

Neurodevelopmental toxicity in the mouse neocortex following prenatal exposure to acetamiprid

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Abstract

Acetamiprid (ACE) belongs to a widely used class of pesticides known as neonicotinoids. ACE binds selectively to insect nicotinic acetylcholine receptors and was previously considered relatively safe in mammalian species; however, recent studies have demonstrated ACE-mediated toxicity related to vertebrate nicotinic acetylcholine receptor activation. The potential for neurotoxicity following exposure to ACE in utero is unknown. Therefore, we evaluated the effects of repeated prenatal ACE exposure (5 mg/kg, oral doses administered to pregnant dams) on neurogenesis, neuronal distribution and microglial activation in the dorsal telencephalon on embryonic day (E)14 and in the neocortex on postnatal day 14. Immunohistochemical and morphological analyses on E14 revealed hypoplasia of the cortical plate and decreased neurogenesis in mice exposed to ACE from E6 to E13, whereas newborn ACE-exposed mice showed an abnormal neuronal distribution in the neocortex. Additionally, ACE-exposed mice showed increased numbers of Iba1-immunoreactive and amoeboid-type microglia as well as an increased M1/M2 microglial ratio. These findings suggest that prenatal ACE exposure induces neurodevelopmental toxicity and increases microglial activation in the developing brain.

Keywords: microglia; neocortex; neonicotinoids; neurogenesis; neuronal distribution.

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