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## PHYSICAL EXERCISE ACTIVATES THE MU OPIOID SYSTEM IN HUMAN BRAIN

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### Objectives

Physical exercise reduces stress and anxiety, elevates mood, and relieves pain, but the underlying neurobiological mechanisms responsible for these psychophysical effects remain largely unknown. The central opioidergic mechanisms likely modulate these effects and also the exercise-induced euphoria ("runner's high"). In this study, we sought to test the opioid hypothesis of exercise-induced euphoria by measuring  $\mu$ -opioid receptor availability *in vivo* in healthy males twice, before and after aerobic exercise.

### Methods

Five recreationally active healthy men (age: 24 $\pm$ 2 years, BMI: 23 $\pm$ 1.6, VO<sub>2max</sub>: 49.1 $\pm$ 6.3 mL/kg/min) were studied with positron emission tomography (PET) and a bolus injection of [<sup>11</sup>C]carfentanil. Participants underwent two consecutive [<sup>11</sup>C]carfentanil PET scans in random order: after rest and after 60 min of aerobic endurance cycling, on separate days. Cycling was performed at a workload between aerobic and anaerobic thresholds (158 $\pm$ 40W) predetermined individually in maximal oxygen uptake test. Voxel-wise  $\mu$ -opioid receptor availability was quantified with simplified reference tissue model using occipital cortex as the reference region, and statistical parametric mapping was used to compare availability maps between the two conditions.

### Results

Acute exercise increased the availability of  $\mu$ -opioid receptors in anterior cingulate cortex, prefrontal and temporal cortex (cluster-level FDR-corrected p-value < 0.05). ROI analysis indicated that exercise increased  $\mu$ -opioid receptor availability 7-10% in these regions.

### Conclusion

This study provides preliminary evidence that acute exercise modulates the brain  $\mu$ -opioid system in recreationally active men. The  $\mu$ -opioid activation may be responsible for various beneficial psychophysical effects of physical exercise. Individual differences in these mechanisms may reveal why some people enjoy physical exercise more than others.