olfactory system, the neurotoxic effects of a gestational exposure to air pollution are questioned and poorly investigated.

Objective: The present work aims to study the effects of a controlled gestational exposure to diesel exhaust (DE), at levels closely reflecting those of the urban human population, on the olfactory system development in rabbits.

Materials and methods: Pregnant rabbits were exposed nose-only to clean air or to diluted (1 mg/m^3) filtered DE from gestational day 3 (GD3) to day 28, 2 h/d, 5 d/w. At GD28, 12 females (5 controls and 7 exposed) were sacrificed to collect fetal olfactory mucosa (OM) and bulb (OB) for anatomical and chemical measures. At postnatal day 2 (PND2), 62 control and 55 polluted pups from 18 litters (9 controls and 9 exposed) were examined for their odor-guided behavior in response to the presentation of the rabbit mammary pheromone 2-methyl-3-butyn-2-ol (2-NBT).

Results: Electron microscopy analysis of OM and OB revealed in exposed fetuses the presence of nanosize particles (20–48 nm) in the olfactory sensory neurons and the glomerular layer of the OB, along with cellular and axonal hypertrophy. OB of exposed animals exhibited higher levels of serotonin and lower levels of dopamine and its metabolites. Finally, the behavioral response to 2-NBT at PND2 was altered in exposed rabbits.

Conclusions: The present gestational exposure to DE affects the neuro-olfactory development of the rabbit offspring, and altered early olfactory-based behaviors. Because of the known anatomical and functional continuum between the olfactory system and the rest of the brain, such early alterations could be indicative of disturbances in higher integrative structures.

Financial support: ANSES & ADEME (PNR-EST 2014-1-190).

http://dx.doi.org/10.1016/j.toxlet.2016.07.482

PP21.10
Acute and subchronic effects of antipsychotic drugs on cognitive and social deficits after adolescent toluene exposure in mice

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Introduction: Abuse of toluene-containing products by adolescents is a significant public health issue. Our previous study revealed that adolescent toluene exposure produces enduring social deficits and cognitive impairment at adulthood in mice. Antipsychotics are generally used to treat psychotic symptoms in toluene abusers clinically.

Objective: The present study examined the predictive validity of this model by evaluating the beneficial effects of antipsychotics on cognitive impairment and social dysfunction after toluene exposure.

Materials and methods: Male NMRI mice received injection per day of either toluene (750 mg/kg) or oil at postnatal day P35–P39 and P42–P46. Novel object recognition test and social interaction were conducted after 7-day washout period to confirm the toluene-treated animals with long-lasting behavioral impairment. Thereafter, the acute and subchronic effects of antipsychotics, including haloperidol, clozapine and risperidone were evaluated.

Results: All these antipsychotics reduced the social withdrawal, whereas clozapine and risperidone, but not haloperidol, attenuated the cognitive impairment when they were administered 1 h prior to the behavioral tests. Subchronic treatment of antipsychotics for 14 days produced the same improving effects as acute study and the effects lasted at least 14 weeks. These findings suggest that clozapine and risperidone might be better than haloperidol to treat the behavioral disorders related to toluene abuse.

Financial support: NSC 99-2314-B-400-005-MY3.

http://dx.doi.org/10.1016/j.toxlet.2016.07.483

PP21.11
Extracellular calcium concentration and channel activity involved in aminoglycoside-induced hair cell toxicity in the zebrafish lateral line

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Introduction: Ototoxic damage often caused by antibiotic aminoglycosides leads to the loss of hair cells. Since aminoglycosides are effective at infection treatment, it is imperative to discover new approach to prevent hearing loss and permit safe use of aminoglycosides. The alterations in cytosolic calcium homeostasis play an important role in aminoglycoside-induced sensory hair cell death. However, the involvement of cytoplasmic membrane calcium channels in aminoglycoside ototoxicity is not clear.

Objective: The present study determined the role of calcium and its channel activity in ototoxicity induced by aminoglycosides.

Materials and methods: In this study, the lateral lines of zebrafish were used to investigate the effects of verapamil, a calcium channel blocker, and Bay K8644, a calcium channel activator, on aminoglycoside (neomycin and gentamycin)-induced hair cell toxicity which was detected *in vivo* by the dye FM1-43FX, a reliable indicator to assess hair cell viability.

Results: The data showed that verapamil significantly attenuated both aminoglycosides induced hair cell loss, whereas Bay K8644 enhanced their ototoxicity. Interestingly, the loss of hair cells induced by both aminoglycosides was respectively reduced and reinforced under extracellular high calcium (3.3 mM) and low calcium (33 μM) concentrations compared with normal calcium (330 μM) condition. Furthermore, Bay K8644 partly inhibited the protective action of extracellular high calcium on hair cell death mediated by the aminoglycoside treatment.

Conclusions: These findings indicate that both extracellular calcium concentration and calcium channel activity influence hair cell loss from aminoglycoside toxicity.

Financial support: NSC100-2320-B-004-003-MY3.

http://dx.doi.org/10.1016/j.toxlet.2016.07.484