Inhibition of protein kinase C decreases sensitivity of GABA receptor subtype to fipronil insecticide in insect neurosecretory cells.

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Résumé en anglais	Phosphorylation by serine/threonine kinases has been described as a new mechanism for regulating the effects of insecticides on insect neuronal receptors and channels. Although insect GABA receptors are commercially important targets for insecticides (e.g. fipronil), their modulation by kinases is poorly understood and the influence of phosphorylation on insecticide sensitivity is unknown. Using the whole-cell patch-clamp technique, we investigated the modulatory effect of PKC and CaMKinase II on GABA receptor subtypes (GABAR1 and GABAR2) in DUM neurons isolated from the terminal abdominal ganglion (TAG) of Periplaneta americana. Chloride currents through GABAR2 were selectively abolished by PMA and PDBu (the PKC activators) and potentiated by Gö6983, an inhibitor of PKC. Furthermore, using KN-62, a specific CaMKinase II inhibitor, we demonstrated that CaMKinase II activation was also involved in the regulation of GABAR2 function. In addition, using CdCl(2) (the calcium channel blocker) and LOE-908, a blocker of TRPγ, we revealed that calcium influx through TRPγ played an important role in kinase activations. Comparative studies performed with CACA, a selective agonist of GABAR1 in DUM neurons confirmed the involvement of these kinases in the specific regulation of GABAR2. Furthermore, our study reported that GABAR1 was less sensitive than GABAR2 to fipronil. This was demonstrated by the biphasic concentration-response curve and the current-voltage relationship established with both GABA and CACA. Finally, we demonstrated that GABAR2 was 10-fold less sensitive to fipronil following inhibition of PKC, whereas inhibition of CaMKinase II did not alter the effect of fipronil.
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