

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.

For more information visit www.intechopen.com



Interaction Between Exposure to Neurotoxicants and Drug Abuse

Francisca Carvajal, Maria del Carmen Sanchez-Amate,
Jose Manuel Lerma-Cabrera and Inmaculada Cubero

*University of Almeria/Department of Neuroscience and Health Sciences, Almeria,
Spain*

1. Introduction

Humans are continuously exposed to a variety of environmental neurotoxicants. Over the past 30 years, at least 100,000 chemicals, including pesticides, food additives, drugs, and cosmetics, have been registered for commercial use in the United States (Muir & Howard, 2006). Twenty years ago, about 750 chemicals had shown neurotoxic effects in laboratory animals (Anger, 1984). Actually, the number is thought to exceed a thousand, although no authoritative estimate of the real number of neurotoxicants is available (Grandjeand & Landrigan, 2006).

About two-thirds of all agricultural use of xenobiotics involves herbicides and about one-eighth involves insecticides; approximately 20% of usage is fungicides, fumigants, and other pesticides (United States Environmental Protection Agency [U.S. EPA], 2001). Organophosphate insecticides represent 50% of all the insecticide use worldwide. In fact in Europe, the use of pesticide on crops exceeds 140,000 metric tons (The use of plant protection products in the European Union. Data 1992–2003. Eurostat statistical books [http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/KS-76-06-669/EN/KS-76-06-669-EN.PDF]). Although European policies to reduce pesticide use have been introduced, according to EU statistical data for 1992–2003, annual pesticide consumption has not decreased. Estimates made by the World Health Organization (WHO) indicate that three million acute organophosphate poisonings and over 200,000 deaths may occur annually in the world (Ferrer & Cabral, 1995; WHO, 1990). Thus, exposure to neurotoxic compounds has become in a serious public health problem worldwide.

Numerous reports have indicated a link between xenobiotic exposure and human health, including disturbances in the CNS (for a review, see Costa et al., 2008). Moreover, numerous studies have reported long-term neurological and neurobehavioral sequelae following a pesticide poisoning event (Delgado et al., 2004; Rosenstock et al., 1991; Steeland et al., 1994). Thus, humans exposed to acute or chronic levels of organophosphate (OP) compounds, a potent neurotoxic widely employed in industry, households and agriculture for pest control, exhibit long-term alterations in neuropsychological performance and cognitive processes, such as processing speed, visual attention, visuosperceptual abilities, memory impairment and problem solving (Farahat et al., 2003; Fiedler et al., 1997; Roldan-Tapia et al., 2004, 2006;

Steenland et al., 1994). Also, emotional deficits have been found after exposure to OPs (Savage et al., 1998; Yokoyama et al., 1998). Pesticide exposure has been correlated with emotional disturbances such as anxiety increases, depression and suicide risk (London et al., 2005; Roldan-Tapia et al., 2006).

On the other hand, the use of pesticides in agriculture has been linked with several dopamine-associated CNS disorders including Parkinson's Disease (PD) (Dick, 2006) and Attention-Deficit/Hyperactivity Disorder (ADHD) (Bouchard et al., 2010). Specifically, pesticide exposure is a risk factor for PD (Ascherio et al., 2006; Brown et al., 2006; Dick, 2006) and recent studies have shown that it may contribute to ADHD prevalence (Bouchard et al., 2010). Given that dopamine (DA) has been identified as the critical neurotransmitter in the reward circuit mediating substance abuse (for a review, see Di Chiara & Bassareo, 2007), exposure to certain environmental neurotoxicants might influence the development of drug addiction. There are numerous reports associating neurotoxicant exposure and dopaminergic disorders such as PD and ADHD in the literature; however studies examining any potential effects of neurotoxicants on drug addiction are just recently being conducted and published, in spite of the fact that drug abuse is an important public health problem leading to serious negative consequences for individuals and society. Estimates of the total overall costs of substance abuse in the United States, including health- and crime-related costs, exceed \$600 billion annually (Office of National Drug Control Policy, 2004). This includes approximately \$235 billion for alcohol abuse (Rehm et al., 2009). Thus, these data stresses the need for new scientific research aimed toward the assessment of neurochemical and neurobiological mechanisms underlying exposure to neurotoxicants and drug abuse.

2. Environmental neurotoxicants and drug abuse

In recent years, a growing body of clinical evidence has revealed that acute, intermittent or continuous exposure to a wide variety of chemically unrelated environmental pollutants (such as volatile organic chemicals, woods preservatives, solvents, or organophosphate pesticides) might result in the development of multiple chemical intolerance (Miller, 2001) and increased sensitivity to drugs of abuse (Newlin, 1994; Sorg & Hochstatter, 1999). The general population is exposed to multiple agents, either as intrinsically complex mixtures or as separate substances, such as specific drugs. Since the behavior of any given chemical in the body is affected by other chemicals, there is a need to study the toxicological and behavioral effects of environmental neurotoxicant mixtures and drugs. Since both environmental neurotoxicants and drug abuse present a health hazard to the population, these studies should merit special attention. Moreover, such studies would open new perspectives to the promising and exciting scientific field that tries to bridge environmental health sciences, toxicology and drug research.

A large variety of studies in animals (Mutti et al., 1988; Von Euler et al., 1991, 1993) and humans (Edling et al., 1997) have demonstrated that repeated volatile organic compound exposure have deleterious effects on the dopaminergic system. The most ubiquitous volatile organic compound is formaldehyde (Form). Acute exposure to formaldehyde can cause eye, nose, throat, and skin irritation, whereas long-term exposure has been linked to certain cancers as well as asthma (Daisey et al., 2003). Furthermore, numerous animal studies on the

adverse effects of formaldehyde on behavioral responses to cocaine have revealed drug-pollutant cross-sensitization (Sorg et al., 1996, 1998, 2001).

In 1996, Sorg and her collaborators demonstrated that animals pretreated with repeated high-level formaldehyde inhalation (1h/day x 7days) showed a significantly enhanced locomotor response to cocaine compared to controls, an indicator that specific limbic pathways may have been sensitized (Sorg et al., 1996). However, the same pattern of exposure, but with low-level formaldehyde doses failed to cause behavioral sensitization to cocaine (Sorg et al., 1998) suggesting that formaldehyde effects on behavioral response to cocaine are dose-dependent.

Paradoxically, long-term low-level formaldehyde exposure (1h/day x 5days/week x 4 weeks) produced behavioral sensitization to later cocaine injection, suggesting altered dopaminergic sensitivity in mesolimbic pathways (Sorg et al., 1998). More specifically, this study has shown that repeated exposure to a relatively low-level volatile organic compound, formaldehyde, amplifies behavioral responses to cocaine. Taking together, these data suggests that the effect of formaldehyde on the cross-sensitization to cocaine depends both on the dose and on the pattern of exposure to this volatile organic compound (Sorg et al., 1998).

