Ionic Mechanism of $GABA_A$ Biphasic Synaptic Potentials in Gustatory Nucleus of the Solitary Tract[a]

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ABSTRACT: Gamma-aminobutyric acid (GABA) is the principal neurotransmitter of synaptic inhibition in the gustatory nucleus of the solitary tract (rNST). High-frequency activation of GABA neurons in the rNST results in biphasic inhibitory postsynaptic potentials (IPSPs) that are initially hyperpolarizing but then became depolarizing. Our results indicate that high-frequency stimulation evokes redistribution of Cl^- and K^+ ions that shifts IPSP reversal potential in a more positive direction, which produces a biphasic or depolarizing IPSP.

Single shock stimuli applied to the solitary tract evoke complex postsynaptic potentials in rostral nucleus of the solitary tract (rNST) neurons consisting of a short-latency excitatory component followed by a longer-latency inhibitory component. We have found that the excitatory component can be blocked by glutamate receptor blockers (20 μM 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX) and 50 μM D-2-amino-5-phosphovalerate (AP5)). Moreover, by increasing the stimulus strength it is then possible to directly activate inhibitory interneurons in rNST eliciting hyperpolarizing inhibitory postsynaptic potentials (IPSPs) that are not contaminated by excitatory synaptic potentials.[2]

Usually, application of γ-aminobutyric acid (GABA) to neurons of the rostral (gustatory) nucleus of the solitary tract (rNST) results in a concentration-dependent membrane hyperpolarization.[5] However, electrical stimulation in the presence of gluatamte receptor blockers at frequencies that mimic the *in vivo* firing rate of afferent taste fibers results in biphasic IPSPs that are initially hyperpolarizing but then become *depolarizing.*

We have examined the ionic mechanisms of these rNST biphasic synaptic potentials in rats using whole cell patch clamp recordings in horizontal brainstem slices. Since other investigators[4] have suggested that HCO_3^- is responsible for the depolarizing phase of the biphasic responses, we used a HCO_3^--free superfusate and found that the character of the biphasic IPSPs was unaltered indicating that HCO_3 ions are not involved in the depolarizing phase of the biphasic IPSPs in rNST. However, we did find that the external K^+ concentration played a role in the biphasic IPSPs. Even though $GABA_A$-

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activated channels are permeable to only negative ions (Cl^- and HCO_3^-)[3] manipulation of the extracellular K^+ concentration changed the GABA reversal potential. Higher concentration of extracellular K^+ shifts the reversal potential to a more positive value. In addition, Benninger *et al.*[1] have shown that stimulation of GABAergic neurons results in an elevation of the extracellular K^+ concentration. We have therefore concluded that tetanic stimulation produces an elevation of extracellular K^+ and accumulation of intracellular Cl^- resulting in a change of the IPSP reversal potential. This redistribution of Cl^- and K^+ produces a decay of the hyperpolarizing IPSP amplitude and as a consequence can result in biphasic or depolarizing IPSPs. While the possible role of biphasic IPSPs in the rNST is not known, in the hippocampus it has been suggested that they lead to increases in dendritic calcium that are necessary for various forms of synaptic plasticity. It is therefore possible that biphasic IPSPs in rNST are similarly involved in synaptic plasticity.

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