

AAMR

Collaborative on  
Health and the  
Environment  
(LDDI)



Institute for  
Children's  
Environmental  
Health

## LINKING ENVIRONMENTAL EXPOSURES WITH PSYCHOLOGICAL DISORDERS

### Linking Environmental Exposures with Psychological Disorders Fact Sheet

The role of neurotoxicants in the etiology of psychological disorders is increasingly being recognized. A considerable body of research shows that neurotoxic exposures may be associated with deficits in IQ, learning, memory, and attention as well as behavioral changes. Less well-developed but emerging data reveal that exposure to environmental agents with neurotoxic effects may result in a spectrum of psychological disturbances, such as anxiety, depression, conduct disorders and schizophrenia. Most studies and clinical reports focus on high-dose exposures that would only be encountered by accident or perhaps in an occupational setting. There are even fewer studies of the impacts of low-dose and chronic exposure to neurotoxic agents and study results are often mixed. In short, new research suggests that psychological disorders can be influenced by environmental agents though the data are limited in many, but not all cases.

Below is a brief compilation of the small body of research that has found associations between environmental toxicants and mental health disorders. Studies finding no association are not included. Study design limitations have been noted in most cases to help provide perspective. In addition, readers should use a note of caution when extrapolating the effects seen in animal studies to the effects on humans.

#### **Anxiety Disorder**

##### Mercury

- A small study of 16 chemical workers conducted five years after their exposure to neurotoxic levels of organic mercury concluded that mercury may contribute to **anxiety, depression and phobic avoidance**. These workers were exposed to very high levels of mercury for a considerable time. (Powell 2000)
- Another small study of 13 men acutely exposed to inorganic mercury vapor found associations with **depression, anxiety and social withdrawal**. (Haut et.al. 2000)

##### Pesticides

- A four-year study of 761 residents of Colorado farms using herbicides and insecticides noted that “neurological effects resulting from a pesticide poisoning may **decrease concentration and cause irritability**...” (Beseler and Stallones, Oct 2003)
- A Brazilian study of 37 workers chronically exposed to low levels of the organophosphate pesticides chlorpyrifos and acephate showed almost half of the workers had psychiatric

diagnoses, including generalized **anxiety disorder, panic disorder and social anxiety**. (Salvi 2003)

- An animal study in which rats were given doses of 1.0, 3.0 and 7.0 mg/kg of cyhalothrin, a synthetic pyrethroid insecticide, showed evidence that it induces **anxiety-like symptoms**, with the effect being dose-related. (Righi 2003)
- Results of an animal study at Washington State University indicated that repeated exposure to low levels of lindane may produce persistent changes in **anxiety-related neural** circuitry. Animals pre-treated with lindane continued to show evidence of fear in the presence of an odor weeks after the fear-provoking stimulus previously associated with the odor was discontinued. (Cloutier 2006)

## **Conduct Disorder**

### Lead

- A study of 301 public-school boys associated lead exposure with an increased risk for **antisocial and delinquent behavior**. Teachers of 11-year-old boys with high bone lead levels reported increased **social and attention problems, delinquent behavior and anxious/depressed** symptoms. Parents and teachers of boys with high bone lead levels judged them to be more **aggressive and antisocial** than boys with low lead levels. ("High lead" classification refers to those boys with blood lead levels above the median; "Low lead" are those with levels below the median) (Needleman Feb96)
- A study of 195 subjects compared prenatal and postnatal blood lead levels with parental and self-report of delinquent behaviors. The researchers found that prenatal blood lead exposure greater than 10 micrograms per deciliter is associated with an increase of more than 2.3 delinquent acts compared with study subjects with less than or equal to blood lead levels of 5 micrograms per deciliter or less. Significantly higher rates of delinquent behavior is associated with a categorical blood lead level measured prenatally and at 78 months of age, although not by average childhood blood lead level. (Dietrich et al. 2001)

