The Potential Effect of Caffeine and Nicotine Co-administration on the Induction of Alzheimer's disease

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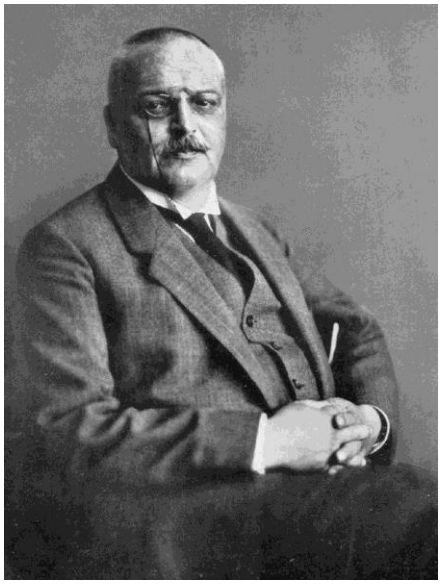
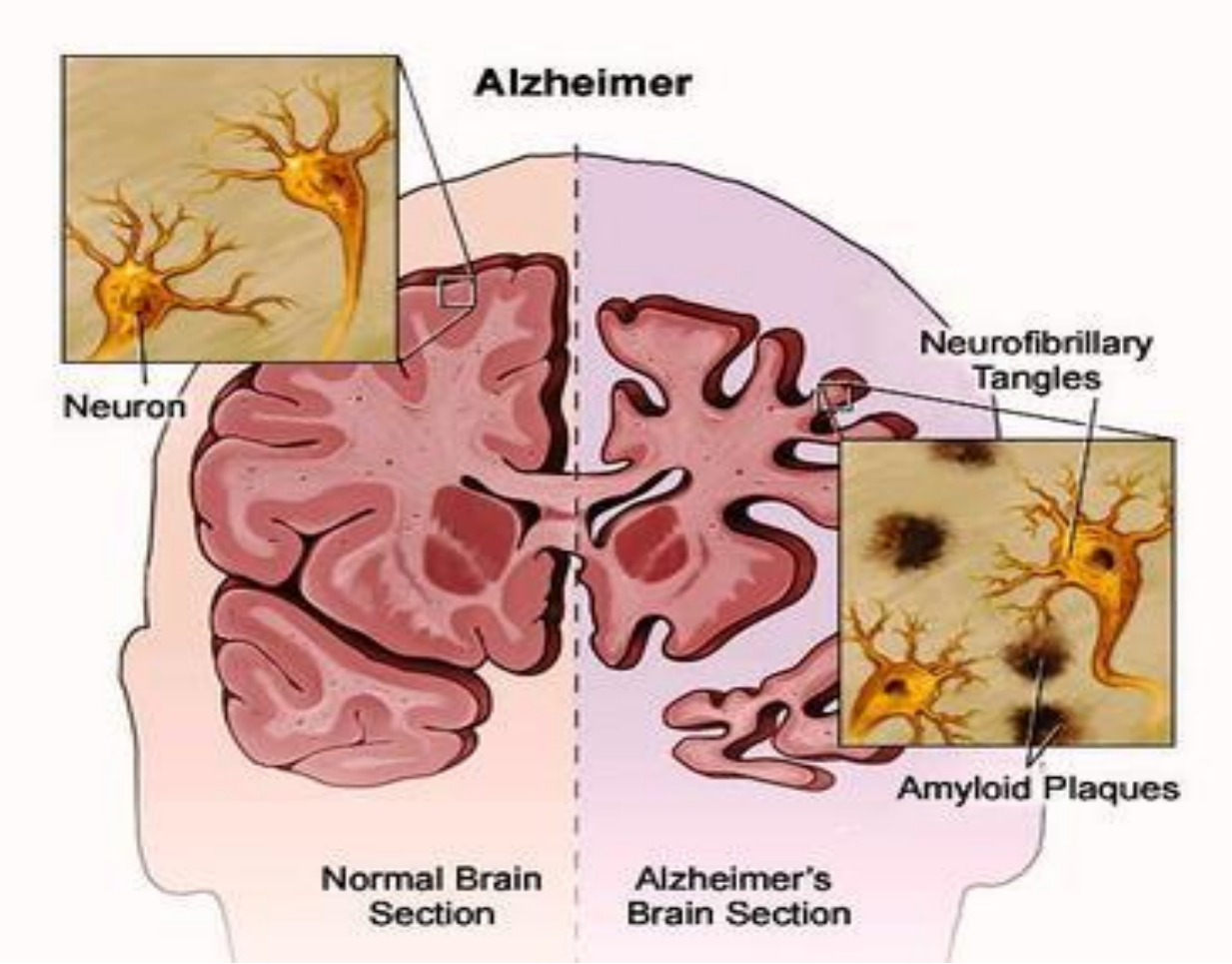
Alzheimer’s disease

Alzheimer's disease (AD) is a progressive neurodegenerative disease characterized clinically by cognitive decline and memory loss

It was first described by German psychiatrist and Neuropathologist Alois Alzheimer in 1906

