

Title: Olfactory bulb plasticity during complex perceptual learning in mice

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Olfaction is critical in many behaviors, such as research for food, predator avoidance or reproduction. To accomplish these behaviors successfully, an animal must be able to discriminate very close olfactory stimuli with great accuracy. Discrimination performances can be modified by perceptual learning which is defined as an increase in discrimination capabilities of two perceptually close odorants after exposure to this pair of odorants. One of the key supporting structures of this learning is the olfactory bulb (OB) (Mandairon et al. 2008). Interestingly, in the OB, granule cells, a type of inhibitory interneurons, are the target of an important adult neurogenesis originating in the subventricular zone of the lateral ventricles. Previous work showed that adult-born neurons are required for perceptual learning in mice (Moreno et al. 2009).

Until now, studies have analyzed behavioral performances and neurogenic correlates during simple olfactory perceptual learning, involving only one pair of odorants. However, in real life, animals are exposed to more complex olfactory environments. Thus, in this study, we investigated how the animal adapts its perceptive abilities when exposed to more odor pairs and examined the underlying neurogenic modulations.

We showed that i) increasing the complexity of perceptual learning leads to the discrimination of more odor pairs, ii) perceptual learning increased adult-born cell density independently of the complexity of enrichment (using Brdu labelling of adult-born neurons), iii) increasing the complexity of perceptual learning enhances the functional recruitment of adult-born neurons (using *zif268* expression), iv) increasing the complexity of perceptual learning increases structural plasticity of adult-born neurons (labelled by GFP-expressing lentivirus), and v) structural plasticity is specific of adult-born neurons since it is not observed in neurons born during ontogenesis (using lentivirus injection at P1).

All together, these results showed that increasing complexity of perceptual learning increases structural plasticity of adult-born neurons (but not of neurons born during ontogenesis) as well as their involvement in processing the learned odorants. Enhancing the complexity of the task thus intensifies adult-born neuron plasticity resulting at the behavioral level in discrimination of a higher number of perceptually similar odorants.