

HIERARCHICAL CONTROL OF DOPAMINE NEURON-FIRING PATTERNS BY NEURONAL NICOTINIC RECEPTORS

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Nicotine elicits dopamine release by stimulating nicotinic acetylcholine receptors (nAChRs) on dopaminergic neurons. However, a modulation of these neurons by endogenous acetylcholine has not been described.

We recorded, *in vivo*, the spontaneous activity of dopaminergic neurons in the VTA of anaesthetized wild-type and nAChR knockout mice and their response to nicotine injections. Deleting $\alpha 7$ or $\beta 2$ subunits modified the spontaneous firing patterns, demonstrating their direct stimulation by endogenous acetylcholine.

Quantitative analysis further revealed four principal modes of firing, each depending on the expression of particular nAChR subunits and presenting unique responses to nicotine. The prominent role of the $\beta 2$ subunit was further confirmed by its selective lentiviral re-expression in the VTA.

These data suggest a hierarchical control of dopaminergic neuron firing patterns by nAChRs: activation of $\beta 2^*$ -nAChR switches cells from a resting to an excited state, whereas activation of $\alpha 7^*$ -nAChRs finely tunes the latter state but only once $\beta 2^*$ -nAChRs have been activated.

References:

Mameli-Engvall M., Evrard A., Pons S., Maskos U., Svensson T.H., Changeux J.P., Faure P. (2006) *Neuron* 50, 911–921.