Copper neurotoxicity in rat substantia Nigra and striatum is dependent on DT-diaphorase inhibition

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The dependence of copper neurotoxicity on DT-diaphorase inhibition was suggested from results obtained from a cell line derived from substantia nigra. Therefore, the aim of this study was to evaluate whether CuSO4 neurotoxicity in vivo, which was evaluated by determining the contralateral rotation and loss of tyrosine hydroxylase immunostaining, was dependent on DT-diaphorase inhibition by dicoumarol. Animals unilaterally and intranigrally injected with 0.25 nmol of CuSO4 and 2 nmol of dicoumarol presented a significant and characteristic contralateral rotational behavior ($P < 0.01$) when they were systemically stimulated with apomorphine (0.5 mg/kg s.c.), similar to that observed in rats injected unilaterally with 6-hydroxydopamine as a positive control. The behavioral effects correlated with the lost of tyrosine hydroxylase-positive staining, since animals unilaterally and intranigrally injected with 0.25 nmol of CuSO4 together with 2 nmol of dicoumarol exhibited extensive loss of tyr