

Participant 7. Nofer Institute of Occupational Medicine, Lodz, Poland (NIOM)

The group from the Nofer Institute of Occupational Medicine is directed by **Professor Slawomir Gralewicz**, Chief of the Laboratory of Neurotoxicology at the Department of Toxicology and Carcinogenesis. Professor Gralewicz has 35 years of experience in conducting behavioural and electrophysiological experiments on laboratory animals, and 15 years of experience in neurotoxicological investigations.

Since 1990, Dr. Gralewicz' group has been involved in behavioural and electrophysiological studies on the long-term neurotoxic effects of low-level exposure to selected organophosphate pesticides and organic solvents. The battery of behavioural implemented are very sensitive in the detection of subtle behavioural disturbances appearing in rats weeks after a 28-day exposure to some solvents at levels approaching the adopted MAC values. Interestingly, low concentrations appeared more effective in producing these effects which suggests a hormetic dose-response relationship (an inverted U-curve). Electrophysiological methods in use include detection and assessment of a peculiar, but surprisingly common in laboratory rats, form of spontaneous seizure activity – bursts of spike-wave discharges (SWD). The proven relationship of this EEG pattern to the level of general arousal (negative) and animal age (positive), makes it a possible and quite sensitive indicator of some neurotoxic effects of exposure (e.g. accelerated aging). To this purpose, two rat strains, SWD strain and SWD-free strain have been bred out in the Institute breeding facility.

Recently, the pharmacological challenge technique has been implemented and used extensively in detection of the effects of exposure. Currently being implemented is the startle-response technique. The area of interest has been extended and encompasses the interaction of non-chemical and chemical stressors in the induction of neurotoxic insults.

Selected recent publications

Gralewicz A, Lutz P, Szymczak W. Hyposensitivity to amphetamine following exposure to chlorphenvinphos – protection by amphetamine preexposure. *Acta Neurobiol. Exp.* 60, 203-207, (2000).

Gralewicz S, Wiaderna D, Stetkiewicz J, Tomas T. Spontaneous spike-wave discharges in rat neocortex and their relation to behaviour. *Acta Neurobiol Exp.* 60, 323-332 (2000).

Gralewicz S, Wiaderna D. Behavioral effects following subacute inhalation exposure to m-xylene or trimethylbenzene in the rat. A comparative study. *NeuroToxicology* 22, 79-89, (2001).

Gralewicz S, Lutz P, Tomas T. Behavioural responsiveness to amphetamine or scopolamine following repeated exposure to chlorphenvinphos in rats. *Acta Neurobiol Exp.* 62, 75-83, (2002).

Gralewicz S. Behavioral sensitization to amphetamine induced by a single i.p. dose of oxotremorine in the rat.
Acta Neurobiol Exp. 62, 93-98 (2002).

Gralewicz S, Wiaderna D, Lutz P. Behavioral sensitivity to amphetamine after repeated exposure to an organophosphorous pesticide in the rat. Effect of coexposure to restraint.
Int J Occup Med Environ Health 15, 229-238, (2002).