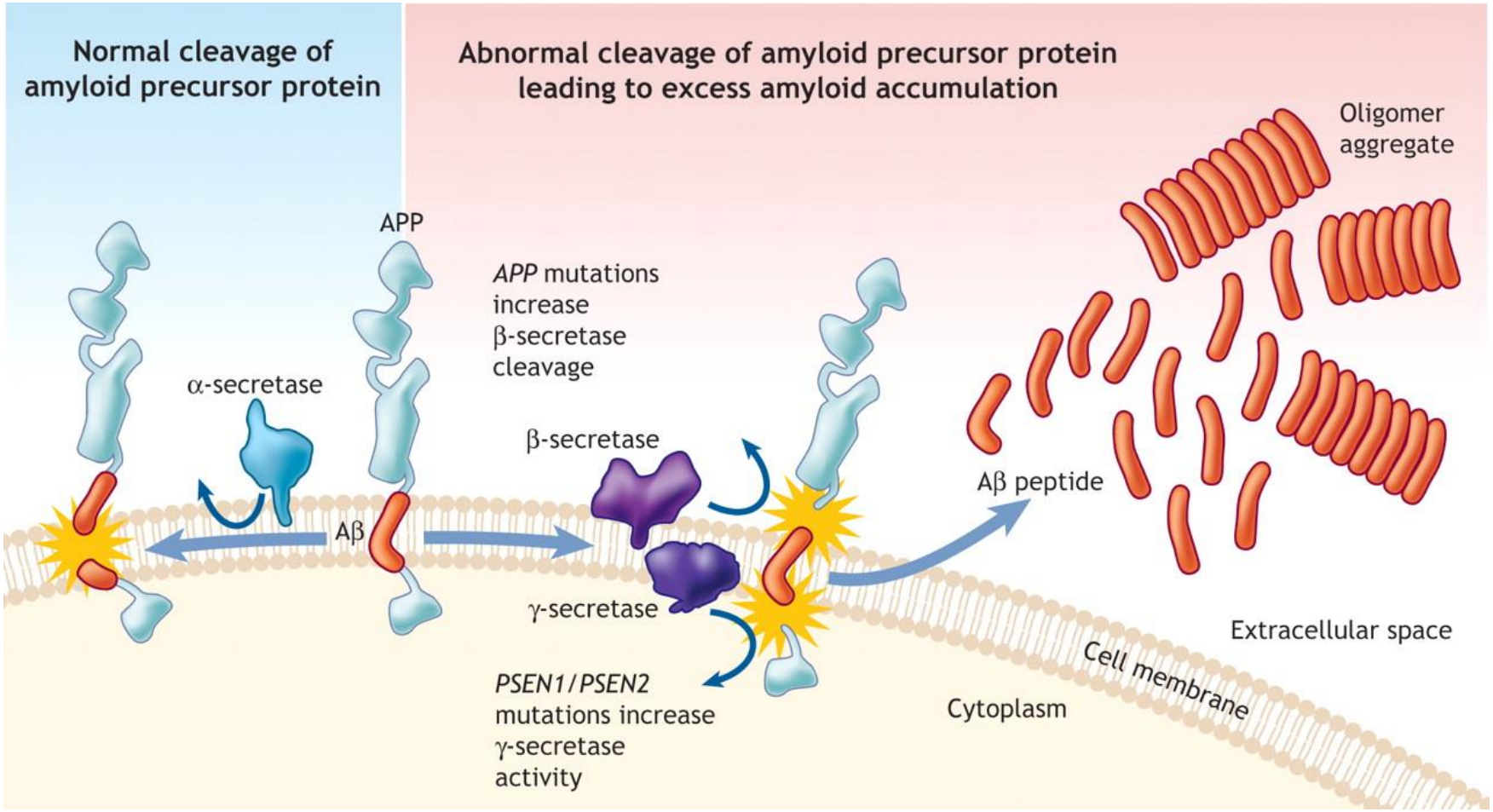


Pathological hallmarks of AD



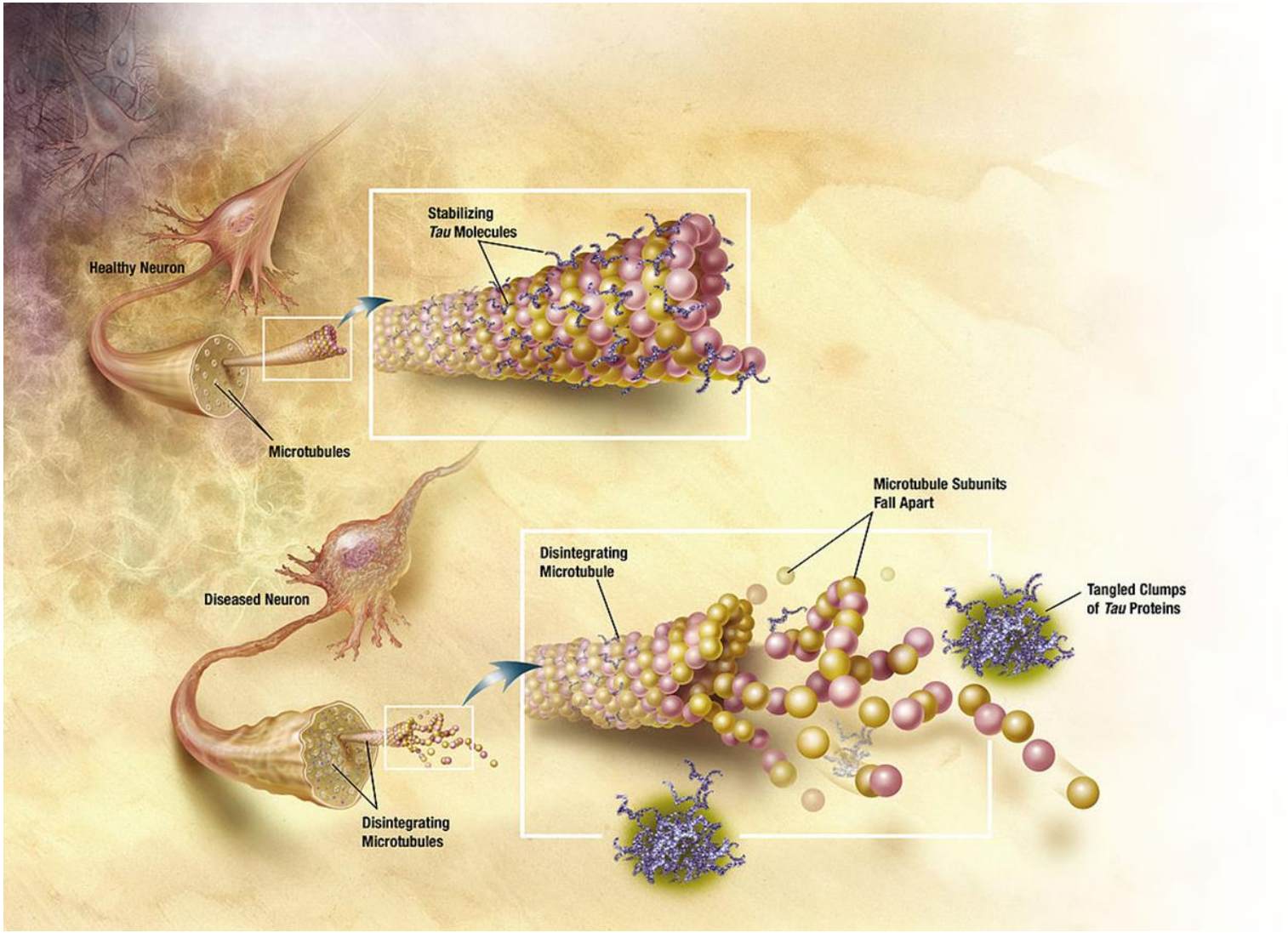
https://neurowiki2012.wikispaces.com/Down+Syndrome

