Defining the role of the olivo-cochlear system in the development of the auditory system in rats and mice

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Neural circuits that process sensory information require electrical activity during development to promote maturation and refine synapses. Early spontaneous (sensory-independent) activity occurs in discrete bursts of action potentials separated by long periods of silence. Studies in the visual system indicate that bursting activity originates in the retina, pointing to an important role of sensory organs in activity-dependent neuronal development. How is bursting activity generated in the auditory system? This is an important question due to the existence of neuronal feedback *via* the olivo-cochlear (OC) system, an inhibitory cholinergic pathway located in the ventral brainstem. To begin addressing this question we performed electrophysiological recordings in the ventral brainstem of anesthetized neonate rats (n = 69, between P0-11). We found that central auditory neurons fire action potentials in a precise sequence of mini-bursts prior to the onset of hearing. We next obtained *in vivo* whole cell recordings from identified auditory brainstem neurons and observed that firing was driven by EPSPs (n=6/6, ages P1-6). Interestingly, the proportion of bursting units increased with age, and after P4 only bursting units were observed. This stereotyped pattern is very similar to that recorded in primary auditory neurons in cochlear explants (Tritsch *et al.*, 2007), suggesting that OC feedback is not necessary to generate bursting activity. Therefore, we hypothesized that the OC system could be involved in regulating the observed increase in bursting units during early postnatal development. To test the hypothesis we are performing electrophysiological experiments in 9 nicotinic receptor knockout animals, where OC function is compromised (Vetter *et al.*, 1999). The hypothesis predicts that the proportion of bursting cells in knockout mice will increase at earlier ages than in heterozygous or wild type littermates.

Tritsch NX, Yi E, Gale JE, Glowatzki E, Bergles DE. (2007) *Nature* **450**: 50-5.

Vetter DE, Liberman MC, Mann J, Barhanin J, Boulter J, Brown MC, Saffiote-Kolman J, Heinemann SF, Elgoyhen AB. (1999) *Neuron* **23**: 93-103.