

SEROTONIN 5-HT_{2C} RECEPTOR ACTIVATION INCREASES EXPRESSION OF PKC γ and PKC ζ IN AN ISOLATED RAT SPINAL CORD PREPARATION.

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Protein kinase C (PKC) activation is implicated in the induction of long-lasting events including neuropathic pain (PKC γ ; Malmberg et al, Science 1997) and hippocampal LTP (PKC ζ ; Osten et al, J Neurosci 1996). Serotonin 5-HT_{2C} receptor activation induces a long-lasting facilitation of spinal reflexes (LLRF) perhaps due to its G_q-mediated activation of PKC. We used immunolabeling to see if 5-HT_{2C}-induced LLRF was associated with activation of PKC γ and PKC ζ isoforms (membrane translocation).

The isolated hemisected spinal cords of postnatal 14 day-old rats were incubated in saline under quiescent control conditions and following electrical stimulation of dorsal roots and/or application of 5-HT_{2C} receptor agonists (DOI or MK212). Counts of immunopositive PKC γ and PKC ζ labeled cells were separated topographically into dorsal horn, intermediate gray and ventral horn regions. In control conditions, PKC γ and PKC ζ expression dominated in dorsal horn and intermediate gray. For PKC ζ , experimental procedures that involved electrical stimulation, activation of 5-HT_{2C} receptors or both caused significant increases in expression in the intermediate gray. Notably, the largest increase occurred when LLRF was induced, and only under these conditions were significant increases also seen in the ventral horn. In dorsal horn, no expression changes were observed for PKC ζ under any conditions. For PKC γ , observed changes were generally the opposite. In dorsal horn, 5-HT_{2C} receptor activation, electrical stimulation of afferents or both resulted in significant expression increases. While there was a general trend for increased expression in the intermediate gray matter, in ventral horn, expression either decreased or remained unchanged.

In sum, since 5-HT_{2C} receptor expression dominates in the intermediate gray and ventral horn, the observed changes in PKC ζ expression are more consistent with those expected to contribute to the observed reflex plasticity (LLRF). Supported by NIH grant NS40893.