## **Depression**

### Lead

- A cross-sectional study on low-level lead exposure concluded that lead can contribute to **depression and anxiety**. It further supports the idea that lead exposure can play a role in psychiatric problems including general stress on the central nervous system (Rhodes et. al. 2003)
- In a prospective study of lead neurotoxicity, exposed foundry workers with blood lead levels over 40 micrograms per deciliter showed increased rates of **depression, confusion, anger, fatigue and tension**. (Baker et. al. 1983)

### Organophosphates

- **Depression, along with anxiety, irritability and restlessness** represent the most prominent emotional symptoms from acute and moderate organophosphate poisonings. (Mearns 1994); (Metcalf & Holmes 1969)
- Long-term psychological effects of long-term low-level exposure to organophosphates have not been adequately studied. Some studies have found adverse psychological effects but not all. (Mearns 1994)
- One study by Salvi showed a significant decrease in **depressive mood disorder** among agricultural workers when they stopped using organophosphate pesticides. (Salvi 2003)

- Another study showed that **depression** was 5 times as likely when individuals reported pesticide poisoning in a population of farm workers. (Stallones 2002)

Solvents

- Occupational exposure to organic solvents has been associated with increased psychiatric symptoms, particularly **depression**. (Hakkola 1994); (Linz et al.1986); (Morrow, Kamis, & Hodgson 1993); (Struwe, Mindus, & Jonsson 1980).

**Schizophrenia**

Lead Exposure

- One study has found that lead exposure during pregnancy may be associated with **schizophrenia** later in life. The study results showed that elevated lead exposure (greater than 15 micrograms per deciliter) during gestation increased the odds of developing schizophrenia later in life by two and half times. (Opler 2004)
- Another study has found that low levels of lead exposure can overstimulate an enzyme in the brain that is implicated in **bipolar disorder** and **schizophrenia**. This over-stimulation of this enzyme Protein Kinase C contributes to a subset of symptoms involving the dysregulation of thought affect, and behavior, which are features of many neuropsychiatric disorders. (Birnbaum 2004). This suggests that gene-environment interactions may be important and that lead may have some greater impact for people who are genetically predisposed.

**Environmental Toxicant Exposures that Have Been Associated with Psychological Disorders in Research Studies\***

<b>Disorder/ Exposure</b>	<b>Anxiety Disorder</b>	<b>Conduct Disorder</b>	<b>Depression</b>	<b>Schizophrenia</b>
Lead	XX	XX	XX	XX
Mercury	XX		XX	
Organophosphates	XX		XX	
Solvents	XX		XX	

\*This chart summarizes the information described above showing possible associations between environmental toxicants and adverse mental health outcomes. Please note that these associations are based on a small body of emerging research and are not necessarily conclusive suggesting further studies are needed to substantiate these findings.

