

Effects of physical exercise on brain glucose metabolism in a mouse model of Down Syndrome: a PET imaging study

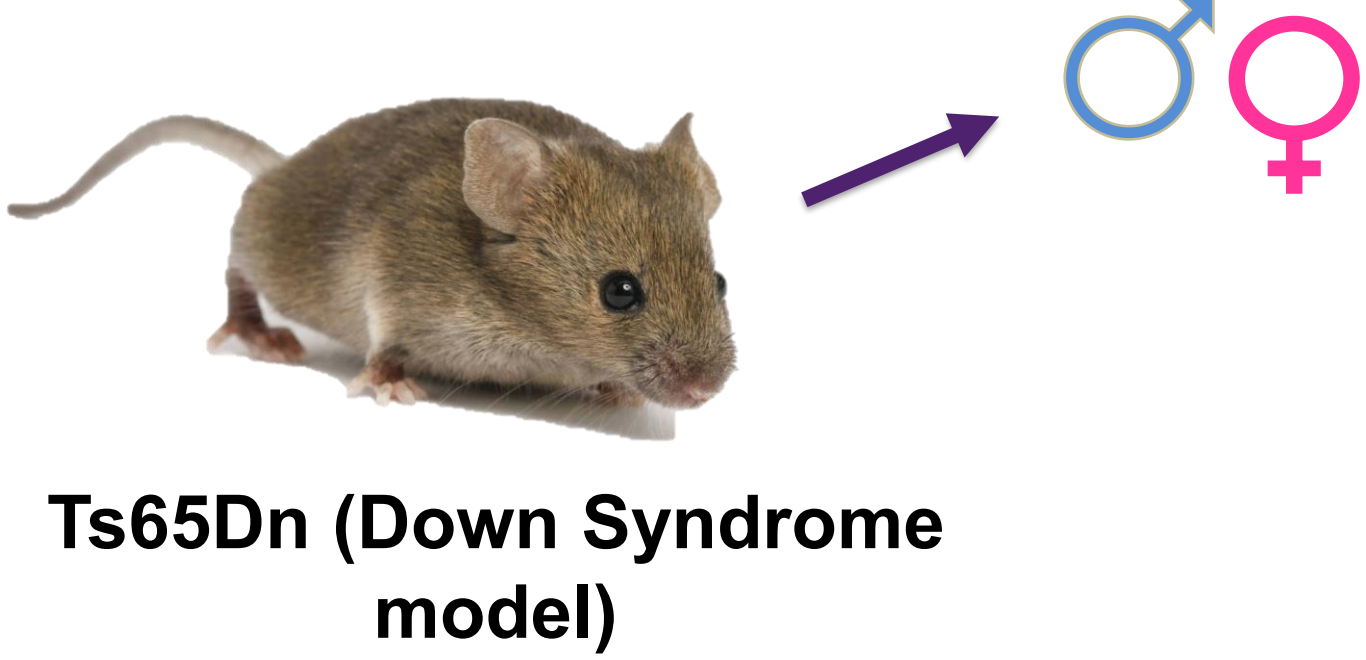
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INTRODUCTION

Individuals with Down syndrome (DS) have an elevated lifetime risk of developing dementia. Thus, it is important to look for interventions that prevent or delay pathological alterations before symptoms occur. Physical activity is a non-pharmacological intervention with potential benefits for brain health. This study aimed to evaluate the effects of physical exercise on brain glucose metabolism and behavior in a mouse model of DS.

METHODS

1. Animal model



*Ethics committee approval CEUA/FMUSP 1811/2022, 2065/2024

2. Experimental groups

1. SEDENTARY

No therapeutic intervention

2. EXERCISE

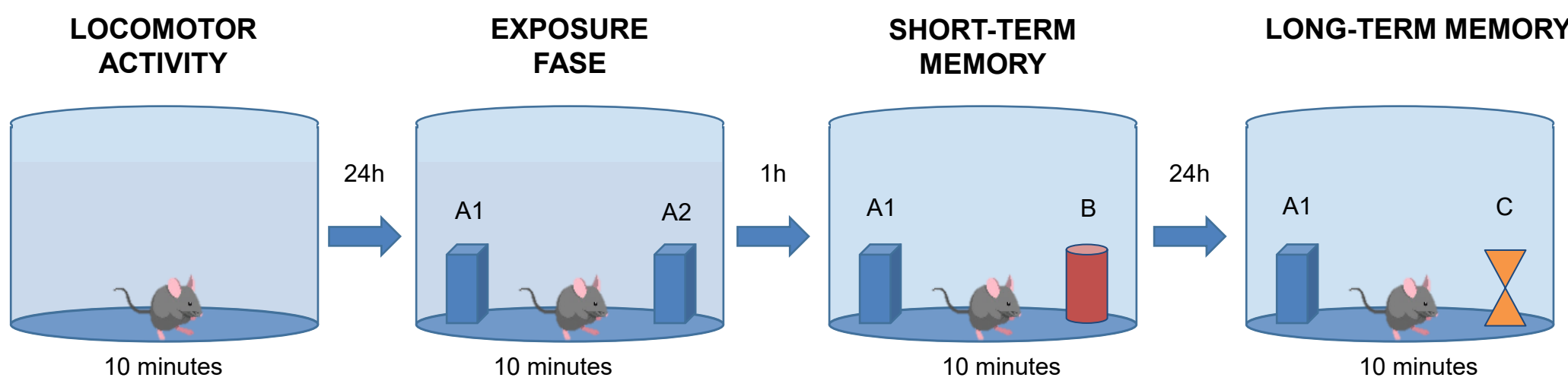
Physical activity on a treadmill from 2 to 4 months of age, 3 times/week

