Lamotrigine Effect on GABA Transmission in Angelman Syndrome?

To the Editors:

We read Dion et al.'s (2007) report of effectiveness of lamotrigine against both partial and generalized seizures in patients with Angelman syndrome. In their discussion of the possible mechanisms, the authors suggested that although the best documented antiepileptic effect of lamotrigine seems to be mediated by blockade of voltage-dependent sodium channels and no direct effect has been demonstrated on GABAA receptors, interference with inhibitory GABAA-neurotransmission might be considered. More precisely, modulation of the expression of the GABRB3 gene, which encodes the β3 subunit of GABAA receptors, is possible, as exemplified by expression enhancement in rat-cultured hippocampal cells following chronic administration of lamotrigine (Wang et al 2002). If confirmed in vivo in humans, this might concern not only patients with a chromosome 15q11-q13 deletion containing GABRB3 but also the other molecular classes of Angelman syndrome, consistent with the "UBE3AGABRB3" hypothesis (Dan and Boyd, 2003). According to the latter, neuronal network hypersynchrony documented in Angelman syndrome is related to deficient recruitment of β3 subunit-containing GABAA receptors due to reduced UBE3A gene expression in all molecular classes, and additional decrease in β3 subunit due to reduced GABRB3 gene expression in deletion cases (Dan et al. 2004a,b). This might provide a novel, pharmacogenomic antiepileptic effect of lamotrigine in Angelman syndrome.

Bernard Dan, Stewart G. Boyd, Karine Pelc, Guy Cheron

Department of Neurology, H^opital
Universitaire des Enfants Reine Fabiola
Universit´e Libre de Bruxelles (ULB)
15 Avenue JJ Crocq, 1020 Brussels, Belgium
Department of Clinical Neurophysiology
Great Ormond Street Hospital for Children, London
United Kingdom
Laboratory of Neurophysiology
and Movement Biomechanics
Univerit´e Libre de Bruxelles (ULB)

Brussels, Belgium
bernard.dan@ulb.ac.be