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PLASTICITY IN THE NUCLEUS ACCUMBENS FOLLOWING HIGH FREQUENCY STIMULATION OF THE VENTRAL TEGMENTAL AREA *IN VIVO*.

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Plasticity in the dopaminergic mesolimbic pathway is increasingly recognised as a contributing factor associated with addiction(Gerdeman *et al.* 2003).However, little is known about the mechanisms that enable DA receptors to modulate synaptic plasticity. To address these questions, we used extracellular recording *in vivo* to examine changes in cell firing patterns that may occur in the Nucleus Accumbens (NAc) following periods of high frequency stimulation (HFS) in the ventral tegmentum (VTA). Here we report how different types of neuronal responses are affected.

Bipolar stimulating electrodes were placed in the VTA of urethane (1.2 g/kg i.p.) anaesthetized male Wistar rats (n=22) and recordings made in the NAc; animals were humanely killed at the end of the experiments. Stimuli are comprised of bursts of 5 pulses (50ms), 20 Hz every 20 seconds. Average stimulating current was less than 1.4 mA. To investigate the effect of HFS (comprising 10 trains of 10 pulses delivered at 200Hz with an inter-train interval of 2s delivered 3 times at 20 s intervals) a normalized firing ratio was computed, from peristimulus time histogram (PSTH), by dividing the number of spikes occurring at a given latency by the number of stimuli during a given period. This ratio indicates the probability of generating an action potential in the receptive cell, and thus synaptic efficiency. Synaptic plasticity was measured as a ratio variation following HFS.

Of the 60 neurons recorded in the NAc, 49 (82%) responded to stimulation in the VTA. HFS induced changes in firing ratios of 31 neurons; 14 were potentiated and 17 depressed. Potentiation and depression increased slowly during the 1 hr period following HFS, both reaching peak values, 180 ± 46 % and 55 ± 7 % (mean ± s.e.m) of baseline respectively. Comparisons between latencies of potentiated (9.2 ± 1.4 ms), depressed (6.3 ± 0.8 ms) and unchanged responses (9.6 ± 1.2 ms) show that depressed responses occurred in neurons with a significantly shorter latency (un-paired t-test, $p<0.05$). The latencies were not altered following HFS.

The difference in latencies observed suggests two neuronal populations with different sensitivity to HFS. The slow time course of the change may be explained by the modulatory role of DA and an interaction between DA and other neurotransmitter systems within the NAc.

Gerdeman GL, Partridge JG, Lupica CR & Lovinger DM (2003). *Trends in Neurosciences*, **26**, 184-192.

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Where applicable, the experiments described here conform with Physiological Society ethical requirements.