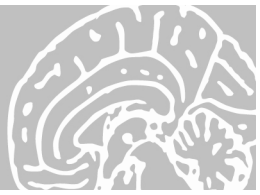
Do valproate potentially improve outcome of acute middle cerebral artery infarction?



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Stroke is the most common life-threatening neurological disease and the major cause of disability in Taiwan. Ischemic incident of brain is the most common stroke type. Current therapies for acute ischemic stroke are aimed at early recanalization of the occluded cerebral vessel to minimize brain damage and to modify the ischemic cascade pathway in order to rescue injured neurons. Thrombolysis with recombinant tissue plasminogen activator (rtPA) is presently the only approved therapy for acute ischemic stroke, and eligible patients treated with rtPA show better neurological performance. However, rtPA thrombolysis is not an ideal therapy because of the narrow therapeutic window and the strict patient selection requirements. Thus, there is a clear clinical urgency to develop novel and effective neuroprotective drugs or new strategies to improve current treatment for patients experiencing acute ischemic stroke. A growing body of evidence from animal stroke models suggests that valproate comprises multiple mechanisms that contribute both neuroprotective and neurotrophic effects against ischemic stroke. Well-established data have demonstrated that valproate treatment in rodent ischemic stroke models markedly reduces infarct volume and improves functional outcome. The mechanisms likely involve inhibition of histone deacetylases (HDACs), which induce neuroprotective molecules that suppress ischemia-induced neuroinflammation, protect against blood-brain barrier disruption, and promote angiogenesis, thus facilitating functional recovery. An open-label controlled trial with valproate was conducted in Tri-Service General Hospital for investigating whether valproate improves functional recovery in patients with acute middle cerebral artery (MCA) infarction. It demonstrated that valproate treatment significantly improves functional outcome in patients with acute MCA infarction.