

influence of quality control. *Blood Press Monit* 2002;7:169–77.

- [5] Wingfield D, Freeman GK, Bulpitt CJ et al. Selective recording in blood pressure readings may increase subsequent mortality. *QJM* 2002;95: 571–7.

Li-Jian Li
Pei-Shan Wang
Department of Public Health
Tianjin Medical University
No.22, QiXiang Tai Road

Heping District
Tianjin 300070
PR China
Tel.: +86 22 23542663; fax: +86 22 23542676 (L.-J. Li)
E-mail address: ljltj2005@yahoo.com.cn (L.-J. Li)

Tong Liu
Department of Cardiology
Second Hospital of Tianjin Medical University
Tianjin 300211
PR China

doi:10.1016/j.mehy.2005.02.001

On the similarity of cocaine and 3,3'-iminodipropionitrile

Peter Kovacic [1] discussed the role of oxidative metabolites of cocaine in toxicity and addiction. One of Kovacic's arguments is a mechanistic similarity to the action of neurotoxin 3,3'-iminodipropionitrile (IDPN). However, this argument is not supported by current knowledge.

IDPN is well known for inducing neurobehavioural changes in rodents [2]. Several authors, as those cited by Kovacic, have tried to relate these effects to oxidative stress in the brain, or to block IDPN's behavioural and brain chemical effects by antioxidant treatments. However, the behavioural effects of IDPN are identical to those of a bilateral labyrinthectomy [2,3], and are associated with degeneration of the vestibular sensory hair cells [2–4]. Similar behavioural effects and vestibular hair cell loss are caused by allylnitrile ($\text{CH}_2=\text{CH}-\text{CH}_2-\text{CN}$) [5] and *cis*-crotonitrile ($\text{CH}_3-\text{CH}=\text{CH}-\text{CN}$) [6], while *trans*-crotonitrile cause neither of both effects [6]. Thus, IDPN does not induce dyskinesia, but a loss of vestibular function that results in impaired motor control. If oxidative stress has a role in IDPN behavioural toxicity, this needs to be studied in the inner ear, not the brain. In any case, in opposition to Kovacic's suggestion [1], the similarity between IDPN and cocaine in metabolism to an *N*-hydroxy derivative is not relevant to IDPN behavioural toxicity, because the same toxicity is caused by IDPN analogues that lack the imino group and are thus unable to form similar derivatives.

Acknowledgement

Supported by Grant BFI2003-01606 from MCyT (Spain).

References

- [1] Kovacic P. Role of oxidative metabolites of cocaine in toxicity and addiction: oxidative stress and electron transfer. *Med Hypotheses* 2005;64:350–6.
- [2] Llorens J, Demêmes D, Sans A. The behavioral syndrome caused by 3,3'-iminodipropionitrile and related nitriles in the rat is associated with degeneration of the vestibular sensory hair cells. *Toxicol Appl Pharmacol* 1993;123: 199–210.
- [3] Llorens J, Rodríguez-Farré E. Comparison of behavioral, vestibular, and axonal effects of subchronic IDPN in the rat. *Neurotoxicol Teratol* 1997;19:117–27.
- [4] Seoane A, Demêmes D, Llorens J. Relationship between insult intensity and mode of hair cell loss in the vestibular system of rats exposed to 3,3'-iminodipropionitrile. *J Comp Neurol* 2001;439:385–99.
- [5] Balbuena E, Llorens J. Behavioural disturbances and sensory pathology following allylnitrile exposure in rats. *Brain Res* 2001;904:298–306.
- [6] Balbuena E, Llorens J. Comparison of *cis*- and *trans*-crotonitrile effects in the rat reveals specificity in the neurotoxic properties of nitrile isomers. *Toxicol Appl Pharmacol* 2003;187:89–100.

Jordi Llorens
Universitat de Barcelona
Departament de Ciències Fisiològiques II
Feixa Llarga s/n
08907 Hospitalet de Llobregat, Catalunya, Spain
Tel.: +34 93 4024277; fax: +34 93 4024268
E-mail address: jlllorens@ub.edu

doi:10.1016/j.mehy.2005.02.024