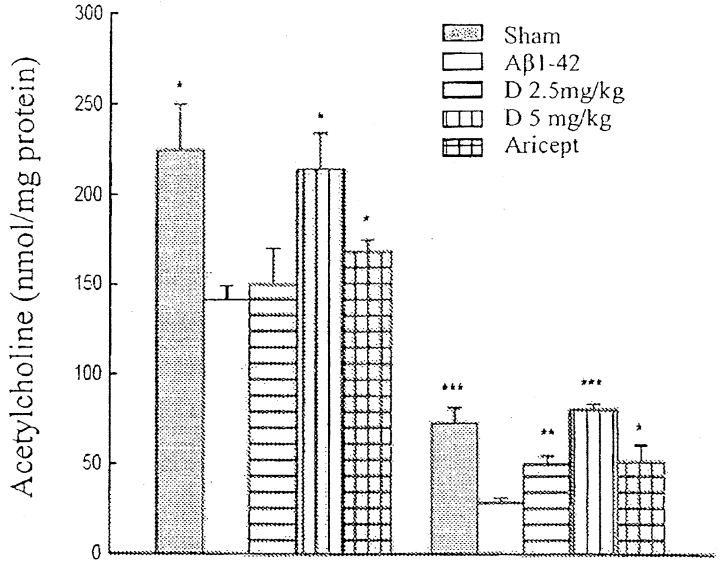


Fig. 13A

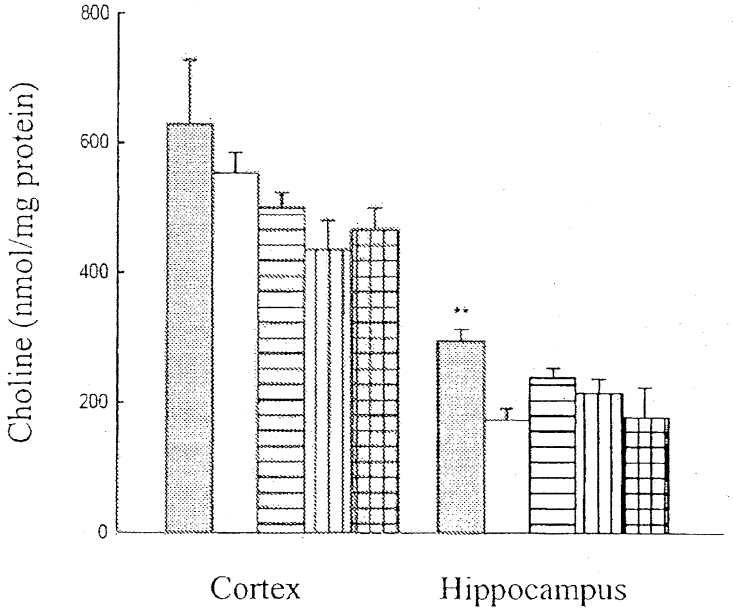


Fig.13B

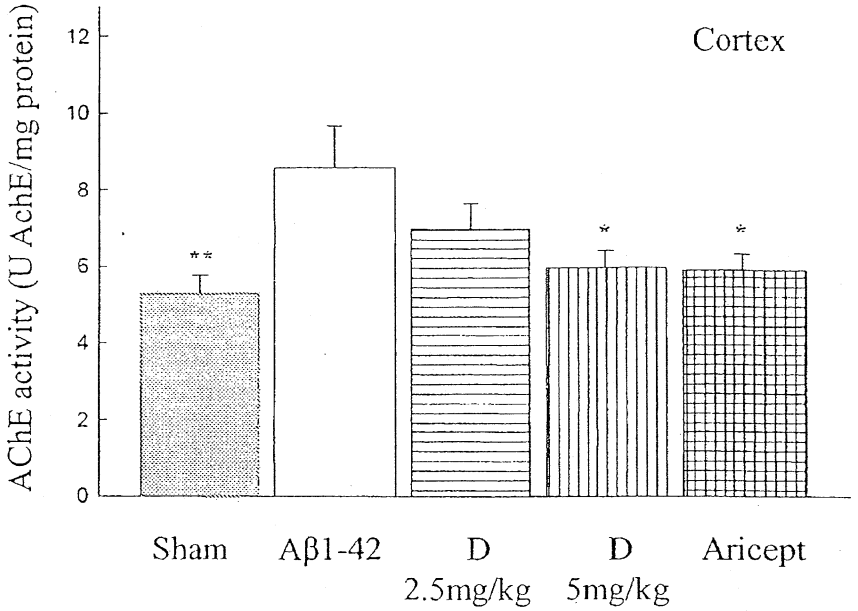


Fig. 14A

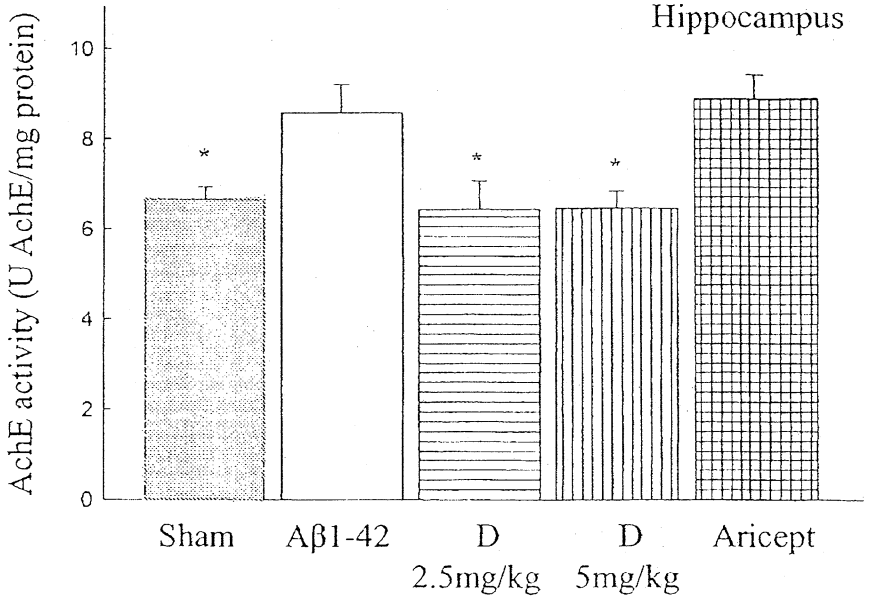


Fig. 14B