

### **Estrogen can down-regulate human catechol-*O*-methyltransferase (COMT) gene transcription: a novel link between estrogen and Parkinson's disease**

Xie Tao†, Ho Shu Leong†, David Ramsden‡

Division of Neurology†, University Department of Medicine, University of Hong Kong, Queen Mary Hospital, and Department of Medicine, University of Birmingham‡, Queen Elizabeth Hospital, UK.

Differences in COMT activity determine individual variations in levodopa response in Parkinson's disease (PD). Regulation of COMT transcription by endogenous compounds, although is important to PD, has never hitherto been explored. We have, for the first time, showed that physiological concentrations of 17- $\beta$ -estradiol can down-regulate human 1.3 kb COMT mRNA levels in MCF-7 cells (estrogen receptor-positive), but not in HeLa cells (estrogen receptor-negative), in a time- and dose-dependent manner. Sequence analyses in our newly cloned extended proximal and distal promoters revealed several half-palindromic estrogen-response elements (EREs) and liver-specific transcription factor binding (CEBP) sites. Co-transfection of COMT promoter-reporter constructs into COS-7 cells showed that 17- $\beta$ -estradiol down-regulated COMT promoter activities in an estrogen receptor-dependent mechanism. Deletion analyses further revealed that this estrogenic effect was mediated by fragments with half-palindromic EREs in the proximal promoter and a 323-bp fragment with only CEBP sites in the distal promoter. Our findings also demonstrate for the first time the mechanism of estrogenic inhibition of COMT transcription. This novel link between estrogen and Parkinson's disease may help to explain gender-related differences in clinical manifestations in PD, and suggest that estrogen replacement therapy may be helpful in post-menopausal women with PD.

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#### **REVIEW OF TRIGEMINAL NEURALGIA IN A REGIONAL NEUROLOGY CLINIC**

Tsang KL, Cheung RTF, Ho SL. Division of Neurology, University Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong

**BACKGROUND:** We reviewed the demographic profile, clinical presentation and treatment response of patients with trigeminal neuralgia who are being followed in our neurology clinic.

**METHODS:** The records of patients with the diagnosis of trigeminal neuralgia attending our Neurology Clinic at Sai Ying Pun Polyclinic, Hong Kong between 1st October 1997 and 31st October 1998 were reviewed retrospectively.

**RESULTS:** Twenty-seven patients with trigeminal neuralgia were identified; there were 17 females and 10 males. All were Chinese, and their mean age was 62 (range 25 to 80). The mean age of onset was 52. Fourteen patients had right-sided involvement, while left side was affected in 13. The ophthalmic, maxillary and mandibular divisions were involved in 4, 23 and 13 patients respectively. Twelve patients had 2 nerve root areas being affected. Regarding triggering factors, 15 patients had a trigger point on the skin; 10 at the angle of the mouth or naso-labial fold, 3 at the maxilla and 2 at the supra-orbital area. Twenty-one patients had their attacks triggered by stimuli to the mucosa or teeth, and 5 patients had no specific precipitating factor. MRI study of the brainstem and trigeminal nerve was performed in 16 patients, and 15 studies were normal. Only one patient was found to have vascular compression on the corresponding trigeminal nerve. Carbamazepine was used as first line treatment in all patients, and 21 (84%) showed satisfactory response. Six (24%) patients required more than one medication to control their symptoms, but the response remained sub-optimal.

**CONCLUSIONS:** Our results are similar to the reported series with slight female preponderance and onset after 40. The prevalence of ophthalmic branch involvement is higher than that reported in the literature. Abnormal findings on MRI studies are rare, and so MRI is recommended only for resistant cases or those with associated cranial nerve deficits. Carbamazepine remains the most effective medication.