ENDOGENOUS-EXOGENOUS CHEMICALS WITH NEUROTOXIC POTENTIAL

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Introduction: While certain highly reactive chemicals are neurotoxic at high environmental concentrations, low endogenous concentrations of the same substances are required for normal neurophysiological function. **Methods/Results:** Airborne pollutants carbon monoxide, hydrogen sulfide, nitric oxide and cyanide are each employed as endogenous gasotransmitters [1], while high concentrations are associated with various neurological disorders. The pyrrole-forming neurotoxic gamma-diketone metabolites of certain aliphatic (*n*-hexane) and aromatic solvents (1,2-diethylbenzene) cause axonal polyneuropathy, yet gamma-diketones are present in solvent-unexposed subjects, and their urinary pyrrole derivatives increase in diabetes mellitus, a major cause of polyneuropathy [2]. Formaldehyde, the common metabolite of two naturally occurring epi/genotoxic neurotoxins (MAM, L-BMAA) linked to a prototypical neurodegenerative disease (Western Pacific Amyotrophic Lateral Sclerosis and Parkinsonism-Dementia Complex) [3], is a neurotoxic and carcinogenic xenobiotic, but the substance is an indispensable component of one-carbon metabolism essential for biosynthetic reactions and epigenetic modulation [4]. Elevated levels of endogenous formaldehyde have been linked to Alzheimer disease [5]. **Conclusions:** Such considerations suggest that understanding the relationship between the endogenous functions and effects of such highly reactive chemicals may illuminate both how their endogenous mis-regulation may contribute to neurological disease and the mechanisms underlying their neurotoxic effects from exposure to high concentrations. As taught by Paracelsus (1491-1541), the "Poison is in everything, and no thing is without poison. *The dosage makes it either a poison or a remedy*."

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7994231/;
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9291117/;
2. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7113121/;
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