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Regulation of Neuronal Activity by GluD1 Current in Brain Slices

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Ion channel function of native delta glutamate receptors ($GluD_R$s) is incompletely understood. Previously, we and others have shown that activation of G_q protein-coupled receptors (GPCR) produces a slow inward current carried by $GluD1_R$. $GluD1_R$ also carry a tonic cation current of unknown origin. Here, using voltage-clamp electrophysiological recordings from adult male and female mouse brain slices containing the dorsal raphe nucleus, we find no role of on-going G protein-coupled receptor activity in generating or sustaining tonic $GluD1_R$ current. Neither augmentation nor disruption of G protein activity affected tonic $GluD1_R$ current, suggesting that on-going G protein-coupled receptor activity does not give rise to tonic $GluD1_R$ current. Further, tonic $GluD1_R$ current was unaffected by the addition of external glycine or D-serine, which influence $GluD2_R$ current at millimolar concentrations. Instead, GPCR-stimulated and tonic $GluD1_R$ current is regulated by external calcium. In current-clamp recording, block of $GluD1_R$ channels hyperpolarized the membrane by ~10 mV at subthreshold potentials, reducing excitability. Thus, $GluD1_R$ carry a G protein-independent tonic current that contributes to subthreshold neuronal excitation in the dorsal raphe nucleus.