β-amyloid plaques



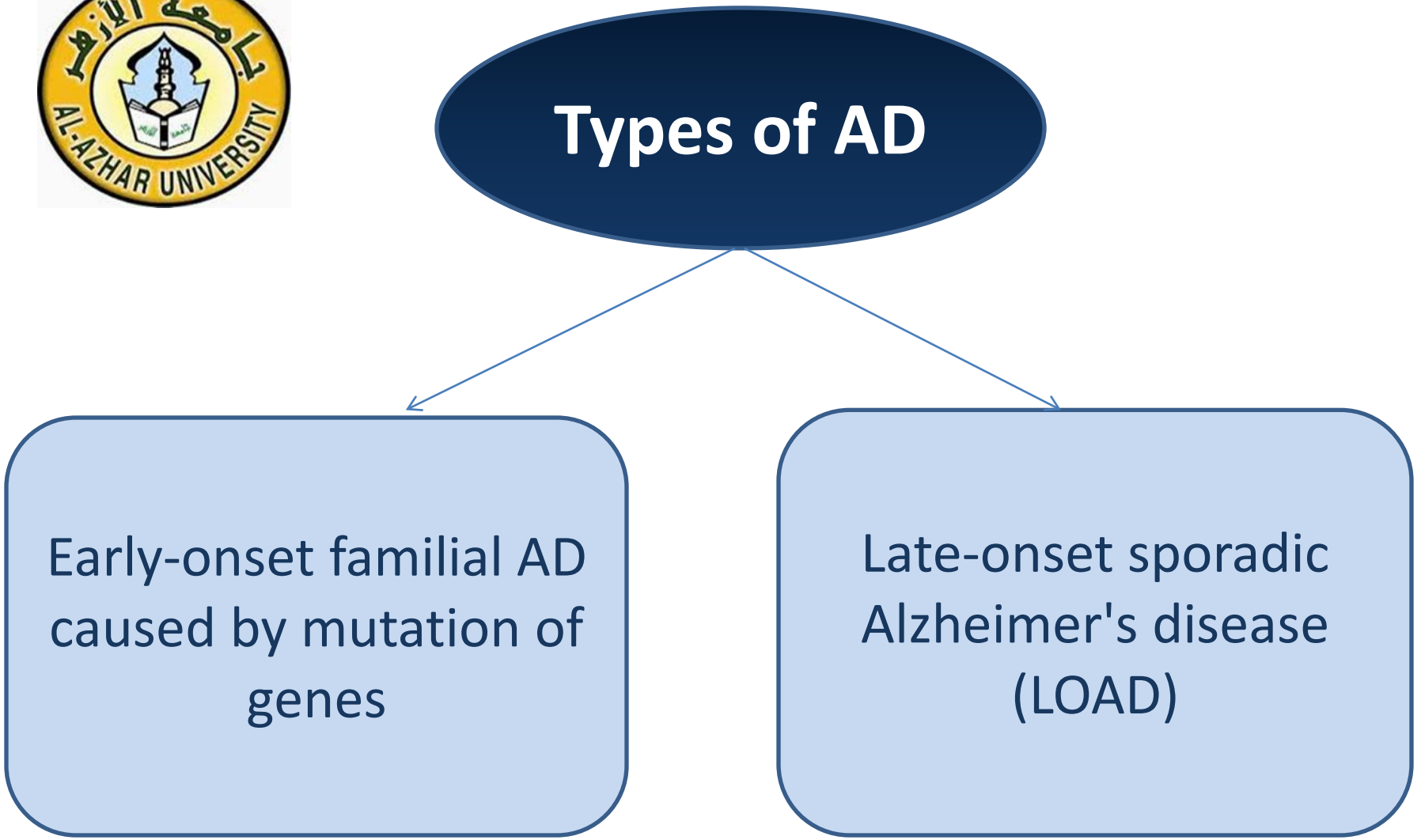
Lianne Friesen and Nicholas Woolridge

Neurofibrillary tangles



https://commons.wikimedia.org/wiki/File:TANGLES_HIGH.jpg

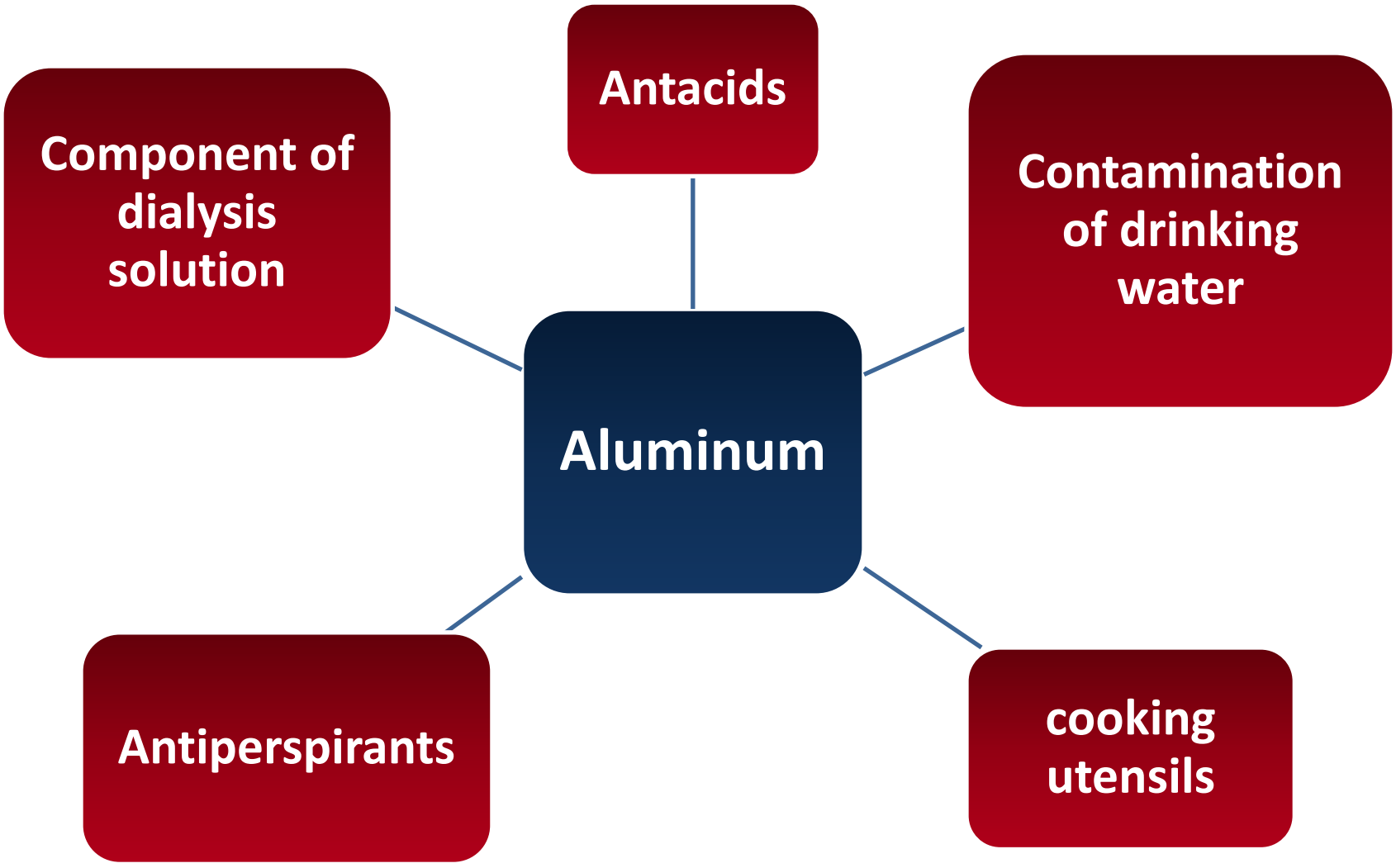
Types of AD


Early-onset familial AD caused by mutation of genes
Late-onset sporadic Alzheimer's disease (LOAD)

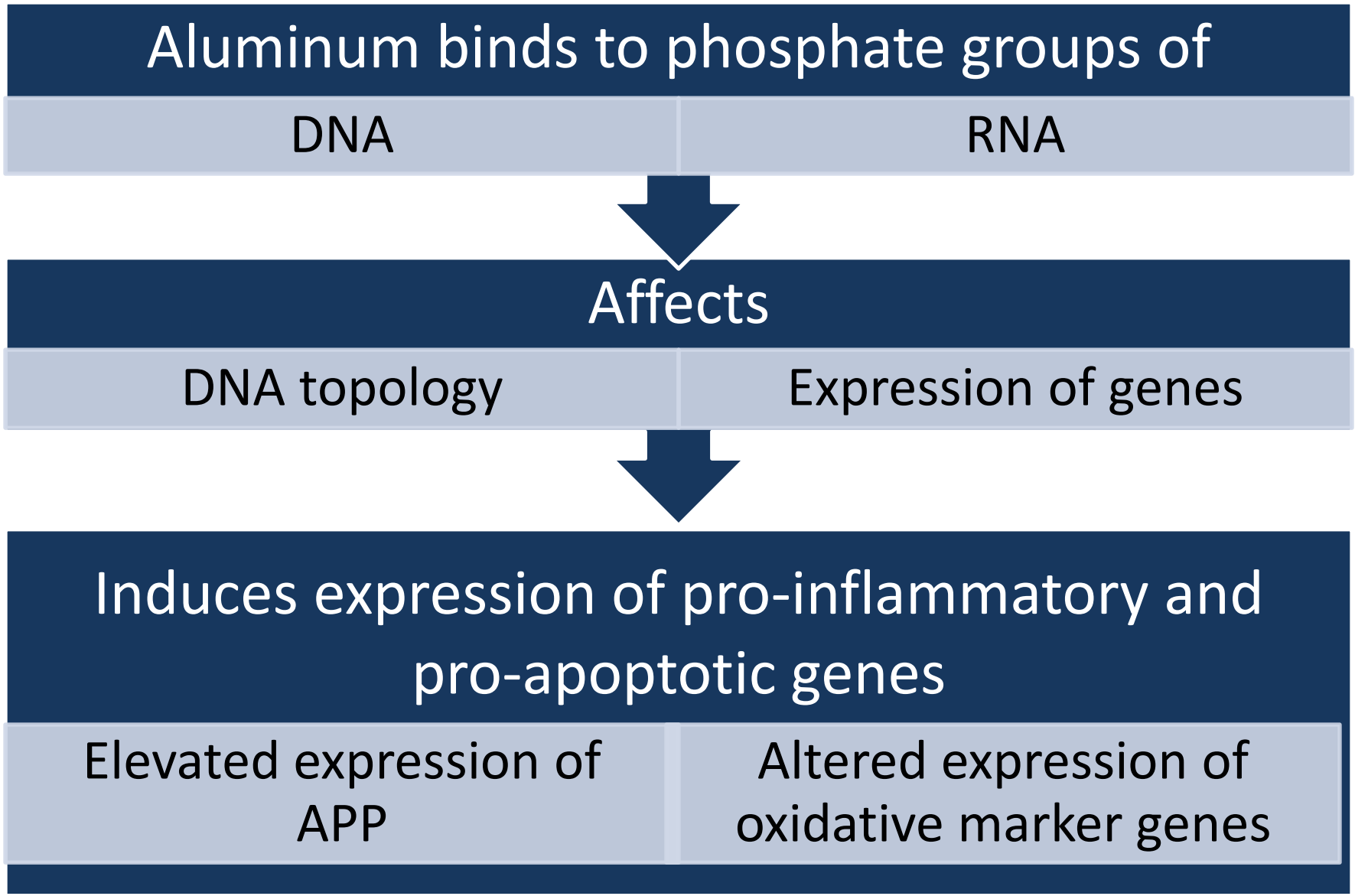
Aluminum

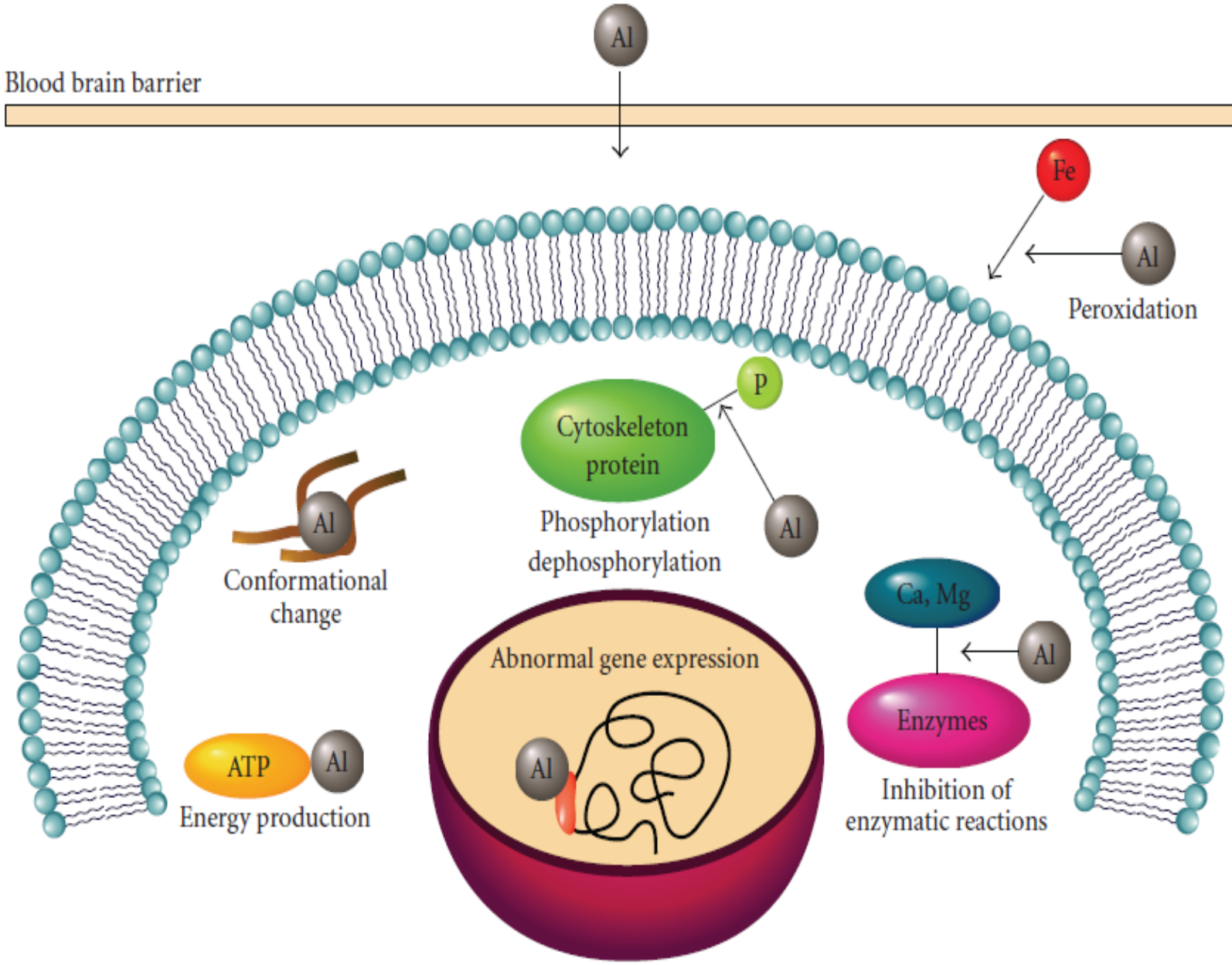
Aluminum is a well established neurotoxin and is suspected to be linked with various neurodegenerative diseases including Alzheimer's disease

