MEDIAL FOREBRAIN BUNDLE STIMULATION INDUCES SHORT- AND LONG-LASTING CHANGES IN DOPAMINE NEURON ACTIVITY: INVOLVEMENT OF THE CANNABINOID AND GLUTAMATE RECEPTORS

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Stimulation of the medial forebrain bundle (MFB) induces an enduring potentiation of behaviour directed at obtaining additional stimulation (intracranial self-stimulation). Considerable body of evidence suggests that ventral tegmental area (VTA) dopamine (DA) neurons are involved in the rewarding effects of MFB self-stimulation. It was assessed whether MFB stimulation, like drugs of abuse, may induce short or long-lasting modifications in DA neuron activity, which may underlie its strong rewarding and reinforcing properties.
We utilized standard single cell extracellular recordings from VTA DA neurons in anesthetized rats. DA cells were antidromically identified from the stimulation of MFB. After a single train (40 stimuli in 1 s), DA neurons responded with a short-lasting inhibition of firing (<1 s), followed by a phasic (~ 1 min) increase in spontaneous firing rate and bursting discharge (to 125.7±4.7 % and 137.9±14.5 % of baseline, respectively). Short lasting DA cell responses were followed by a delayed and long-lasting change in firing activity. Hence, we observed a reduction of firing rate (57.8±16.5% of baseline, $P<0.001$) and bursting discharge (30.3 ±16.3% of baseline, $P<0.05$) which persisted for more than 30 minutes. Metabotropic glutamatergic and endocannabinoidergic transmissions play a major role in short- and long-term forms of synaptic plasticity in the VTA. Thus, we studied whether the mGLUR1 receptor antagonist JNJ16259685 (JN) and the CB1 cannabinoid receptor antagonist SR141716A (SR) modulate the early and/or the delayed response of DA cells to MFB stimulation. SR (1 mg/kg, i.v.) modulated the short-latency response to train stimulation but had no effect on the delayed inhibition of DA neurons. JN (0.125 mg/kg i.v.) enhanced the early inhibitory response whereas modulated train induced decrease in burst firing.
Our results indicate that MFB stimulation evoked a modification of DA neuron activity over multiple time scales, possibly the results of synaptic plasticity. The cannabinoid and metabotropic glutamate receptors are involved in the early and delayed phases of DA neuron responses.