Furthermore, humans are routinely exposed to heavy metals through a variety of sources (air, food, water or soil). Thus, prolonged exposure to heavy metals, such as cadmium, copper, lead, nickel, and zinc can cause deleterious health effects in humans (for a review, see Järup, 2003). Mainly, heavy metal exposure can directly influence behavior by impairing mental and neurological function, influencing neurotransmitter production and use, and altering numerous metabolic body processes. The adverse effects of heavy metal exposure are well documented; however, few studies have been carried out to understand their effects on drug use. Next, we are going to describe the effect of two heavy metals (lead and manganese) over the incidence of drug abuse.

The symptoms of acute lead poisoning are headache, irritability, abdominal pain and various symptoms related to the nervous system. Additionally, populations exposed to environments with high lead concentrations may show an increase in the incidence of drug abuse (Ensminger et al., 1997). Experimental studies show that adult lead exposure decreases behavioral sensitivity to cocaine (Burkey et al., 1997; Nation et al., 1996). Animal studies have found evidence that chronic lead exposure in adulthood causes a delay in the development of cocaine-induced locomotor sensitization, as well as a decrease in the magnitude of the locomotor response (Nation et al., 1996). Operant responses, rather than only simple behavioral responses, such as locomotor activity, are also affected by lead exposure. Thus, chronic lead exposure caused cocaine-induced disturbance attenuation in fixed-interval responding (Burkey et al., 1997). In agreement with these data, there are studies showing attenuated cocaine-induced increases in extracellular dopamine levels in the nucleus accumbens region after chronic lead exposure (Nation & Burkey, 1994).

By contrast, the evidence suggests that, after perinatal lead exposure, early developmental lead exposure may increase sensitivity to the reinforcing effects of cocaine and heroin in adulthood (Nation et al., 2004). Several studies have shown that acute administration of cocaine to rats developmentally exposed to low levels of lead produces an attenuation of drug reinforcement according to a conditioned place preference (CPP) paradigm (Miller et

al., 2000), and a drug discrimination preparation (Miller et al., 2001). A similar pattern of attenuation is evident in studies that examined the effects of developmental chronic low-level lead exposure on morphine-induced CPP (Valles et al., 2003). Thus, these studies suggest that lead exposure during development can cause long-term changes in the response that these individuals give to drugs of abuse in adulthood, probably reducing the reinforcing properties of drugs.

Consistent with these data, there is experimental evidence indicating that exposure to another heavy metal, manganese (Mn), has had effects on psychostimulant vulnerability too. Thus, Mn exposure in young adult rats leads to a reduced behavioral response to amphetamines (Vezer et al., 2007). Interestingly, Mn-exposed rats show opposite locomotor responsiveness when challenged with different doses of cocaine (Reichel et al., 2006). Specifically, postnatal Mn exposure causes increased locomotor activity in combination with lower doses of cocaine; and an attenuated locomotor response in combination with high doses of cocaine. These data suggests that Mn exposure can increase dopaminergic receptor sensitivity. In fact, postnatal Mn exposure caused persistent declines in DAT protein expression and [3H] dopamine uptake in the striatum and nucleus accumbens, as well as long-term reductions in striatal dopamine efflux into adulthood (McDougall et al., 2008).

Another set of experiments was carried out to study the effects of pesticides on drug-induced behavior. These studies have shown, for example, that the daily administration of a oral dose of herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) during gestation and development up to post-natal day 23 (PND23) increases an animal's sensitivity to amphetamine (Duffard & Evangelista de Duffard, 2002).

Also, it has been shown that exposure to another pesticide, chlorpyrifos, causes alteration in several drug-induced responses. For example, tolerance to locomotor effects was shown after a dopaminergic agonist challenge with amphetamine 30 days after exposure to CPF (Lopez-Crespo et al., 2007). In a separate study, the motivational and reward properties of amphetamine were decreased in the place preference paradigm months after CPF administration (Sanchez-Santed et al., 2004). Based on these studies, it has been proposed that CPF intoxication may produce long-term hyposensitivity in the dopaminergic system. Recent studies have found that monoamine levels decreased dramatically in the nucleus accumbens 30 days after CPF exposure (Moreno et al., 2008). Other organophosphates, such as chlorphenvinphos, also cause changes in the dopaminergic system. Thus, behavioral studies have shown that 3 weeks after acute exposure to high doses of chlorphenvinphos (CVP), there is an hyposensitivity to behavioral responsiveness to amphetamine and scopolamine (Gralewicz et al., 2000; Lutz et al., 2000, 2005). Furthermore, exposure to chlorphenvinphos prevents behavioral sensitization to amphetamine (Lutz et al., 2006).

3. Environmental neurotoxicants and ethanol intake

As described in the previous section, several studies have shown the interaction between neurotoxicants and the abuse of certain drugs, such as cocaine, amphetamines or morphine. Given that ethanol (EtOH) is one of the most commonly used drugs worldwide, next we will present the specific literature referring to neurotoxicant exposure and its relationship to ethanol intake.

The great majority of people in modern society regularly consume ethanol. In fact, about 100 billion Euros on alcoholic beverages are spent annually by Europeans, which is reflected by the high rate of alcohol consumption per capita of 10 liters of pure ethanol per year. But, consuming and abusing these huge amounts of alcohol is clearly a problem, with enormous health and socioeconomic effects worldwide. According to the Alcohol-Related Disease Impact (ARDI) tool, from 2001–2005, there were approximately 79,000 deaths annually attributable to excessive alcohol use. Thus, excessive alcohol use is the 3rd leading lifestyle-related cause of death for people in the United States, after tobacco addiction and obesity (McGinnis & Foege, 1999). The economic cost of ethanol abuse is estimated at greater than \$235 billion every year (Rehm et al., 2009), including health care costs, lost worker productivity, and crime.

Several studies have suggested a relationship between several neurotoxic agents and alcohol intake. First of all, we will focus on the interaction between lead exposure and alcohol intake. The exposure to this heavy metal has already been linked to reduced behavioral sensitivity to cocaine (Burkey et al., 1997; Nation et al., 1996). Also, populations exposed to environments with high lead concentrations may show an increase in the incidence of drug abuse (Ensminger et al., 1997). Epidemiological data has revealed that alcoholic industrial workers have higher blood lead levels than their non alcoholic colleagues, suggesting that alcoholic workers could be more susceptible to the toxic effects of lead (Cezard et al., 1992; Dalley et al., 1989).

Animal studies have found evidence that ethanol exposure for 8 weeks resulted in a marked increase in the accumulation of lead in the blood (Gupta & Gill, 2000a) and brain (Gupta & Gill, 2000b) of animals exposed to lead, making them more vulnerable to the toxic effects of lead. Thus, for example, levels of lead in the brain were approximately twice higher in lead and ethanol co-exposed animals than in animals exposed to lead alone (Gupta & Gill, 2000b). Another set of experimental studies has shown that mice treated chronically with lead exhibit some alterations in ethanol-induced behaviours, such as a reduction in ethanol-induced locomotor activity (Correa et al., 1999). In a self-administration task, dietary lead exposure led to lever pressing at a significantly lower rate than the control group (Nation et al., 1991). Apparently, lead toxicity reduces sensitivity to ethanol effects. Moreover, when subjects were exposed simultaneously to lead and ethanol, the level of dopamine decreased significantly, and was accompanied with increased norepinephrine levels (Flora & Tandom, 1987; Gupta & Gill, 2000b).

