Electrophysiological effects of etomidate on neurons of primary sensory cortex in rat

Introduction: The primary somatosensory cortex（S1）is the senior nerve center of the specific projection system , one of the key brain structures for central processing of somatic noxious information to produce pain perception. At present, most investigation in the mechanism of general anesthesia is focused on thalamus and hippocampus, which refers to consciousness and memory. But the local effects of anesthetics on the specific projection system are barely reported. Our previous *in vivo* studies have demonstrated that the spontaneous activity in S1 was weakened under propofol anesthesia (propofol inhibits the spontaneous activity of S1). However, no *in vivo* information is available for the properties of electrophysiology of pyramidal neurons in S1. We therefore studied the electrophysiological actions of etomidate (Et) on pyramidal neurons in S1 area slices of juvenile rats.

Aim: Using whole cell patch-clamp techniques, we investigated the effects of Et on sodium channels, potassium channels and action potential (AP) of pyramidal neurons in S1.

Methods: After the preparation and maintenance of the slices as well as electrophysiological and pharmacological techniques are used, Near steady-state, voltage-current relationships were obtained by applying ramp commands during voltage-clamp condition (and AP were obtained during current-clamp condition). According to the different kinds of ion channels, the slices were divided into the sodium channels group, the potassium channels group and the AP group. Each group contains control group and the experiment group. The control group was perfused with normal ACSF; the experiment group was perfused with ACSF containing

different concentrations of Et. Then by applying various protocols, we investigated if the Et could dose-dependently affect the activation process, the deactivation process and the de-inactivation process of the sodium channels; the activation process of the potassium channels; and the electronic portrait of single AP.

Results:

1. Action potentials: When perfused with increasing concentrations of Et, the threshold potential of neurons was ascended, action potential amplitude was decreased, duration of threshold potential to peak potential was widened, and slope of depolarization was slowed(Fig.1).

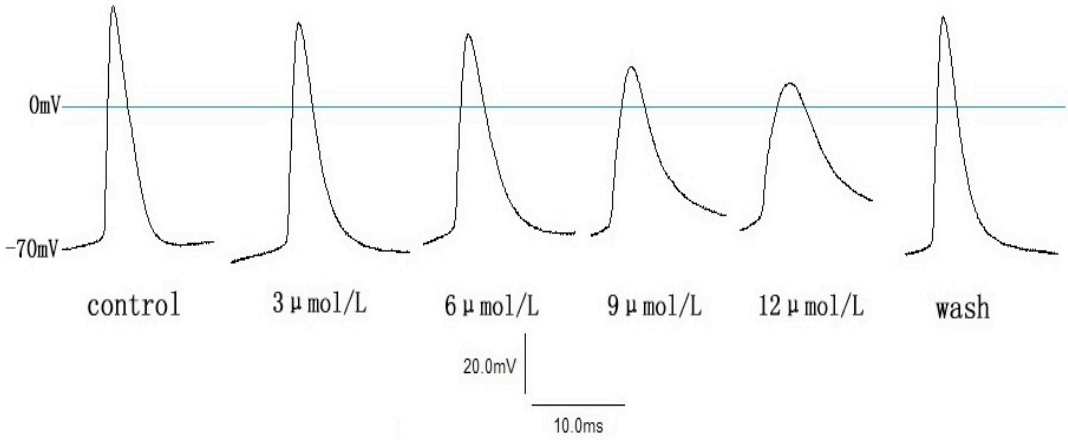

Fig.1 Et could dose-dependently change the electronic portrait of single APTable.1

2. The sodium currents on pyramidal neurons in S1 was remarkably decreased under different concentrations of Et; however, different concentrations of Et did not affect the activation property of sodium current on pyramidal neurons in S1; Et could dose-dependently hyperpolarize the steady-state inactivation curve of sodium currents on pyramidal neurons in S1; and prolong the time course of the recovery from inactivation.

3. The transient outward potassium currents on pyramidal neurons in S1 was dose-dependently reduced by Et; furthermore, Et could dose-dependently depolarize the steady-state activation curve of

transient outward potassium currents on pyramidal neurons in S1; however, Et dose-dependently activated the delayed rectification potassium channels without affecting the activation property of delayed rectification potassium current.

Conclusions:

We demonstrated for the first time that etomidate dose-dependently suppressed the excitability of neurons through blocking neural sodium channels and potassium channels, which may contribute to the mechanisms of Et-induced general anesthesia.