Effects of lamotrigine on human motor cortex plasticity.

Abstract:
Besides its use in epilepsy, lamotrigine (LTG) is also effective as mood stabilizer. The pathophysiology of mood disorders may incorporate a dysfunction of neuronal plasticity and animal experiments suggest that mood stabilizers influence induction of long-term potentiation (LTP) and -depression (LTD), two major forms of synaptic plasticity. However, the exact modes of action of LTG and its impact on neuronal plasticity in humans remain unclear. Here, we tested the effects of a single oral dose of LTG (300 mg) on motor cortical plasticity induced by paired associative stimulation (PAS(25)), a protocol that typically induces LTP-like plasticity, in 26 young healthy adults in a placebo-controlled, randomized, double-blind crossover design. We stratified analysis of the LTG effects according to the individual PAS(25) response in the placebo session (14 LTP-responders vs. 12 LTD-responders). Plasticity was indexed by motor evoked potential (MEP) amplitudes recorded before and for 60 min after PAS(25). LTG resulted in a significant reduction of the LTP-like MEP increase in the LTP-responders and a reduction of the LTD-like MEP decrease in the LTD-responders, with the majority of LTD-responders even showing an MEP increase. In summary, LTG differentially modulated cortical plasticity induced by non-invasive brain stimulation in human subjects depending on their individual intrinsic propensity for expressing LTP-like or
LTD-like plasticity. Findings contribute to our understanding of the anticonvulsant and antidepressant clinical effects of LTG, which have been suggested to occur, at least in part, through downregulation of LTP (epilepsy) and LTD (depressive disorders).