As with lead, simultaneous exposure to aluminium and ethanol also deplete brain dopamine (DA) and 5-hydroxytryptamine (5-HT) levels, when compared to rats given aluminium alone (Flora et al., 1991). Also, the concentration of aluminium in the blood and liver was significantly higher in rats exposed to both aluminium and ethanol than in those exposed only to aluminium. These results suggest that prolonged ethanol consumption may increase the rats' susceptibility to certain effects of aluminium.

3.1 The relationship between organophosphate exposure and ethanol intake

Decades ago, an interesting study showed that 114 agricultural workers suffering acute organophosphate intoxication developed intolerance to nicotine- and ethanol-containing beverages (Tabershaw & Cooper, 1966). Another epidemiological study, carried out by

Spiegelberg in 1961, described persistent intolerances for alcohol and nicotine among Germans who had manufactured chemical weapons, including organophosphate nerve agent, during World War II (Spiegelberg, 1961). These studies were the first to propose the existence of a relationship between organophosphate compound exposure and ethanol intake. In addition, more recently, clinical reports have shown that a significant percentage (66%) of Gulf War veterans reported that alcohol beverages, even a can of beer, made them feel ill (Miller, 2001). Unfortunately, there are not many epidemiological studies considering organophosphate exposure as a determinant of ethanol intake.

In agreement with clinical data, Overstreet and his colleagues reported that Flinder rats, which had been bred for increased sensitivity to organophosphate poisoning, showed enhanced responses to ethanol or nicotine (Overstreet et al., 1996, 2001). Thus, Flinder Sensitive Line (FSL) rats exhibited a significantly greater ethanol-induced (Overstreet et al, 1990, 1996) and nicotine-induced hypothermic response (Overstreet et al, 1996; Schiller & Overstreet, 1993) compared to its parallel bred counterparts, the Flinder Resistant Line (FRL) rats. It suggests that FSL rats, selectively bred for increased cholinergic responses, also show an increased sensitivity to the effects of alcohol or nicotine.

Taken together, clinical and experimental evidence strongly points to the existence of important, but poorly understood, neurobiological interactions between organophosphate exposure and ethanol intake. Therefore, we investigated the impact of OP exposure on voluntary alcohol consumption from a molecular and a behavioral approach in an animal model. To that aim, we employed an experimental model in Wistar rats based on the administration of a single high dose (250 mg / kg) of the organophosphate chlorpyrifos (CPF). CPF is an OP used worldwide in the agricultural industry and in households as a pesticide (Pope, 1999; Richardson, 1995). The primary mechanism of acute toxic action of these compounds is acetylcholinesterase (AChE) inhibition, which results in acute cholinergic over stimulation at nicotine and muscarinic synapses of the peripheral, autonomic and central nervous system (Lotti, 2001; Richardson, 1995). Additionally, non-AChE targets such as the monoaminergic (Aldridge et al., 2003; Dam et al., 1999; Moreno et al., 2008), the gabaergic (Rocha et al., 1996; Sánchez-Amate et al., 2002), or the glutamatergic systems (Gultekin et al., 2007) have also been proposed as alternative mechanisms involved in the acute lethal action and/or side effects of short and long-term OP exposure.

After subcutaneous administration, CPF keeps acetylcholinesterase (AChE) activity mildly inhibited for weeks. This unique biochemical profile points to the long-lasting presence of the compound in the body (Bushnell et al., 1993; Pope et al., 1992). Since CPF-induced AChE inhibition is not associated with overt cholinergic toxicity (Bushnell et al., 1993; Pope et al., 1992), exposure to high doses of this OP has been used in animal research to investigate the neurobehavioral effects of OP exposure during a wide temporal window of approximately 8-12 weeks (Richardson, 1995). Thus, exposure to a single subcutaneous injection of CPF would provide an animal model to conduct extensive neurobehavioral testing during a long interval of approximately 8 weeks.

The two-bottle choice paradigm provides a convenient method for a rapid screening of alcohol preferences in rats. Thus, early paradigms assessing the reinforcing effects of alcohol typically used an oral preference paradigm where animals were allowed to drink alcohol or water. In fact, free choice procedures are widely employed for selection of rat lines with genetically determined high or low ethanol preference (Files et al., 1997; Sinclair et al., 1989).

Eight weeks after CPF administration, Wistar rats were allowed to drink ethanol in a two bottle paradigm (water vs. 8%-20% w/v ethanol) to evaluate if pre-exposure to the organophosphate caused them long-lasting avoidance. In this long-term drinking model, changes in alcohol-drinking behavior occur over time between CPF and vehicle-treated rats. Thus, the CPF pretreated rats showed lower ethanol consumption and ethanol preference than the control group at 8, 15, and 20% ethanol concentration (Carvajal et al., 2007). These results are consistent with clinical and experimental data showing that exposure to organophosphates might be linked to increased ethanol sensitivity and reduced voluntary consumption of ethanol-containing beverages in humans.

Since different factors might contribute to alcohol consumption, from week 4 to week 8 after CPF administration, an additional set of neurobiological, physiological, and behavioral responses to ethanol were evaluated. First, we analyzed whether CPF alters gustatory sensory processing as measured by taste preferences for sucrose, quinine and saccharin. CPF-pretreated rats showed the same taste preference pattern as vehicle-treated rats. Secondly, we verified that ethanol avoidance was not secondary to ethanol-induced flavor aversion disturbances since both CPF- and vehicle-treated rats showed a similar pattern of flavor avoidance in response to ethanol. Finally, we explored the sedative/hypnotic properties of alcohol as assessed by the righting reflex. These data showed that 4 weeks after poisoning, CPF-treated rats showed enhanced sensitivity to the sedative properties of ethanol not associated with altered blood ethanol levels.

It is possible that increased ethanol sensitivity is partially mediated by several CPF toxicity mechanisms (for more details, see Carvajal et al., 2007). As noted above, the main CPF action mechanism is acetylcholinesterase inhibition. For example, it was demonstrated that administering cholinesterase inhibitors, galantamine or desoxypeganine, reduces alcohol consumption in alcohol-preferring rats (Doetkotte et al., 2005; Mann et al., 2006). Also, CPF decreases nicotinic alpha-7nACh receptor density (Slotkin et al., 2004), with a known role in ethanol intake and ethanol-induced sedation (Bowers et al., 2005; de Fiebre and de Fiebre, 2005). In this regard, there have been significant studies showing, at least at the genetic level, that knockout mice lacking alpha-7nAChR receptor specifically show reduced ethanol intake and increased sedation to ethanol (Bowers et al., 2005; de Fiebre and de Fiebre, 2005). Finally, alternative noncholinesterasic CPF neurotoxicity mechanisms (Casida and Quistad, 2004) might also cause ethanol avoidance (for more details, see Carvajal et al., 2007). However, future experimental research is required to test more specifically the implication of these CPF toxicity mechanisms in ethanol avoidance.

