Shifted health effects in animals exposed to psychological stress and toxicants

Pamela G. Tucker, MD
Medical officer, ATSDR/DTEM/EMESB

Background

- In 1994, ATSDR began a project to compile the knowledge related to the psychological effects on communities exposed to toxicants.
- As part of that project, an expert panel workshop was held September 1995 entitled the Psychological Responses to Hazardous Substances.
- One of the research questions posed was- Are there interactions between chronic stress and neurotoxicants that could shift the dose-response curve for neurotoxicants?

Background

- During the 1980s, toxicologists investigated the effects of various stressors on laboratory animals and how it affected health effects from exposures to toxicants.
- They were investigating psychological stress as a confounder in their toxicological investigations.
- Recently, investigators have been considering whether or not there is synergy between psychological stress and exposure to toxicants in animals, leading to increased health effects.

Statement of the problem

Are there increased health effects from concurrent exposure to psychological stress and toxicants?

What is stress?

- “The external and internal forces that are applied to organisms or other biological systems, and changes in biological systems that occur as a consequence of these forces.” (Hoffman and Parsons, 1991)
- Change leading to “ a measurable alteration of a physiological (or behavioral, biochemical or cytological) steady state which is induced by environmental change.”
- “Any environmental change that acts to reduce the fitness of an organism.”

Approach to the problem

- A specific animal model needs to be developed to test the hypothesis about the synergism between stress and specific health effects of chemicals.
- Known laboratory stresses for animals can be used such as: auto-analgesia, reactivity (startle response), restraint stress, foot shock with and without escape.

Evidence to date- Positive studies

- Lead plus restraint stress in pregnant rats lead to persistently elevations of glucocorticoids in female offspring but not in male offspring. (DA Cory-Slechta et al., 2004)
- Perfluorooctane sulfonate (PFOS) plus stress in pregnant mice resulted in reduced fetal weight and increased fetal toxicity than previously reported studies of PFOS exposure alone. (Fuentes et al., 2006;
- PFOS plus stress exposure in pregnant rats showed mixed results on neurobehavioral effects in offspring. PFOS alone shows delayed neural maturation. Stress without PFOS exposure caused acclerated maturation. PFOS plus stress caused diminished activity in an open-field test. (Fuentes et al., 2007)

Evidence to date-Positive studies

- Prenatal stress affects sensitivity to caffeine in the adult offspring. (Pohorecky et al., 1989)
- Concurrent maternal stress and arsenic and methylmercury exposure in mice resulted in significant exacerbation of exposure-related developmental effects. (Colomina et al., 1997)
- Adult rats were exposed concurrently to the neurotoxic pesticide, dieldrin and inescapable, uncontrollable stress. This combination caused behavioral deficits in adult animals that other experimental parameters did not. (Carlson and Rossellini, 1987)

Evidence to date-Negative studies

- Uranium exposure plus stress in pregnant rats did not shift dose-related health effects. (Sanchez et al., 2006, Albina et al., 2005)
- Concurrent manganese and stress exposure in mice did not alter dose-response effects. (Torrente M, et al., 2002)
- With joint exposure to heavy metals and stress in pregnant rodents, the maternal stress enhances the metal-induced fetal toxicity only at doses that are clearly toxic to the dam. (Domingo et al., 2004)

Evidence to date-negative studies

- Concurrent exposure to maternal restraint stress and aluminum did not alter aluminum induced post natal developmental effects in mice. (Colomina et al., 2005)

Conclusions to date

- The evidence suggests that in some specific substances with some types of stressors, differences in response to toxic exposures are seen in experimental animals such as rats.
- The health effects seen are complex and shifted, ie., sometimes toxic exposure plus stress causes worsening of the adverse effects of the toxin; other times, the combination of exposure to stress and toxins leads to resistance to the health effects of a toxicant.

Implications for Risk Assessment

- During the past decade, EPA has examined a new multifactorial model for risk assessment that may take into account community factors such as poverty and cumulative stress and how that may generate unique vulnerabilities to toxic exposure.
- March 2010 - EPA is hosting a conference to examine how various forms of stress may impact communities exposed to disproportionately high levels of toxicants.