

# Pharmacological activation of the dopamine D4 receptor prevents morphine-induced impairment of adult neurogenesis in the subventricular zone: functional implications in odor discrimination learning

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## **Topic & Theme selection**

**Main Topic:** D.1.a: Olfaction

**Secondary Topic:** E.1.q: Pharmacology

## **Title**

### **Abstract Body**

**Abstract body:** Morphine reduces adult neurogenesis in the subventricular zone (SVZ) and therefore the integration of newly generated neurons in the local olfactory bulb circuit. However, the effects of opioids drugs on the olfactory perception have been scarce studied, although some data suggests that they interfere with olfactory function, and the underlying mechanisms are unknown. We have previously shown that the activation of the dopamine D4 receptor (D4R) prevents both morphine addiction -by modulating dopamine signaling from nigral dopamine cells- and the development of morphine-induced analgesic tolerance -by regulating the primary circuit of pain and GABA/glutamate balance within the dorsal horn. Here, we hypothesize that the D4R could also counteract the impairment of olfaction associated with morphine. We investigated the effect of chronic paradigm of combined treatment of morphine with the D4R agonist PD168,077 on SVZ neurogenesis in adult rats using immunohistochemistry and its functional implications by an olfactory discrimination test. Results showed that, in the SVZ, D4R activation counteracted morphine-induced depletion of newly generated glial cells (astrocytes and oligodendrocytes) and neuroblasts as well as the increase of tyrosine hydroxylase expression. Besides, three weeks of chronic administration of morphine impaired olfactory discrimination between a pair of odorants, which was completely prevented by the co-administration with PD168,077. The present results deepen in the dopaminergic regulation of olfaction and give support for the existence of antagonistic functional D4R-MOR interaction in olfactory bulb and SVZ that could help to the development of new pharmacology strategies for the treatment of pain reducing side-effects of morphine.

### **Keywords**

**Keywords:** Yes

**Keyword 1:** olfaction

**Keyword 2:** morphine

**Keyword 3:** dopamine D4 receptor

**Keyword 4:** olfactory bulb

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