In summary, administration of a single high dose of CPF to adult Wistar rats elicited long-lasting reduced voluntary ethanol drinking and increased sedation to ethanol without evidence of altered ethanol metabolism, which indicates that CPF-ethanol neurobiological interactions may exist. Thus, there is the interesting possibility that some OPs such as CPF might induce long-lasting neural disturbances in brain systems critically involved in neurobehavioral responses to ethanol.

Investigating specific brain targets has been proposed as an important tool for developing our understanding of behavioral, emotional and cognitive impairments caused by OP compounds (Gupta, 2004). Considering this, in another study we explore whether CPF exposure induces significant disturbances in basal and/or ethanol-evoked neural activity in

a set of cholinceptive brain regions critically involved with neurobiological responses to ethanol. For this purpose, brain regional c-fos expression in response to acute ethanol (1.5 or 3.0 g/kg, i.p.) or saline solution was assessed in adult male Wistar rats previously injected with either a single high dose of CPF (250 mg/kg, sc) or vehicle. Results showed that first, CPF exposure did not modify the regional c-fos expression in response to acute ethanol administration; and secondly, CPF administration reduces long-term basal c-fos expression in the arcuate hypothalamic nucleus.

The arcuate hypothalamic nucleus AgRP/NPY expressing cells have been hypothesized to have a key role in voluntary ethanol consumption (Kalra & Kalra, 2004; Thiele et al., 2003). Taking together this fact and the present observation that long-term CPF exposure blunts c-fos expression in this brain region, one tempting hypothesis is that CPF causes long-term inhibition of neural activity in AgRP/NPY expressing cells in the Arc leading to reduced voluntary ethanol consumption. However, future behavioral and molecular studies are required to understand more extensively the role of Arc neural disturbances in long-term and long-lasting CPF-induced ethanol avoidance.

Although experimental data shown here constitute only an initial exploration of the putative relationship between organophosphate exposure and ethanol intake, both preclinical and experimental literature, and the preliminary findings of this study, suggests that further research is warranted. The use of well controlled animal models aiming to characterize the neurobiological mechanisms of drug/pollutant interactions would open new perspectives to this new scientific field that bridges environmental health sciences, toxicology, and drug research (Miller, 2001). Also, such research may result in public health and prevention programs that produce significant improvements in the integrity of long-term cognitive and behavioral outcomes.

4. Conclusion

In this chapter, we have provided a brief overview of this new scientific field that bridges environmental health sciences, toxicology, and drug research. In recent years, a large variety of studies have shown that different environmental neurotoxicants can lead to vulnerability to drug abuse. However, neurobiological interactions between environmental pollutants and drugs of abuse are still poorly understood. In the particular case of pesticides, both clinical and experimental research have shown that exposure to organophosphates might be linked to increased ethanol sensitivity and reduced voluntary consumption of ethanol-containing beverages. However, the mechanisms by which organophosphates may exert their effects on ethanol intake have yet to be elucidated. Accordingly, further laboratory and epidemiological research into the role of pesticides, and specifically chlorpyrifos, exposure in alcohol intake is needed. These studies appear to demonstrate a link between environmental neurotoxicant exposure and drug addiction, although much work needs to be done to further identify and characterize the underlying mechanisms involved.

5. Acknowledgment

This work was supported by Spanish grants from the Ministerio de Ciencia y Tecnología [PM/99-1046, SEJ2006-03629], Junta de Andalucía [CTS-280], and FEDER [UNAM05-23-006].

6. References

- Anger, W.K. (1984). Neurobehavioral testing of chemicals: impact on recommended standards. *Neurobehavioral Toxicology and Teratology*, Vol.6, No.4, (March 1984), pp. 147-153, ISSN 0275-1380.
- Aldridge, J.E.; Seidler, F.J.; Meyer, A.; Thillai, I. & Slotkin, T.A. (2003). Serotonergic systems targeted by developmental exposure to chlorpyrifos, effects during different critical periods, *Environmental Health Perspective*, Vol.111, No.14, (November 2003), pp. 1736-1743, ISSN 0091-6765
- Ascherio, A.; Chen, H.; Weisskopf, M.C.; O'Reilly, E.; McCullough, M.L.; Calle, E.E.; Schwarzschild, M.A. & Thun M.J. (2006). Pesticide exposure and risk for Parkinson's disease, *Annals of Neurology*, Vol.60, No.2, (August 2006), pp. 197-203, ISSN 1531-8249
- Bouchard, M.F.; Bellinger, D.C.; Wright, R.O. & Weisskopf, M.G. (2010). Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides, *Pediatrics*, Vol.125, No.6, (May 2010), pp. 1270-1277, ISSN 0031-4005
- Bowers, B.J.; McClure-Begley, T.D.; Keller, J.J.; Paylor, R.; Collins, A.C. & Wehner, J.M. (2005). Deletion of the alpha7 nicotinic receptor subunit gene results in increased sensitivity to several behavioral effects produced by alcohol, *Alcoholism: Clinical and Experimental Research*, Vol.29, No.3, (March 2005), pp. 295-302, ISSN 0145-6008
- Brown, T.P.; Rumsby, P.C.; Capelton, A.C.; Rushton, L. & Levy, L.S. (2006). Pesticides and Parkinson's disease—is there a link? *Environmental Health Perspectives*, Vol.114, No.2, (February 2006), pp. 156-164, ISSN 0091-6765
- Burkey, R.T.; Nation, J.R.; Grover, C.A. & Bratton, G.R. (1997). Effects of chronic lead exposure on cocaine-induced disturbance of fixed-interval behavior, *Pharmacology, Biochemistry and Behavior*, Vol.56, No.1, (January 1997), pp. 117-121, ISSN 0091-3057
- Bushnell, P.J.; Pope, C.N. & Padilla, S. (1993). Behavioral and neurochemical effects of acute chlorpyrifos in rats: Tolerance to prolonged inhibition of cholinesterase, *The Journal of Pharmacology and Experimental Therapeutics*, Vol.266, No.2, (August 1993), pp. 1007-1017, ISSN 0022-3565
- Carvajal, F.; Lopez-Grancha, M.; Navarro, M.; Sanchez-Amate, M.C. & Cubero, I. (2007). Long-lasting reductions of ethanol drinking, enhanced ethanol-induced sedation, and decreased c-fos expression in the Edinger-Westphal nucleus in Wistar rats exposed to the organophosphate Chlorpyrifos, *Toxicological Science*, Vol.96, No.2, (April 2007), pp. 310-320, ISSN 1096-6080
- Carvajal, F.; Sanchez-Amate, M.C. & Cubero, I. (2011). A single high dose of chlorpyrifos reduces long-term basal c-fos expression in the rat arcuate hypothalamic nucleus. In preparation
- Casida, J.E. & Quistad, G.B. (2004). Organophosphate toxicology: safety aspects of nonacetylcholinesterase secondary targets, *Chemical Research in Toxicology*, Vol.17, No.8, (August 2004), pp. 983-998, ISSN 0893-228X.
- Cezard, C.; Demarquilly, C.; Boniface, M. & Haguenoern, J.M. (1992). Influence of the degree of exposure on lead on relations between alcohol consumption and the biological indices of lead exposure, epidemiological study in a lead acid battery factory,

