# Key elements of neurotransmitter pathways as biomarkers of effect of neuroactive compounds with different primary mode of action

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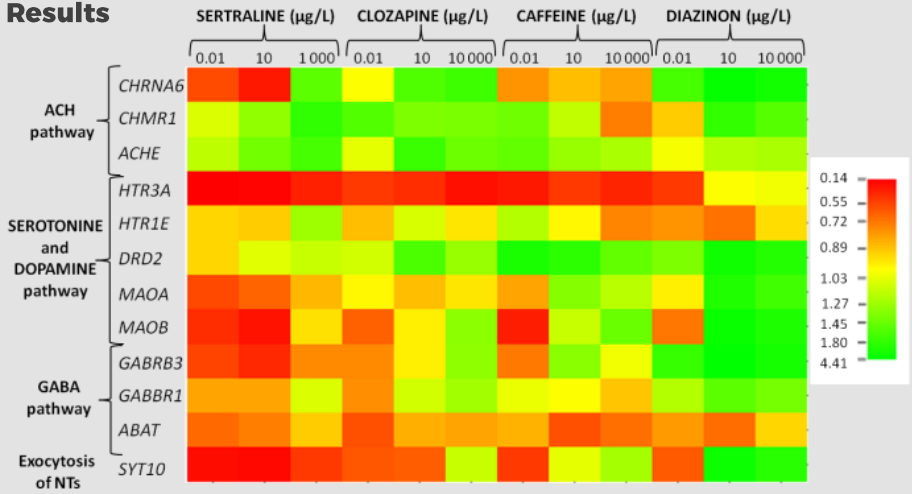
## Introduction

- Neuroactive compounds (NCs) are a newly recognized hazard in the aquatic environment, with possible adverse effects on aquatic ecosystems and implications to human population.
- Lack of well-characterized and widely accepted biomarkers of effect of NCs represent a challenge in development of biomarker-based strategy for impact assessment of NCs.
- In this study, we provide data on mechanism of toxic effects of NCs, regardless their primary mode of action, to contribute to the database on possible and most responsive biomarkers of effect of NCs.

## Material and Methods

- *In vitro* experimental model: human neuroblastoma SH-SY5Y cell line.
- Test compounds: antidepressant sertraline, antipsychotic drug clozapine, stimulant and pharmaceutical caffeine, organophosphate pesticide diazinon.
- Target parameters: key elements of neurotransmitter (acetylcholine, serotonin, dopamine and GABA) pathways and exocytosis of neurotransmitters.
- Method: quantitative real-time PCR (RQ-PCR) gene expression analyses.

## Results




**ACH pathway:** *CHRNA6* - nicotinic receptor α subunit 6; *CHMR1* - muscarinic receptor 1; *ACHE* - acetylcholinesterase;
**Serotonine and dopamine pathway:** *HTR3A* - serotonin receptor 3A; *HTR1E* - serotonin receptor 1E; *DRD2* - dopamine receptor D2; *MAOA* - monoamine oxidase A; *MAOB* - monoamine oxidase B;
**GABA pathway:** *GABRB3* - GABA A receptor subunit β3; *GABBR*1 - GABA B receptor subunit1; *ABAT* - 4-aminobutyrate aminotransferase;
**Exocytosis of neurotransmitters:** *SYT10* - synaptotagmin 10.

## Comments and Conclusions

- **Predominant stimulation of expression of the responsive genes in treatment by organophosphate pesticide diazinon and inhibition in treatment by pharmaceuticals imply to differential effects of various groups of NCs, with possible relevance in development of biomarker-based strategy for NCs.**
- ***HTR3A* and *SYT10* distinguish as the most sensitive parameters to tested NCs and promising candidates for biomarkers of effect of NCs, regardless their primary MoA.**
- ***DRD2A*, *MAOA*, *MAOB* and *GABRB3* might be promising candidates for sensitive biomarkers of effects specific for the group of organophosphate pesticides.**
- **The relevance of the selected parameters as early responses leading to adverse effects in exposed organisms need to be further explored through *in vivo* and *in situ* studies, considering also Adverse Outcome Pathway (AOP) database for implications of adverse outcomes.**

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