One strategy to understand bipolar disorder is to study the mechanism of action of mood stabilising drugs, such as valproate and lithium. This approach has implicated a number of intracellular signalling elements, such as GSK3β, ERK/MAPK, or protein kinase C. However, we found that lamotrigine did not modulate any of these targets, which is intriguing given that its profile in the clinic differs from that of valproate or lithium, with greater efficacy to prevent episodes of depression than mania. The primary target of lamotrigine is the voltage-gated sodium channel, but it is unclear why inhibition of these channels might confer antidepressant efficacy. In healthy volunteers, we found that lamotrigine had a facilitatory effect on the BOLD response to transcranial magnetic stimulation (TMS) of the frontal cortex. This effect was in contrast to an inhibitory effect when TMS was applied over motor cortex. In a follow-up study, a similar facilitatory effect was observed in a larger cohort of healthy subjects, whereas valproate inhibited frontal cortical TMS-induced BOLD response. In vitro, we found that lamotrigine (3-10 µM) enhanced the power of gamma frequency network oscillations induced by kainic acid in the rat hippocampus, an effect that was not observed with valproate (100 µM). These data suggest that lamotrigine has a positive effect on corticolimbic network function that may differentiate it from other mood stabilisers. The results are also consistent with the notion of corticolimbic network dysfunction in bipolar disorder.