- British Journal of Industrial Medicine*, Vol.49, No.9, (September 1992), pp. 645–647, ISSN 0007-1072
- Correa, M.; Miquel, M.; Sanchis-Segura, C. & Aragón, C. (1999). Effects of chronic lead administration on ethanol-induced locomotor and brain catalase activity, *Alcohol*, Vol.19, No.1, (August 1999), pp. 43-49, ISSN 0741-8329
- Costa, L.G. ; Giordano, G.; Guizzetti, M. & Vitalone, A. (2008). Neurotoxicity of pesticides: a brief review, *Frontiers in Bioscience*, Vol.13, No.1, (January 2008), pp. 1240–1249, ISSN 1093-9946
- Daisey, J.M.; Angell, W.J. & Apte, M.G. (2003). Indoor air quality, ventilation and health symptoms in schools: an analysis of existing information, *Indoor Air*, Vol.13, No.1, (March 2003), pp. 53–64, ISSN 0905-6947
- Dalley, S.; Girre, C.; Hispard, E.; Tomas, G. & Fournier, L. (1989). High blood lead levels in alcoholics : wine vs. Beer, *Drug Alcohol Dependence*, Vol.23, No.1, (January 1989), pp. 45–48, ISSN 0376-8716
- Dam, K.; Garcia, S.J.; Seidler, F.J. & Slotkin, T.A. (1999). Neonatal chlorpyrifos exposure alters synaptic development and neuronal activity in cholinergic and catecholaminergic pathways, *Developmental Brain Research*, Vol.116, No.1, (August 1999), pp. 9-20, ISSN 0165-3806
- de Fiebre, N.C. & de Fiebre, C.M. (2005). Alpha7 nicotinic acetylcholine receptor knockout selectively enhances ethanol-, but not beta-amyloid induced neurotoxicity, *Neuroscience Letters*, Vol.373, No.1, (January 2005), pp. 42–47, ISSN 0304-3940
- Delgado, E.; McConnell, R.; Miranda, J.; Keifer, M.; Lundberg, I.; Partanen, T. & Wesseling C. (2004). Central nervous system effects of acute organophosphate poisoning in a two-year follow-up, *Scandinavian Journal of Work, Environment & Health*, Vol.30, No.5, (October 2004), pp. 362–370, ISSN 0355-3140
- Di Chiara, G. & Bassareo, V. (2007). Reward system and addiction: what dopamine does and doesn't do, *Current Opinion in Pharmacology*, Vol.7, No.1, (February 2007), pp. 69-76, ISSN 1471-4892
- Dick, F.D. (2006). Parkinson's disease and pesticide exposures, *British Medical Bulletin*, Vol.79–80, No.1, (January 2007), pp. 219–31, ISSN 0007-1420
- Doetkotte, R.; Opitz, K.; Kiianmaa, K. & Winterhoff, H. (2005). Reduction of voluntary ethanol consumption in alcohol-preferring alko alcohol (AA) rats by desoxypeganine and galanthamine, *European Journal of Pharmacology*, Vol.522, No.1-3, (October 2005), pp. 72–77, ISSN 0014-2999
- Duffard, R. & Evangelista de Duffard, A.M. (2002). Environmental chemical compounds could induce sensitization to drugs of abuse, *Annals of New York Academy of Science*, Vol.965, (June 2002), pp. 305–313, ISSN 0077-8923
- Edling, C.; Hellman, B.; Arvidson, B.; Andersson, J.; Hartvig, P.; Lilja, A.; Valind, S. & Langstrom, B. (1997). Do organic solvents induce changes in the dopaminergic system? Positron emission tomography studies of occupationally exposed subjects, *International Archives of Occupational and Environmental Health*, Vol.70, No.3, (August 1997), pp. 180–186, ISSN 0340-0131
- Ensminger, M.E.; Anthony, J.C. & McCord, J. (1997). The inner city and drug use: initial findings from an epidemiological study, *Drug and Alcohol Dependence*, Vol.48, No.3, (December 1997), pp. 175–184, ISSN 0376-8716

- Farahat, T.M.; Abdelrasoul, G.M.; Amr, M.M.; Shebl, M.M.; Farahat, M.M. & Anger, W.K. (2003). Neurobiological effects among workers occupationally exposed to organophosphorous pesticides, *Occupational and Environmental Medicine*, Vol.60, No.4, (April 2003), pp. 279-286, ISSN 1351-0711
- Ferrer, A. & Cabral, R. (1995). Recent epidemics of poisoning by pesticides, *Toxicology Letters*, Vol.82-83, (December 1995), pp. 55-63, ISSN 0378-4274
- Fiedler, N.; Kipen, H.; Kelly-McNeil, K. & Fenske, R. (1997). Long-term use of organophosphates and neuropsychological performance, *American Journal of Industrial Medicine*, Vol.32, No.5, (November 1997), pp. 487-496, ISSN 0271-3586
- Files, F.J.; Denning, C.E.; Hyytia, P.; Kiiianmaa, K. & Samson, H.H. (1997). Ethanol-reinforced responding by AA and ANA rats following the sucrose-substitution initiation procedure, *Alcoholism: Clinical and Experimental Research*, Vol.21, No.4, (June 1997), pp. 749-753, ISSN 0145-6008
- Flora, S.J. & Tandon, S.K. (1987). Effect of combined exposure to lead and ethanol on some biochemical indices in the rat, *Biochemical Pharmacology*, Vol.36, No.4, (February 1987), pp. 537-541, ISSN 0006-2952
- Flora, S.J.; Dhawan, M. & Tandom, S.K. (1991). Effects of combined exposure to aluminium and ethanol on aluminium body burden and some neuronal, hepatic and haematopoietic biochemical variables in the rat, *Human and Experimental Toxicology*, Vol.10, No.1, (January 1991), pp. 45-48, ISSN 0960-3271
- Gralewicz, S.; Lutz, P. & Szymczak, W. (2000). Hyposensitivity to amphetamine following exposure to chlorphenvinphos protection by amphetamine preexposure, *Acta Neurobiologiae Experimentalis*, Vol. 60, No.2, (April 2000), pp. 203-208, ISSN 0065-1400
- Grandjean, P. & Landrigan, P.J. (2006). Developmental neurotoxicity of industrial chemicals, *The Lancet*, Vol.368, No.9553, (December 2006), pp. 2167-2178, ISSN 0140-6736
- Gultekin, F.; Ozturk, M. & Adogan, M. (2000). The effect of organophosphate insecticide chlorpyrifos-ethyl on lipid peroxidation and antioxidant enzymes (in vitro), *Archives of Toxicology*, Vol.74, No.9, (November 2000), pp. 533-538, ISSN 0340-5761
- Gupta, V. & Gill, K.D. (2000a). Lead and ethanol coexposure: implications on the dopaminergic system and associated behavioral functions, *Pharmacology, Biochemistry and Behaviour*, Vol.66, No.3, (July 2000), pp. 465-474, ISSN 0091-3057
- Gupta, V. & Gill, K.D. (2000b). Influence of ethanol on lead distribution and biochemical changes in rats exposed to lead, *Alcohol*, Vol.20, No.1, (January 2000), pp. 9-17, ISSN 0741-8329
- Harwood, H.J.; Fountain, D. & Livermore, G. (1998). Economic costs of alcohol abuse and alcoholism, *Recent Development in Alcoholism*, Vol.14, pp. 307-30, ISSN 0738-422X
- Järup, L. (2003). Hazards of heavy metal contamination, *British Medical Bulletin*, Vol.68, No.1, (December 2003), pp.167-182, ISSN 0007-1420
- Kalra, S.P. & Kalra P.S. (2004). Overlapping and interactive pathways regulating appetite and craving, *Journal of Addictive Disease*, Vol.23, No.3, (July 2004), pp. 5-21, ISSN 1055-0887

