U50,488H, a kappa-selective opioid agonist and neurotensin (NT) have been shown to have an additive effect on the modulation of body temperature (Tb) when given in combination (Handler, et al., JPET, 1995). Central administration of dynorphin (DY), the endogenous kappa agonist, in combination with NT, lacks this additive effect. NT and U50 were injected alone and in combination over a range of doses (U50, 25 - 100 µg; NT, 0.125 - 2.50 µg) and Tb was measured for 3 hr post injection. A dose of 25 µg failed to induce statistically significant hypothermia while all other doses of U50 or NT, either alone or in combination, caused a significant decrease in Tb. When U50 and NT were given in combination, the effect was additive. Pretreatment with the kappa-selective antagonist, nor-binal-torphimine (nor-BNI, 20 nmol, icv, t = 60 min) blocked the kappa-modulated effect. This blockade of the kappa receptor and modulatory effect on Tb was seen even at the lowest combined dose of U50/NT (25/0 125 µg). This suggests there is an interaction between kappa opioid and neurotensin receptors in terms of the modulation of Tb. The data further suggest the lack of central effect of the DY/NT combination may be due to the lack of potency of DY as an agonist and its degree of selectivity for the kappa receptor.