Peripheral mechanoreceptor activation modulates mesolimbic GABA and dopamine neurons and ameliorates withdrawal symptoms in ethanol dependent rats

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Introduction

The therapeutic benefits to the supraspinal CNS attributed to mechanical stimulation (MStim) are poorly understood. There is a growing body of evidence that suggests MStim can modulate substrates of the supraspinal CNS.

Methods

Electrophysiological, pharmacological, neurochemical, surgical, and behavioral techniques were utilized on male Wistar rats.

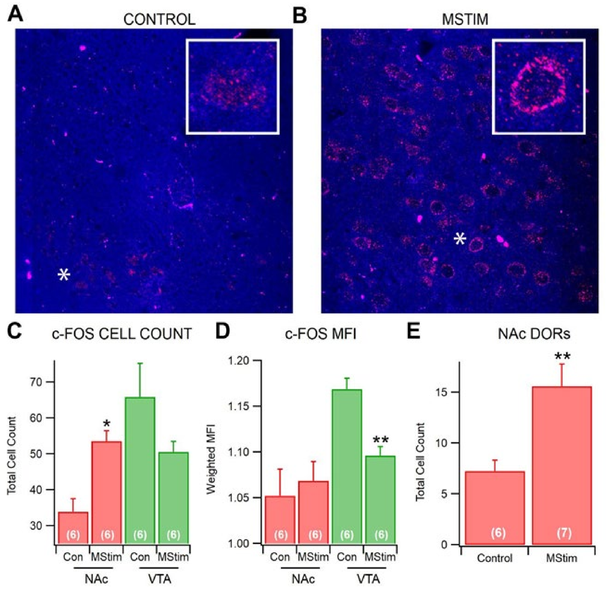

Figure 1: MStim **activates neurons and induces translocation of DORs in the NAc.** (A,B) Increased expression of DORs (red; TH is blue) in the NAc 2-hours post MStim compared to control. Insets show magnified views at point on 40X image indicated by the *. Note the translocation of DORs to the cell membrane. (C) Increased number of neurons in the NAc, but not the VTA, expressing c-FOS 2 hrs post MStim. (D) Decreased expression of c-FOS mean fluorescent intensity (MFI) in the VTA, but not in the NAc, 2 hrs post MStim. (E) Total number of NAc cells expressing DORs 2 hrs post MStim.

