

The therapeutic effect of intranasal administration of exogenous cholesterol in the R6 / 2 mouse model of Huntington's disease

21st July 2022

By K. Ahmed, S. Gillio Tos , S. Varisco

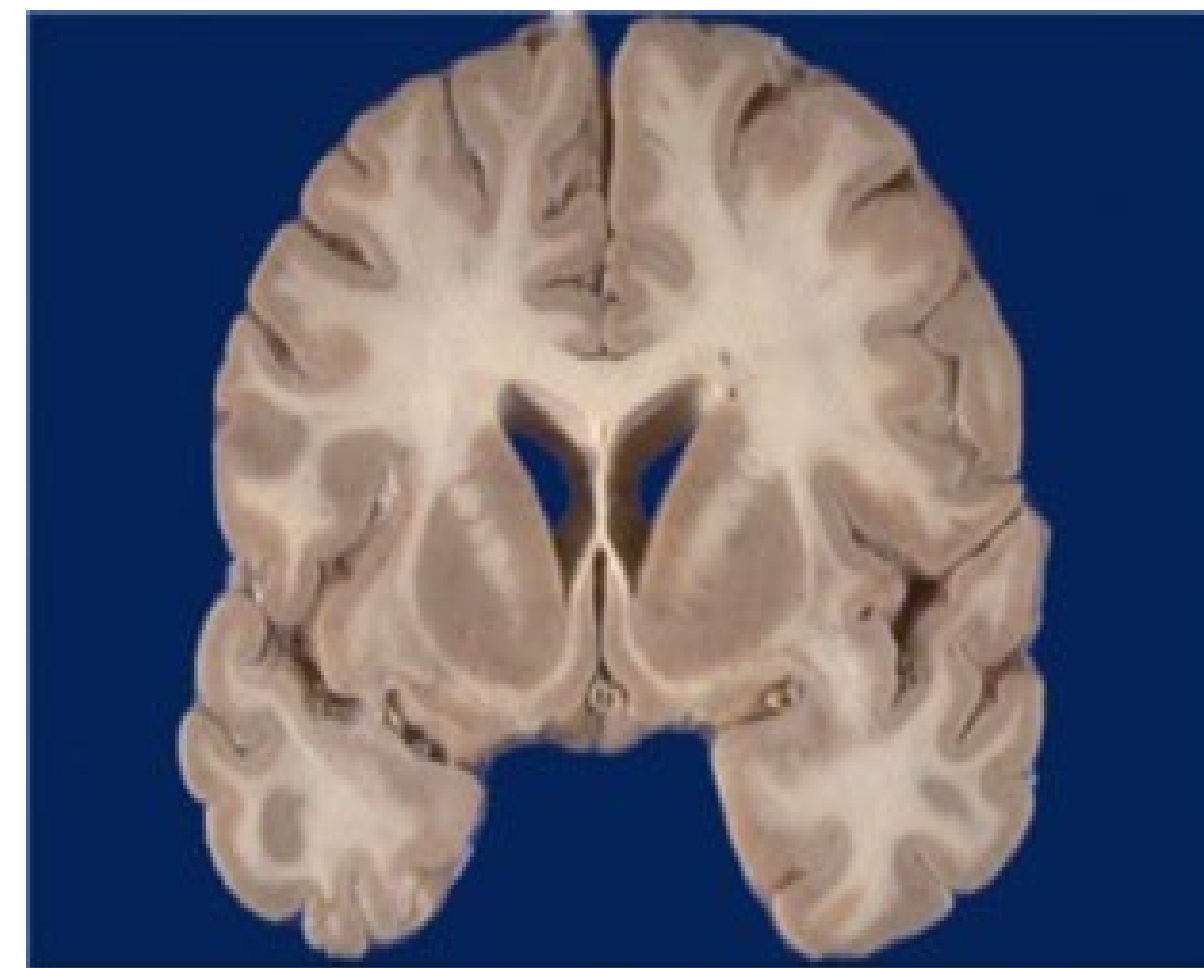


ISTITUTO DI RICERCHE
FARMACOLOGICHE
