Mossy fiber long-term depression (LTD) has been shown to be triggered by either pharmacological or synaptic activation of Group II metabotropic glutamate receptors (mGluRs) whereas other studies indicate that synaptic activation of mGluRs is very limited. Therefore, we reexamined the role of Group II mGluRs for the induction of mossy fiber LTD. The complete depression of field potentials (fEPSPs) by 1 microM (2S,2'R,3'R)-2-(2',3'-Dicarboxycyclopropyl)glycine (DCG-IV) only partially reversed upon removal of the drug but fEPSPs were completely restored by the Group II antagonist 2S-2-amino-2-(1S,2S-2-carboxycyclopropyl-1-yl)-3-(xanth-9-yl)propanoic acid (LY341495) (3 microM). In contrast, fEPSPs returned back to baseline within 30 min after a brief application of 0.2 microM DCG-IV suggesting that the incomplete reversal of higher concentrations may be due to a residual receptor occupancy rather than to an induction of LTD. LY341495 itself did not increase fEPSPs and also blocked the inhibition of (2S,1'S,2'S)-2-(2-carboxycyclopropyl)glycine (L-CCG-I) (20 microM) and (1S,3R)-1-aminocyclopentane-1,3-dicarboxylic acid (ACPD) (10 microM) and its effect was mimicked by CPPG (50 microM). Furthermore, stimulation at 1 Hz for 15 min induced an LTD of 81% +/- 3% and 80% +/- 4% in the absence and presence of LY341495, respectively (n = 7, 5). Finally, we found that synaptic activation of Group II mGluRs during 15 min of 1-Hz stimulation only produces an inhibition of release by 8% +/- 1% (30 degrees C, n = 3).
data suggests that pharmacological activation of Group II mGluRs is fully reversible per se and does not produce a long lasting depression and that activation of Group II mGluRs is neither necessary nor sufficient for the induction of mossy fiber LTD.