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**N**owadays, it is quite acknowledged that inhalant abuse crosses all demographic, ethnic, and socioeconomic boundaries causing significant morbidity and mortality particularly in school-aged and older children. Solvent inhalants are not illegal, easily accessible and inexpensive; which makes young people at an increased risk for their abuse and consequences including death.

Several studies were undertaken to elucidate the possible mechanisms(s) of inhalant abuse and toxicity. Some studies revealed that deaths associated with their abuse were traumatic and capable of killing directly probably via cardiac mechanism. Other studies showed that inhalants can lead to severe damage to bone marrow, liver, kidney, brain, and heart.

Various reports ascribed the neurotoxicity of inhalants to their effects on brain neurotransmitters. Inhalants were found to increase GABAA, glycine and 5-HT<sub>3</sub> receptor activation. Toluene, TCE, benzene and diethyl ether produce anxiolytic effects, suggesting that they act as positive modulators of GABAA receptors. Toluene acutely inhibits nicotinic ACh receptors; whereas acute toluene exposure was shown to regulate hippocampal muscarinic receptor binding and could disrupt the activity of numerous voltage-gated ion channels, calcium signaling, ATPases and G-proteins.

Other studies reported that toluene, benzene, diethyl ether, TCE, and xylene may block the NMDA receptors resulting in CNS depression. Prolonged exposure to toluene increased levels of brain NMDA receptors. Toluene was reported to inhibit two types of potassium channels in brain cells. Exposure to toluene increased dopamine levels in the rat prefrontal cortex and striatum and increased neuronal firing in the ventral tegmental area (VTA) in a manner similar to other drugs of abuse which could be integral to the rewarding

Toluene caused alterations in catecholamines synthesis and utilization in a number of studies. The neurobiological effects of toluene may be mediated by GABA and glutamate receptors.

In a recent study in our laboratory, single and daily repeated Toluene inhalation significantly altered levels of brain neurotransmitters. Toluene increased levels of glutamate and decreased levels of GABA. Toluene single and repeated daily inhalation increased 5-HT and dopamine levels in rat's brain.

In this presentation, a trial is undertaken to throw some light on the role of brain neurotransmitters in solvent inhalant abuse and neurotoxicity. This might help in finding more adequate methods to treat and overcome the deleterious hazards of abusing these toxic substances.



Elkoussi is a professor of Pharmacology and Toxicology in Assiut College of Medicine. He obtained his PhD in 1972 and in 1982 and 1984 was granted postdoctoral fellowships in the University of Florida College of Pharmacy. From 1990 to 1994 he worked as a Senior Research Scientist in the Center for Drug Design and Delivery and Center for Drug Discovery, University of Florida and also worked as pharmacologist and as a regulatory affairs manager in pharmaceutical research companies in USA and Egypt. In 2002 Prof. Elkoussi obtained a Hubert Humphrey Fellowship at Johns Hopkins University. He published over 50 manuscripts in international journals and presented several lectures and research work in many international conferences and supervised several Masters and PhD theses in experimental and clinical pharmacology and toxicology. Prof. Elkoussi main areas of interest includes: drug abuse, drug design & delivery, drug interactions, biological evaluation of drug activity, pharmacokinetics, pharmacotherapy, pharmacovigilance as well as phytotherapy. For the last 2 decades; Prof. Elkoussi has

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