Pyrethroid insecticide neurotoxicity

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Pyrethroid insecticides are one of the most widely used pesticides to combat agricultural pests and malaria. Compared with the group of the organophosphorus pesticides acting via the inhibition of acetylcholine esterase in either insects or mammals, the neurotoxic mechanism of pyrethroids is thought to be more species specific. Moreover, pyrethroids are the pesticide of choice in controlling bed bugs, parasitic insects feeding on human blood, which since 1995 are increasing in prevalence. The editors are pleased that David Soderlund from New York accepted our invitation to contribute a comprehensive review about the molecular mechanisms of pyrethroid neurotoxicity (Soderlund 2012). This is not only appreciated since neurotoxicity is one of the cutting-edge topics in toxicology (Frimat et al. 2010; Liu et al. 2010; Pamies et al. 2010; Romero et al. 2010; Sriram et al. 2010; Wagner et al. 2010; Ge et al. 2011; Hardelauf et al. 2011; Li et al. 2011; Nakamura et al. 2011; Takahasi et al. 2011; Wang et al. 2011; Yen et al. 2011) but also because recently the safety of pyrethroid insecticides has been discussed controversially. Traditionally pyrethroid insecticides are considered as relatively safe. They compromise the function of voltage-gated sodium channels in insect neuronal membranes, which explains their insecticidal properties. In contrast, mammalian sodium channels were considered as much more resistant. Although this seems to apply in general, it has become clear that besides insensitive mammalian sodium channels (e.g. $\text{Na}_v 1.2$) also more sensitive isoforms exist (such as $\text{Na}_v 1.3$, $\text{Na}_v 1.6$ or $\text{Na}_v 1.8$). Moreover,

pyrethroids may besides sodium channels also target voltage-gated calcium and chloride channels. Thus, another ongoing discussion is to which degree children are more susceptible than adults. The effects of pyrethroids on sodium channels are comparable to the mode of action of some anticonvulsants (e.g. phenytoin) that are associated with the foetal hydantoin syndrome (FHS) a neurodevelopment disorder occurring in epileptic women using these drugs during pregnancy (Bjorling-Poulsen et al. 2008). The review article of David Soderlund gives differentiated and comprehensive answers to these questions and is highly recommended to everybody interested in ion-channel-mediated neurotoxicity.

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