3. PET imaging



The animals were anesthetized and received an intravenous injection of the radiotracer. Then, the animals woke up for biodistribution time (45 minutes).
A 15-minute static image was acquired.
VOI analysis – SUV (Standardized Uptake Value).

4. Behavioral assessment



RESULTS

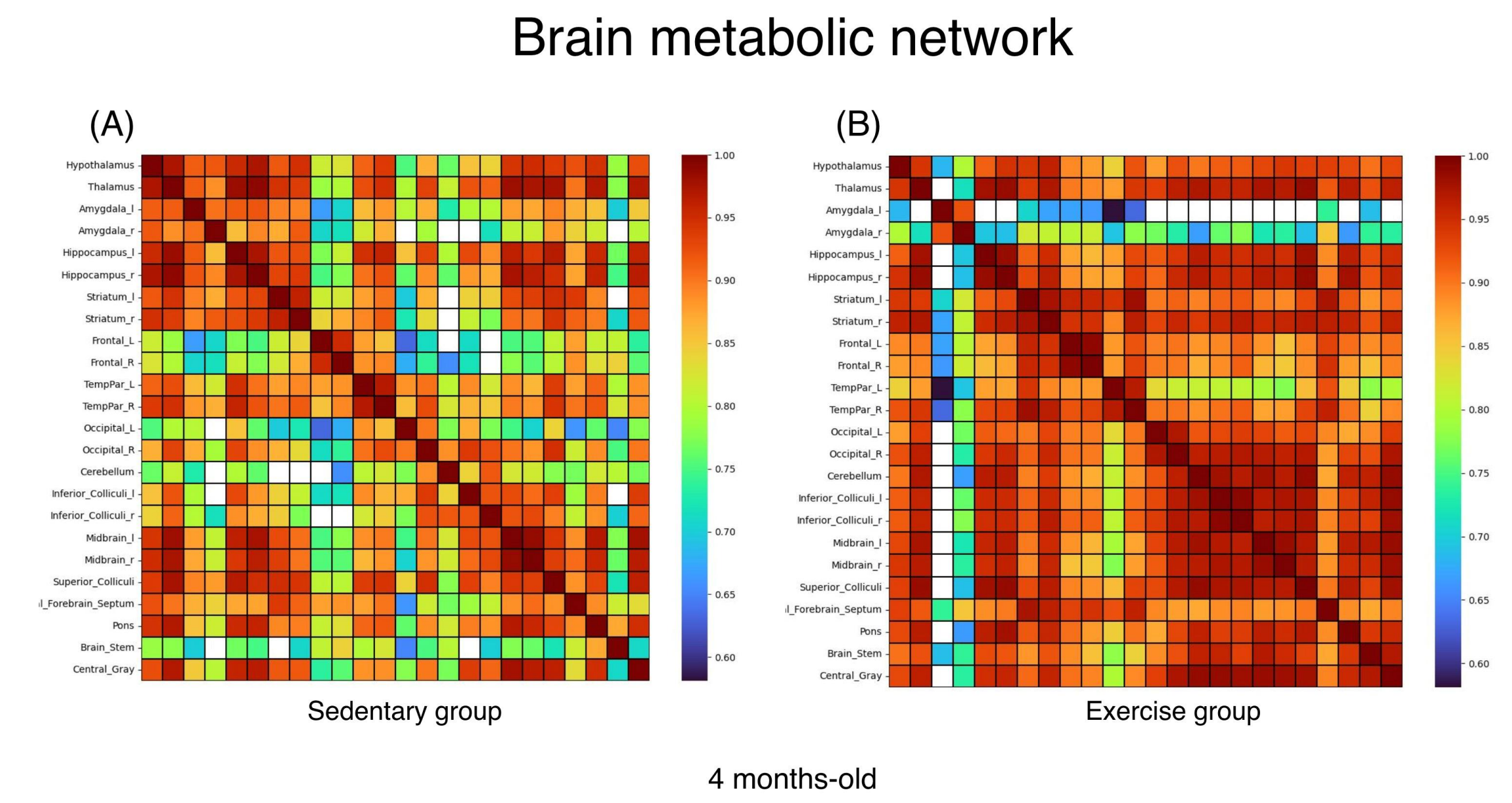


Figure 1: Brain Adjacency matrices for sedentary (n = 20) and exercise (n = 25) groups using [¹⁸F]FDG SUV data. Metabolic networks shows that, while the sedentary-group seems to have a cluster encompassing hypothalamus, thalamus, amygdalas, hippocampus and striatum, the exercise-group demonstrated a general more connected network, with a cluster in occipital cortex, cerebellum, midbrain, superior and inferior colliculi also a smaller cluster in pons, brain stem and central gray.