MARIO NEGRI · IRCCS

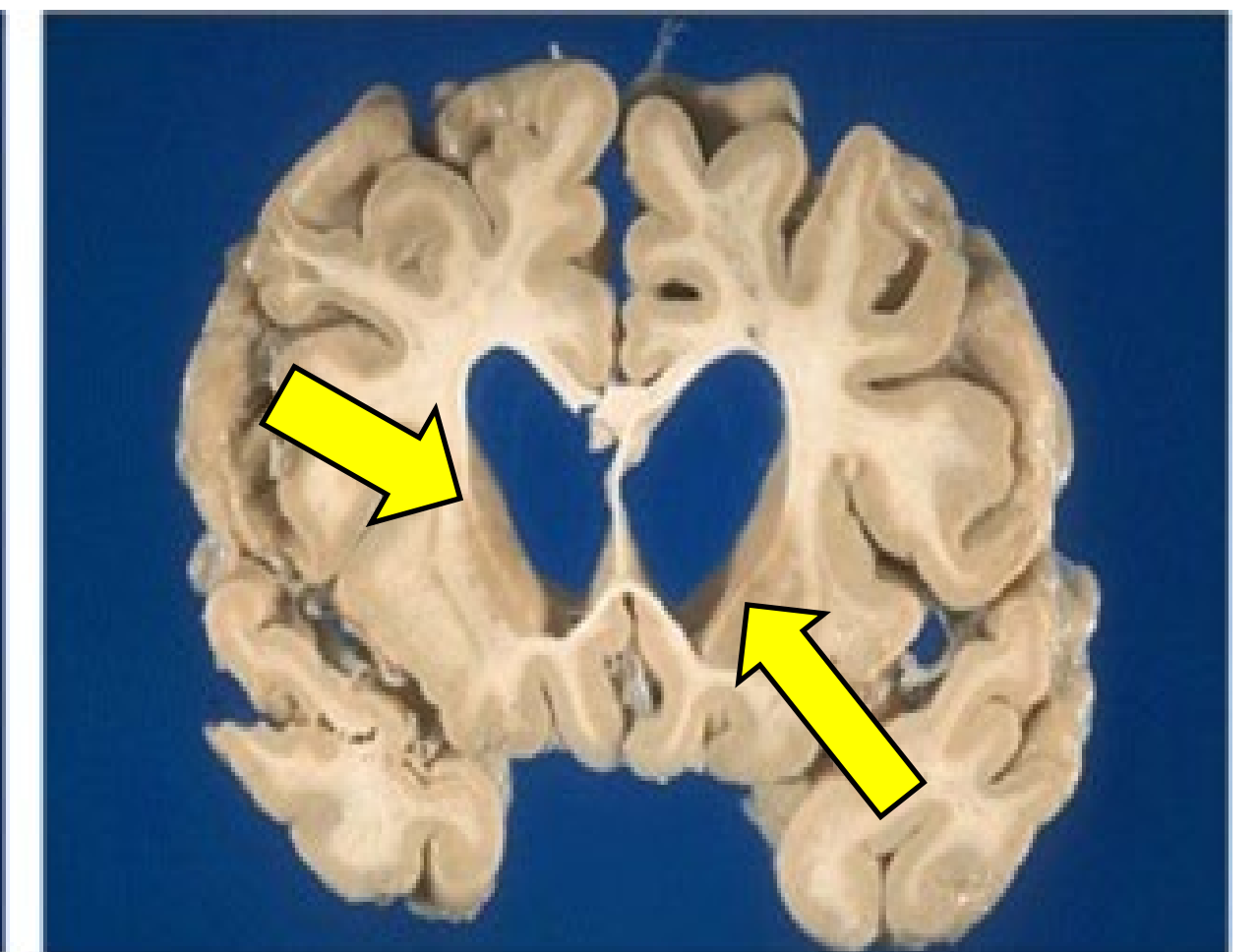
Huntington Disease

Huntington's Chorea

- **Neurodegenerative** disease that causes brain atrophy
- A stretch of the **HTT protein** is expanded
- **Rare** diseases (1/10 000)
- Motor, cognitive, psychiatric **symptoms**

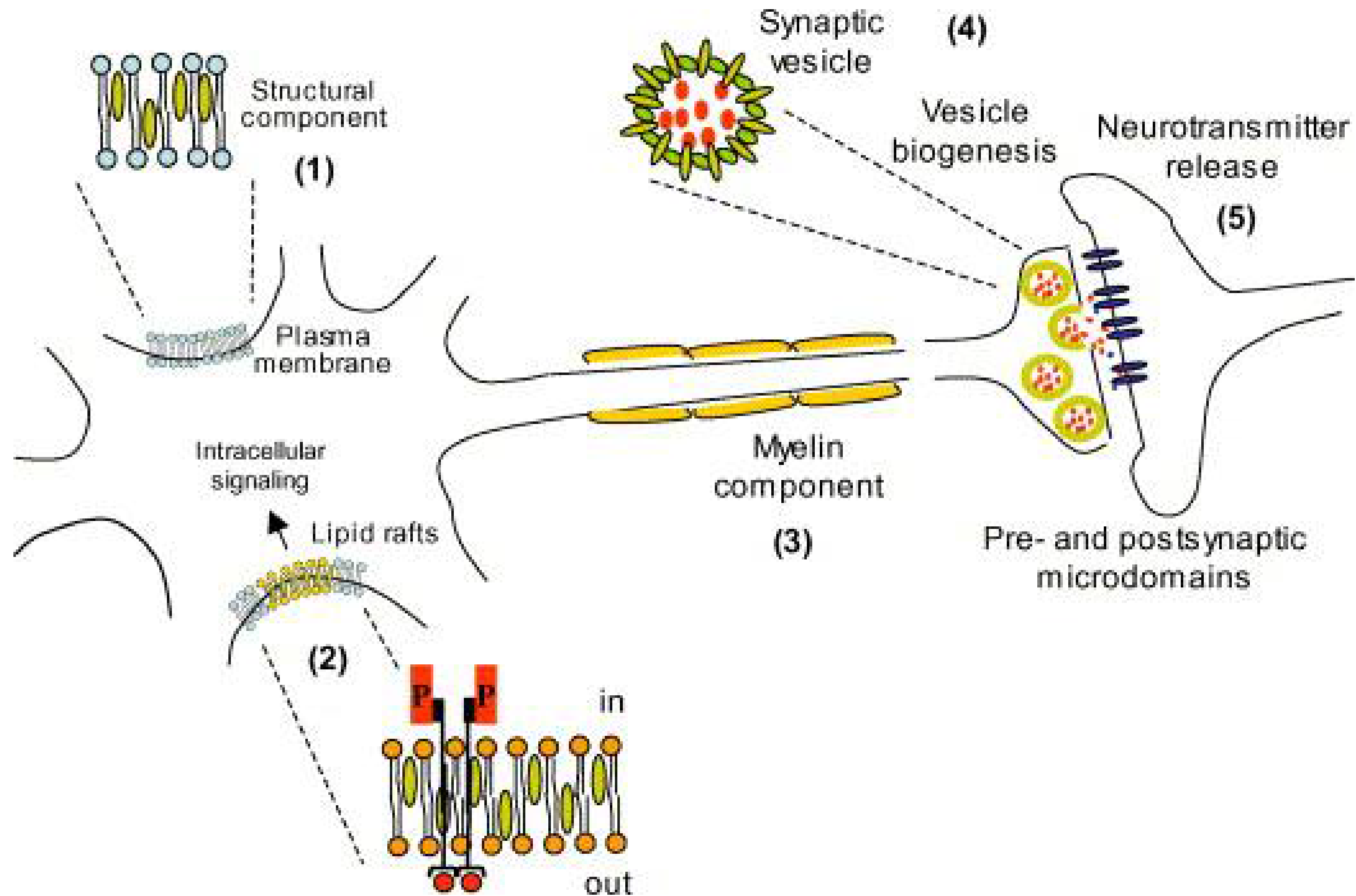


NORMALE



HD

Cholesterol



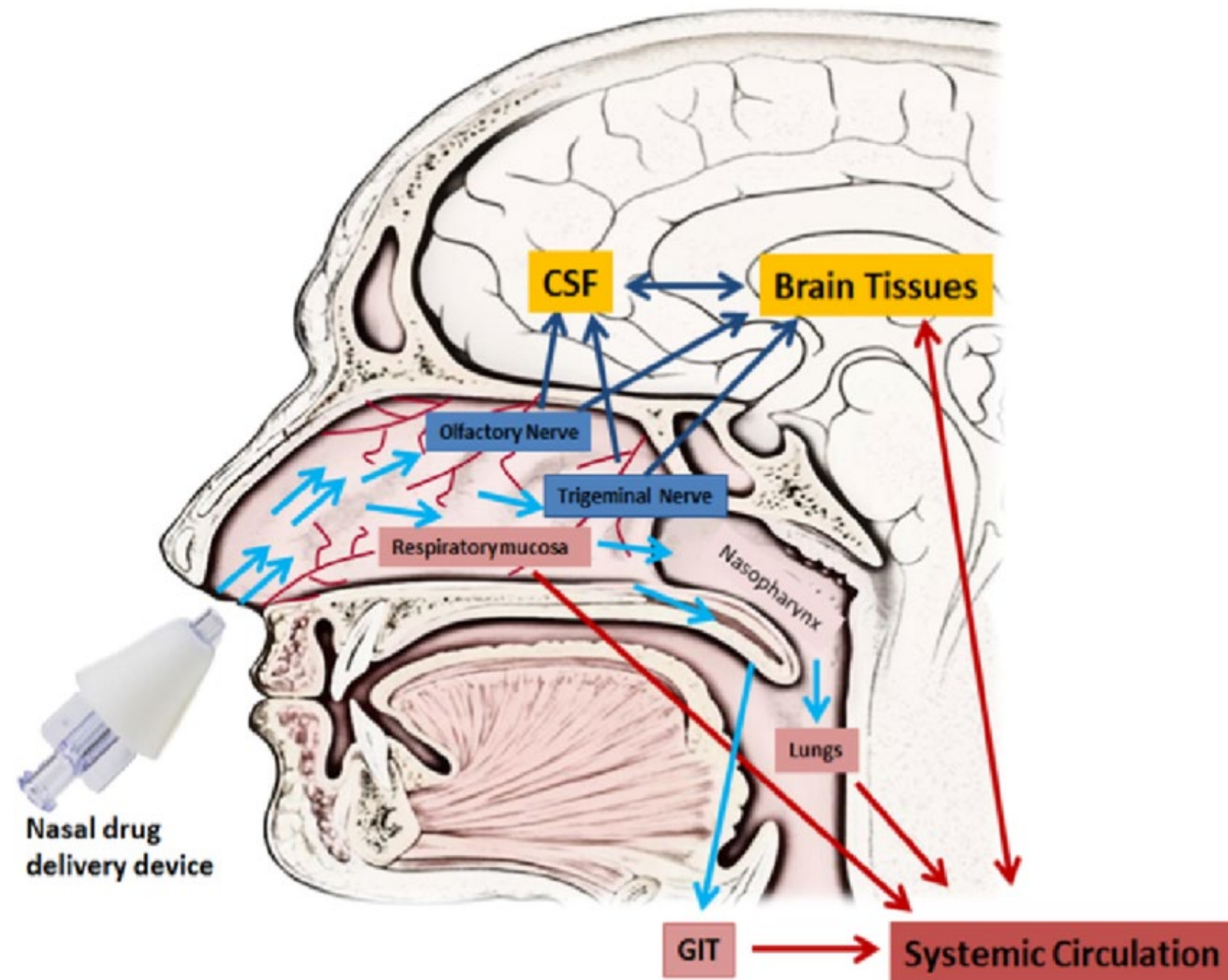
Cholesterol

Myelin

HD

Nose-to-Brain Delivery

Nose-to-Brain Therapy and Liposomes

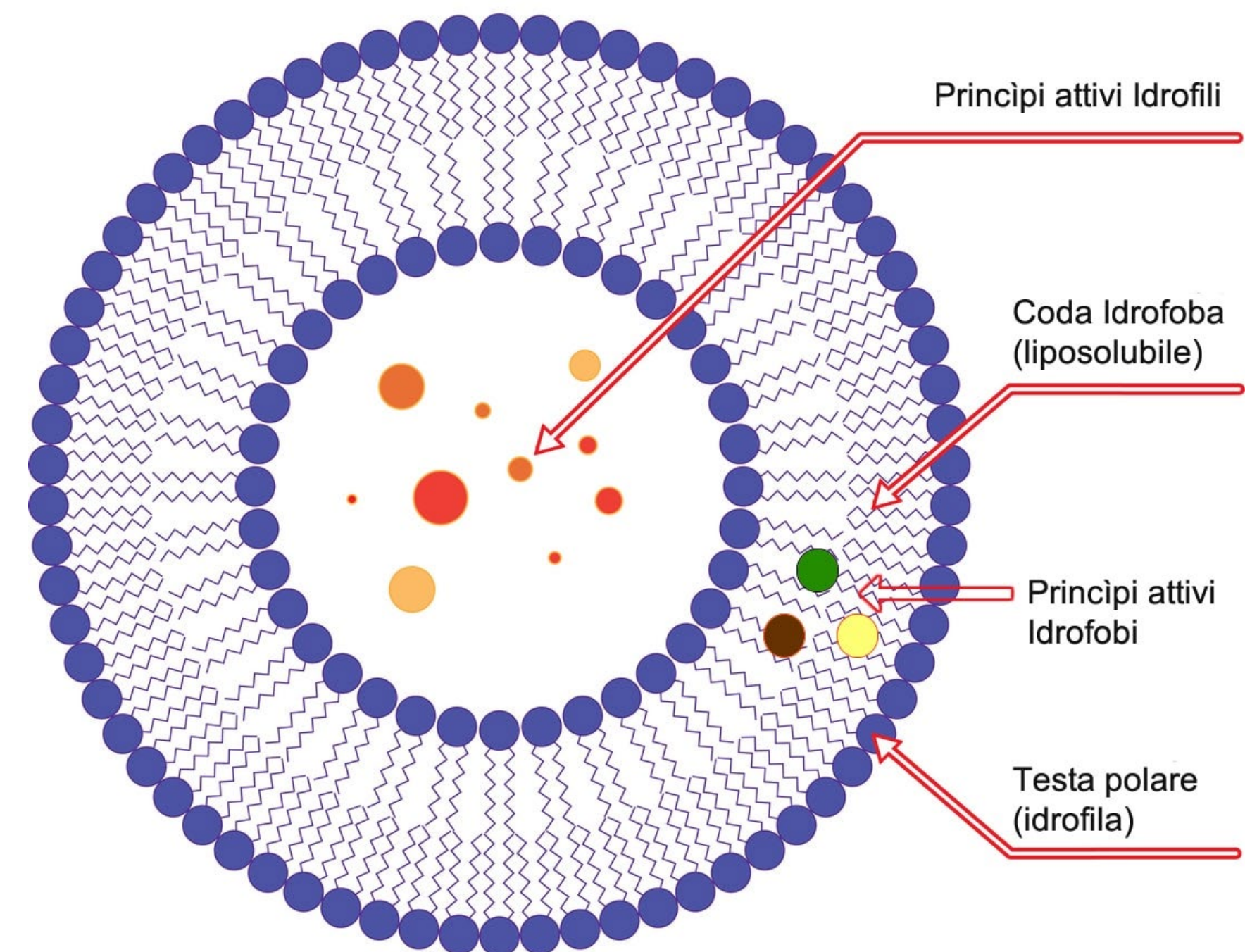


DISADVANTAGES

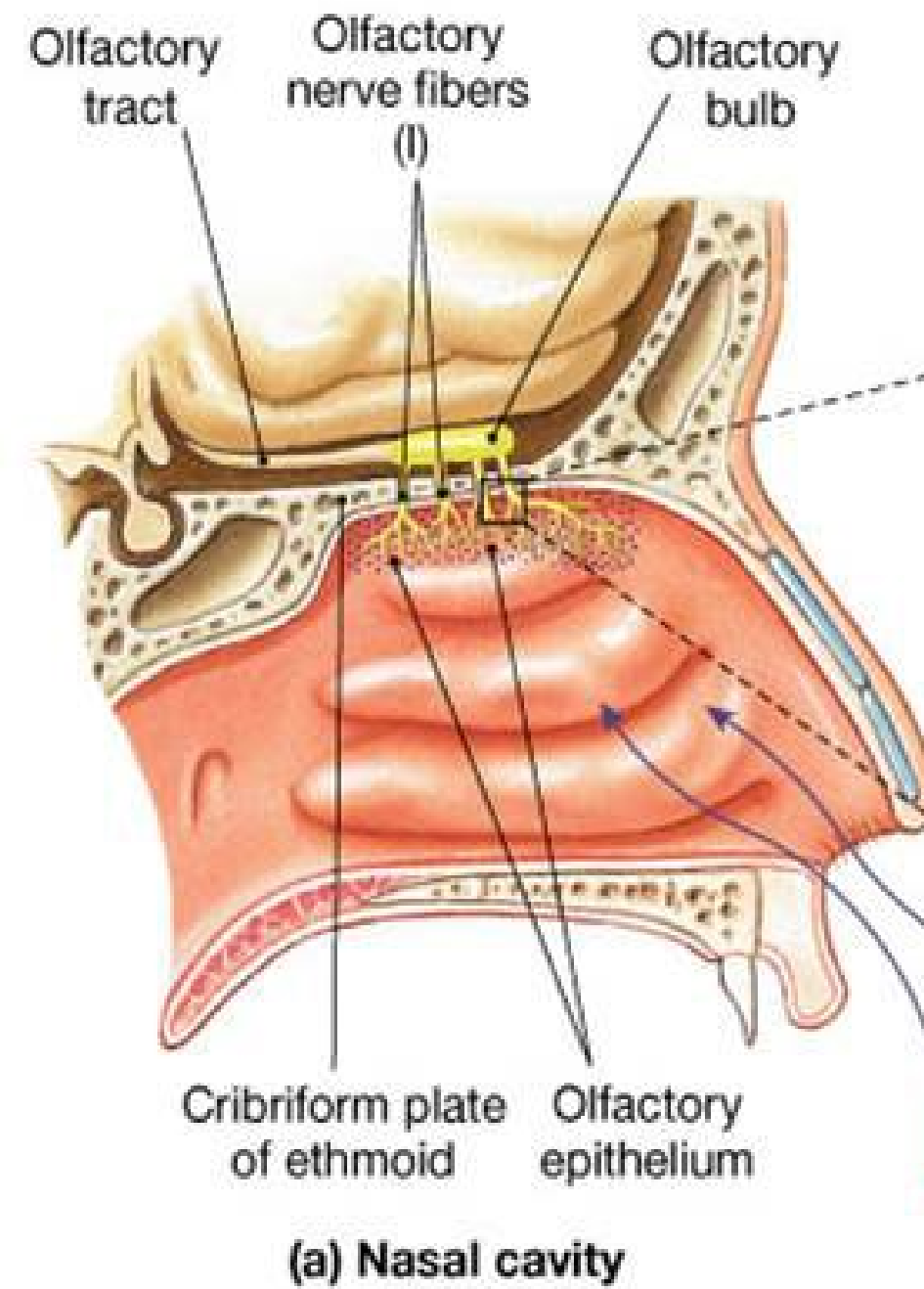
- Limited injection volume
- Risk of irritation or interference with inflammatory agents
- Possibility of a quick elimination

ADVANTAGES

- Crossing of the BBB
- Fast onset of action
- Possibility of self-injection



Nose-to-brain pathways



Olfactory Epithelium

Olfactory Nerve

Olfactory Bulbs

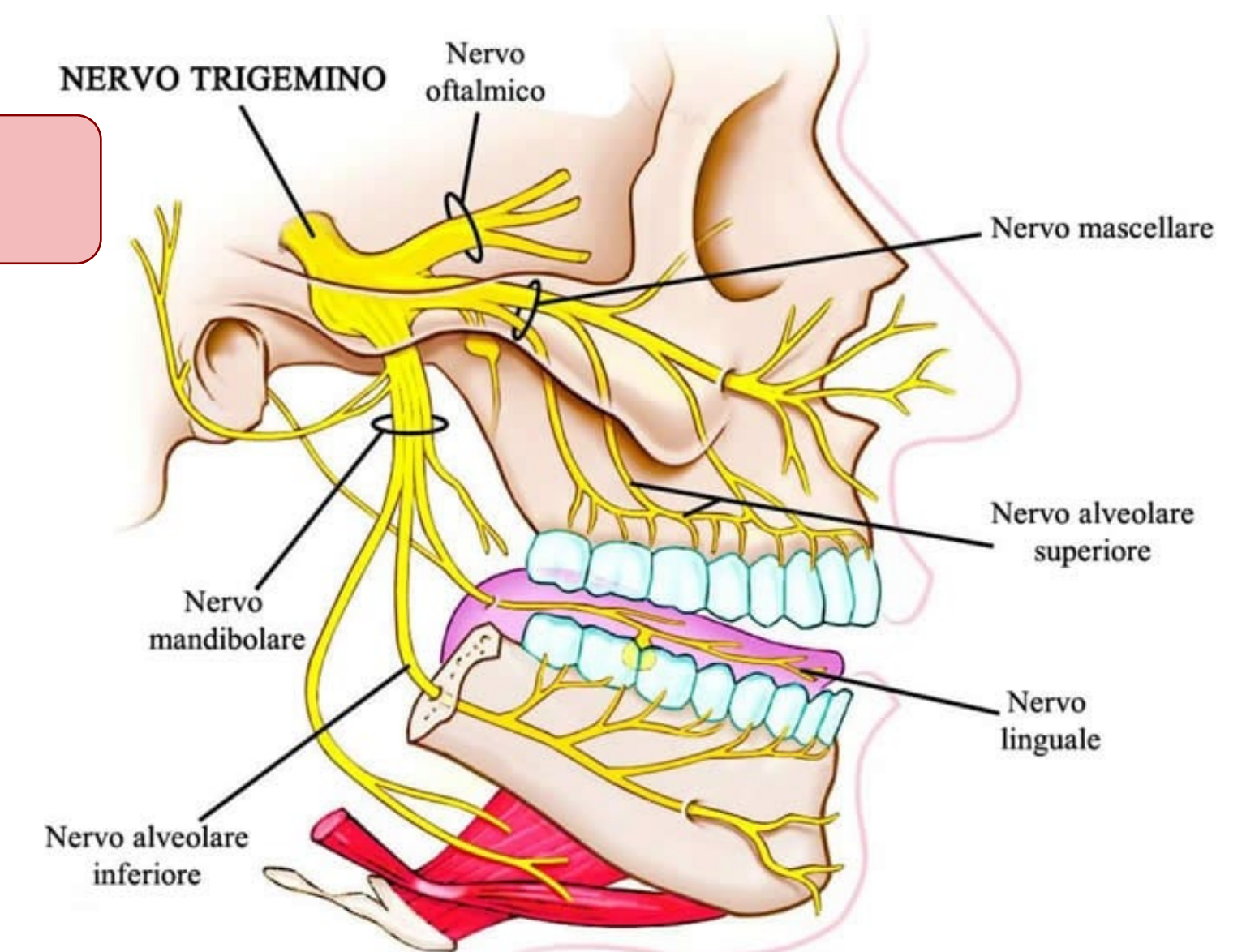
CNS

Nose Injection

Respiratory Epithelium

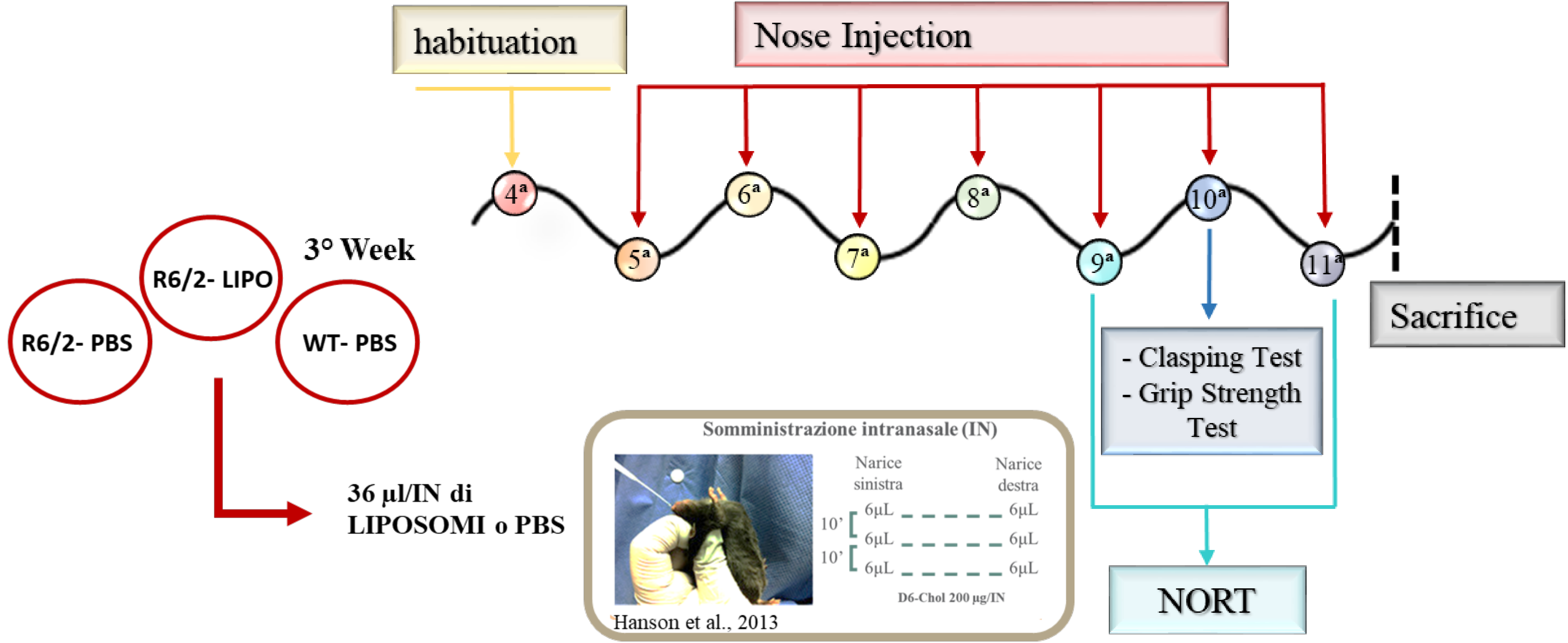
Trigeminal Nerve

Brain Bridge



Chronic Treatment

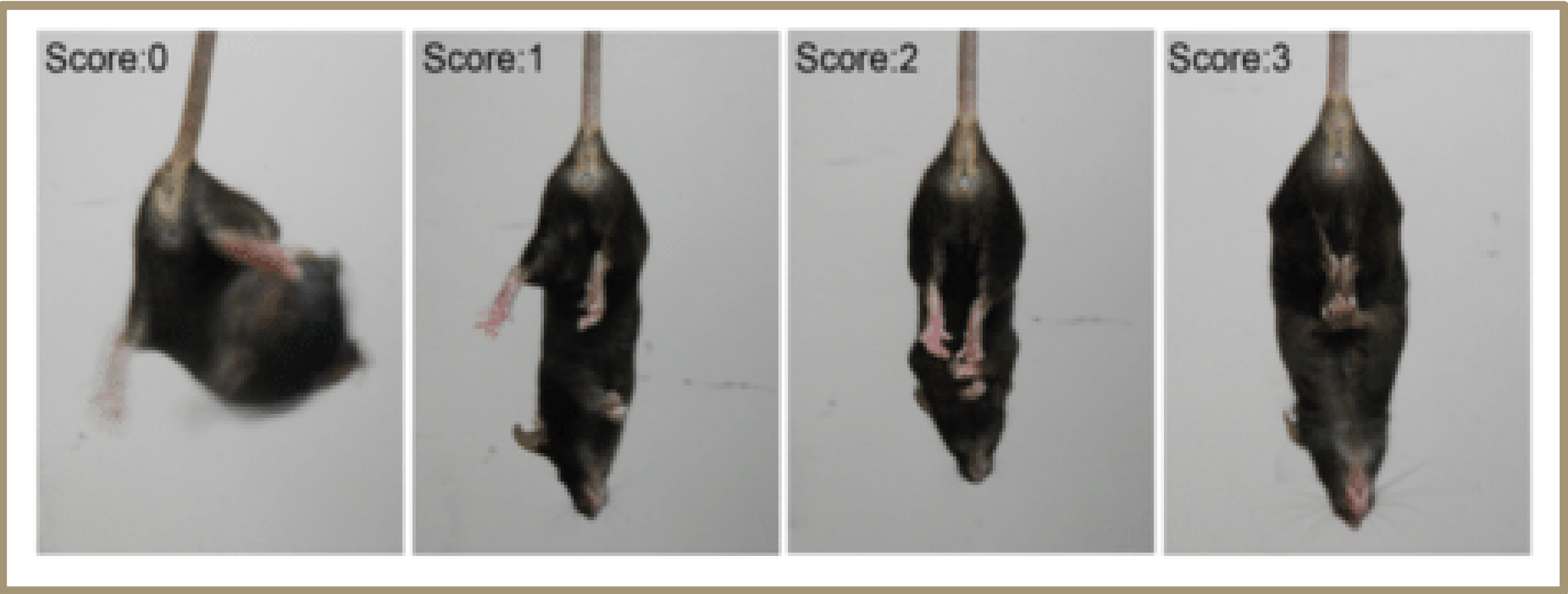
Repeated Treatment



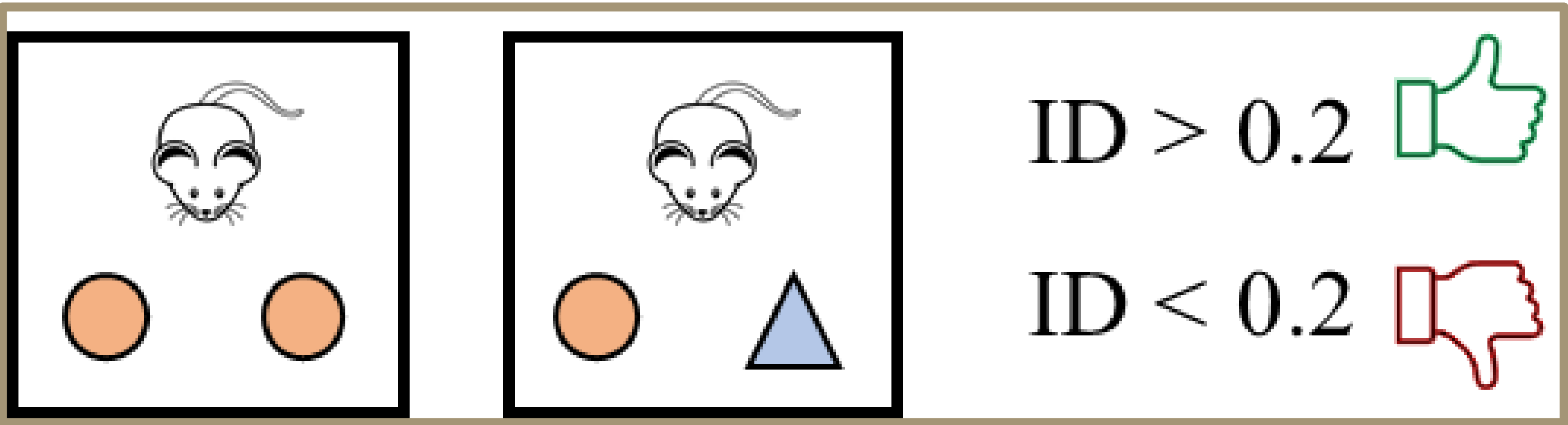
Behavioral tests



Grip Strength Test



Clasping Test



Novel Object Recognition Test

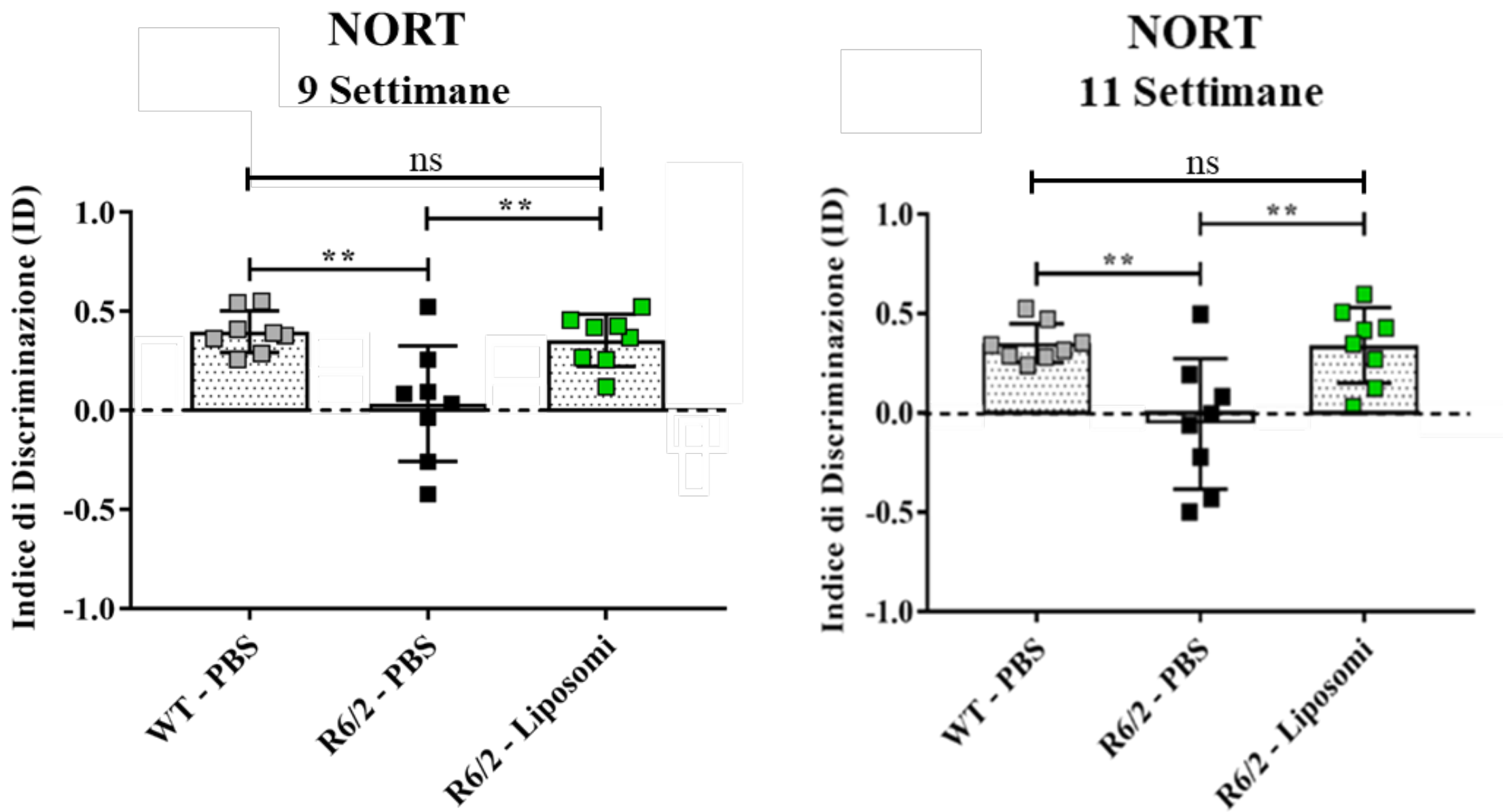
Results

Gruppo	Media ± SD
WT- PBS	88.28 ± 12.65 gr
R6/2 PBS	57.78 ± 10.34 gr
R6/2 LIPOSOMI	75.18 ± 6.00 gr

Grip Strength Test

Gruppo	Media ± SD
WT- PBS	0.14 ± 0.18
R6/2 PBS	2.16 ± 0.34
R6/2 LIPOSOMI	1.22 ± 0.49

Clasping Test



Novel Object Recognition Test

THANK YOU