

# Modelli *in vitro* per la valutazione della neurotossicità del metilmercurio. Stato attuale delle conoscenze

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## KEY WORDS

Methylmercury; *in vitro* models; neurotoxicity

## SUMMARY

***In vitro models for assessment of the neurotoxicity of methylmercury - current state of knowledge.*** **Background:** *In adults, MeHg poisoning is characterized by damage to discrete anatomical areas of the brain (visual cortex, loss of neurons from the granule layer of the cerebellum). However, the immature central nervous system (CNS), which is extremely sensitive to MeHg neurotoxicity, shows a diffuse and widespread damage disorganization of cerebral cortex cytoarchitecture, disappearance of granule cells with narrowing of the molecular layer. While adverse effects have been unequivocally demonstrated in poisoning incidents in humans (visual abnormalities, sensory impairment of the extremities, cerebellar ataxia, hearing loss, muscle weakness, tremor and mental deterioration), the implications of lower level exposures, such as those occurring in fish-eating populations, are still controversial. The high affinity of MeHg for thiol groups makes proteins and peptides bearing cysteines the predominant targets for structural and functional modification by MeHg in all subcellular compartments. Methods:* *The identification of MeHg cellular and sub-cellular targets in the CNS is complicated by the fact that it is difficult to observe the outcomes directly in vivo. In neurobiology, in vitro cell culture techniques have been successfully developed and employed to address specific questions of cell biology and nervous system functioning and provide a means to systematically study the complexity of cellular functions of the CNS elements. Moreover, they provide a convenient experimental tool for testing possible functions or postulates in vivo that otherwise might not be conducted. Results:* *Several mechanisms have been proposed as being implicated in the neurotoxic effects of MeHg. Examples of MeHg molecular effects which may be relevant to risk assessment are presented, including cell death mode, effects on microtubules, calcium signalling, oxidative stress, effects on neurotransmitter systems. Conclusions:* *Molecular and cellular approaches permit exploration of early biological responses to chemical or physical agents and definition of the role of these early effects in altered cellular structure and function.*

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