[¹⁸F]FDG Uptake and Graph Metrics for Significant Regions

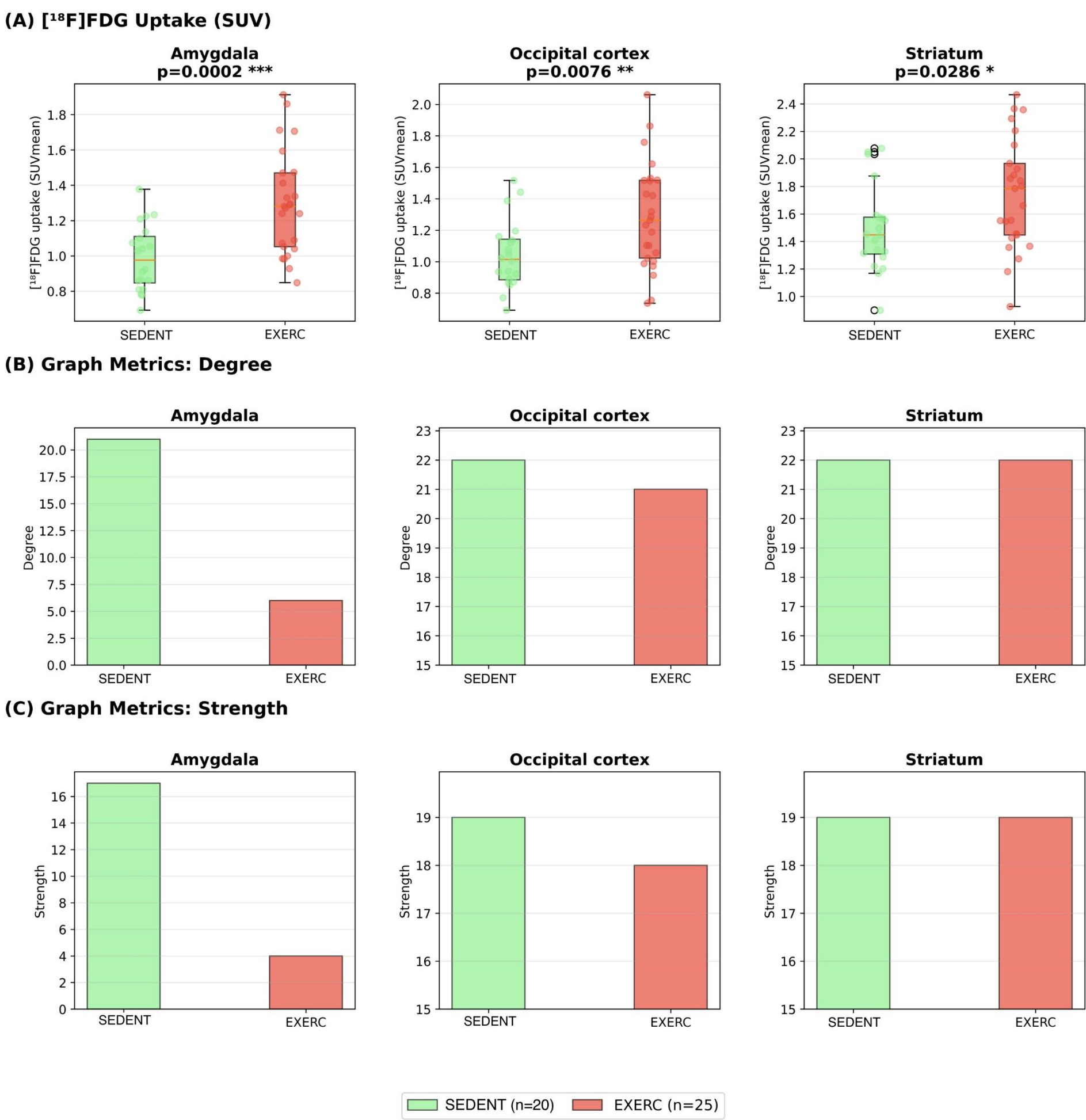


Figure 2: (A) VOI analysis: [¹⁸F]FDG uptake of sedentary (n = 20) and exercise groups (n = 25) considering amygdala, occipital cortex and striatum at 4 months-old. T-test, data presented as mean ± sd. Graph metrics derived from covariance analysis: degree (B) and strength (C). Group-wise analysis demonstrated that the exercise-group had higher SUV in amygdalas (p<0.001), occipital cortex (p=0.0076) and striatum (p=0.0286). Covariance analysis showed that these regions demonstrated different network metrics between groups, with amygdala demonstrating less degree and strength in the exercise-group.

