Impaired GABAergic transmission by amitraz in primary hippocampal cells.

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INTRODUCTION

Amitraz is a formamidine pesticide. Many amitraz poisoning cases in humans have been reported worldwide and still being described up today. Amitraz has been reported to be a neurotoxic compound inducing convulsion among other effects. The alpha-2 adrenergic agonist and/or local anesthetic-like properties of these compounds have been reported as likely responsible for the seizure enhancing effects. Moreover, other mechanism could be implicated. In this regard Amitraz it is an inhibitor of H1 receptor and the inhibition of histamine H1 receptor has also been implicated in seizure induction. Amitraz seizure induction could be mediated by some of the mechanism commented through a dysfunctions on GABAergic systems.

METHODS

To confirm if amitraz disrupt GABAergic transmission by local anesthetic-like action, inhibition of H1 receptor and activation of alpha-2 receptor, we evaluated, in primary hippocampal neurons, the effect of amitraz (0.01µM 100µM) with or without idazoxan (1 µM) and/or n-methylhistaprodifen (30µM) and lidocaine (20mM) co-treatment on 4-aminobutyrate aminotransferase (GABAT), Glutamate Decarboxylase 65 (GAD65), succinate-semialdehyde dehydrogenase (SSADH) gene expression and GABA levels after 24h treatment.

RESULTS

We observed that amitraz alter GABAergic transmission disrupting the expression of GAD 65 and thus GABA levels. These effects were mediated partially by H1 and alpha-2 receptors suggesting that other mechanism could be implicated.

CONCLUSIONS

These data help to explain the way amitraz induce seizures and a way to protect against this effect in the cause of poisoning.