Biphasic Expression of NF-kappaB in Experimental Subarachnoid Hemorrhage in vivo and vitro

Wanchun You MD; Mengliang Zhou; Wei Li M.D.; Zong Zhuang; Xiangjun JI MD; Yong Tang; Jixin Shi MD, PhD

Department of Neurosurgery, Jinling Hospital, School of Medicine,Nanjing University, 305 East Zhongshan Road, Nanjing, 210002, Jiangsu, People's Republic of China

Introduction

It has been proven that nuclear factor-kappa B (NF-?B) is activated as a well-known transcription factor in the brain after subarachnoid hemorrhage (SAH). However, the panoramic view of NF-?B activity after SAH remained obscure.

Methods

Cultured neurons were incubated with hemoglobin to produce SAH model in vitro and were separated into 7 groups: control group and 1h, 3h, 6h, 12h, 24h, 48h hemoglobin incubation groups. One-hemorrhage rabbit SAH model was induced by the injection of autologous blood into cisterna magna. Thirty-six New Zealand rabbits were divided into 6 groups: control group and day 1, day 3, day 6, day 10, day 14 SAH groups. NF-?B activity was detected by electrophoretic mobility shift assay (EMSA) and immunohistochemistry. Real-time polymerase chain reaction (PCR) was performed to assess the downstream genes of NF-?B . NeuN Immunofluorescence and lactate dehydrogenase (LDH) quantification were used to estimate the neuron injury in vivo and in vitro.

Results

Double drastically elevated phases of NF-?B activity were detected in the brain on day 1 to day 3 and day 10 after SAH in vivo. Meanwhile, NF-?B activity showed significant increasing and biphasic peaks in 1h and 12h groups in vitro. The downstream gene expressions showed an accordant phase peaks. NeuN positive cells decreased significantly in day 3 and day 10 groups. LDH leakage exhibited significantly increasing in hemoglobin incubation groups.

Conclusions

Biphasic increasing of NF-?B activity were induced in vivo and in vitro, and the early peak indicated the injury role on neuron survival, and the late peak may involve in the deteriorated effects on neurons.

Learning Objectives

We aim to discover the molecular mechanism of brain injury after SAH, especially the NF-?B activation in vivo and vitro experiment.

References

Nijboer CH, Heijnen CJ, Groenendaal F, May MJ, van Bel F, Kavelaars A (2008) A Dual Role of the NF-?B Pathway in Neonatal Hypoxic-Ischemic Brain Damage. Stroke 39:2578-2586.