Behavior and locomotor activity

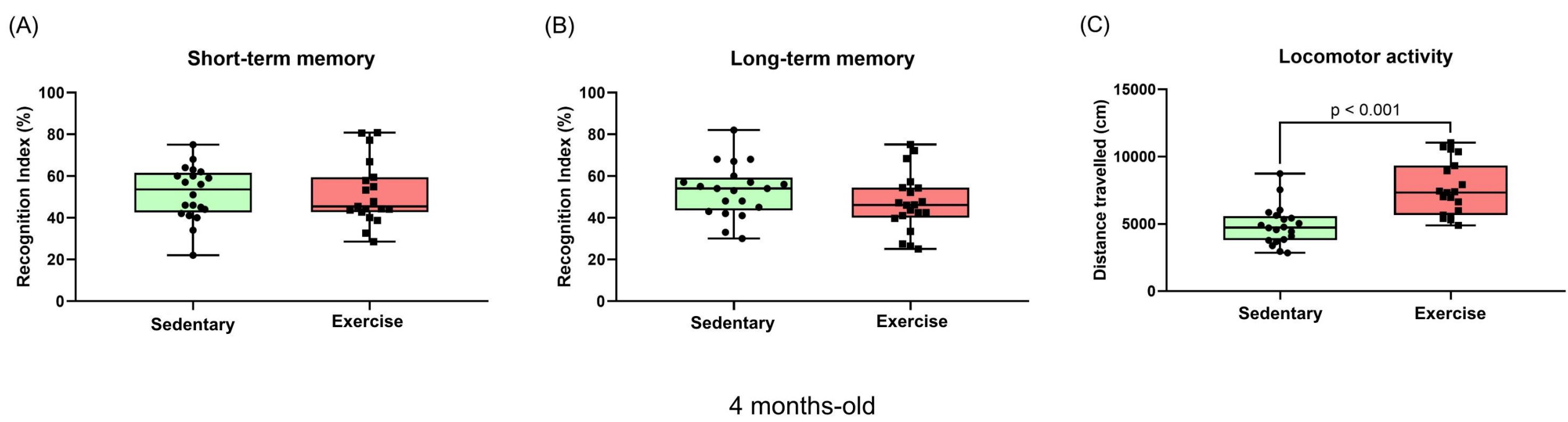


Figure 3: (A) Short-term memory indexes of sedentary (n = 20) and exercise (n = 19) groups. (B) Long-term memory indexes of sedentary (n = 20) and exercise (n = 19) groups. (C) Locomotor activity of sedentary (n = 20) and exercise (n = 19) groups. The molecular alterations in the brain did not affect short- nor long-term memory, however the exercise group demonstrated higher locomotor activity (p<0.001).

CONCLUSIONS

Our results demonstrated that Ts65Dn mice that underwent physical exercise presented more connected brain networks, with higher correlation in key brain regions to motor control and movement. Also, this intervention increased brain glucose metabolism in cortical and subcortical brain regions and promoted higher locomotor activity. Together, these findings indicate an improvement in brain energetic efficiency, which may contribute to neuroprotective effects. However, it is important to evaluate these animals throughout the aging process to better understand the physical exercise impact.

REFERENCES

- Fortea J, Zaman SH, Hartley S, Rafii MS, Head E, Carmona-Iragui M. Down syndrome and Alzheimer's disease: insights into biomarkers, clinical symptoms, and pathology. *Lancet Neurol.* 2025.
- Parrini M, Ghezzi D, Deidda G, Medrihan L, Castroflorio E, Alberti M, et al. Aerobic exercise and a BDNF-mimetic therapy rescue learning and memory in a mouse model of Down syndrome. *Sci Rep.* 2017;7(1):16825.
- Chumin EJ, et al. Brain metabolic network covariance and aging in a mouse model of Alzheimer's disease. *Alzheimers Dement.* 2024.
- Hanna C, Hamilton J, Amavut E, Blum K, Thanos PK. Brain Mapping the Effects of Chronic Aerobic Exercise in the Rat Brain Using FDG PET. *J Pers Med.* 2022;12(6):860.

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