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Letter to the Editor

Does Copper Ameliorate the Vestibular Toxicity of Iminodipropionitrile (IDPN)?

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Since its discovery (Delay et al., 1952), the behavioural toxicity of IDPN in laboratory rodents has attracted the interest of many authors. Already in the 1960s, some authors indicated the similarity of the IDPN syndrome with that associated with dysfunction of the vestibular system (Chou and Hartmann, 1964; Slagel and Hartmann, 1965). Now, Henrik A. Hartmann (2005) reports the results of some experiments in which a high copper diet seems to diminish both the behavioural toxicity of IDPN and the presence of axonal swellings in the spinal cord. The work is driven by the idea that the severe neurological signs that follow developmental copper deficiency ''are quite similar to those produced by IDPN in rats''.

I would like to point out that the vestibular hypothesis for IDPN has been confirmed in the meantime. It has been demonstrated that IDPN causes degeneration of the vestibular sensory hair cells (Llorens et al., 1993; Llorens and Rodríguez-Farré, 1997; Seoane et al., 2001), and direct comparison indicates that the behavioural effects of IDPN are identical to those of a bilateral labyrinthectomy (Llorens et al., 1993; Llorens and Rodríguez-Farré, 1997). A good correlation is observed between the behavioural effects and the vestibular pathology following acute, subacute and subchronic exposure regimes (Llorens et al., 1993; Llorens and Rodríguez-Farré, 1997; Seoane et al., 2001). In contrast, IDPN dosing schedules that induce axonal swellings in the spinal cord, but no hair cell loss, do not induce behavioural signs (Llorens and Rodríguez-Farré, 1997). Behavioural effects identical to those caused by IDPN and vestibular hair cell loss are also caused by allylnitrile (CH_2=CH–CH_2–CN) (Balbuena and Llorens, 2001). Both behavioural changes and vestibular pathology are induced by the *cis*-isomer, but neither effect is induced by the *trans*-isomer of crotononitrile (CH_3–CH=CH–CN) (Balbuena and Llorens, 2003). Thus, the behavioural effects of IDPN do not depend on spinal cord lesions, but on a loss of vestibular function that results in impaired motor control.

Is copper deficiency associated with vestibular deficits? The description by Hartmann of the symptoms of this condition (seizures, tremor, wild running, catatonia) does not suggest so. In any case, if copper supplementation mitigates the behavioural effects of IDPN, the pathological correlate should be investigated in the inner ear, not the spinal cord.

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