- London, L.; Flisher, A.; Wesseling, C.; Mergler, D. & Kromhout, H. (2005). Suicide and exposure to organophosphate insecticides, cause or effect? *American Journal of Industrial Medicine*, Vol.47, No.4, (April 2005), pp. 308–321, ISSN 0271-3586
- Lopez-Crespo, G.; Carvajal, F.; Flores, P.; Sanchez-Santed, F. & Sanchez-Amate, M.C. (2007). Time-course of biochemical and behavioural effects of a single high dose of chlorpyrifos, *Neurotoxicology*, Vol.28, No.3, (May 2007), pp. 541–547, ISSN 0161-813X
- Lotti, M. (2001). Clinical toxicology of anticholinesterase agents in humans. In: *Handbook of Pesticide Toxicology. Second edition*, R.I. Krieger, (Ed.), 1043-1085, Academic Press, ISBN 978-0-12-426260-7, San Diego.
- Lutz, P.; Gralewicz, S.; Kur, B. & Wiaderna, D. (2005). Amphetamine- and scopolamine-induced locomotor activity following treatment with chlorphenvinphos or chlorpyrifos in rats, *International Journal of Occupational Medicine and Environmental Health*, Vol.18, No.2, (April 2005), pp. 115–125, ISSN 1232-1087
- Lutz, P.; Tomas, T.; Gralewicz, S. & Nowakowska, E. (2000). Long-term effects of acute exposure to chlorphenvinphos on behavioural responsiveness to amphetamine and scopolamine in rats, *International Journal of Occupational Medicine and Environmental Health*, Vol.13, No.3, (July 2000), pp. 215–222, ISSN 1232-1087
- Lutz, P.; Wiaderna, D.; Gralewicz, S. & Kur, B. (2006). Exposure to chlorphenvinphos, an organophosphate insecticide, prevents from behavioural sensitization to amphetamine, *International Journal of Occupational Medicine and Environmental Health*, Vol.19, No.2, (April 2006), pp. 132–141, ISSN 1232-1087
- Mann, K.; Ackermann, K.; Diehl, A.; Ebert, D.; Mundle, G.; Nakovics, H.; Reker, T.; Richter, G.; Schmidt, L.G.; Driessen, M.; Rettig, K.; Opitz, K. & Croissant, B. (2006). Galantamine: a cholinergic patch in the treatment of alcoholism: a randomized, placebo-controlled trial, *Psychopharmacology (Berl)*, Vol.184, No.1, (January 2006), pp. 115–21, ISSN 0033-3158
- McDougall, S.A.; Reichel, C.M.; Farley, C.M.; Flesher, M.M.; Der-Ghazarian, T.; Cortez, A.M.; Wacan, J.J.; Martinez, C.E.; Varela, F.A.; Butt, A.E. & Crawford, C.A. (2008). Postnatal manganese exposure alters dopamine transporter function in adult rats: Potential impact on nonassociative and associative processes, *Neuroscience*, Vol.154, No.2, (June 2008), pp. 848–860, ISSN 0306-4522
- McGinnis, J.M. & Foege, W.H. (1999). Mortality and Morbidity Attributable to Use of Addictive Substances in the United States, *Proceedings of the Association of American Physicians*, Vol.111, No. 2, (February 1999), pp. 109–118, ISSN 1525-1381
- Miller, C.S. (2001). Toxicant-induced loss of tolerance, *Addiction*, Vol.96, No.1, (January), pp. 115–139, ISSN 0965-2140
- Miller, D.K.; Nation, J.R. & Bratton, G.R. (2000). Perinatal exposure to lead attenuates the conditioned reinforcing properties of cocaine in male rats, *Pharmacology, Biochemistry and Behavior*, Vol.67, No.1, (September 2000), pp. 111–119, ISSN 0091-3057
- Miller, D.K.; Nation, J.R. & Bratton, G.R. (2001). The effects of perinatal lead exposure to lead on the discriminative properties of cocaine and related drugs, *Psychopharmacology*, Vol.158, No.2, (November 2001), pp. 165–174, ISSN 0033-3158

