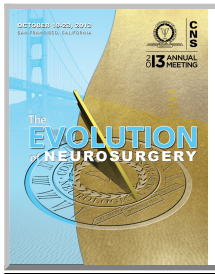

Role of Hyperhomocysteinemia in the Development of Intracranial Aneurysms

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Introduction

Hyperhomocysteminemia is involved in vascular injury and may participate in coronary disease or stroke. Whether hyperhomocysteminia facilitates the growth and/or rupture of cerebral aneurysms is unknown. In this study we explored the role of hyperhomocysteinemia in the development of cerebral aneurysms using a well-defined animal model.

Methods

Thirteen week-old female Sprague-Dawley rats were subjected to bilateral oophorectomy, ligation of the right common carotid artery and fed an 8% high-salt diet. Two weeks later they underwent ligation of bilateral posterior renal arteries. The animals were then divided into 2 groups treated with and without 1g/kg/day methionine in the drinking water. A third group rat was sham. The animals were observed for 12 weeks.

Conclusions

Hyperhomocysteinemia may promote the formation and growth of intracranial aneurysm, in association with increased oxidative stress, apoptosis and degradation of extracellular matrix. To confirm whether the vascular degradation is directly caused by hyperhomocysteinemia, further studies are underway.

Results

Plasma homocysteine level was increased by 6 folds with oral methionine administration. The incidences of aneurysm rupture were the same in both groups. However there is a higher incidence of multiple aneurysm formation in the methionine group, and the aneurysm size was larger. Oxidative stress-related NOX4, Rac1, and apoptosis-related Rac1 were up-regulated in the methionine group. The expression of MMP-9 was also increased as was the ratio of MMP-9 to TIMP2 but not of MMP-9 to TIMP1, suggesting vascular degradation due to an imbalance between the activation and inhibition of extracellular matrix metalloprotease.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) describe hyperhomocysteinemia as a possible factor in cerebral aneurysm development, and 2) discuss possible mechanisms by which homocysteinemia exsert vascular injury.

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