A role for endogenous CRH in the hippocampus?

Benjamin Gunn¹, Yuncai Chen², Gary Lynch² and Tallie Z. Baram¹,²

¹Pediatrics, ²Anatomy / Neurobiology, University of California-Irvine, Irvine, CA 92697-4475

Rationale
- CRH is a central component of the stress response.
- Neurons within the hippocampus express CRH, CRH receptors (CRHR’s) and this neuropeptide is released in this brain region during stress.
- Important in mediating stress-related effects upon learning and memory.
- Exogenous application of CRH modulates neuronal excitability in the hippocampus.
- Is there evidence of an endogenous CRH “tone?”

The hippocampus is a “hot spot” of receptors for key stress mediators.

Hippocampal principal neurons.
- Express a number of receptors for key stress mediators.
- These receptors are expressed in discreet subcellular domains.
- Inhibitory and excitatory afferents innervate distinct domains of principal cells.
- How the effects of these various stress mediators integrate to modulate neuronal function and plasticity will be crucial in determining the response to stress.

CRH is expressed in hippocampal interneurons in the CA1 and CA3.

The Crh-ires-cre mouse line can be used to reliably identify CRH expressing neurons in the hippocampus

Does endogenous CRH modulate excitatory synaptic transmission in the hippocampus CA3?

Properties of spontaneous excitatory postsynaptic currents (sEPSCs).

Inhibition of CRHR1 signalling has modest effects upon the peak amplitude and decay time of sEPSCs.

However, the frequency of sEPSCs is attenuated following treatment with the CRHR1 antagonist NBI 30775 (1 μM).

A mean decrease in the sEPSC frequency of ~25%.

The effects of NBI 30775 (1 μM) appear to be reversible.

Summary
- Inhibition of CRHR1 signaling significantly reduces the frequency of sEPSCs recorded from CA3 pyramidal cells.
- This suggests that endogenous CRH modulates excitatory synaptic transmission in the CA3 region in an acute brain slice preparation.

Future Directions
- To characterise the properties of CRH-expressing interneurons within the hippocampus using CRH-tdTomato mice.
- Further elucidate the mechanism(s) underlying CRH modulation of excitatory transmission within the hippocampus.
- Investigate the effect that stress has upon the function of CRH interneurons and how this influences their interaction with principal neurons.

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Electrophysiology.
Male WT mice (P21-40) were killed by decapitation, brains were dissected and horizontal slices (300-350 μm) prepared using standard procedures. All electrophysiological recordings were made under standard conditions as previously described (Gunn et al, 2013).