

Accepted Manuscript

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PII: S0304-3940(17)30861-3
DOI: <https://doi.org/10.1016/j.neulet.2017.10.035>
Reference: NSL 33179

To appear in: *Neuroscience Letters*

Received date: 5-9-2017
Revised date: 17-10-2017
Accepted date: 19-10-2017

Please cite this article as: Stephanie von Holstein-Rathlou, Nicolas C. Petersen, Maiken Nedergaard, Voluntary running enhances glymphatic influx in awake behaving, young mice, *Neuroscience Letters* <https://doi.org/10.1016/j.neulet.2017.10.035>

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Voluntary running enhances glymphatic influx in awake behaving, young mice

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Highlights

- We assessed glymphatic activity in young mice after five weeks of voluntary running.
- Exercise increases glymphatic influx in awake but not in anesthetized animals.
- Glymphatic influx is enhanced in hypothalamus, ventral, and lateral cortex.
- CSF tracer influx declines during running itself.

Abstract

Vascular pathology and protein accumulation both contribute to cognitive decline, whereas exercise can slow vascular degeneration and improve cognitive function. Recent investigations suggest that glymphatic clearance measured in aged mice while anesthetized is enhanced following exercise. We predicted that exercise would also stimulate glymphatic activity in awake, young mice with higher baseline glymphatic function. Therefore, we assessed glymphatic function in young female C57BL/6J mice following five weeks voluntary wheel running, as compared to sedentary mice. The active mice ran a mean distance of 6 km daily. We injected fluorescent tracers in cisterna magna of awake behaving mice and in ketamine/xylazine anesthetized mice, and later assessed tracer distribution in coronal brain sections. Voluntary exercise consistently increased CSF influx during wakefulness, primarily in the hypothalamus and ventral parts of the cortex, but also in the middle cerebral artery territory. While glymphatic activity was higher under ketamine/xylazine anesthesia, we saw a

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