D045 - Chloride homeostasis modulates synaptic plasticity in the superficial dorsal horn of the spinal cord

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The efficacy of GABAA/glycine-mediated inhibition in the adult brain relies on the capacity of central neurons to extrude chloride (Cl-) to maintain a low intracellular Cl- concentration. In neurons, Cl- extrusion is critically dependent on the K+-Cl- cotransporter 2 (KCC2). However, the expression of KCC2 is not homogeneous throughout the CNS. This heterogeneity may affect how different neurons integrate synaptic inputs and, thereby, how they express synaptic plasticity. We have previously found that the expression of KCC2 follows a distribution gradient across the superficial dorsal horn (SDH), with low levels of KCC2 in lamina I and higher levels in lamina II. To explore if differences in Cl- homeostasis across the SDH affect synaptic plasticity, we recorded field postsynaptic potentials (fPSPs) evoked by dorsal root stimulation, at different depths in the SDH from a whole spinal cord preparation. After a stable baseline, long-term potentiation (LTP) was induced by low frequency stimulation (LFS: 2Hz, 2min) to the same dorsal root. To explore the role of KCC2 in the propensity of LTP, we bath applied the selective KCC2 antagonist VU0240551 (10 μM). We found that LTP developed faster and stronger in superficial recordings, where KCC2 levels are low, while LTP was increasingly weaker in deeper recordings. VU0240551 application abolished the gradient in LTP across the SDH, suggesting a direct involvement of KCC2. These experiments suggest that chloride homeostasis modulates the propensity for synaptic plasticity, as higher KCC2 activity is directly linked with reduced LTP in the SDH.