Peripheral MSTIM Ameliorates Withdrawal Symptoms from Alcohol

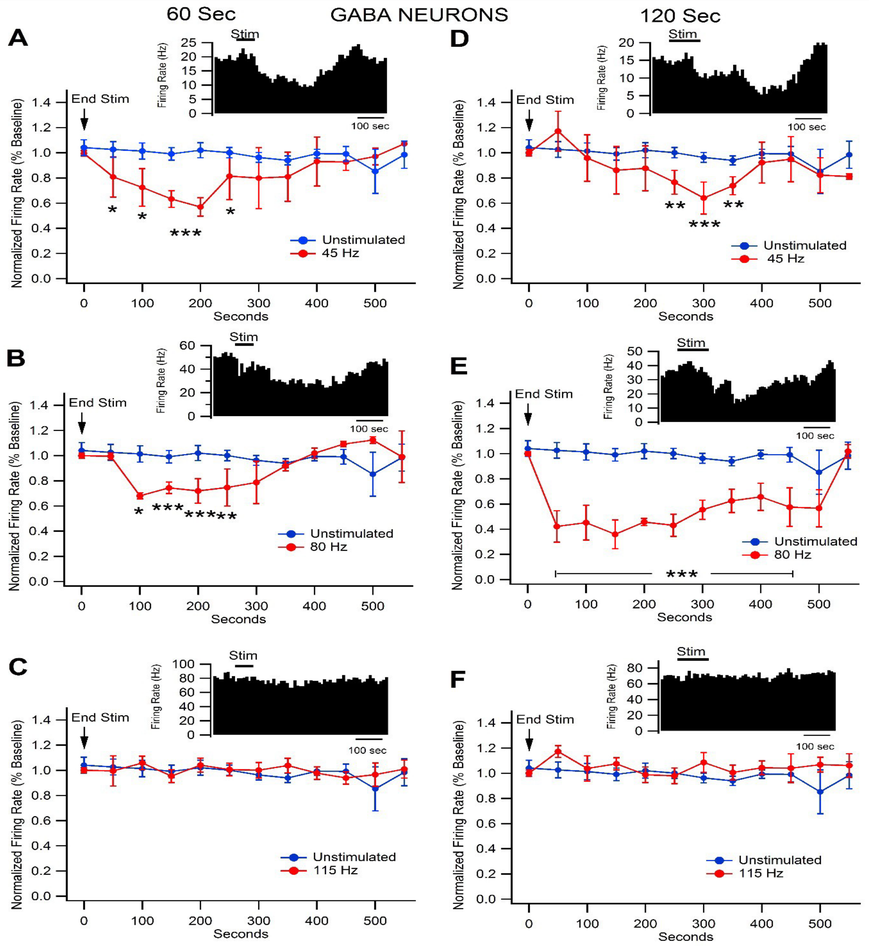

Figure 2: **Frequency and duration-dependent effects of peripheral subcutaneous vibration at the C7-T1 vertebral level on GABA neurons firing rate in the VTA.** A, B, and C - Time course data for 45, 80 and 115 Hz stimulation for 60 sec and D, E and F for 120 sec stimulation Representative firing rate traces are inlaid.

Discussion

Peripheral MStim provided protection against chronic EtOH withdrawal symptoms and dependence-induced insensitivity of VTA GABA neurons to ethanol reintroduction. Behavioral indices of withdrawal were substantively ameliorated with concurrent MStim treatment. These findings suggest the need to explore the specific role of mechanoreceptor-based therapies in the treatment of substance abuse.

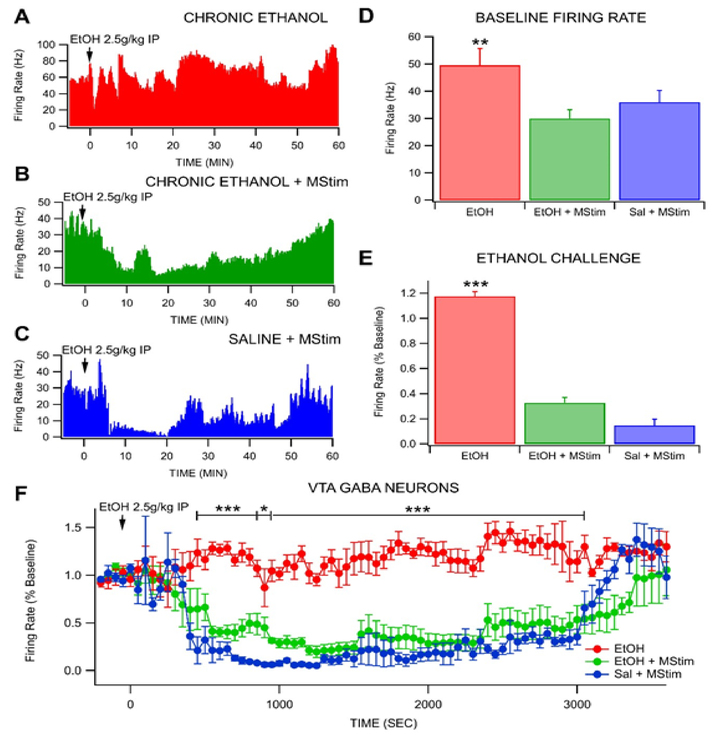

Figure 3: **Effect of ethanol on VTA GABA neuron firing after ethanol reinstatement during withdrawal.** (A-C) Representative traces for GABA neuron response for (A) EtOH alone, (B) EtOH + MStim and (C) saline + MStim. (D) Baseline firing rate differences between the three groups. Note that EtOH alone maintained a higher baseline firing rate. (E) MStim blocks chronic EtOH-induced desensitization of GABA neurons to EtOH reinstatement. (F) Time course data with 50 sec bins demonstrating disparate effects among groups.

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