

Newsletter 1

Worldwide, serious concern has arisen about the increased incidence of learning and developmental disorders in children. From a scientific point of view, there is no doubt that exposure to neurotoxic chemicals during early brain development can adversely affect learning and development. The European commission-funded project DENAMIC will develop tools and methods for screening of neurotoxic effects of low-dose mixtures of pesticides and a number of common environmental pollutants possibly resulting in (subclinical) effects on learning (cognitive skills) and developmental disorders in children (e.g ADHD, autism spectrum disorders and anxiety disorders). The investigation of such a relationship in humans and providing plausible mechanistic reasons for this by using the developed tools are the major objectives of DENAMIC.

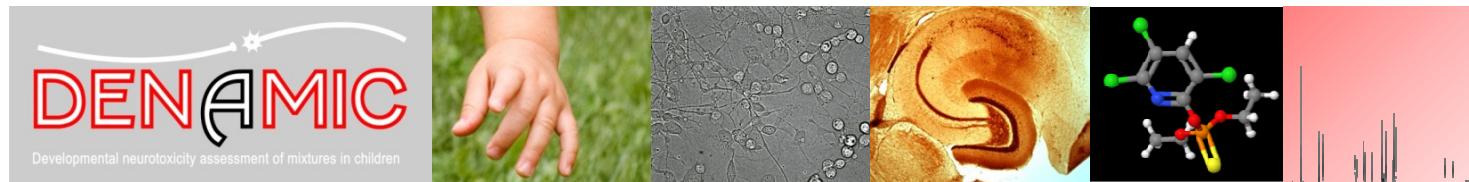
Because of recent concerns of cognitive and neurobehavioral effects related to pesticide exposure and if proven necessary the possibility to protect future generations by regulatory measures, this research will primarily focus on possible neurotoxic effects of pesticides. Nonetheless, several other common environmental pollutants are known neurotoxicants and are therefore also included. As both pesticides as well as some of these environmental contaminants may very well have a similar mechanism in common, possible mixture effects via human exposure will also be included in DENAMIC. To obtain human relevant information, a mixture exposure method for the investigation of neurotoxic hazard from real-life neonatal exposure is included.

Which chemicals are studied?

DENAMIC will primarily focus on possible neurotoxic effects of pesticides (organophosphates, carbamates, pyrethroids, organochlorines, paraquat). Other common environmental pollutants such as flame retardants (PBDEs), phosphate-based plasticizers/flame retardants (TCPP, TCP), perfluorinated compounds (PFOS, PFOA), phthalates and metals (methylHg) are also included



DENAMIC consortium: Kick-off meeting, Amsterdam, 31 Jan- 1 Feb 2012



Newsletter 1

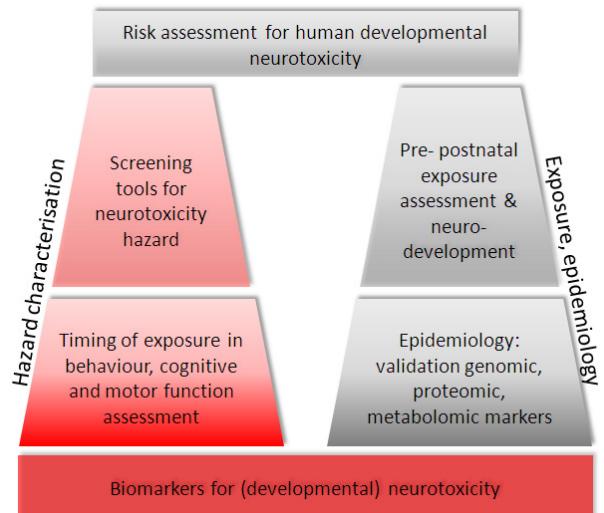
Approach

The research in DENAMIC consists of two distinct pillars:

- 1) hazard characterization
- 2) exposure/epidemiology

Hazard characterization

The DENAMIC hazard characterisation includes in vitro, ex vivo and in vivo studies using innovative models spanning molecular, cellular and multicellular (functional) processes, brain slices, brain and behaviour with a focus on neuronal development. In vitro screening methods for neurotoxicity will be developed and validated with individual model chemicals and mixtures thereof. The focus is on assays for direct cellular neurotoxicity, neuronal function, and neurodevelopment.



To further investigate the mechanism(s) of action of neurotoxic chemicals and validate the in vitro models, ex vivo, in vivo (behavioural) neurotoxicity, and cognitive function models will be developed. In addition, an early life-stage zebrafish model will be developed to study neurotoxicity and behaviour development. The emphasis is on differences in exposure timing, critical windows during neuronal development and consequences on susceptibility. The underlying mechanisms of observed effects on behavior and cognitive function will also be studied. An important aspect is the development of biomarkers for (developmental) neurotoxicity in animal models using (epi-)genomics, proteomics and metabolomics.

Exposure/epidemiology

DENAMIC investigate differences in prenatal and neonatal exposure to a selected number of suspected neurotoxic environmental pollutants in four different European regions. Data and samples from existing European cohorts with different exposure profiles from Norway, Netherlands, Slovakia and Spain will be made available for DENAMIC. These studies will also be used to study possible associations between the selected environmental pollutants with neurodevelopmental outcome, in particular cognitive development (e.g. ADHD).

In addition, a new tailor-made cohort of mother-child pairs is set up. In this specific cohort, associations between chemical exposure and learning (cognitive) and neurobehavioural (ADHD, ASD, anxiety) development or disorders will be studied. The tailor-made cohort will also be used to test the validity and usability of the integrated screening tools and methods for neurotoxicity developed in the hazard characterization. This study will be used to explore the relevance of selected biomarkers.

Coordinator:
Pim Leonards
 Institute for Environmental Studies
 VU University Amsterdam
 +31 20 5989 509
 pim.leonards@ivm.vu.nl

Subcoordinator:
Milou ML Dingemans
 Institute for Risk Assessment Sciences
 Utrecht University
 +31 30 2534387
 m.dingemans@uu.nl

This project is carried out with financial support from the European Community's Seventh Framework Programme [FP7/2007-2013], grant agreement n° 282957.

For more information www.denamic-project.eu