LOW CONCENTRATIONS OF COUMAPHOS DO NOT AFFECT BRAIN DEVELOPMENT AND FUNCTION

HOJNIK Nataša, ČEH Katerina, MAJDIČ Gregor

2nd SloLASA, Ljubljana, 2014
ORGANOPHOSPHATES (OP)
main representatives of insecticides

- **organic compounds** with **phosphorus**
- phosphatic bind (P=O) and thiophosphatic bind (P=S)

→ **INSECTICIDAL ACTIVITY**: irreversible inhibition of enzyme acetylcholinesterase (AChE)

AChE is important component of the human nervous system → poisoning
THE EFFECTS OF CONSTANT EXPOSURE TO LOW CONCENTRATIONS OF OP

Intensive use of OP ➔ contamination of the environment

- High sensitivity during development ➔ abnormalities later in life
MECHANISMS = ?

• **Effects on the developing fetus:**
  - Oxidative stress
  - Increased permeability of blood-brain barrier
  - Migration, proliferation, differentiation of the Ach target cells
  - Other brain proteins
• **Endocrine disruptor**
BEHAVIOUR

- Cognition abnormalities (memory)
- Mental disorders (anxiety, depression, …)
- Abnormal social behaviour (autism)
COUMAPHOS

Organophosphate insecticide:

- Extermination of the mite Varroa jacobsoni – beekeeping (EU); Extermination of ticks carrying Babesia bigemina - cattle (USA)

- Relatively safe representative of OP

→ Found in honey: RISK
THE AIM OF OUR STUDY

• to examine consequences of long-term exposure to low doses of coumaphos during fetal development → neuropsychiatric disorders

• **Behavioural differences in adult mice**: standard behavioural tests
METHODOLOGY

Mouse line: balb/c

14 days before mating

COUMAPHOS
Coumaphos + DMSO
Control (DMSO)

1 mg/kg
0.1 mg/kg

BEHAVIOURAL TESTS

Age: 70 days

No exposure to coumaphos after P21

6 – 8 days

Sacrifice

N
0

No exposure to coumaphos after P21
1) ELEVATED PLUS MAZE (EPM)

- Anxiety-like behaviour
- Time spent in closed/open arms
2) MARBLE BURYING TEST

- Anxiety-like behaviour
- Number of buried marbles
3) SOCIAL RECOGNITION TEST

- Social memory
- Interest in stimulus mouse
4) OPEN FIELD TEST (OFT)

- general activity, anxiety-like behaviour
- Time spent in outer/inner zones
5) FORCED SWIM TEST (FST)

- depression-like behaviour
- Floating/ swimming
EPM – The number of the entries into the open arm
Social recognition test: duration of sniffing - female

![Graph showing duration of sniffing for different conditions.](image-url)
Social recognition test: duration of sniffing - male
OFT – Time mobile
DIRECTLY EXPOSED ANIMALS IN ADULT LIFE

Results consistent with results presented in July cDNA Microarrays.
CONCLUSION

- females: **significant trend for anxiety-like behaviour**
- *EPM: anxiolytic effect of coumaphos - ?*

- **Sex differences → expected difference;**
  - EPM: *the difference between sexes is increasing with higher doses*