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Poster Session

Angiogenesis

UNDERSTANDING HOW DIFFERENT STROKE RISK FACTORS AFFECT ANGIOGENESIS IN EXPERIMENTAL CEREBRAL ISCHEMIA IN CO-MORBID RATS ANALYZED BY DCE-MRI

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Abstract

Introduction

During the last three decades, although there has been a large effort to understand the pathophysiology of cerebral ischemia, none of the drugs and neuroprotective strategies useful in experimental studies have succeeded clinically. To increase the translation to humans, the Stroke Therapy Academic Industry Roundtable (STAIR) has recommended to consider different stroke risk factors and imaging techniques in experimental studies[(1)]. As well as acute treatment, the study of long term post-stroke neurorepair mechanisms, such as angiogenesis, may offer new opportunities of treatment with a broader therapeutic window. Angiogenesis, a process increased after cerebral ischemia around the affected brain area, is reduced by risk factors such as age and obesity[(2,3)]. Dynamic enhanced-contrast imaging (DCE-MRI) is an imaging technique widely used in cancer disease to study angiogenesis, but poorly explored in the stroke field[(4)]. Our purpose was to study the influence of different stroke risk factors on the angiogenic process and its evolution after stroke in an experimental model of cerebral ischemia using DCE-MRI.

Methods

Twenty month-old corpulent (JCR:LA Cp/Cp, a model of atherosclerosis and obesity) and lean rats were used. Experimental stroke was induced by transient MCAO (90 min) by ligature. Post-stroke angiogenesis was analyzed by DCE-MRI made at 3, 7 and 28 days after tMCAO using a Bruker Biospec BMT 47/40 system (Bruker, Ettligen, Germany) operating at 4.7 T and using a 5-cm anatomically shaped homemade surface coil. Using a T1-weighted imaging sequence, 80 serial MR images were acquired before, during, and after intravenous administration of Gd-DTPA (0.2mmol/kg). Then angiogenesis, determined by brain vessel perfusion, permeability and tissue volume fractions, was analyzed by the Kety-Tofts mathematical model. To confirm MRI findings, immunofluorescence techniques were performed on brain sections. Finally, endothelial progenitor cells (EPCs) properties were evaluated using cultures of spleen EPCs from those animals.

Results

At 7 and 28 days after tMCAO, aged lean animals showed higher brain perfusion in the infarcted area than that observed in corpulent rats and, in both, a reduction in the angiogenic parameters was observed at 28d compared with the 7d time point (140% of MRI signal relative to the basal at 7d versus 118% at 28d). Histological examination confirmed that lean rats had a higher number of blood vessels in the affected area than corpulent rats at 28d. Finally, EPCs cultured from aged lean rats showed more adhesion and migration when compared with EPCs from corpulent rats, demonstrating that risk factors affect the angiogenic properties of these cells.

Conclusions

Our results show that co-morbidities impair the angiogenesis process after cerebral ischemia, and confirm that DCE-MRI is a useful technique to evaluate this process in a non-invasive way.

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