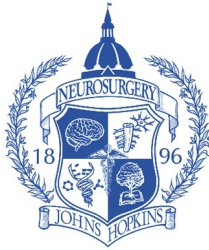


Expression of the Pro-Inflammatory Cytokine IL-1b in a Murine Transgenic Haptoglobin Model of SAH

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Introduction

Inflammation plays a critical role in the pathogenesis of vasospasm after aneurysmal subarachnoid hemorrhage (aSAH). The Hp2-2 genotype appears to be pro-inflammatory, and predisposes to symptomatic vasospasm. IL-1b is a pro-inflammatory cytokine released by macrophages and monocytes, which acts through distinct pathways to promote inflammatory cell recruitment. We generated transgenic Hp2-2 mice and measured IL1b expression, before and 24 hours post-SAH and compared it to the expression of wild type(Hp1-1) mice.

Methods

Transgenic C57Bl6-Hp2-2 mice were developed and expanded in colony; wild-type Hp1-1 animals were used for comparison. Animals were randomized to 3 groups per genotype: no-interventions (baseline, n=5), surgery-without-SAH (n=10), or surgery+SAH (n=10) and were perfused/euthanized 24-hours post-SAH. The common carotid artery(CCA), femoral artery(FA), olfactory bulbs(OB), forebrain(FB), caudate/putamen(C/P), brainstem/basilar artery(BS/BA), and cerebellum(CER) were processed for proteomic analysis(mouse cytokine array system, Bioplex23plex, Bio-Rad, Minneapolis, MN)

Results

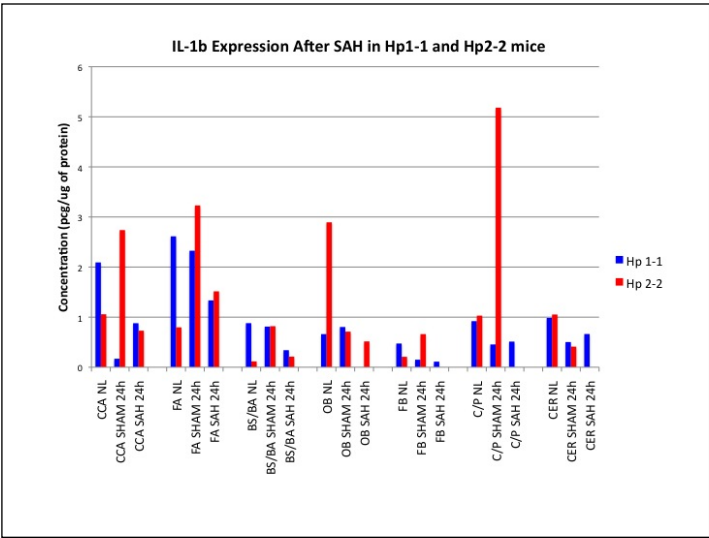
At baseline, IL-1b was higher in Hp2-2s than in Hp1-1s in the OB(2.89±0.10 vs. 0.66±0.01), C/P(1.03±0.08 vs. 0.92±0.10), and CER(1.06±0.08 vs. 0.98±0.13) and lower in the CCA(1.06±0.06 vs. 2.09±0.27), FA(0.80±0.13 vs. 2.61±0.13), BS/BA(0.12±0.0 vs. 0.88±0.10), and FB(0.21±0.02 vs. 0.47±0.03).

After surgery without SAH, IL-1b levels were higher in Hp2-2 than in Hp1-1 animals in the CCA(2.74±0.25 vs. 0.17±0.00), FA(3.23±0.25 vs. 2.32±0.09), BS/BA (0.82±0.04 vs. 0.81±0.09), FB(0.66±0.04 vs. 0.15±0.01), and C/P(5.18±0.38 vs. 0.46±0.07) and lower in the OB(0.71±0.00 vs. 0.80±0.03) and CER(0.41±0.04 vs. 0.50±0.04).

After SAH, IL-1b was higher in Hp2-2 animals in FA (1.52±0.21 vs. 1.33±0.12) and OB (0.52±0.02 vs. 0.00±0.00) and lower in CCA (0.73±0.09 vs. 0.88±0.24) and BS/BA (0.21±0.01 vs. 0.34±0.03). Data were not available for FB, C/P, and CER.

References:

Chaichana KL, Pradilla G, Huang J, Tamargo RJ (2010) Role of inflammation (leukocyte-endothelial cell interactions) in vasospasm after subarachnoid hemorrhage. World Neurosurg 73: 22-41.



Conclusions

Hp2-2 genotype is associated with lower baseline IL-1b levels that increase after surgery with/without SAH when compared to Hp1-1 mice.

Findings suggest that IL-1b contributes to inflammation after SAH, and that its activity is more pronounced in animals with an Hp2-2 genotype in this model.

Learning Objectives

To understand the role of IL-1b in the pathogenesis of cerebral vasospasm. To determine differences in IL-1b expression in animals with different haptoglobin genotypes.