Exposure to Aluminum



Neurotoxicity of Aluminium



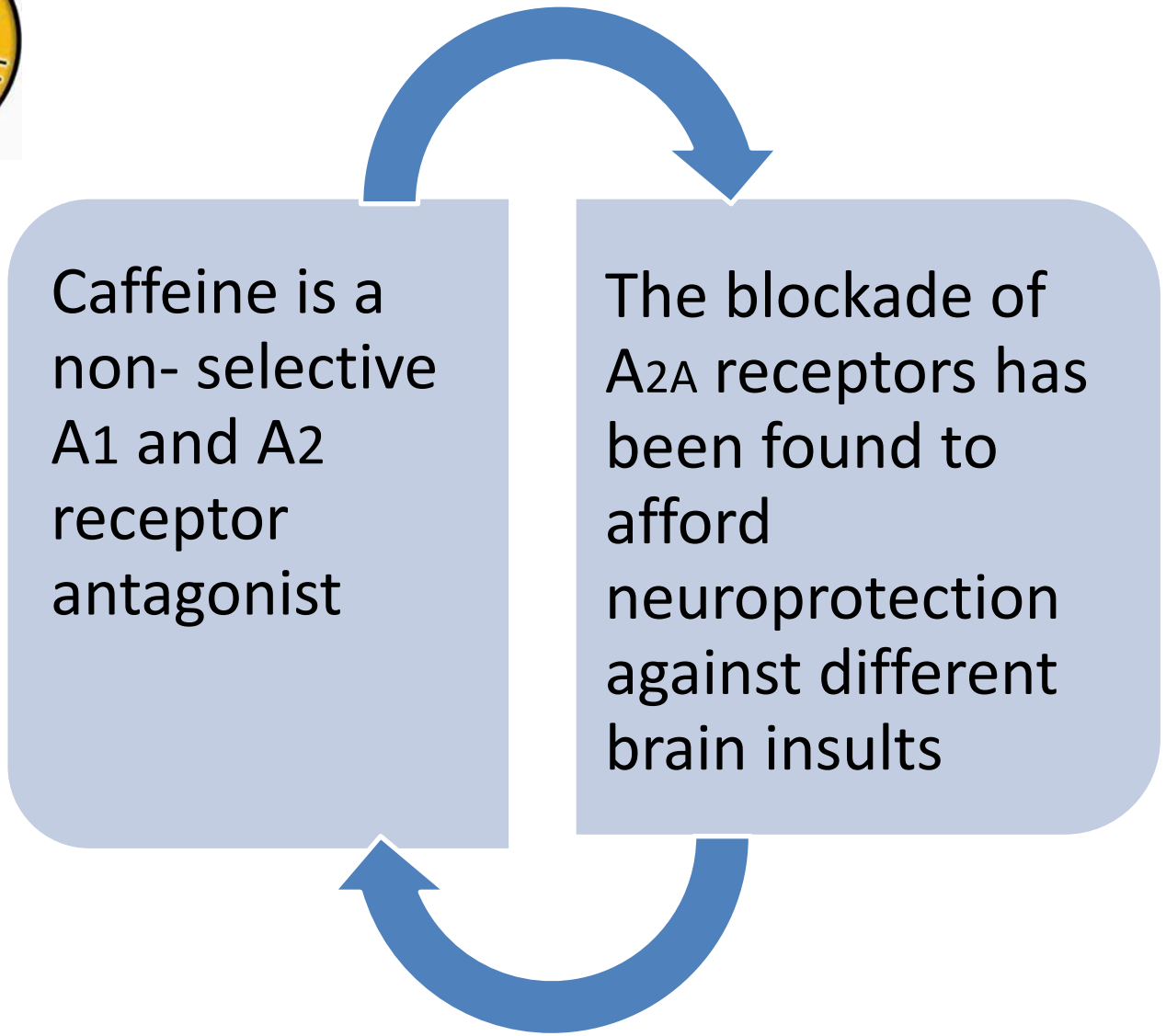


(Masahiro Kawahara and Midori Kato-Negishi)

Caffeine and nicotine are the most commonly co-used psychostimulants

Caffeine

The most widely consumed psychoactive drug present primarily in coffee and tea.


Caffeine is a non- selective A1 and A2 receptor antagonist
The blockade of A2A receptors has been found to afford neuroprotection against different brain insults

Caffeine acts also by increasing

- Cortical activity
- Cerebral energy metabolism
- Extracellular Ach concentration

Antioxidant

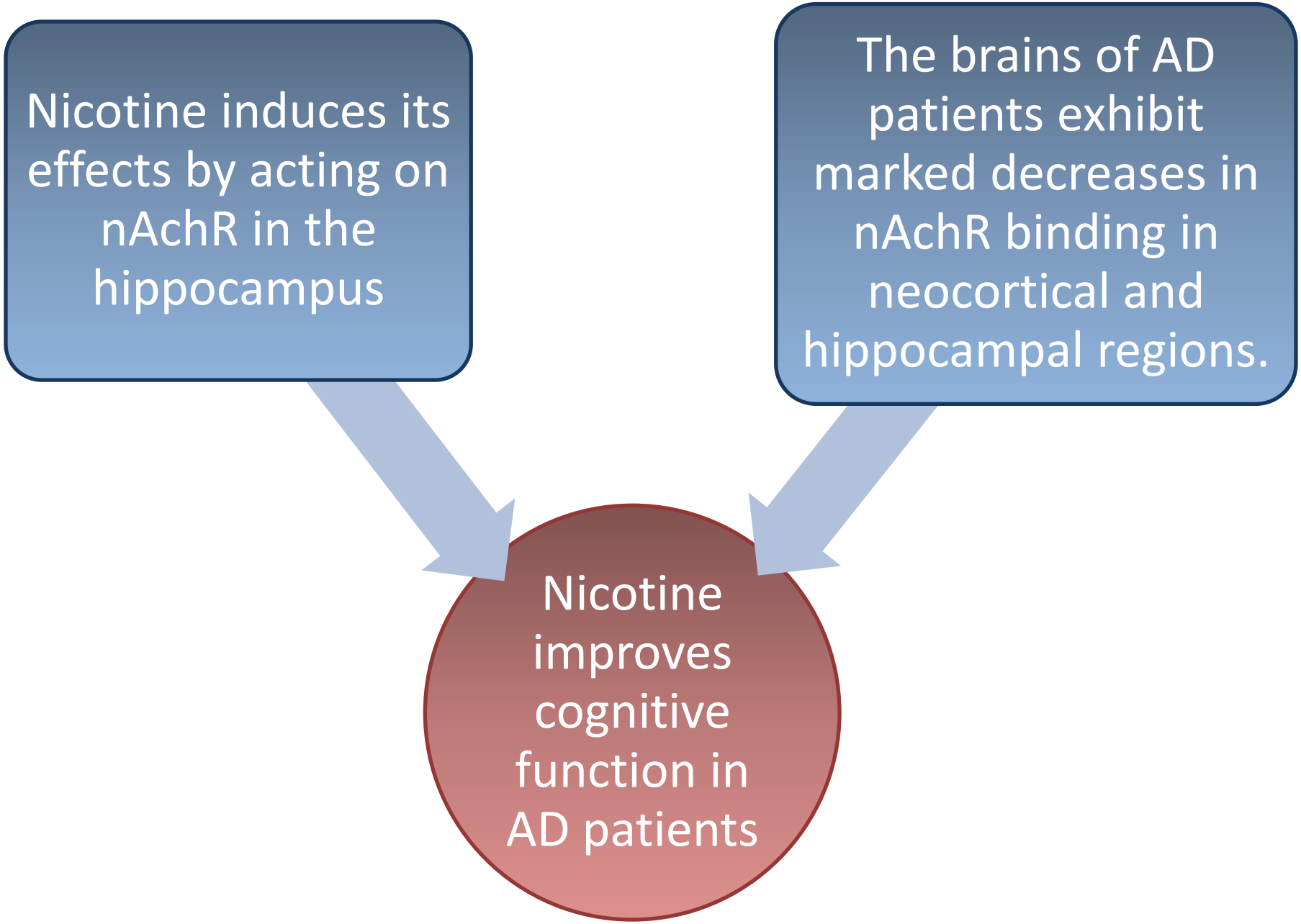
prevents the neurons from oxidative damage

Reduces the risk of chronic degenerative diseases

Nicotine

A major component of cigarette smoke

Has been shown to improve cognitive function in AD patients


Nicotine induces its effects by acting on nAchR in the hippocampus
The brains of AD patients exhibit marked decreases in nAchR binding in neocortical and hippocampal regions.
Nicotine improves cognitive function in AD patients

Nicotine acts also by

- Increasing the expression of BDNF mRNA in the hippocampus
- Attenuating the impairment of LTP and spatial memory associated with chronic stress
- Antioxidant effects

AIM OF THE WORK

Study the behavioral ,biochemical, and histopathological changes induced by caffeine or nicotine during induction of AD in rats.

Evaluate the influence of caffeine and nicotine co-administration against aluminum-induced AD in rats.

MATERIALS AND METHODS

Animals

Forty male Sprague Dawley rats, weighing 180-220 g were used.

Design of the work

Five groups of rats were used and received daily for five weeks

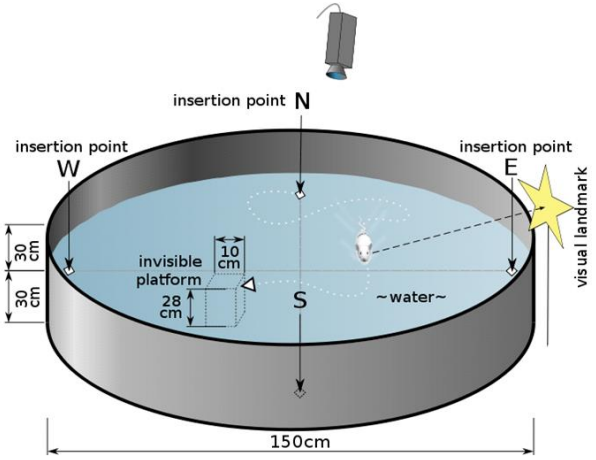
1. Control (Saline)
2. $ALCL_3 .6H_2O$ (70 mg/kg, IP)
3. $ALCL_3$+ Caffeine (5mg/kg, IP)
4. $ALCL_3$ + Nicotine (1mg/kg, SC)
5. $ALCL_3$ + Caffeine + Nicotine

1. Behavioral experiments

Forced swimming test

Morris water maze test

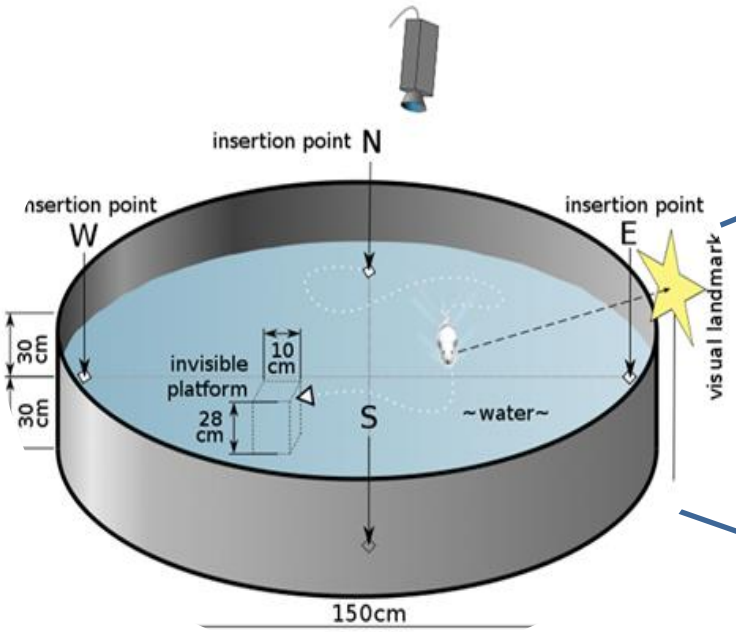
Conditioned avoidance test



Parameters

- Immobility score
- Swimming score
- Climbing score

Parameters

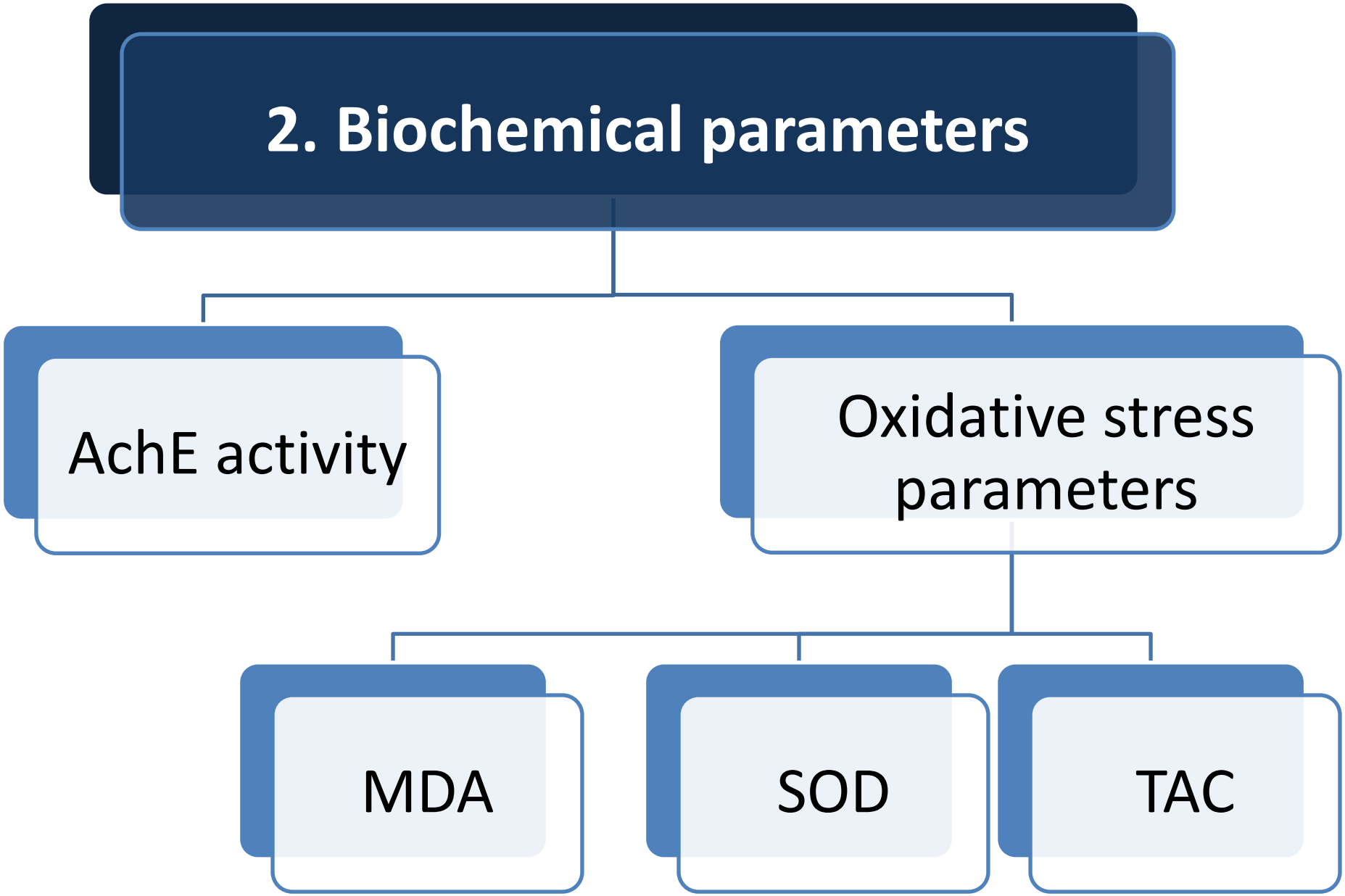


Learning ability

Memory trial

Parameters

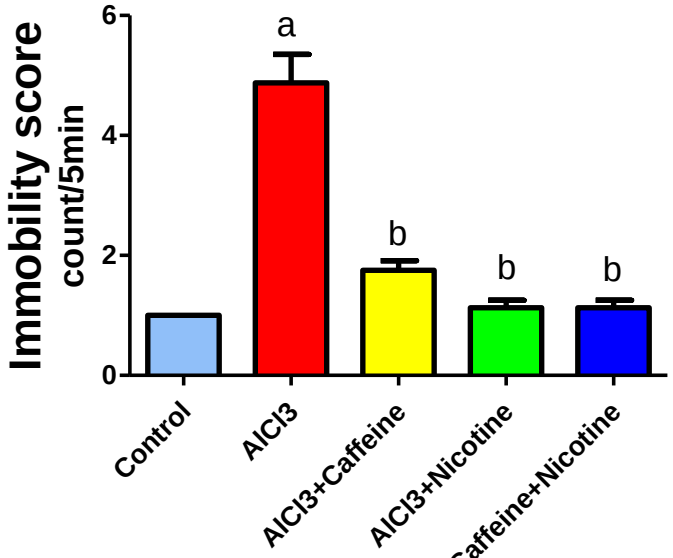
Numbers of trials performed by rats to avoid the electric shock at 1st & 2nd days of the experiment

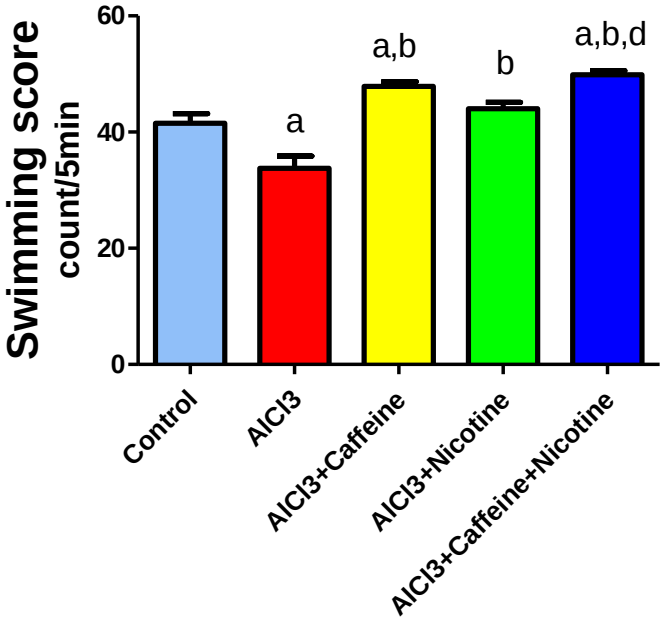

2. Biochemical parameters
AchE activity
Oxidative stress parameters
MDA
SOD
TAC

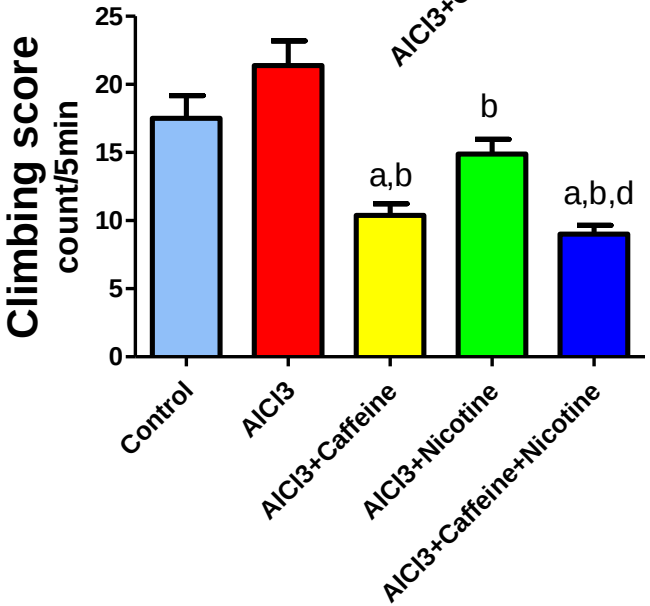
3. Histopathological examination of the brain

RESULTS

Forced swimming test







Significant $p<0.05$:

a: from control

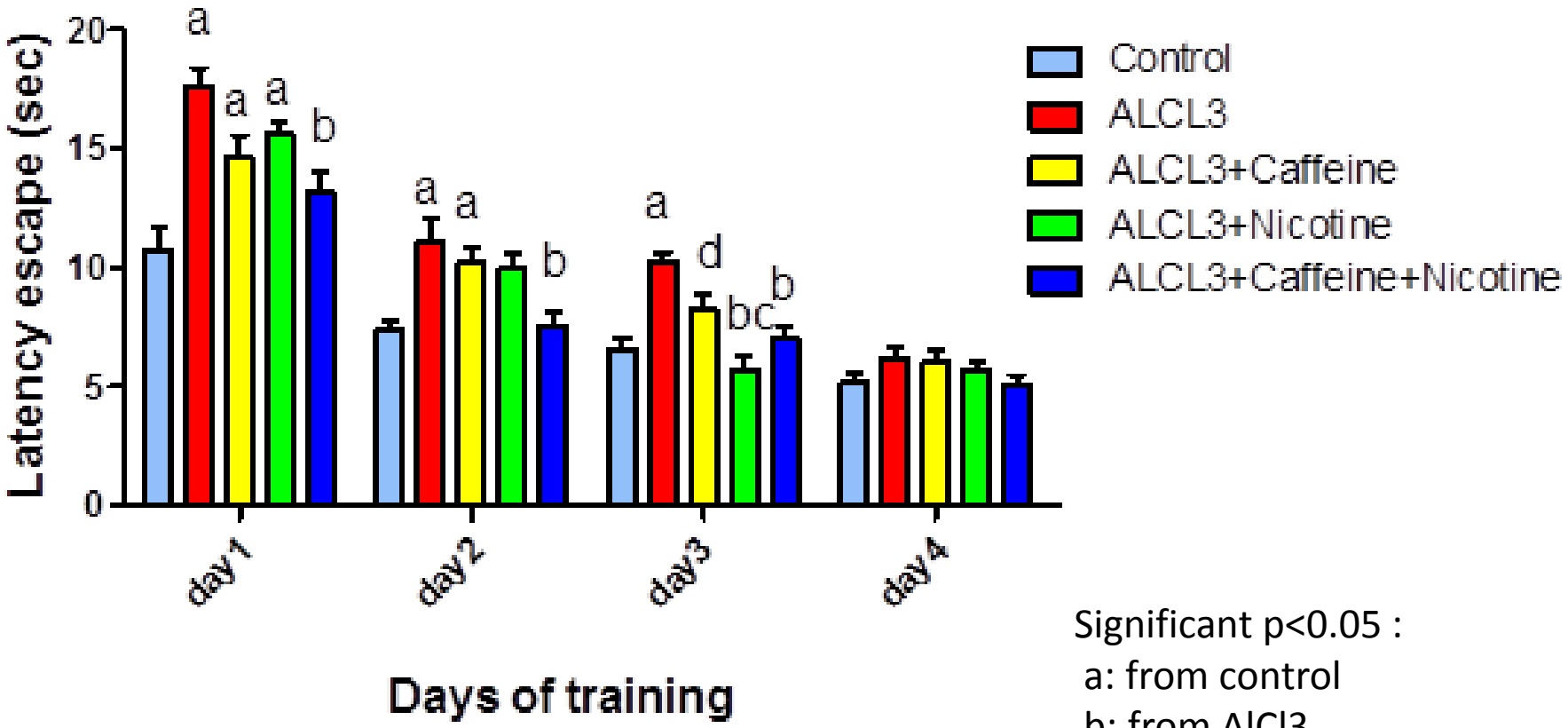
b: from AlCl3

c: from AlCl3 +Caffeine

d: from AlCl3 +Nicotine

Morris water maze

learning ability



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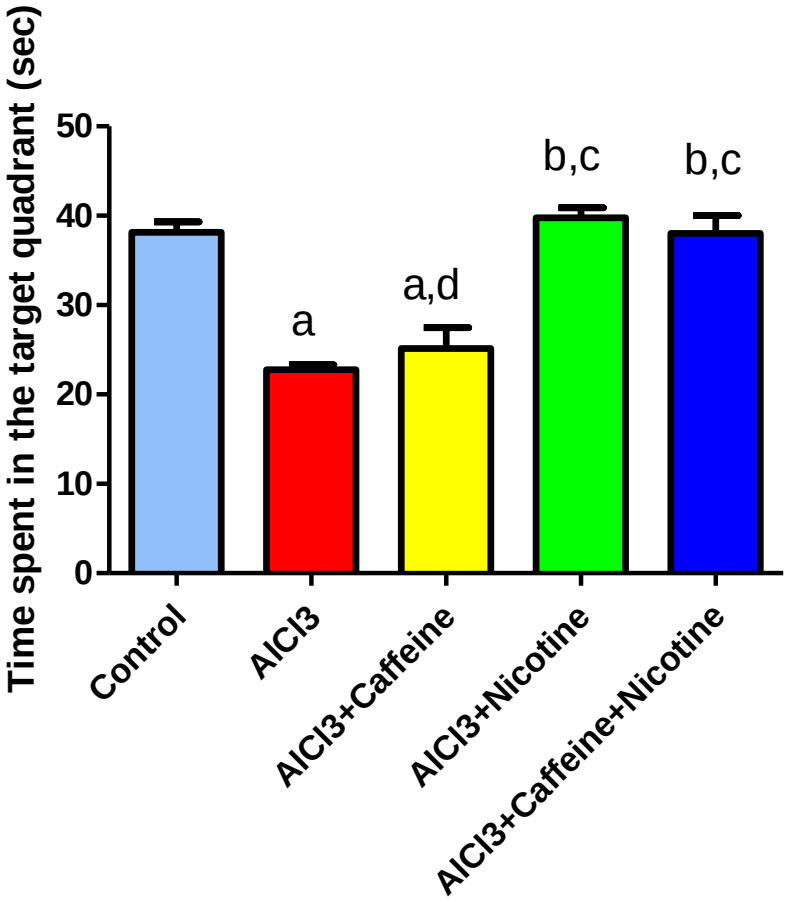
Morris water maze

memory trial



Significant $p<0.05$:

a: from control

b: from AlCl3

c: from AlCl3 +Caffeine

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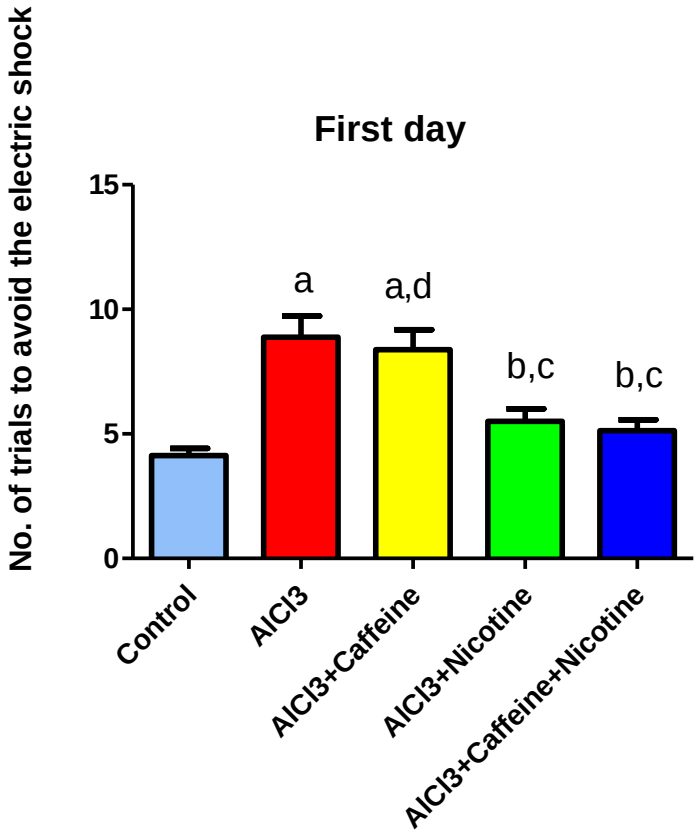
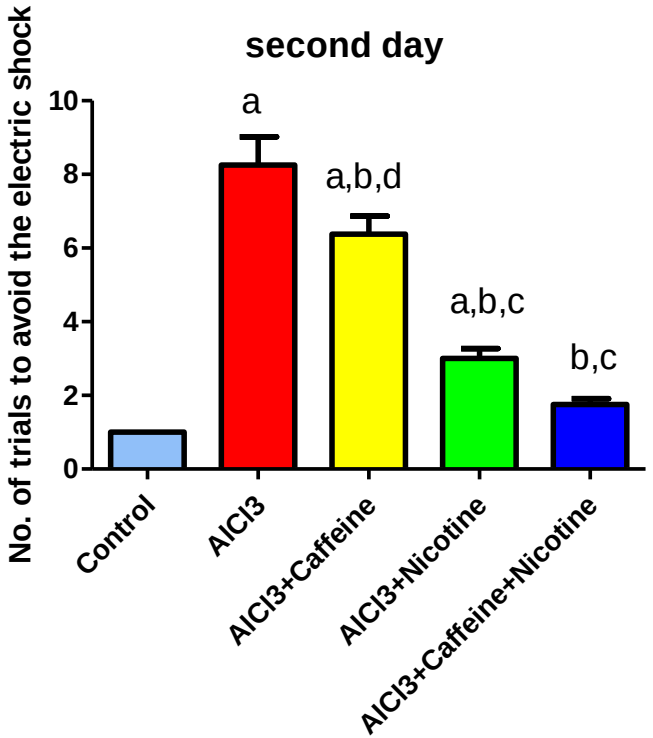
Conditioned avoidance test

Number of trials to avoid the electric shock





Significant $p<0.05$:

a: from control

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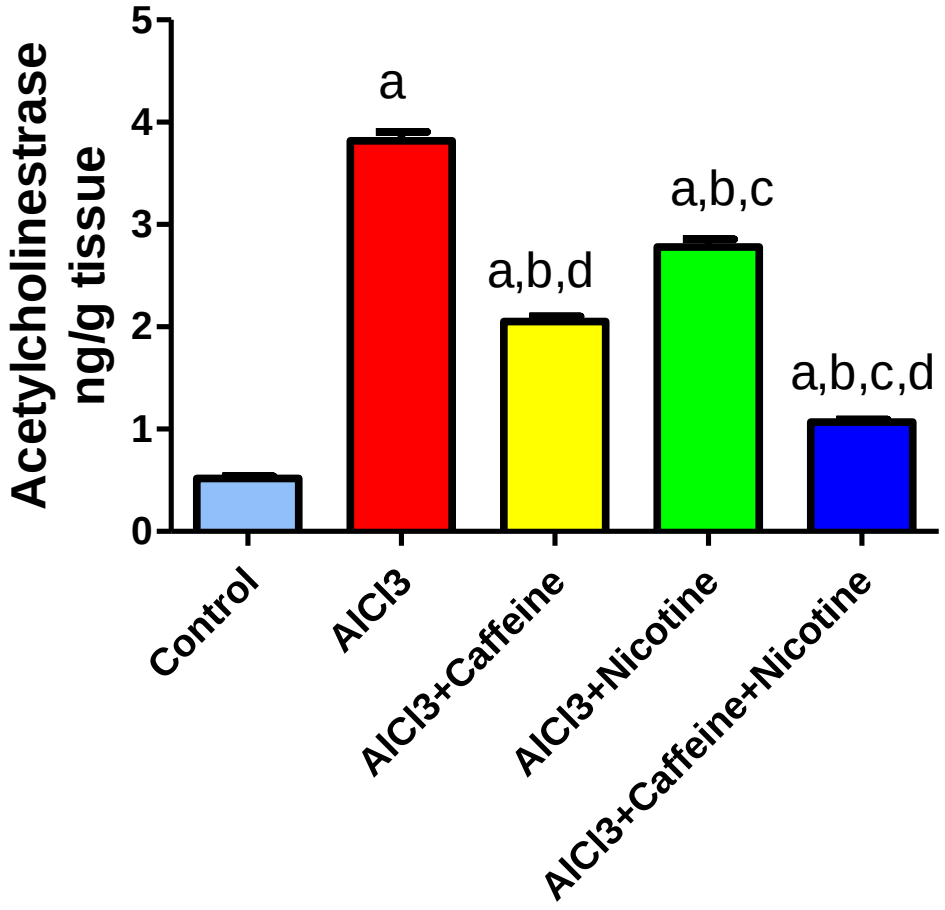
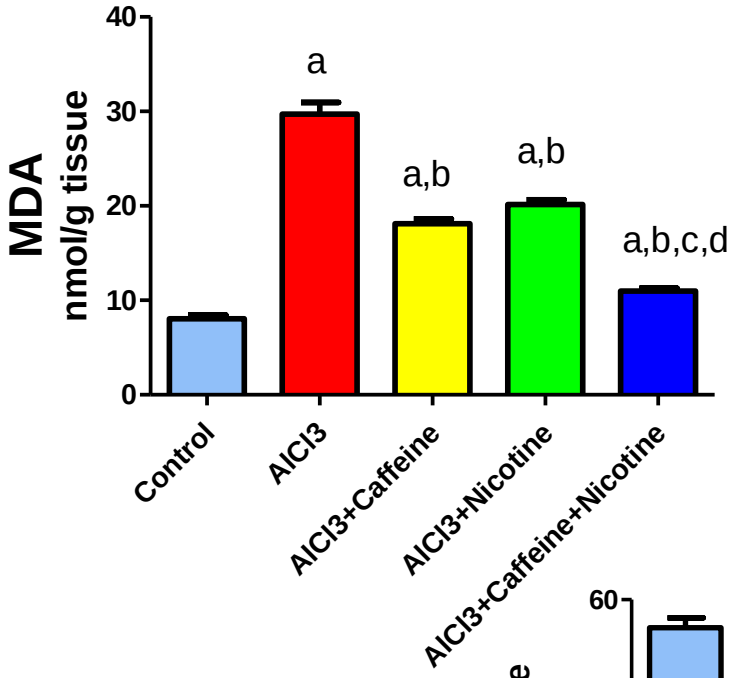
Biochemical parameters

