Intracranial fluids dynamics alterations and cortical thickness

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Abstract

Objectives: The issue of cortical atrophy is important in normal aging and disease since it is associated with cognitive [1] and physical impairments [2]. Cortical atrophy is potentially a relevant biomarker for the early diagnosis of Alzheimer's disease (AD) [3,4].

The vascular component is also an integral part of AD and other late-life neurodegenerative diseases. Abnormalities in blood flow appear before accumulation of abnormal proteins in AD [5–7]. The occlusion of capillaries by neutrophils are significantly higher in AD animal models than control and reduction of those occlusions with an antibody increases both blood flow and cognitive capacities [8]. Vascular alterations lead to hypoperfusion, oxidative stress and inflammation, which in turn lead to damage of neurons, glia and myelin, predominantly in the white mater [9].

Implication of vascular pathologies for gray matter remains unclear. A recent study showed that altered cerebral hemodyamics in asymptomatic carotid artery stenosis is associated with cortical thinning [10]. However there is no proven link between vascular pathologies and cortical thinning. We propose to explore brain aging with a combined biomechanical and imaging approach in order to assess both fluid dynamics alterations and brain structural modifications.

We hypothesize that there is a link between altered cerebral hemodynamics and loss of cortical thickness during brain aging.

Methods: 80 patients suspected of hydrocephalus were prospectively involved. All patients complain of gait alteration, urinary difficulties, mild apathy and ventriculomegaly on brain imaging. They all underwent brain MRI with T1 weighted images to quantify cortical thickness and phase contrast images to measure arterial, venous and CSF velocities. Lumbar infusion test was also performed to gauge lumbar pressure, a surrogate marker of intracranial pressure (ICP), and CSF dynamics. The cortical volumetric segmentation was done by an automatic post-processing analysis with FREESURFER and local thicknesses were assessed with CorThiZon [3]. Venous, arterial and CSF velocities were measured from PCMRI with BIOFLOWIMAGE software. ICP and CSF dynamics were extracted form infusion tests. Pearson correlations were calculated between cortical thickness and arterial, venous and CSF velocities, but also ICP and derived indices.

Results: Mean cortical thickness is positively correlated with mean ICP ($r = 0.48$, $p = 0.001$), ICP pulse amplitude ($r = 0.43$, $p = 0.001$), arterial flow ($r = 0.44$, $p = 0.001$), aqueductal CSF flow($r = 046$, $p = 0.001$), but negatively correlates with venous flow ($r = -0.44$, $p = 0.001$)

Conclusions: We demonstrate that cortical thickness is correlated with arterial and CSF pulsatility. The causality is more complex since it involves local microcirculation that could not be directly measured. However the association between intracranial pulsatility and gray matter thickness suggests that there is a relationship between vascular alterations at the macroscale level and the pathobiology of cortical atrophy.

References

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