A role for kainate receptors in mood disorders

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Most excitatory synapses in the brain use the amino acid glutamate as a neurotransmitter. Since the excitatory properties of glutamate were postulated nearly 40 years ago, an extraordinary wealth of data has accumulated on the types of synaptic responses triggered by this neurotransmitter. A more precise specification of ionotropic glutamate receptors into three types based on the agonist that activates or binds to them indicates the existence of AMPA, kainate and NMDA receptors as the main effectors of glutamate at synapses. Our understanding of the molecular properties of kainate receptors (KARs) and their involvement in synaptic physiology lag far behind that for other receptors, but it has progressed significantly over the last 30 years. A plethora of studies indicate that KARs are important mediators of the pre- and postsynaptic actions of glutamate[1]. The involvement of KARs in synaptic plasticity is now clear[2] and they play a fundamental role in epilepsy through the strategic control of network excitability. Indeed, three clear fields related to the behavior of these receptors have emerged[3]: there are a number of interacting proteins that pace their properties; their activity is unconventional since they can signal through G-proteins, behaving like metabotropic receptors; they seem to be linked to some devastating brain diseases. In the last few years we have accumulated evidences on how these receptors control transmitter release, and more recent results specify their influential role in the maturation of neural circuits during development[4], and provide compelling evidence on their implication in mood disorders. I will present studies using mice with loss and gain of function that may represent new animal models for disentangling the role of these receptors in brain function.

1) Lerma (2003) *Nature Rev Neurosci* 4:481-495.
2) Selak et al. (2009) *Neuron* 63:357-371.
3) Lerma & Marques (2013) *Neuron* 80:292-311
4) Marques et al. (2013). *J. Neurosci.* 33:18298–18310.