Superior neuroprotective effects of nanowired delivery of Chinese celery extract DL-3-n-butylphthalide (DL-NBP) on concussive head injury

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Abstract

Concussive head injury (CHI) is quite common in military personnel during combat operation for which no suitable therapy exists till today. In this investigation, we report that nanodelivery of traditional Chinese medicine, DL-3-n-butylphthalide (DL-NBP) in CHI that was the most effective in reducing brain pathology in CHI if given 2 and 4 h after an 8 h injury or 8 and 12 h after 24 h trauma. Since CHI induces severe brain ischemia and oxidative stress, in this investigation we also examined the effects of TiO_2-DL-NBP on regional cerebral blood flow (CBF) and brain pathology in our rat model of CHI. CHI was inflicted by dropping a weight of 114.6 g on the right parietal skull bone over a distance of 20 cm in anesthetized rats resulting an impact of 0.224 N on the skull surface. This impact induces brain pathology from over 4 h to 24 h. In separate groups of injured animals, administration of TiO_2-nanowired-NBP (40 or 60 mg/kg, i.p.) 2h and 4 h after injury in 8 h survival group and 8 h and 12 h after trauma in 24 h survival group. In the untreated and treated groups, regional CBF (rCBF) in the cerebral cortex, hippocampus, thalamus, hypothalamus, cerebellum and brainstem was measured using [125]-Iodine labeled microspheres (15±0.6 µm o.d.). Untreated CHI resulted in a progressive increase in brain pathology, reduction in the rCBF (-30 to -50%) and development of brain edema formation. TiO_2-NBP resulted in significant improvement in rCBF in all brain areas examined. On the other hand, 80 to 100 mg/kg, dose of normal NBP is needed to induce comparable c reduction in rCBF and brain pathology in CHI. These observations show that nanodelivery of NBP has superior neuroprotective effects in CHI, a feature require additional investigation for clinical relevance.

Biography

Hari Shanker Sharma is the Director of Research (International Experimental Central Nervous System Injury & Repair, IECNSIR), University Hospital, Uppsala University; Professor of Neurobiology (MRC), Docent in Neuroanatomy (UU) and is currently affiliated with Department of Surgical Sciences, Division of Anesthesiology and Intensive Care Medicine, Uppsala University, Sweden. On his research on brain pathology and neuroprotection in different models, he received prestigious awards from The Laerdal Foundation of Acute Medicine, Stavanger, Norway, in 2005 and Distinguished International Scientists Collaboration Award (DISCA) by National Institute on Drug Abuse (NIDA), Baltimore, MD (2006–2008). His current research is focused on the role of nanoparticles in neurodegeneration and neuroprotection and nanodrug delivery for novel treatment strategies supported by European Aerospace Research and Development (EOARD), London, UK and

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