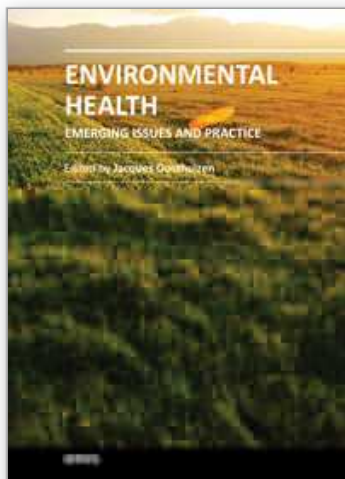
- Moreno, M.; Cañadas, F.; Cardona, D.; Suñol, C.; Campa, L.; Sanchez-Amate, M.C.; Flores, P. & Sanchez-Santed, F. (2008). Long-term monoamine changes in the striatum and nucleus accumbens alter acute chlorpyrifos exposure, *Toxicology Letters*, Vol.176, No.2, (January 2008), pp. 162-167, ISSN 0378-4274
- Muir, D.C. & Howard, P.H. (2006). Are there other persistent organic pollutants? A challenge for environmental chemists, *Environmental Science and Technology*, Vol.40, No.23, (December 2006), pp. 7157-7166, ISSN 0013-936X
- Mutti, A.; Falzoi, M.; Romanelli, A.; Bocchi, M.C.; Ferroni, C. & Franchini, I. (1988). Brain dopamine as a target for solvent toxicity: Effects of some monocyclic aromatic hydrocarbons, *Toxicology*, Vol.49, No.1, (April 1988), pp. 77-82, ISSN 0300-483X
- Nation, J.R.; Dugger, L.M.; Dwyer, K.K.; Bratton, G.R. & Grover, C.A. (1991). The effects of dietary lead on ethanol-reinforced responding, *Alcohol and Alcoholism*, Vol.26, No.4, (July 1991), pp. 473-480, ISSN 0735-0414
- Nation, J.R. & Burkey, R.T. (1994). Attenuation of cocaine-induced elevation of nucleus accumbens dopamine in lead-exposed rats, *Brain Research Bulletin*, Vol.35, No.1, (January 1994), pp. 101-104, ISSN 0361-9230
- Nation, J.R.; Livermore, C.L. & Burkey, R.T. (1996). Chronic lead exposure attenuates sensitization to the locomotor-stimulating effects of cocaine, *Drug and Alcohol Dependence*, Vol.41, No.2, (June 1996), pp. 143-149, ISSN 0376-8716
- Nation, J.R.; Smith, K.R. & Bratton, G.R. (2004). Early developmental lead exposure increases sensitivity to cocaine in a self-administration paradigm, *Pharmacology, Biochemistry and Behavior*, Vol.77, No.1, (January 2004), pp. 127-135, ISSN 0091-3057
- Newlin, D.B. (1994). Drug sensitization, substance abuse, and chemical sensitivity, *Toxicology and Industrial Health*, Vol.10, No.4-5, (July-October 1994), pp. 463-480, ISSN 0748-2337
- Office of National Drug Control Policy (2004). The Economic Costs of Drug Abuse in the United States, 1992-2002. Washington, DC: Executive Office of the President (Publication No. 207303). Available at www.ncjrs.gov/ondcppubs/publications/pdf/economic_costs.pdf
- Overstreet, D.H.; Rezvani, A.H. & Janowsky, D.S. (1990). Increased hypothermic responses to ethanol in rats selectively bred for cholinergic supersensitivity, *Alcohol and Alcoholism*, Vol.25, No.1, (January 1990), pp. 59-65, ISSN 0735-0414
- Overstreet, D.H.; Miller, C.S.; Janowsky, D.S. & Russell, R.W. (1996). Potential animal model of multiple chemical sensitivity with cholinergic supersensitivity, *Toxicology*, Vol.111, No.1-3, (July 1996), pp. 119-134, ISSN 0300-483X
- Overstreet, D.H. & Djuric, V. (2001). A genetic rat model of cholinergic hypersensitivity, implications for chemical intolerance, chronic fatigue, and asthma, *Annals of the New York Academy of Science*, Vol.933, (March 2001), pp. 92-102, ISSN 0077-8923
- Pope, C.N.; Chakraborti, T.K.; Chapman, M.L. & Farrar, J.D. (1992). Long-term neurochemical and behavioural effects induced by acute chlorpyrifos treatment, *Pharmacology, Biochemistry and Behavior*, Vol.42, No.2 (June 1992), pp.251-256, ISSN 0091-3057

- Pope, C.N. (1999). Organophosphorus pesticides, Do they all have the same mechanism of toxicity? *Journal of Toxicology and Environmental Health, Part B Critical Reviews*, Vol.2, No.2, (April-June 1999), pp. 161-181, ISSN 1093-7404
- Rehm, J.; Mathers, C.; Popova, S.; Thavorncharoensap, M.; Teerawattananon Y. & Patra, J. (2009). Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders, *The Lancet*, Vol.373, No.9682, (June 2009), pp. 2223-2233, ISSN 0140-6736
- Reichel, C.M.; Wacan, J.J.; Farley, C.M.; Stanley, B.J.; Crawford, C.A. & McDougall, S.A. (2006). Postnatal manganese exposure attenuates cocaine-induced locomotor activity and reduces dopamine transporters in adult male rats, *Neurotoxicology and Teratology*, Vol.28, No.3, (May-June 2006), pp. 323-332, ISSN 0892-0362
- Richardson, R.J. (1995). Assessment of the neurotoxic potential of chlorpyrifos relative to other organophosphorus compounds: A critical review of the literature. *Journal of Toxicology and Environmental Health*, Vol.44, No.2, (February 1995), pp. 135-165, ISSN 0098-4108
- Rocha, E.S.; Swanson, K.L.; Aravaca, Y.; Goolsby, J.E.; Maelicke, A. & Albuquerque, E.X. (1996). Paraoxon: Cholinesterase-independent stimulation of transmitter release and selective block of ligand-gated ion channels in cultured hippocampal neurons, *The Journal of Pharmacology and Experimental Therapeutics*, Vol.278, No.3, (September 1996), pp. 1175-1187, ISSN 0022-3565
- Roldan-Tapia, L. & Sanchez-Santed, F. (2004). Neuropsychological sequelae of acute poisoning by pesticides containing cholinesterase inhibitors, *Revista de Neurologia*, Vol.38, No.6, (March 2004), pp. 591-597, ISSN 0210-0010
- Roldan-Tapia, L.; Nieto-Escamez, F.A.; del Aguila, E.M.; Laynez, F.; Parron, T. & Sanchez-Santed, F. (2006). Neuropsychological sequelae from acute poisoning and long-term exposure to carbamate and organophosphate pesticide, *Neurotoxicology and Teratology*, Vol.28, No.6, (November-December 2006), pp. 694-703, ISSN 0892-0362.
- Rosenstock, L.; Keifer, M.; Daniell, W.E.; McConnell, R. & Claypoole, K. (1991). Chronic central nervous system effects of acute organophosphate pesticide intoxication, *The Lancet*, Vol.338, No.8761, (July 1991), pp. 223-227, ISSN 0140-6736
- Sánchez-Amate, M.C.; Dávila, E.; Cañadas, F.; Flores, P. & Sanchez-Santed, F. (2002). Chlorpyrifos Shares Stimulus Properties with Pentylentetrazol as Evaluated by an Operant Drug Discrimination Task, *Neurotoxicology*, Vol.23, No.6, (December 2002), pp. 795-803, ISSN 0161-813X
- Sanchez-Santed, F.; Cañadas, F.; Flores, P.; Lopez-Grancha, M. & Cardona, D. (2004). Long-term functional neurotoxicity of paraoxon and chlorpyrifos: behavioural and pharmacological evidence, *Neurotoxicology and Teratology*, Vol.26, No.2, (March-April 2004), pp. 305-317, ISSN 0892-0362
- Savage, E.P.; Keefe, T.J.; Mounce, L.M.; Heaton, R.K.; Lewis, J.A. & Burcar, P.J. (1998). Chronic neurological sequelae of acute organophosphate pesticide poisoning, *Archives of Environmental Health*, Vol.43, No.1, (January-February 1998), pp. 38-45, ISSN 0003-9896
- Schiller, G.D. & Overstreet, D.H. (1993). Selective breeding for increased cholinergic function: Preliminary study of nicotinic mechanisms. *Medical Chemistry Research*, Vol.2, No.8-9 (October 1993), pp. 578-583, ISSN 1054-2523

