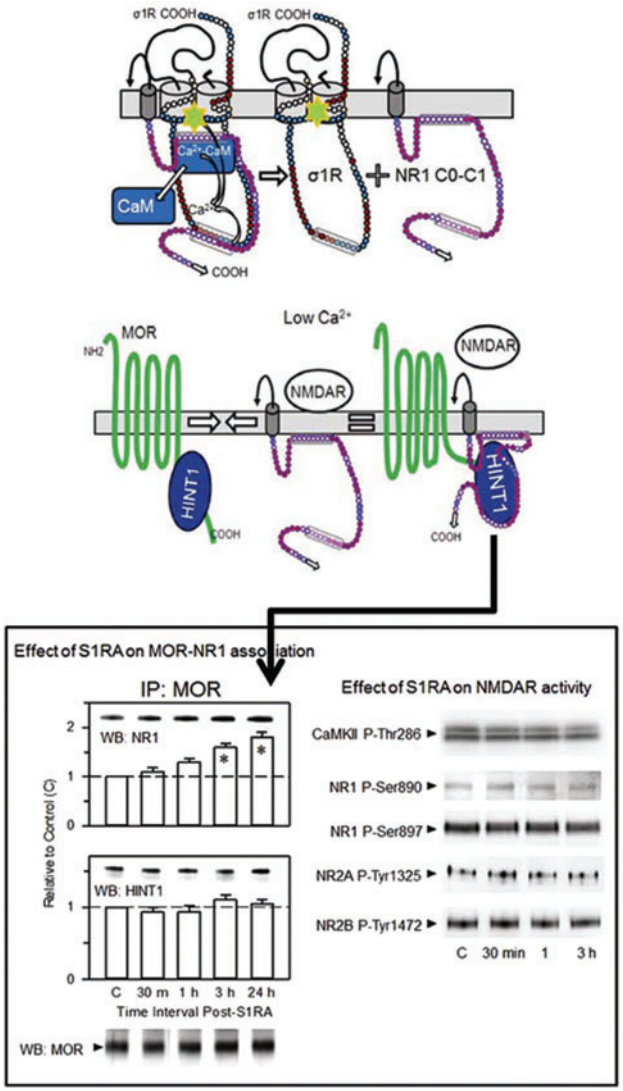

SUPPLEMENTARY FIG. S8. Antagonists of σ1Rs promote the uncoupling of MOR activity from the negative control of glutamate NMDARs. Antagonists of σ1Rs promote the uncoupling of MOR activity from the negative control of glutamate NMDARs. Antagonists of σ1Rs such as S1RA facilitate NR1 C0 binding with Ca^{2+}-CaM to inhibit NMDAR calcium fluxes, indicated by the framed NMDAR without *asterisks*. In the absence of MOR regulation of PLCs, Ca^{2+}-CaM binding further reduces calcium levels in the NMDAR environment, promoting the subsequent release of calcium-depleted CaM from NR1 subunits. In these circumstances, MOR-HINT1 binds with high affinity to NR1 subunits being observed as a time-dependent increase in MOR-NR1 association. In PAG synaptosomes derived from mice treated with only S1RA, the σ1R antagonist produced no other noticeable changes in the other molecular parameters evaluated. Amino acid charge, see key in Fig. 3C.