## Bibliography

- Baker E., Feldman R., White R., Harley J. The role of occupational lead exposure in the genesis of psychiatric and behavioral disturbances. *Acta Psychiatrica Scandinavica, Supplementum* (1983) 303:38-48.
- Beseler, C., Stallones, L. Safety Practices, Neurological Symptoms, and Pesticide Poisoning. *J. Occupational and Environmental Medicine* (2003) Vol. 45, No. 10.
- Birnbaum, S.G., Yuan, P.X., Wang, M., Vijayraghavan, S., Bloom, A.K., Davis, J., Gobeske, K.T., Sweatt, J.D., Manji, H.K., and A.F.T. Arnsten. Protein Kinase C Over-activity Impairs Prefrontal Cortical Regulation of Working Memory. *Science* (Oct 2004) 306: 882-884.
- Cloutier, S., Forquer, M.R., Sorg, B.A. Low Level Lindane Exposure Alters Extinction of Conditioned Fear in Rats. *Toxicology* (2006) Vol. 217, pp 147 – 154.
- Dietrich K., Douglas R., Succop P., Berger O., Bornschein R. Early exposure to lead and juvenile delinquency. *Neurotoxicology and Teratology* (2001) Vol. 23, No. 6 pp 511-518.
- Hakkola M. Neuropsychological symptoms among tanker drivers with exposure to solvents. *Occupational Medicine* (1994) Vol. 44, pp 243-246.
- Haut M., Morrow L., Pool D., Callahan T., Haut J., Franzen M. Neurobehavioral Effects of Acute Exposure to Inorganic Mercury Vapor. *Applied Neuropsychology* (1999) Vol. 6 No. 4, 193-200.
- Lisboa, S., Souza, F. Developmental Lead Exposure Induces Depressive-like Behavior in Female Rats. *Drug and Chemical Toxicology* (Feb 2005) Vol. 28 Issue (1) p.67, 11p.
- Linz DH, deGarmo PL, Morton WE, Wiens AN, Coull BM & Maricle RA, (1986). Organic solvent-induced encephalopathy in industrial painters. *Journal of Occupational Medicine* (1986) Vol.18, pp 119-125.
- Mearns, J., Dunn, J., Lees-Haley, P.R. Psychological Effects of Organophosphate Pesticides: A Review and Call for Research by Psychologists. *J. of Clinical Psychology*, (1994) Vol. 50, No.2, pp 286 – 294.
- Metcalf DR, Holmes JH. EEG, psychological, and neurological alterations in humans with organophosphorus exposure. *Annals of the New York Academy of Sciences* (1969) Vol. 160, pp 357-365.
- Morrow L, Kamis H, & Hodgson MJ. Psychiatric symptomatology in persons with organic solvent exposure. *Journal of Consulting and Clinical Psychology* (1993) Vol. 61, pp 171-174.
- Needleman H, Riess J, Tobin M, Biesecker G, Greenhouse J. Bone Lead Levels and Delinquent Behavior. *JAMA* (Feb 1996) Vol. 275, No.5.
- Opler M, Brown AS, Graziano J, Desai M, Zheng W, Schaefer C, Factor-Litvak P, Susser E. Prenatal Lead Exposure Aminolevulinic Acid, and Schizophrenia. *Environmental Health Perspectives* (April 2004) Vol. 112 No. 5.

Powell, T. Chronic Neurobehavioural Effects of Mercury Poisoning on a Group of Zulu Chemical Workers. *Brain Injury* (2000) Vol. 14, No 9, pp 797-814.

Rhodes D., Spiro A., Aro A., Hu H. Relationship of Bone and Blood Lead Levels to Psychiatric Symptoms: The Normative Aging Study. *Journal of Occupational and Environmental Medicine* (2003) Vol. 45 No. 11.

Righi, D.A., Palermo-Neto, J. Behavioral Effects of Type II Pyrethroid Cyhalothrin in Rats. *Toxicology and Applied Pharmacology* (2003) Vol. 191, pp 167-176.

Salvi, R.M., Lara, D.R., Ghisolfi, E.S., Portela, L.V., Dias, R.D., Souza, D.O. Neuropsychiatric Evaluation in Subjects Chronically Exposed to Organophosphate Pesticides. *Toxicological Sciences*. (2003) Vol. 72, Issue 2, p267.

Savage EP, Keefe TH, Mounce LM, Heaton RK, Lewis JA, Burcar PJ. Chronic Neurological Sequelae of Acute Organophosphate Pesticide Poisoning. *Archives of Environmental Health* (1988) Vol. 43 (No.1).

Sidell, F.R. Soman and sarin: Clinical manifestations and treatment of accidental poisoning by organophosphates. *Clinical Toxicology* (1974) Vol. 7, pp 1-17.

Stallones, L., Beseler, M. Pesticide Poisoning and Depressive Symptoms among Farm Residents. *AEP* (2002) Vol. 12, No. 6, pp 389-394.

Struwe G, Mindus P, & Jonsson B. Psychiatric ratings in occupational health research: A study of mental symptoms in lacquerers. *American Journal of Industrial Medicine* (1980) Vol.1, pp 23-30.

#### **Additional Research Articles for Reference**

Aldridge, J., Slotkin, T. et al, Developmental Exposure of Rats to Chlorpyrifos Leads to Behavioral Alterations in Adulthood, Involving Serotonergic Mechanisms and Resembling Animal Models of Depression. *Environmental Health Perspectives* (May 2005) Vol.113, No. 5.

Burns JM, Baghurst PA, Sawyer MG, McMichael AJ, Tong S. Lifetime Low-level Exposure to Environmental Lead and children's Emotional and Behavioral Development at Ages 11-13 Years: The Port Pirie Cohort Study. *American Journal of Epidemiology* (April 1999) Vol. 149(8), 15.

Colborn T, Neurodevelopment and Endocrine Disruption, *Environmental Health Perspectives: Annual Review Issue* (June 2004) Vol. 112, No. 9.

Holford P, Alzheimer's and dementia: the nutrition connection. Primary Care Mental Health, *Radcliffe Medical Press* (2004) 2:5-12.

Koger S, Schettler T, Bernard W. Environmental Toxicants and Developmental Disabilities: A Challenge for Psychologists. *American Psychologist* (April 2005) Vol. 60(3).

Kreiling JA, Stephens RE, Reinisch CL. Polychlorinated biphenyls target serotonergic neuronal development in *Spisula solidissima* (surf clam) embryos. *FASEB J* (May 2000) Vol. 14(8): A1476.

Mendola P, Selevan SG, Gutter S, Rice D. Environmental Factors Associated With a Spectrum of Neurodevelopmental Deficits. *Mental Retardation and Developmental Disabilities Research Reviews* (2002) 8:188-197.

*Mental Health Weekly* (Feb 2004) Prenatal lead exposure may be linked to schizophrenia. Vol. 14, Issue 8, p7-7.

Morrow L, Stein L, Bagovich GR, Condray R, Scott A. Neuropsychological Assessment, Depression, and Past Exposure to Organic Solvents. *Applied Neuropsychology* (2001) Vol. 8, No. 2, pp 65-73.

Morse DC, Brouwer A, van den Berg KJ, Seegal RF. Prenatal exposure to polychlorobiphenyls: PCB metabolism, thyroid hormone homeostasis and brain development in the rat. *Neurotoxicology* (1996) Vol. 17, Nos. 3/4, pp 631-638.

Needleman H, Gunnoe C, Leviton A, et al. Deficits in psychologic and classroom performance of children with elevated dentine lead levels. *New England Journal of Medicine* (1979) 300:689-695.

Rice D, Parallels between Attention Deficit Hyperactivity Disorder and Behavioral Deficits Produced by Neurotoxic Exposure in Monkeys. *Environmental Health Perspectives* (June 2000) Vol. 108 No. S3.

Sassine, M., et al. Manganese accentuates adverse mental health effects associated with alcohol use disorders. *Biological Psychiatry* (2002) Vol. 51, No.11, p 909.

Seegal RF, Brosch KO, Bush B. Regional Alterations in Serotonin Metabolism Induced by Oral Exposure of Rats to Polychlorinated Biphenyls. *Neurotoxicology* (1986) Vol. 7, No. 1, pages 155-166.

Tanner, CM M.D. and JW Langston, M.D. "Genetics and Parkinson's Disease: Research Points to Environmental Causes; Efforts Now Directed Towards Factors Other Than Heredity." The Parkinson's Institute, Sunnyvale, CA.

Vermeir G, Viaene M, Staessen J, Hond ED, Roels HA. Neurobehavioural investigations in adolescents exposed to environmental pollutants. *Environmental Toxicology & Pharmacology* (May 2005) Vol. 19 Issue 3.