- Sinclair, J.D.; Le, A.D. & Kiiianmaa, K. (1989) The AA and ANA rat lines selected for differences in voluntary ethanol consumption, *Experientia*, Vol.45, No.9, (September 1989), pp. 798–805, ISSN 0014-4754
- Slotkin, T.A.; Southard, M.C.; Adam, S.J.; Cousins, M.M. & Seidler, F. J. (2004). Alpha7 nicotinic acetylcholine receptors targeted by cholinergic developmental neurotoxicants: Nicotine and chlorpyrifos, *Brain Research Bulletin*, Vol.64, No.3, (September 2004), pp. 227–235, ISSN 0361-9230
- Steenland, K.; Jenkins, B.; Ames, R.G.; O'Malley, M.A.; Chrislip, D.W. & Russo, J. (1994). Chronic neurologic sequelae of acute organophosphate pesticide poisoning, *American Journal of Public Health*, Vol.84, No.5, (May 1994), pp. 731–736, ISSN 0090-0036
- Sorg, B.A.; Willis, J.R.; Nowatka, T.C.; Ulibarri, C.; See, R.E. & Westberg, H.H. (1996). Proposed animal neurosensitization model for multiple chemical sensitivity in studies with formalin, *Toxicology*, Vol.111, No.1-3, (July 1996), pp. 135-145, ISSN 0300-483X
- Sorg, B.A.; Willis, J.R.; See, R.E.; Hopkins, B. & Westberg, H.H. (1998). Repeated low-level formaldehyde exposure produces cross-sensitization to cocaine: possible relevance to chemical sensitivity in humans, *Neuropsychopharmacology*, Vol.18, No.5, (May 1998), pp. 385-394, ISSN 0893-133X
- Sorg, B.A. & Hochstatter, T. (1999). Behavioral sensitization after repeated formaldehyde exposure in rats. *Toxicology and Industrial Health*, Vol.15, No.3-4, (April-June 1999), pp. 346–355, ISSN 0748-2337
- Sorg, B.A.; Tschirgi, M.L.; Swindell, S.; Chen, L. & Fang, J. (2001). Repeated formaldehyde effects in an animal model for multiple chemical sensitivity, *Annals of New York Academy of Sciences*, Vol.933, (March 2001), pp. 57–67, ISSN 0077-8923
- Spiegelberg, V. (1961). Psychopathologisch-neurologische Schaden nach Einwirkung Synthetischer Gifte, In: *Wehrdienst und Gesundheit*, vol. III (Darmstadt, Wehr und Wissen Verlagsgesellschaft)
- Tabershaw, I. & Cooper, C. (1966). Sequelae of acute organic phosphate poisoning. *Journal of Occupational Medicine*, Vol.8, No.1, (January 1966), pp.5-20, ISSN 0096-1736
- Thiele, T.E.; Navarro, M.; Sparta, D.R.; Fee, J.R.; Knapp, D.J. & Cubero I. (2003). Alcoholism and obesity: overlapping neuropeptide pathways? *Neuropeptides*, Vol.37, No.6, (December 2003), pp. 321-337, ISSN 0143-4179
- U.S. EPA (2002) Interim Reregistration Eligibility decision for chlorpyrifos. US EPA, Washington, DC, <http://www.epa.gov/oppsrrd1/reregistration/status.html>.
- Valles, R.; Cardon, A.L.; Heard, H.M.; Bratton, G.R. & Nation, J.R. (2003). Morphine conditioned place preference is attenuated by perinatal lead exposure, *Pharmacology, Biochemistry and Behavior*, Vol.75, No.2, (May 2003), pp. 295–300, ISSN 0091-3057
- Vezer, T.; Kurunczi, A.; Naray, M.; Papp, A. & Nagymajtenyi, L. (2007). Behavioral effects of subchronic inorganic manganese exposure in rats, *American Journal of Industrial Medicine*, Vol.50, No.11, (November 2007), pp. 841–852, ISSN 0271-3586
- Von Euler, G.; Ogren, S.O.; Bondy, S.C.; McKee, M.; Warner, M.; Gustafsson, J.A.; Eneroth, P. & Fuxe, K. (1991). Subacute exposure to low concentrations of toluene affects

- dopamine mediated locomotor activity in the rat, *Toxicology*, Vol.67, No.3, (May 1991), pp. 333- 349, ISSN 0300-483X
- Von Euler, G.; Ogren, S.O.; Li, S.M.; Fuxe, K. & Gustafsson, J.A. (1993). Persistent effects of subchronic toluene exposure on spatial learning and memory, dopamine-mediated locomotor activity and dopamine D2 agonist binding in the rat, *Toxicology*, Vol.77, No.3, (March 1993), pp. 223-232, ISSN 0300-483X
- World Health Organization. (1990). Public health impact of pesticides used in agriculture. Geneva: WHO
- Yokoyama, K.; Araki, S.; Murata, K.; Nishikitani, M.; Okumura, T.; Ishimatsu, S. & Takasu, N. (1998). Chronic neurobehavioral and central and autonomic nervous system effects of Tokyo subway sarin poisoning, *Journal of Physiology*, Vol.92, No.3-4, (June-August 1998), pp. 317-323, ISSN 0928-4257

IntechOpen



Environmental Health - Emerging Issues and Practice

Edited by Prof. Jacques Oosthuizen

ISBN 978-953-307-854-0

Hard cover, 324 pages

Publisher InTech

Published online 03, February, 2012

Published in print edition February, 2012

Environmental health practitioners worldwide are frequently presented with issues that require further investigating and acting upon so that exposed populations can be protected from ill-health consequences. These environmental factors can be broadly classified according to their relation to air, water or food contamination. However, there are also work-related, occupational health exposures that need to be considered as a subset of this dynamic academic field. This book presents a review of the current practice and emerging research in the three broadly defined domains, but also provides reference for new emerging technologies, health effects associated with particular exposures and environmental justice issues. The contributing authors themselves display a range of backgrounds and they present a developing as well as a developed world perspective. This book will assist environmental health professionals to develop best practice protocols for monitoring a range of environmental exposure scenarios.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Francisca Carvajal, Maria del Carmen Sanchez-Amate, Jose Manuel Lerma-Cabrera and Inmaculada Cubero (2012). Interaction Between Exposure to Neurotoxicants and Drug Abuse, *Environmental Health - Emerging Issues and Practice*, Prof. Jacques Oosthuizen (Ed.), ISBN: 978-953-307-854-0, InTech, Available from: <http://www.intechopen.com/books/environmental-health-emerging-issues-and-practice/interaction-between-exposure-to-neurotoxicants-and-drug-abuse>

INTECH
open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen