Effects of Transcranial Direct Current Stimulation on Behavior in a Preclinical Rat Model of Ischemic Stroke

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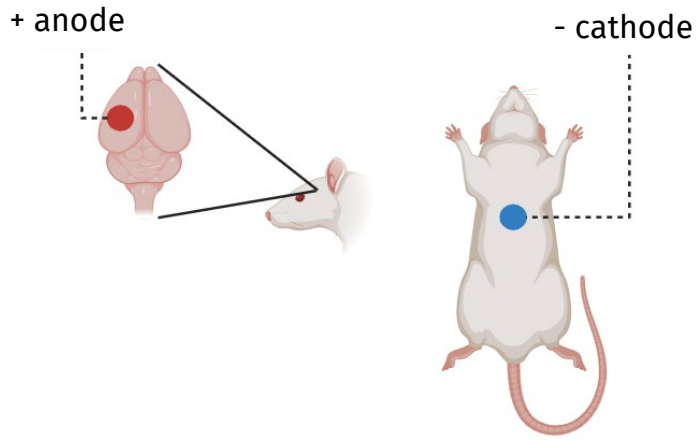
Transcranial Direct-Current Stimulation (tDCS)

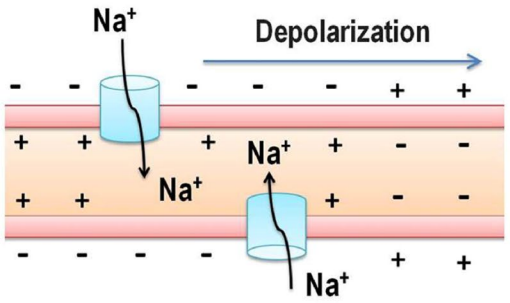
Anodal tDCS

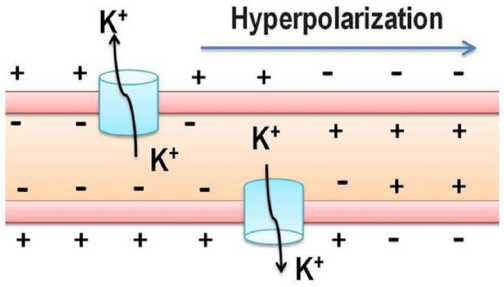


Anodal stimulation → depolarization→ ⬆ neuronal excitability

Cathodal stimulation → hyperpolarization → ⬇ neuronal excitability

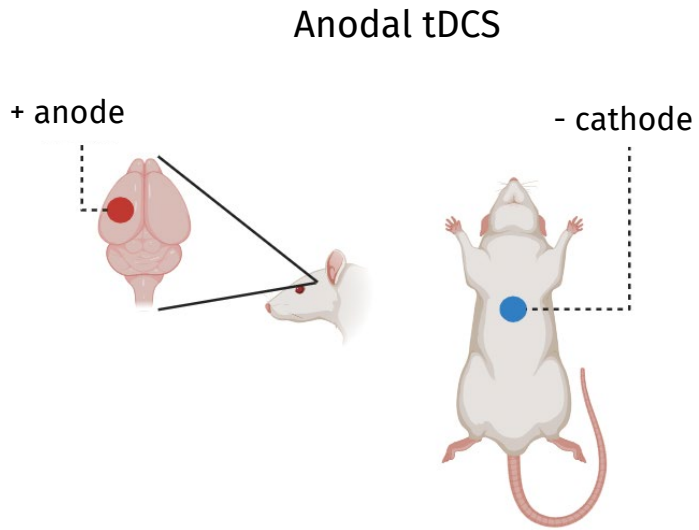
Anodal stimulation	Cathodal stimulation





Rozisky et al. 2016

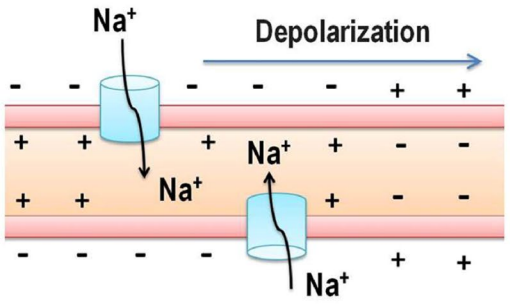
Transcranial Direct-Current Stimulation (tDCS)

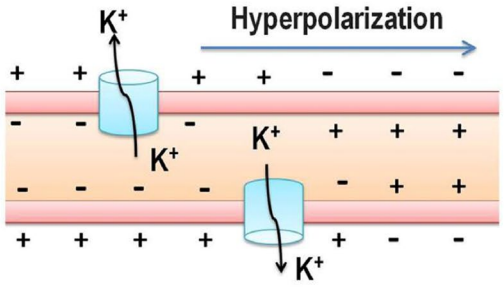


Anodal stimulation → depolarization→ ⬆ neuronal excitability

Cathodal stimulation → hyperpolarization → ⬇ neuronal excitability

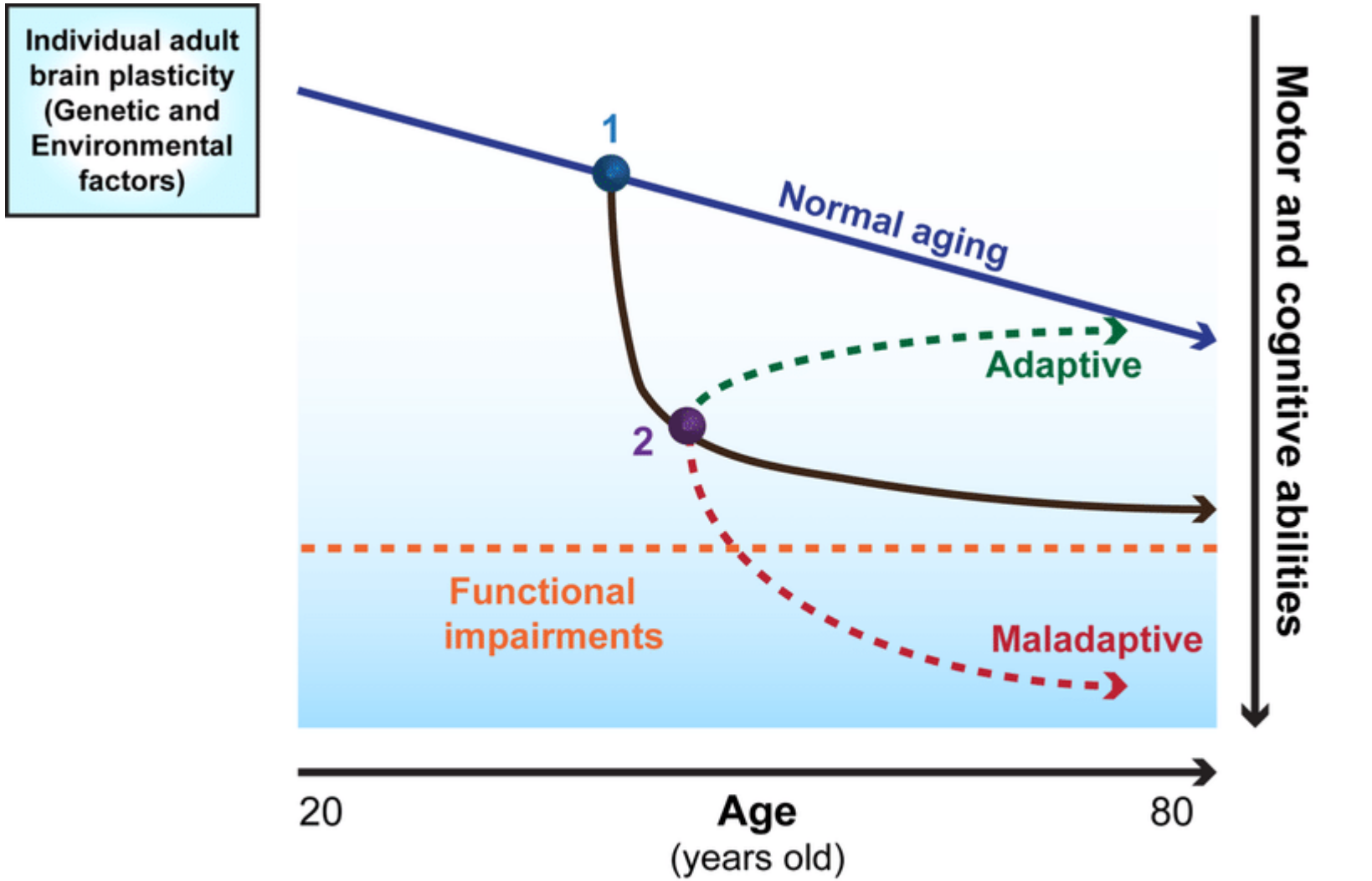
Anodal stimulation	Cathodal stimulation





Rozisky et al. 2016

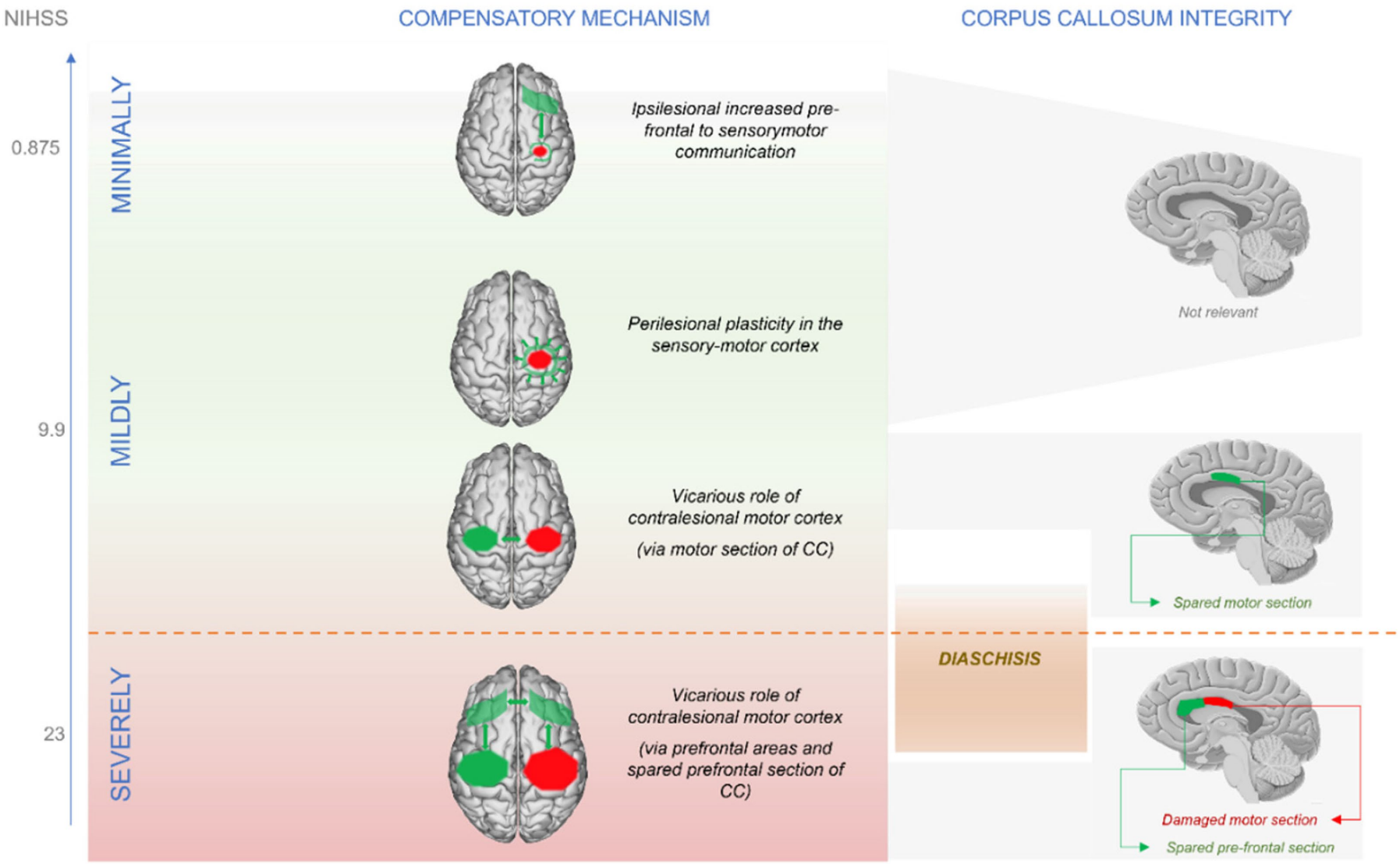
Brain plasticity



1: Insult (traumatic brain injury, stroke), morbidities (eg. depression cancer)

2: Non invasive interventions promoting network plasticity (physical and cognitive training, non invasive brain stimulation)

Pascual-Leone et al. 2011



Interhemispheric competition model:
Adaptive neuroplasticity

A-tDCS on ipsilesional hemisphere
C-tDCS on contralesional hemisphere

Vicariation model:
Maladaptive neuroplasticity

A-tDCS on contralesional hemisphere
C-tDCS on ipsilesional hemisphere

Preclinical Studies of (tDCS) in Stroke

ELSEVIER

Neuroscience & Biobehavioral Reviews

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Non-invasive brain stimulation for functional recovery in animal models of stroke: A systematic review

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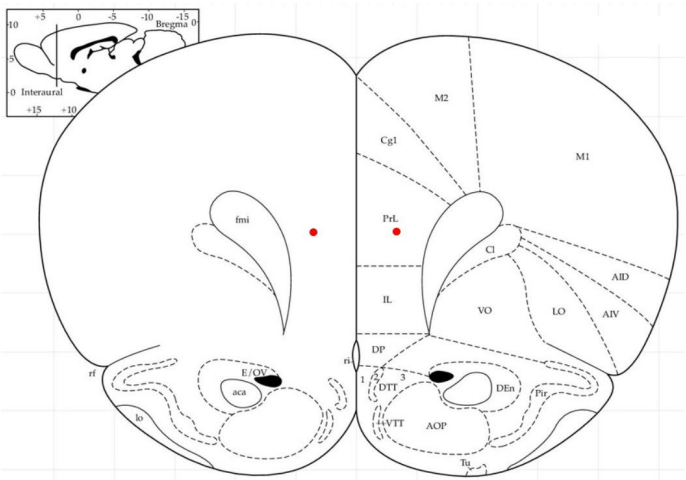
Study Design

Preclinical experimental study in a rat model of stroke induced by endothelin-1 injection targeting the prefrontal cortex.

40 rats (n= 10/group)



AP: +3.0 ML: ±0.7 DV: -4.5

Déziel et al. 2015, 2016, 2017
Weishaupt et al. 2016

➢ **Main objective**

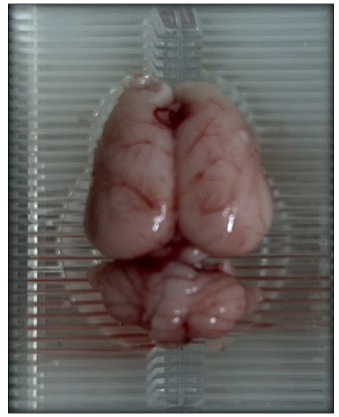
To compare the efficacy of two transcranial direct current stimulation (tDCS) protocols—**anodal vs cathodal stimulation**—in promoting functional recovery after stroke.

➢ **Secondary objectives**

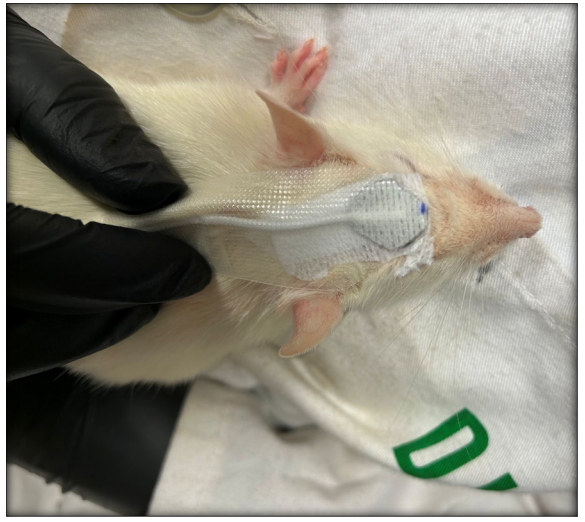
1. To evaluate **executive**, cognitive and motor functions, and emotional behaviors.
2. To assess the expression of serological and histological biomarkers related to inflammation and tissue repair.
3. To measure the volume of the cerebral infarct.

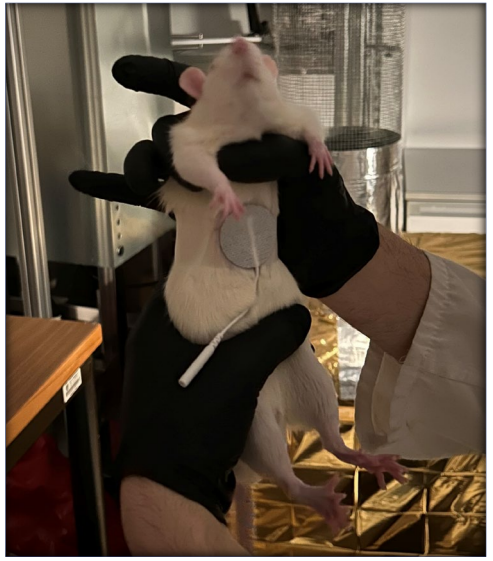
Endothelin-1 model

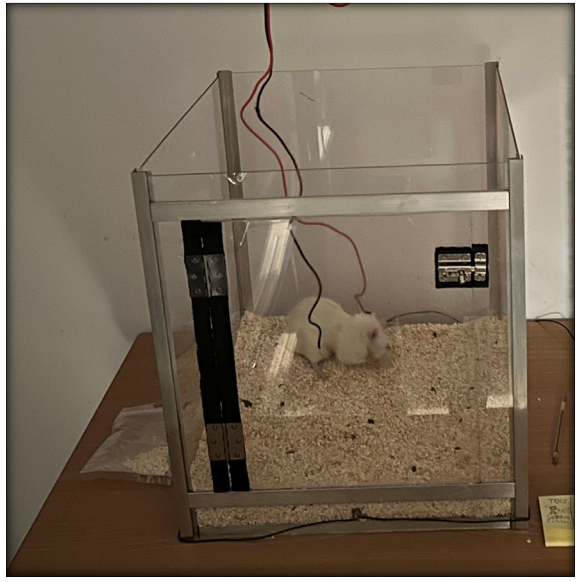
- Low invasiveness
- Low animal mortality
- Speed and simplicity
- Strength and duration of endothelin-1-induced vasoconstriction are strictly dose-dependent
- **Flexible selection of infarct area**



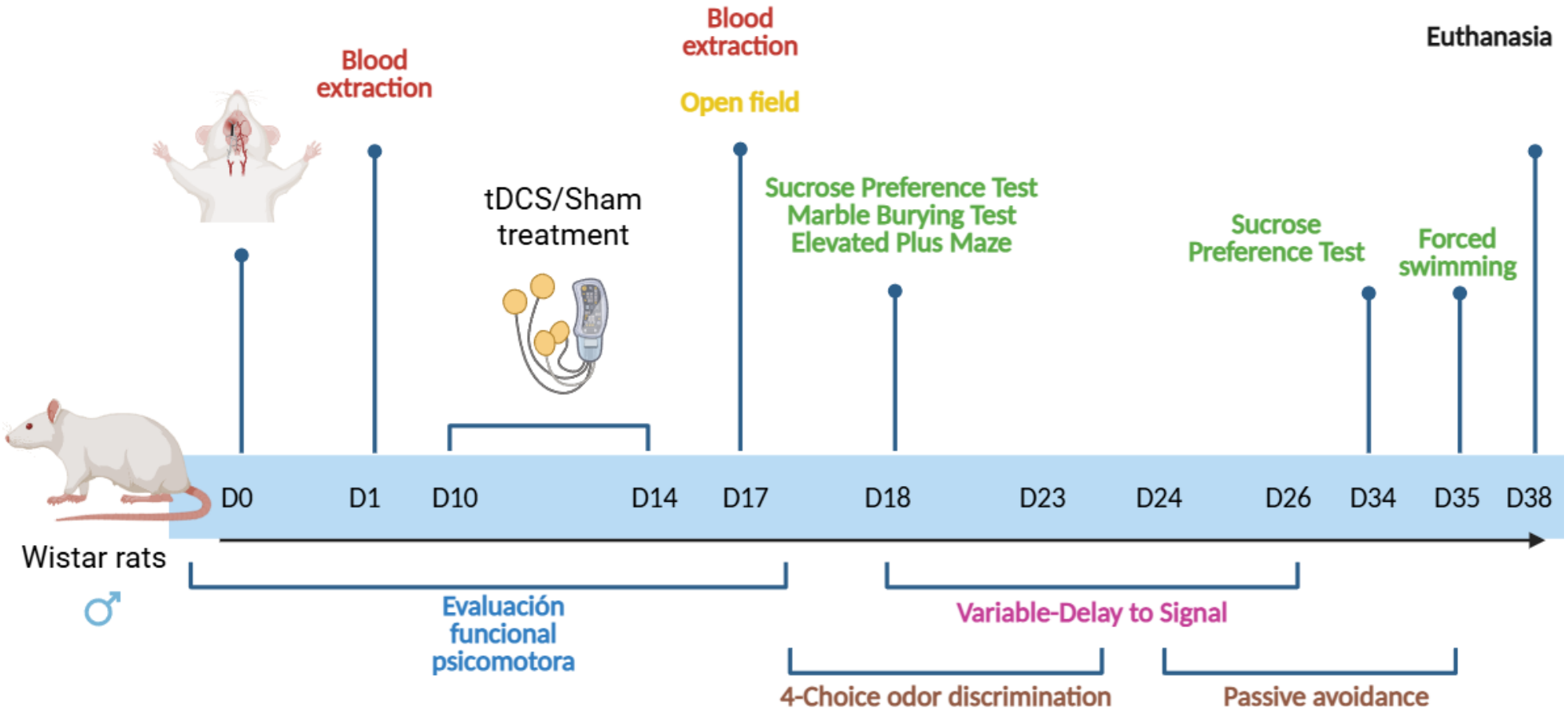
tDCS treatment



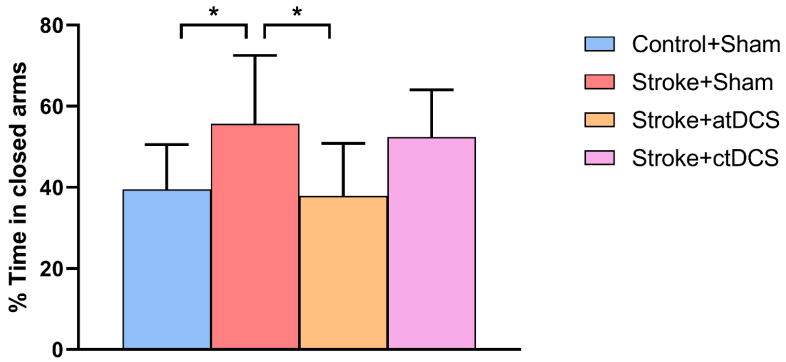


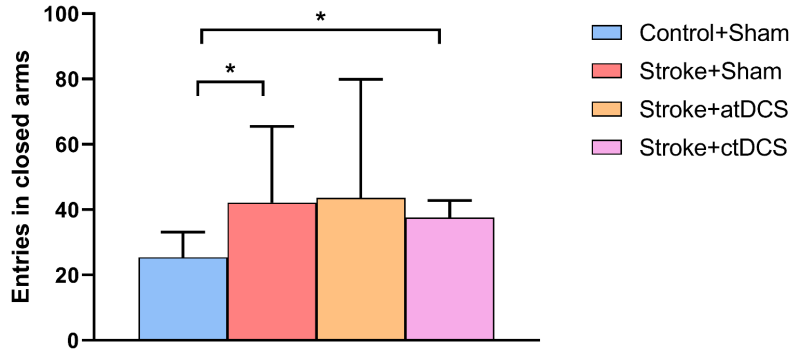


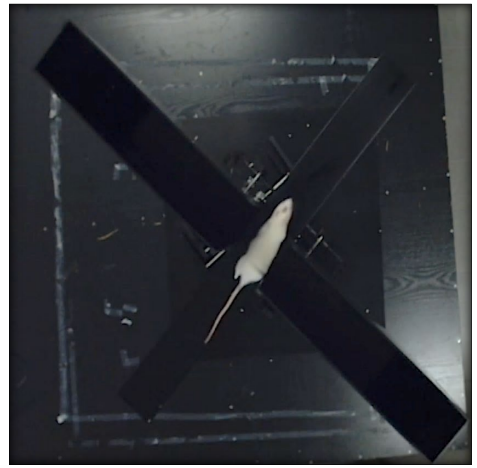
TIMELINE


Blood extraction
Blood extraction
Open field
Euthanasia
tDCS/Sham treatment
Sucrose Preference Test
Marble Burying Test
Elevated Plus Maze
Sucrose Preference Test
Forced swimming
D0
D1
D10
D14
D17
D18
D23
D24
D26
D34
D35
D38
Wistar rats
♂
Evaluación funcional psicomotora
Variable-Delay to Signal
4-Choice odor discrimination
Passive avoidance

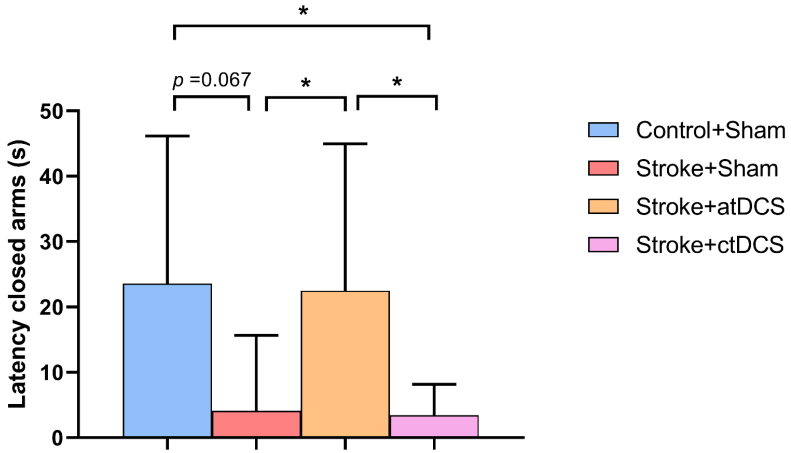
ELEVATED PLUS MAZE

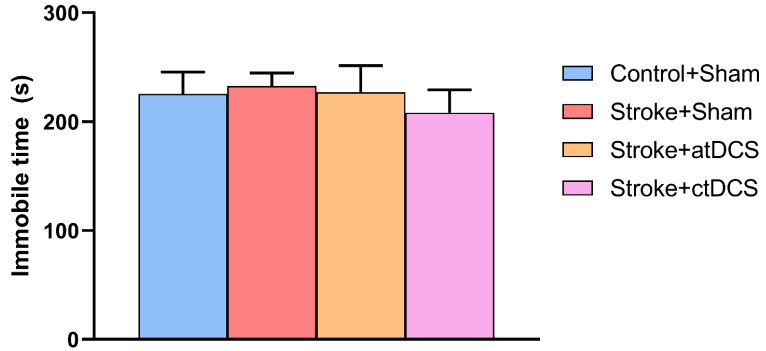






- Stroke group spent more time in the closed arms than the control group
- Stroke + atDCS had similar behaviour than control group



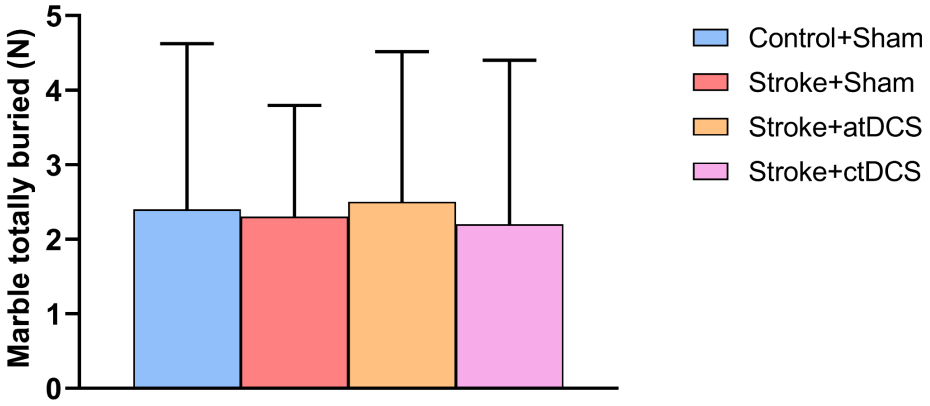


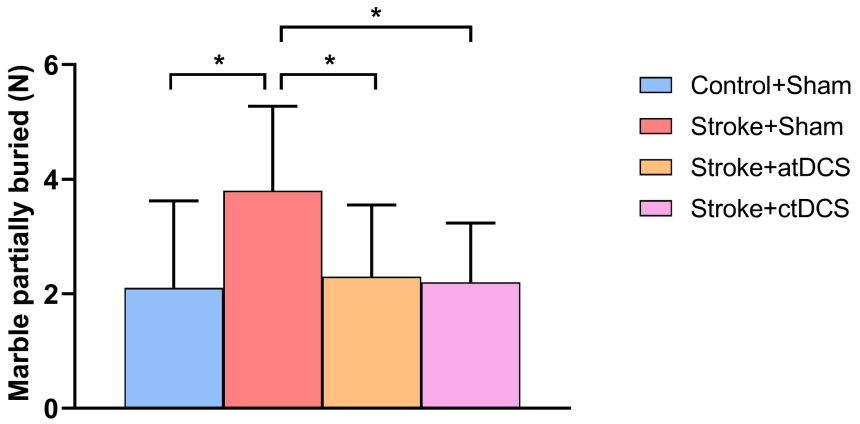
- Stroke group had lower latency than control group
- Stroke + atDCS had similar behaviour than control
- ctDCS group had no effect

-9 equidistant marbles are placed in home box, the rat is left for 30’

-Both fully buried and partially buried marbles are quantified.

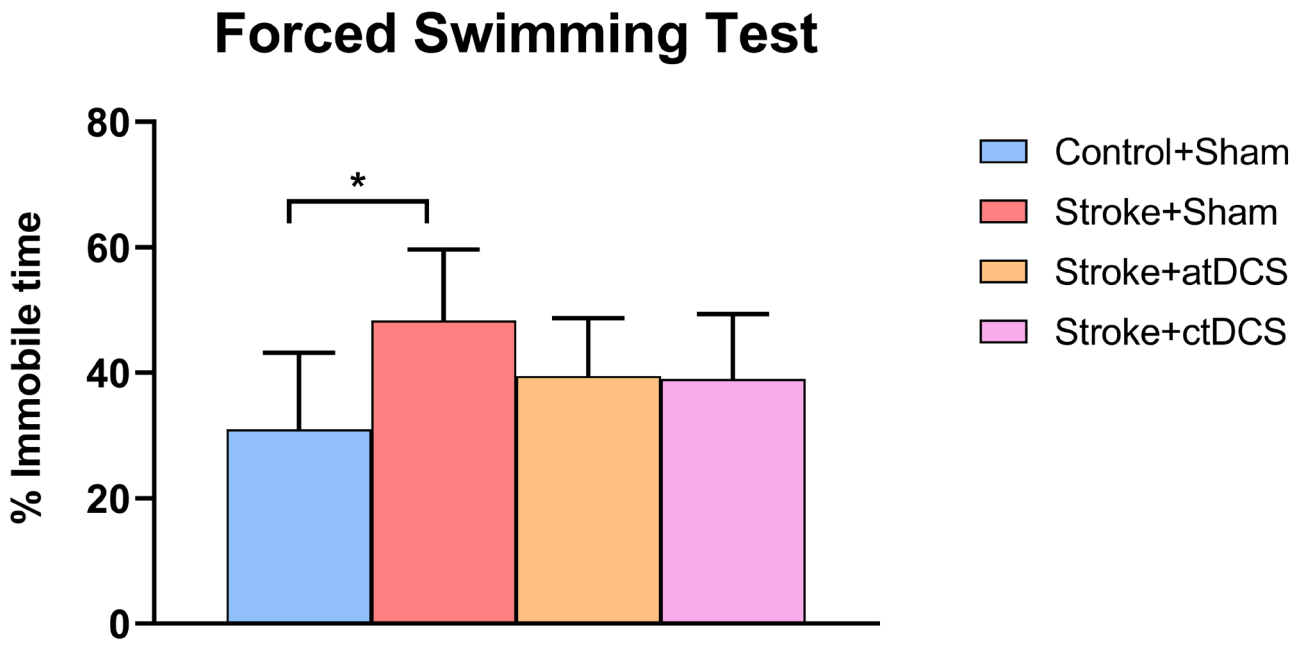
Marble Burying Test





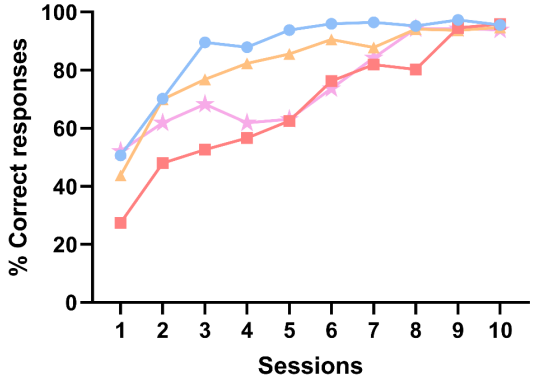
- Rats with stroke had more compulsive behaviour when judged by the higher number of partially buried marbles
- Both atDCS and ctDCS showed recovery of compulsive behaviour

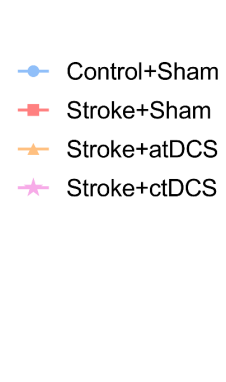
-The animal is placed in a bucket of water at a certain height for 2 minutes and the immobility time during the last minute is measured.

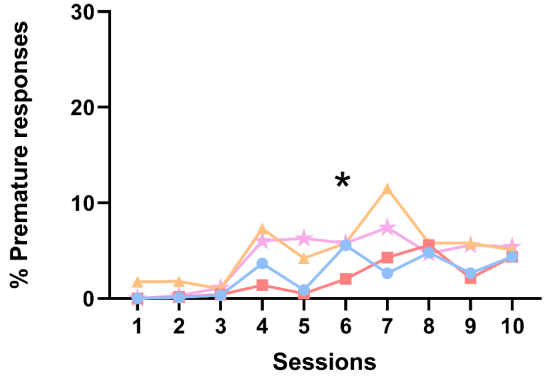


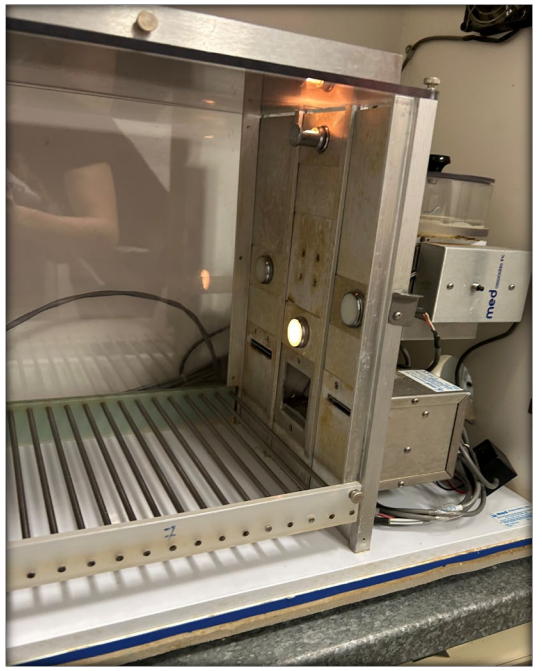
Rats with stroke spent more time immobile, while tDCS treatments showed greater mobility than the stroke group (*P* NS).

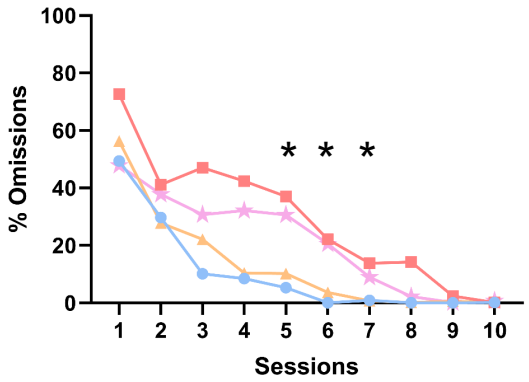
Variable delay-to-signal
(training)