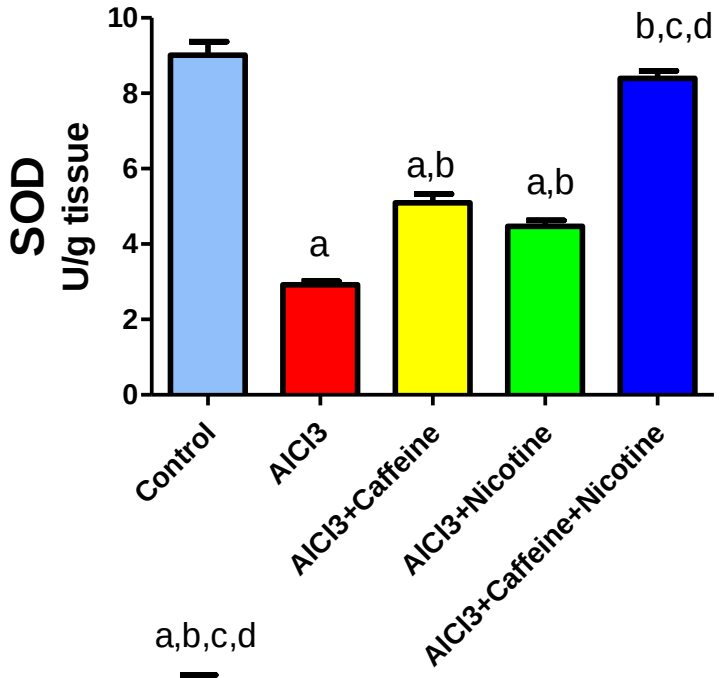
AchE activity

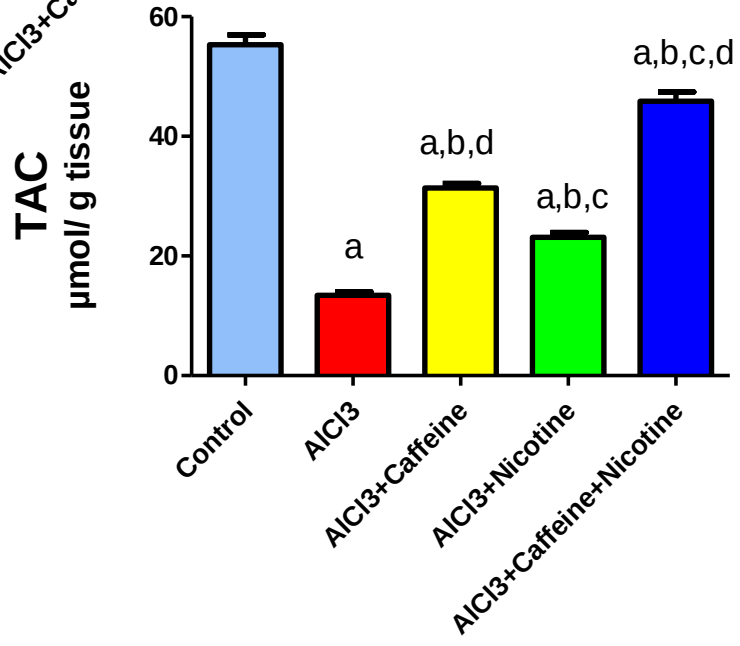


Significant $p<0.05$:
a: from control
b: from AlCl3
c: from AlCl3 +Caffeine
d: from AlCl3 +Nicotine

Oxidative stress parameters





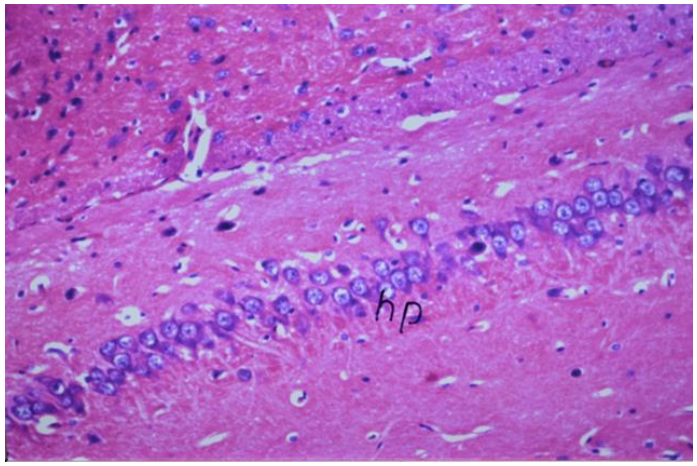


Significant $p<0.05$:
a: from control
b: from AlCl3
c: from AlCl3 +Caffeine
d: from AlCl3 +Nicotine

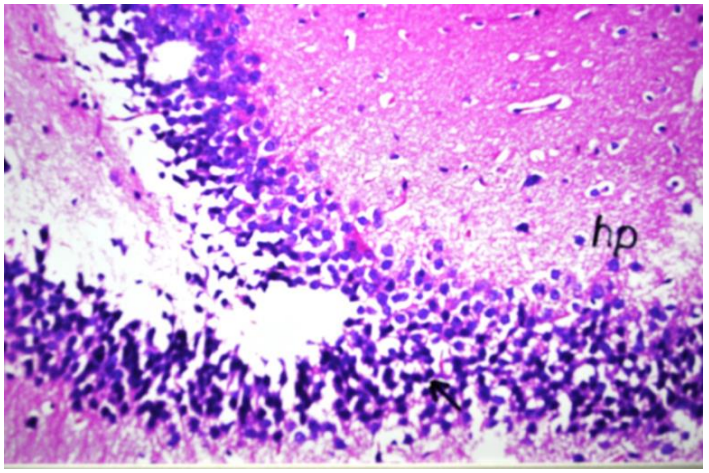
Histopathological examination

Histopathological alterations	Control	ALCL3	ALCL3+Caffeine	ALCL3+Nicotine	ALCL3+Caffeine +Nicotine
Degeneration &pyknosis in hippocampus neurons	–	+++	–	–	–
Eosinophillic plaque formation in striatum	–	+	–	–	–
Gliosis	–	++	–	+	–
Congestion	–	+	–	+	–

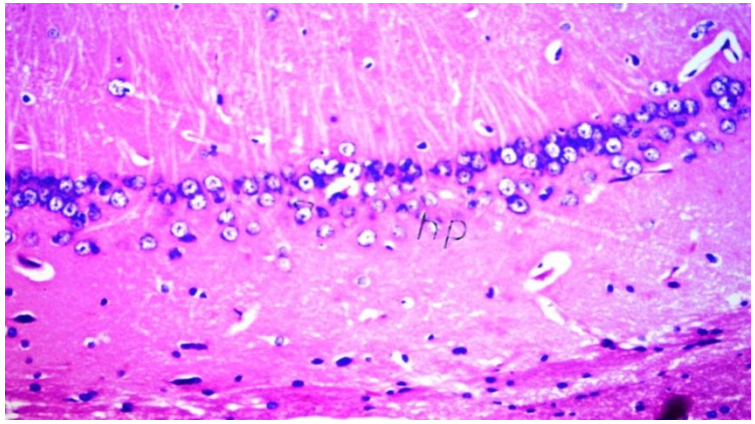
+++ sever ++ moderate + mild - Nil



Brain of rat in control group showing normal histological structure of the hippocampus.



Brain of rat in $ALCL_3$ group showing neuronal degeneration and pyknosis in hippocampus.



Brain of rat in Caffeine and Nicotine co-administration group showing normal histological structure of hippocampus

Conclusions

Aluminum chloride at dose 70mg/kg for five weeks

Impairment of learning and memory

Neuronal degeneration in hippocampus

↑ AchE & MDA

↓ SOD &TAC

Effect of Caffeine

Protect against neuronal degeneration in hippocampus

↓ AchE &MDA

↑ SOD&TAC

The improvement in memory and learning not appeared in all behavioral tests

Effect of Nicotine

Improvement in learning and memory

↓ AchE &MDA

↑ SOD &TAC

Histopathological examination still showed mild gliosis in striatum

Effect of caffeine and nicotine co-administration

More pronounced protecting effect from learning and memory impairment

Prevention of neuronal degeneration in the hippocampus

↓ AchE &MDA

↑ SOD &TAC

Co-administration of caffeine and nicotine can reduce the risk of neuronal degeneration in the hippocampus and attenuate the impairment of learning and memory associated with AD


THANK
YOU!