Shaping adult hippocampal neurogenesis: exercising the brain with cannabinoids

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Background:

Relevance:

- * Neural stem cells >> regenerative potential
 - * Physical exercise >> ↑ brain plasticity
 - * CB2R >> anti-inflammatory/proneurogenic actions
- Develop integrative **therapeutic strategies** to tackle neurological disorders capitalizing on endogenous brain regeneration

Goal:
Investigate the impact of combining physical exercise with CB2R modulation on adult hippocampal neurogenesis

Methods:

Aim 1:

Aim 2:

Results:

Aim 1: *IN VITRO* NEUROGENESIS MODULATION BY CB2R LIGANDS AND NEUROTROPHINS

Cell proliferation

DIV 1, n = 4-6, ***p<0.01, ****p<0.001 using Sidak's multiple comparison test

Neuronal differentiation

DIV 7, n = 4-6, *p<0.05, **p<0.01, ***p<0.001 using Sidak's multiple comparison test

Aim 2: *IN VIVO* NEUROGENESIS AND BEHAVIOR MODULATION BY CB2R LIGANDS

Conclusions:

- “Exercise-like factors” such as BDNF, IGF-1 and VEGF, and CB2R agonist *per se* do not affect cell survival and proliferation in hippocampal neurosphere cultures. Combined treatment (BDNF+IGF-1+VEGF) potentiates the proliferation of hippocampal cells.
- Increasing concentrations of tested compounds induce an acceleration of hippocampal progenitor cells differentiation into neurons which is accompanied by an increase in the number of mature neurons (data not shown). Combined treatment increases substantially this differentiation process.
- CB2R antagonism seems to affect cognitive and anxiety-like behavioural dimensions with clear implications in the regulation of adult hippocampal neurogenesis.

Adult hippocampal neurogenesis