# HIGHLIGHTS

# IN BRIEF

# SLEEP

Hippocampal population activity during the small-amplitude irregular activity state in the rat.

Jarosiewicz, B. et al. J. Neurosci. 22, 1373–1384 (2002)

The authors describe a third sleep state in the rat, which is distinct from rapid eye movement (REM) sleep and normal slow-wave sleep. This state, which follows nearly every REM episode and accounts for around 20% of total sleep, is characterized by a few seconds of low-amplitude electroencephalographic activity and is called S-SIA (sleep small-amplitude irregular activity). During S-SIA, only a few hippocampal cells are active. The authors provide evidence that many of these cells have place fields that include the location where the rat is sleeping.



#### NEUROTECHNIQUES

Visualization of functionally activated circuitry in the brain. Wilson, Y. *et al. Proc. Natl Acad. Sci. USA* **99**, 3252–3257 (2002)

The authors developed a transgenic model to visualize activated neurons. As the *c-fos* gene is rapidly induced in neurons after activation, they used its promoter to drive the expression of a *tau–lacZ* fusion gene. Neuronal activation was accompanied by the expression of  $\beta$ -galactosidase — the *lacZ* product — which diffused to dendrites and axons. They tested whether physiological stimuli could induce  $\beta$ -galactosidase and found that water deprivation led to protein expression in circuits that participate in water homeostasis. This method might have general applications in tracing studies.

#### SYNAPTIC PHYSIOLOGY

Dependence of EPSP efficacy on synapse location in neocortical pyramidal neurons.

Williams, S. R & Stuart, G. J. Science 295, 1907-1910 (2002)

The effect of dendritic location on the potency of a synapse has been the subject of many recent studies. Here the authors show that, in contrast to what has been found in the hippocampus, the size of excitatory potentials in neocortical neurons decreases as distance from the soma increases. However, if distal inputs are co-activated within a narrow time window, then they can provide a significant depolarizing stimulus. So, in neocortical neurons, distal inputs might act as coincidence detectors.

# NEURAL CREST

# About-face

The vertebrate facial skeleton is derived from the cranial neural crest, and patterning of this migratory cell population is a crucial early step in craniofacial development. Each hindbrain segment, or rhombomere (r), expresses a distinct combination of Hox genes, and this 'Hox code' seems to confer positional information on the neural crest. Drew Noden's classic grafting experiments from the early 1980s indicated that rhombomeres and their neural crest derivatives retain their identity if they are transplanted to a different axial level. For example, neural crest precursors that were destined for the first branchial arch still generated first-arch skeletal structures when they were grafted into more posterior regions of the chick hindbrain. However, more recent experiments have shown that r1–6 can be respecified if they are transplanted in a more posterior area of the hindbrain, and that Hox gene expression in the neural crest can be reprogrammed by signals from outside the neural tube. In a new paper, Trainor and colleagues try to reconcile these findings with Noden's data.

One of Noden's results that is often overlooked is that frontonasal neural crest cells also induced firstarch skeletal elements at ectopic sites, even though they do not normally contribute to these structures. Trainor *et al.* propose that both the anterior hindbrain and frontonasal crest grafts could have included tissue from the isthmus, which is a key signalling centre at the mid–hindbrain boundary. Could the isthmus have induced the skeletal duplications?

To find out whether signals from the isthmus could reprogramme Hox gene expression in the neural crest, Trainor *et al.* soaked a bead in the isthmic signalling molecule fibroblast growth factor 8 (FGF8), then implanted it adjacent to r4 in a normal embryo. They found that *Hoxa2*, which is normally expressed in r4 but not in r1, was initially downregulated in the r4 neural crest, but that it was re-activated in crest cells as they



migrated away from the bead. So, although FGF8 can cause transient respecification of r4 neural crest cells, additional signals would presumably be required to suppress their identity permanently.

In a variation of Noden's experiment, the authors transplanted r1 tissue with or without the isthmus into r4, then examined the effects on skeletal development. In the absence of isthmic tissue, the second-arch skeleton developed normally. However, if isthmic tissue was included in the graft, it was replaced by first-arch structures, confirming that Noden's result could have been caused by the inclusion of isthmic tissue in his grafts.

In a previous study, Irving and Mason showed that rl tissue can switch to an r4 identity if transplanted into r4, but only if no isthmic tissue is present in the graft. Taken together with the new data, this indicates that r1 and its neural crest do not have an intrinsic ability to generate first-arch skeletal elements, but that additional isthmic signals are required to suppress the expression of more posterior patterning genes, such as Hoxa2. These findings support the increasingly popular idea that rhombomere and neural crest identity is more plastic than was originally thought, and future studies should help to identify the signals that influence this plasticity.

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# **(3)** References and links

ORIGINAL RESEARCH PAPER Trainor, P. A. et al. Role of the isthmus and FGFs in resolving the paradox of neural crest plasticity and prepatterning. *Science* **295**, 1288–1291 (2002) FURTHER READING Trainor, P. A. & Krumlauf, R. Patterning the cranial neural crest: hindbrain segmentation and *Hox* gene plasticity. *Nature Rev. Neurosci.* **1**, 116–124 (2000) | Irving, C. & Mason, I. Signalling by FGF8 from the isthmus patterns anterior hindbrain and establishes the anterior limit of *Hox* gene expression. *Development* **127**, 177–186 (2000)