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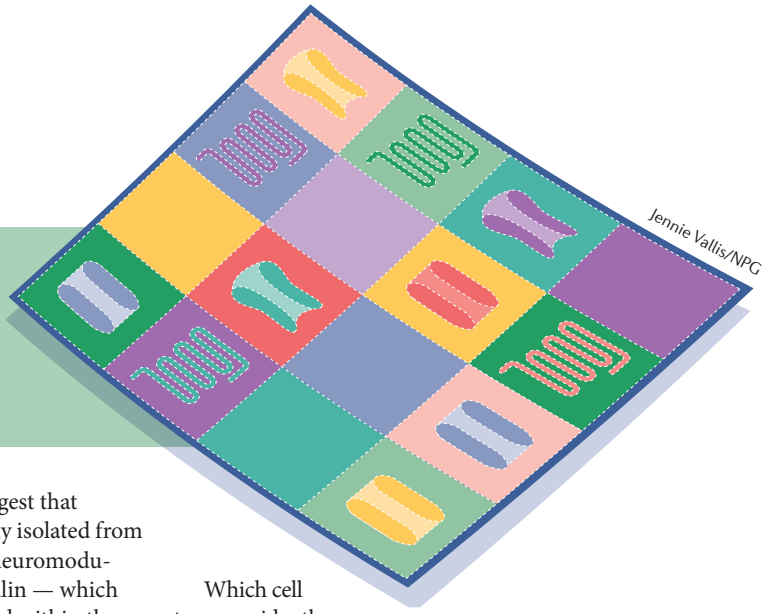

Jennie Vallis/NPG

NEURONAL CIRCUITS

Patch work in the striatum

Patterns of opioid and opioid receptor expression and neuronal connectivity demarcate 'patch' (striosome) and 'matrix' compartments within the dorsal striatum; however, little is known about the circuit structure of these compartments or how they are affected by opioid signalling. Sabatini and colleagues have now dissected the striatal patch microcircuitry in mice and have shown that the endogenous opioid enkephalin acts mainly via δ-opioid receptors (DORs) to suppress inhibitory input to striatal projection neurons (SPNs) in patches.

To examine the cellular composition and connectivity of striatal compartments, the authors performed cell type-specific immunolabelling in brain slices from mice in which two fluorescent proteins were expressed under the control of patch-specific promoters. This revealed compartment-specific patterns of cellular composition: patches contained a higher proportion of the SPNs that contribute to the basal ganglia's 'direct' pathway (dSPNs) than did the matrix, whereas matrix compartments received more inhibitory inputs from parvalbumin-expressing interneurons. There was little evidence of direct intercompartment connectivity, and recordings of synaptic currents in patch SPNs following stimulation in the same patch or in the surrounding matrix indicated that they receive little synaptic input from matrix neurons.

These findings suggest that patches are synaptically isolated from the matrix; however, neuromodulators such as enkephalin — which is specifically expressed within the matrix — represent another possible method of intercompartment communication. Using fluorescence *in situ* hybridization, the authors showed distinct patterns of expression of the receptors for enkephalin — μ-opioid receptors (MORs) and DORs — in the striatum. MOR expression was restricted mainly to patches, whereas DORs were expressed in both compartments. Within patches, dSPNs primarily expressed MORs, whereas SPNs of the 'indirect' pathway (iSPNs) expressed both receptor types.

These patterns of opioid receptor expression provide a potential basis for enkephalin modulation of SPN function. Indeed, bath application of enkephalin to brain slices suppressed evoked inhibitory postsynaptic currents (IPSCs) specifically in patch SPNs (with a particularly marked effect on dSPNs). In the absence of either MORs or DORs, enkephalin still suppressed IPSC amplitude, suggesting that both receptor types contribute to its effects. Activation of either MORs or DORs in brain slices using specific pharmacological agonists was sufficient to suppress SPN IPSCs, but DOR activation had a greater effect.

Which cell type provides the inhibitory input to patch SPNs that is modulated by enkephalin? The authors took brain slices from mice in which channelrhodopsin 2 was expressed in particular classes of GABAergic neurons and examined the effects of enkephalin on light-evoked IPSCs. This revealed that the main cellular targets of enkephalin in patches are the collateral inputs from other SPNs (particularly iSPNs) to dSPNs. Using DOR-specific and MOR-specific agonists, the authors showed that the effects of enkephalin are likely to be mediated primarily by DORs.

The authors found that the overall effect of enkephalin on striatal networks was to disinhibit patch dSPN firing in response to cortical inputs, resulting in an increase in the neuronal firing in patches. Given the selective effects of enkephalin on patches, which receive inputs from limbic-associated cortical regions, these findings suggest that opioid signalling may have a particular influence on goal-directed behaviours.

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ORIGINAL ARTICLE Banghart, M. R. *et al.* Enkephalin disinhibits mu opioid receptor-rich striatal patches via delta opioid receptors. *Neuron* http://dx.doi.org/10.1016/j.neuron.2015.11.010 (2015)

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