**Title:** Functional and structural plasticity of adult-born versus preexisting granule cells of the olfactory bulb during simple and complex perceptual learning in mice

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Olfaction is important in many behaviors such as food search, predator avoidance, conspecific recognition or reproduction. To reliably perform these behaviors, animals must have an olfactory system able to discriminate between odorants. Discrimination performances can be improved by perceptual learning which is an increase in discrimination capabilities between two perceptually close odorants after passive exposure to them. We know that a key supporting structure of this learning is the olfactory bulb (OB). Interestingly, the olfactory bulb is the target of an adult neurogenesis. Indeed, new interneurons (mostly granule cells) are formed throughout life from neural stem cells located in the subventricular zone of the lateral ventricle, which migrate and functionally integrate into the neuronal network. Previous work modulating neurogenesis has shown that adult-born interneurons were required for a perceptual learning task (Moreno et al. 2009). In order to understand the specificity of adult-born neurons, it is important to compare them to preexisting ones. In addition, we asked the question of the respective role of these two populations in conditions of more complex learning. We thus trained mice in perceptual learning tasks with an increasing number of odorant pairs (1, 2, 3 or 6 odor pairs). We showed that i) mice were able to learn to discriminate between two similar odorants of up to 6 odor pairs simultaneously ; ii) adult-born cell density increased with learning independently of its complexity (using Brdu labeling) : iii) adult-born neurons' functional recruitment in the processing of the learned odorant linearly increased with complexity ; iv) during simple perceptual learning, only adult-born neurons (labeled with GFP lentivirus injected in adult mice, P60) activated in response to the learned odorants (Zif268-positive neurons) showed structural plasticity evidenced by an increased spine density both at the apical and basal dendritic domains. During complex perceptual learning these same changes occurred but independently of neuronal activity ; v) in preexisting neurons (labeled with DsRed lentivirus injection at P0-P1), only complex learning elicited an increased spine density and only at the apical dendritic domain.
To summarize, these data suggest that improvement in discrimination is underlain by structural plasticity of adult-born neurons and in a second step preexisting neurons depending on the complexity of learning.