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Altered NMDA receptor-nitric oxide (NO) signaling in the rostral ventrolateral medulla contribute to cardiovascular response of acute ethanol-exposure

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Onsumption of ethanol (EtOH) has many effects on physiological functions particular in the central nerve system and cardiovascular system. Hypotension is one of the main features of acute excessive intake of ethanol (alcohol intoxication). In addition, chronic ethanol consumption has been associated with cardiovascular diseases, including hypertension and stroke. The precise mechanisms underlying ethanol regulation of cardiovascular function remains unclear. It is well known that central N-Methyl-D-Aspartate (NMDA) receptors are implicated in the modulation of glutamatergic transmission and important in regulating neuronal activity. Recent evidence also suggests that nitric oxide is a key neuromodulator within the central nervous system and its production is associated with NMDA receptor activation. The rostral ventrolateral medulla (RVLM) is known as a vasomotor center, which provides the basal sympathetic outflow and maintains blood pressure (BP). This study was carried out to test the hypothesis that NMDA and NO signaling in the RVLM are involved in the regulation of ethanol-induced changes in BP. The BP response was measured in urethane anesthetized SD rats weighing 280-350 g. EtOH (3.2 g/kg) was applied by intraperitoneal injection (IP). The samples of glutamate and NO were collected by micro dialysis every 15 minutes in the RVLM and then analyzed with HPLC-ECD and NOx analyzer, respectively. The results showed that IP ethanol elicited a significant increase in the level of glutamate and NO in RVLM and a reduction in BP. Microinjection of ketamine (an NMDA receptor antagonist) or L-NNA (an NOS inhibitor) into the RVLM, which was applied 5 min after administration of EtOH, attenuated EtOH-induced depressor effects. In addition, microinjection of ketamine suppressed the level of NO production. The results suggest that increases in NMDA receptors activation and enhancement of NO synthase activity in the RVLM may play a major role in ethanol-evoked hypotension.

Biography

Hsuan Lo is a PhD scholar, studied in the Department of Pharmacology and Toxicology at Tzu Chi University. His lab is interested in neuropharmacology particularly in alcohol effects on the central nervous system and cardiovascular function. His studies focus on the mechanism of acute ethanol intake action on the glutamate signaling within the rostral ventral lateral medulla (RVLM). He has performed the whole animal model with practiced skill in RVLM, microinjection of drug and femoral artery surgery for measuring blood pressure, and also have set up the HPLC system to detect the neurotransmitter content. On the other hand, his master's thesis was of Amyloid-beta peptides on NMDA receptor activation in rat sympathetic preganglionic neurons using whole cell, patch clamp technique. All his training has led him to know more about, how the CNS works to control cardiovascular function.

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