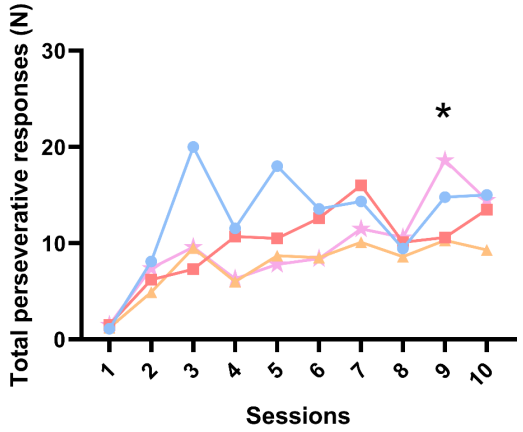




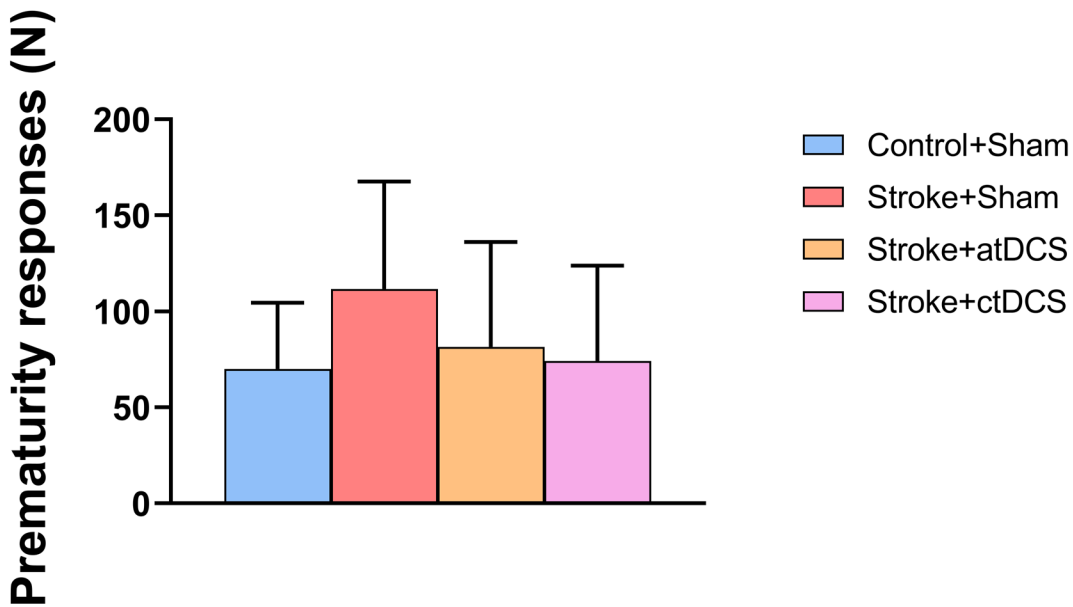




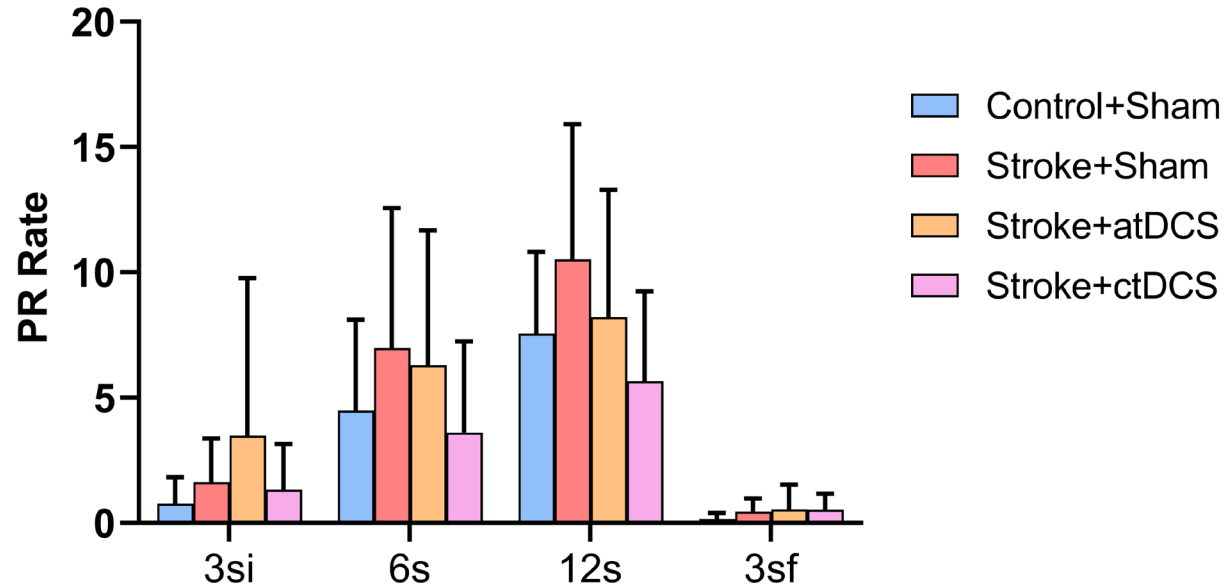




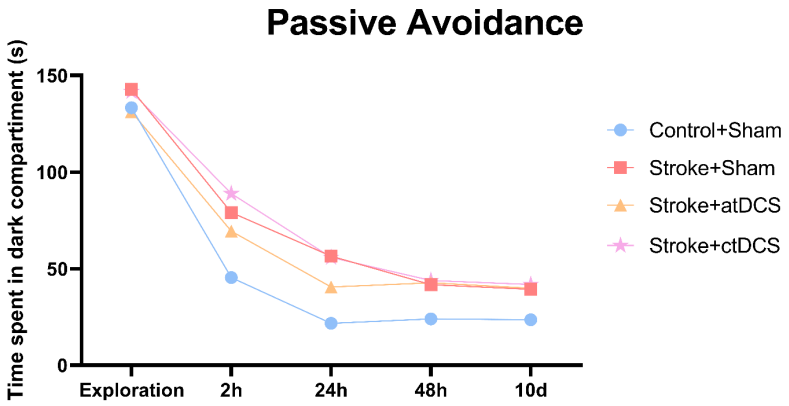
Variable delay-to-signal test

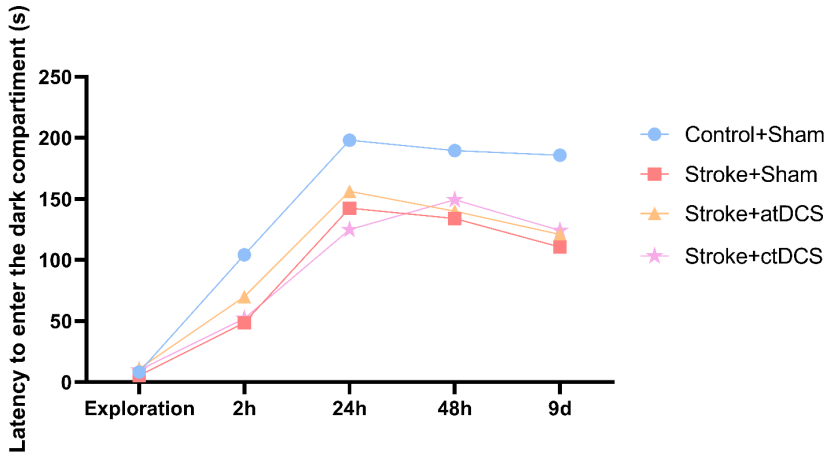


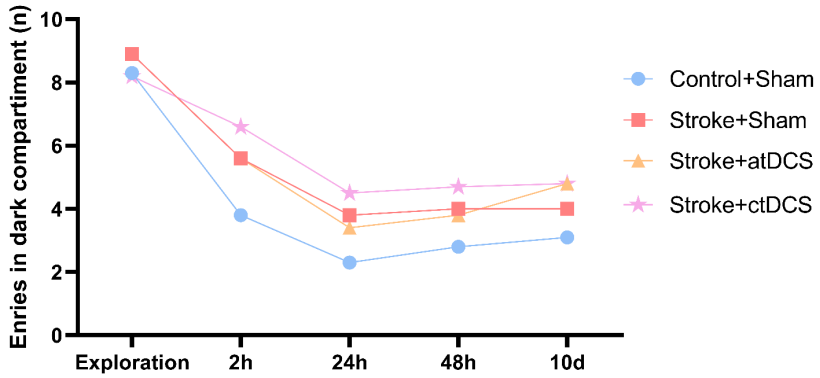
Prematurity Response Rate

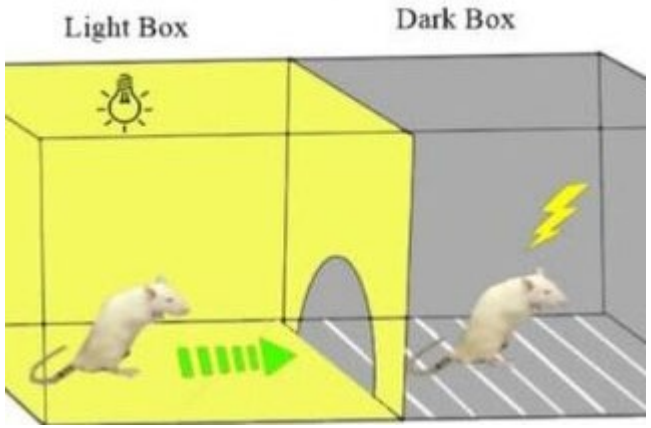


Rats are given a choice between plain water and sucrose water, and how much they drink is quantified. We did not see any anhedonia.

