# Increased hippocampal volume in exercising mice: comparison of control conditions with in vivo voxel based morphometry

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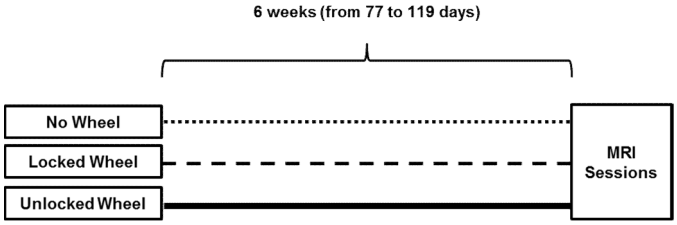
## INTRODUCTION & METHODS

Both human and animal studies have shown that **physical exercise** (primarily aerobic exercise) may have facilitating effects on brain plasticity and cognition[1]. In rodents, improvements of various forms of learning and memory induced by **wheel-running** have been associated with numerous neuroplastic changes such as **increased hippocampal neurogenesis**[2]. A few studies, using **magnetic resonance imaging** (MRI), consistently reported hippocampal volumetric increase relative to non-exercising mice[3-6]. However, the **control group** is commonly limited either to a **locked wheel or no wheel**.

In the present study, we intended to test whether **6 weeks of voluntary wheel-running exercise** during adulthood induced a detectable **volumetric change** in mice brain in comparison to **non-exercised control mice housed either with a locked wheel or without such wheel**.

**54 C57Bl6 males** were randomly assigned to one of the three groups and individually housed for 6 weeks before imaging session

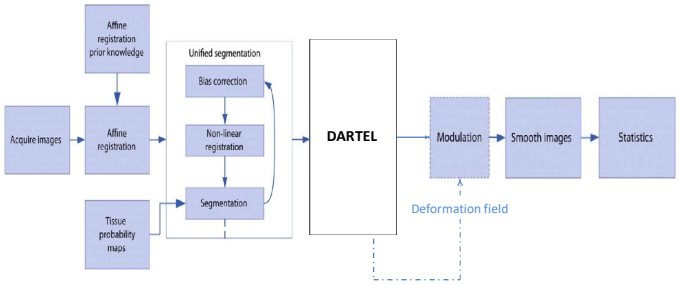



***MRI acquisition:***

- Agilent 9.4 T with 72 mm volume coil, mouse head surface coil receiver.
- 3D anatomical T2 (voxel size: 0.21 mm isotropic).

***Data Analysis:***

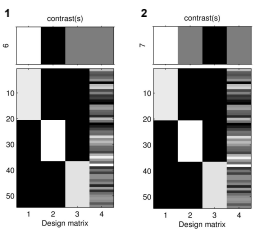
- Dartel software for the preprocessing of the data.




- Voxel Based Morphometry with **SPM mouse toolbox** (SPM 8).
- A **small volume correction** was applied to limit the analysis to the hippocampus.

***Statistical Analysis:***

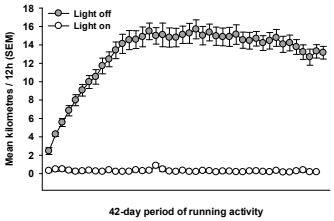
- F test, threshold p < .001 uncorr.
- Intracranial volume (ICV) as co-variable.




Design Matrices of the study.
**1** contrast Wheel > Locked
**2** contrast Wheel > No Wheel.

## RESULTS & DISCUSSION

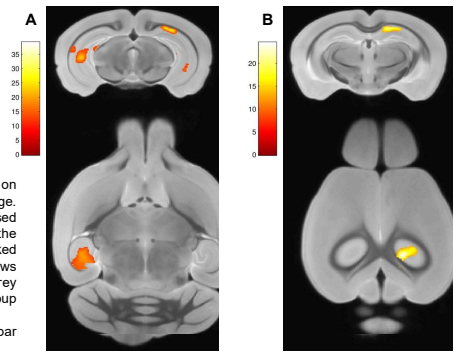
***Behavioral results***




Average distance covered by C57Bl6 mice over the 42 days of free wheel-running activity. Values are mean ± S.EM.

The distance run by the mice progressively increased and reached a plateau. We observed a classical circadian pattern of wheel-running activity, with running activity occurring at night. Besides, individual distances run are highly variable, with a plateau in the rang of 5 and 20 km per 12 hours.

***Imaging results***

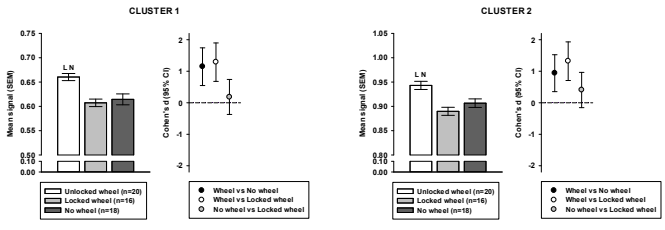



Results of the VBM statistics on the coregistred template image. Panel A shows increased hippocampal grey matter in the wheel group compared to locked group. The panel B shows increased hippocampal grey matter in the wheel group compared to No Wheel group. $p < .001$ uncorrected, scale bar represents $F$ test.

VBM analysis shows significant clusters with increased grey matter volume in the hippocampus when we compare the wheel vs locked wheel groups. Regarding the wheel vs no wheel comparison, significant clusters were observed in the hippocampus.

| | Cluster size | Coordinate x | y | z | $P_{FWE-corr}$ | $Z_{score}$ | $P_{uncorr}$ |
|---|---|---|---|---|---|---|---|
| **Wheel > Locked** | 1531 | 1.7 | -2.2 | -0.8 | 0.001 | 5.22 | 0.000 |
| | 3460 | -3.5 | -3.0 | -3.1 | 0.045 | 4.16 | 0.000 |
| **Wheel > No Wheel** | 955 | 1.1 | -2.5 | -0.8 | 0.028 | 4.29 | 0.001 |
| | 238 | -2.0 | -3.6 | -0.9 | 0.040 | 4.20 | 0.001 |

Those results were confirmed by extracting MRI signal values to compare them among the 3 groups.




Average MRI signal in the 3 groups, extracted from each individual MRI using the two main clusters as mask.

## SUMMARY

In this study, we replicate previous studies depicting an increased hippocampal volume under physical exercise in mice using VBM. Moreover, we certified here that attempting to study the impact of physical exercise on brain volume, control groups with a locked wheel or no wheel are equivalent.

REFERENCES

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