D1-Like Dopaminergic Receptors May Depress The Propofol Excited Regulation of NA(-) Neurons in Rat Ventrolateral Preoptic Area

Background: Accumulating evidence shows ventrolateral preoptic area (VLPO), the center of regulating slow-wave sleep, is a critical nucleus of induction and maintenance of sleep. VLPO contains two principal types of neurons, the noradrenalin-inhibited neurons (NA(−) neurons) and the noradrenalin-excited (NA(+) neurons). NA(−) neurons have three major characteristics: triangular and multipolar in shape, low-threshold spike (LTS) and the firings can be inhibited by noradrenalin. Propofol, a systemic intravenous anesthetic, has been reported to excite NA(−) neurons of rat VLPO, which also have nervous pathway projecting to promote wake nucleus, including dopaminergic pathway. However, there is no evidence whether VLPO can be modulated by dopaminergic system, while the neural mechanisms of unconsciousness induced by general anesthesia are not completely understood.

Methods: Firstly, we identified the NA(-) type neurons based on the pharmacological and morphological characteristics. Spikes and firings of VLPO neurons were recorded respectively by the loose-patch cell-attached technique and in whole-cell mode. Then spontaneous excitatory postsynaptic currents (sEPSCs) and spontaneous inhibitory postsynaptic currents (sIPSCs) were recorded from VLPO cells in acute brain slices of rats. In voltage clamp experiments, sIPSCs were examined in whole-cell configuration at a holding potential of 0 mV in the presence of AP5 (50 μM), 6, 7-dinitroquinoxaline-2, 3-dione (DNQX) (20 μM) and strychnine (1 μM) to block glutamate and glycine receptors.
Membrane potential was clamped at -70 mV when sEPSCs were recorded.

Results: Propofol facilitates the firings of NA(−) neurons and increases the frequency, but not the amplitude and decay time of sEPSCs in NA(−) neurons. Meanwhile, propofol may excite VLPO NA(−) neurons by decreasing the frequency and increasing the amplitude, but not the decay time of sIPSCs. However, D1-like dopaminergic receptors antagonist (SCH23390) but not D2-like dopaminergic receptors antagonist (sulpiride) can partly offset the reduced frequency of sIPSCs effection of propofol. At last, both of SCH23390 and sulpiride have no effect on sEPSCs.

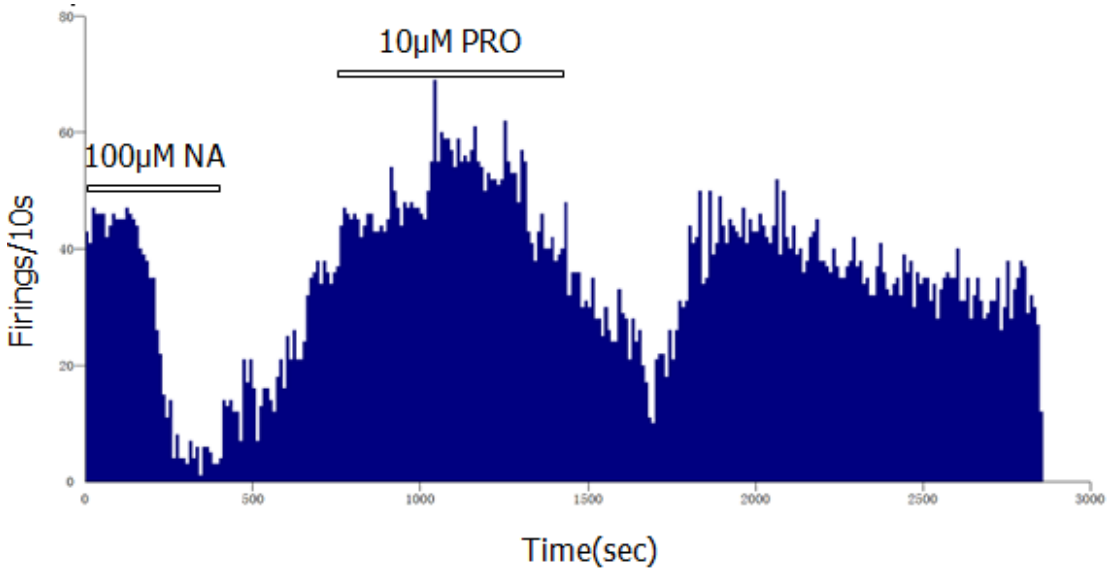

Figure1 The discharges of NA(-) neurons are inhibited by noradrenalin (100 μM). Propofol (10 μM) facilitates the discharges of NA(–) neurons.

Conclusion: Propofol may excite VLPO NA(–) neurons, however, D1-like dopaminergic receptors can depress this effect. Sleep-wake cycle may be involved in the mechanism of unconsciousness induced general anesthesia.

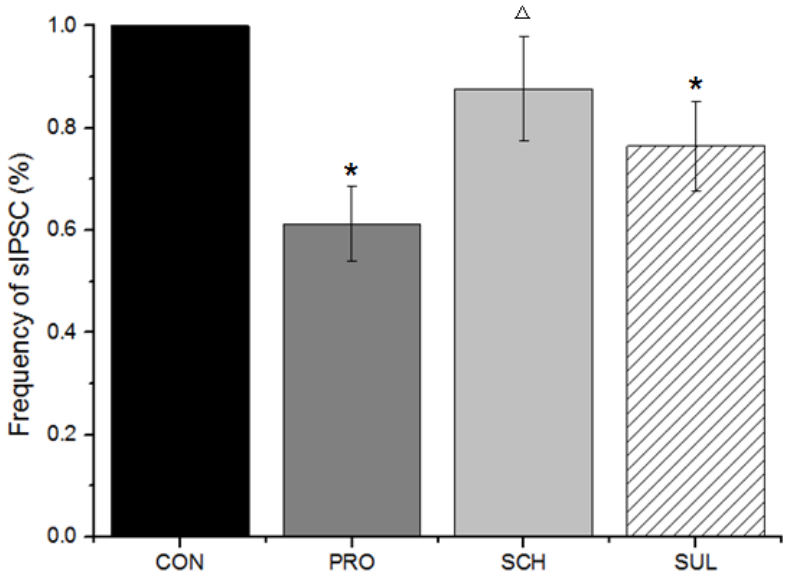

Figure2 Percent changes of sIPSC frequency in NA(–) by different perfusion protocal. (* represents $p<0.05$ compaired with CON group; △ represents $p<0.05$ compaired with PRO group). Perfusion protocal:CON group (ACSF), PRO group (ACSF + 10μM propofol + 100μM dopamine), SCH group (ACSF + 10μM SCH23390 + 100μM dopamine+ 10μM propofol), SUL group (ACSF + 10μM sulpride+ 100μM dopamine + 10μM propofol).