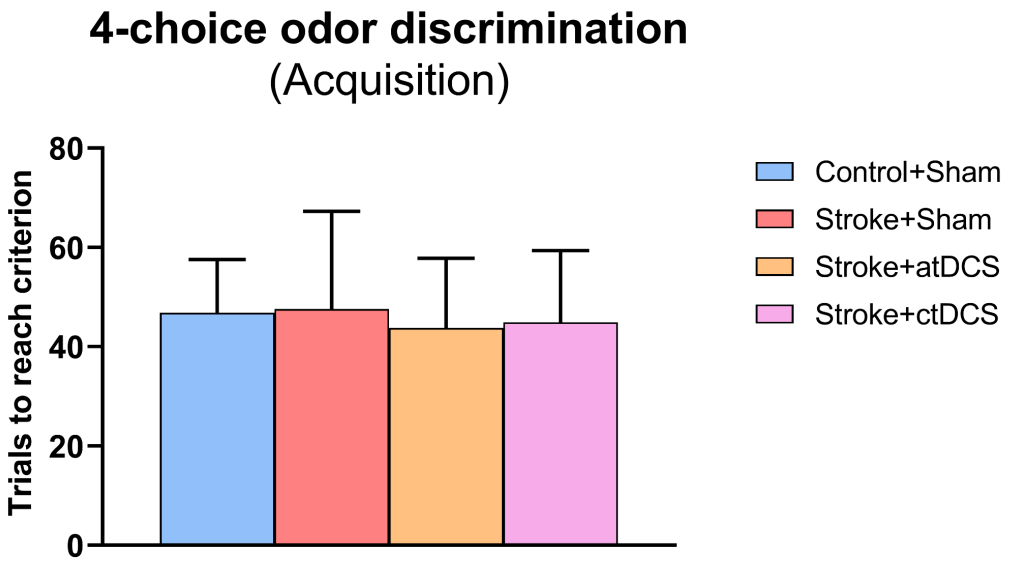


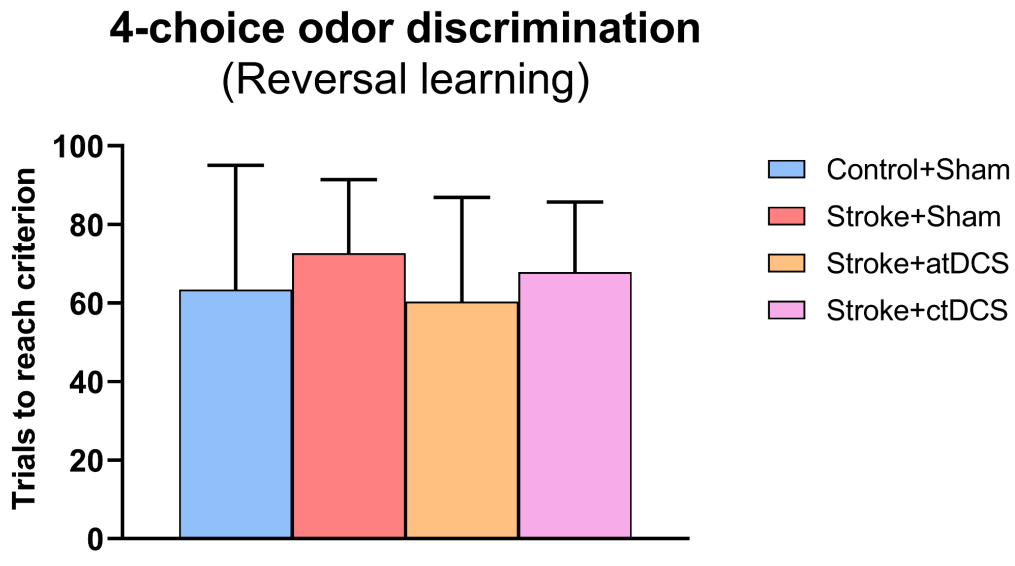


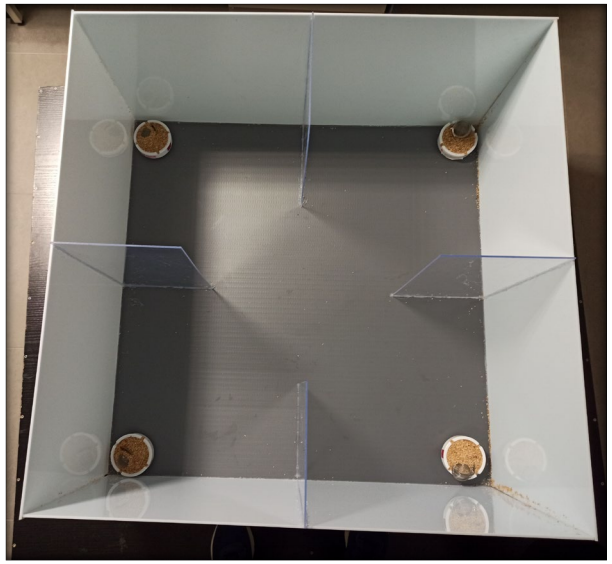




Badeli et al. 2023


4-choice odor discrimination
(Acquisition)
Trials to reach criterion
0
20
40
60
80
Control+Sham
Stroke+Sham
Stroke+atDCS
Stroke+ctDCS


4-choice odor discrimination
(Reversal learning)
Trials to reach criterion
0
20
40
60
80
100
Control+Sham
Stroke+Sham
Stroke+atDCS
Stroke+ctDCS



CONCLUSIONS

- Stroke model affects behaviour:
  - **Compulsivity (MBT)**
  - **Depression (FST)**
  - **Anxiety-like behaviour (EPM)**

- tDCS Treatment
  - Positive effect (atDCS/ctDCS)
  - No effect
  - Positive effect (atDCS)

- Stroke model affects cognitive functions:
  - **Learning (VDS training)**
    - Positive effect (atDCS)

Overall, anodal tDCS seems to have a greater impact on funcional recovery after stroke

Future: Analysis of biomarkers

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