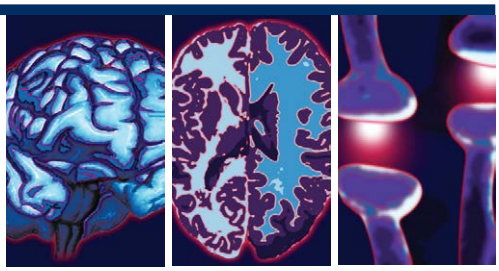

Cerebral Blood Flow, White Matter Micro-Structures and Gray Matter Function in Adult Aged 61-81 Years

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ABSTRACT

Background

Aim of this study was assess cerebral blood flow, white matter micro-structures and gray matter function, and biochemical correlates of oxidative stress in adult aged 61-81 years.

Patients and methods

The study included a total of 50 patients aged from 61 to 81 years. All patients underwent arterial spin labeling (ASL), diffusion tensor imaging (DTI) and biochemical analysis of venous blood concerning values of the selected parameters of oxidative stress.

Results and discussion

Statistically significant correlations between ASL and DTI results were observed, but none correlations between ASL, DTI and biochemical markers of oxidative stress were observed, despite showed reduced effectiveness of the body's natural antioxidant barrier in elderly people.

Conclusions

This study may be regarded preliminary to bigger comparative research. Factors influencing successful prevention of changes and strengthening the defense system may be a direction of further research.

Keywords

Aging, Antioxidant barrier, Cognitive changes, Biochemical changes, Medical imaging

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Introduction

Detailed description of aging in two contexts: biochemical (antioxidant abilities of the organism) and medical imaging (neuronal tissue degeneration) may be helpful in the assessment of functioning of normal aging organism. It may play also useful predictive role in many diseases such as Alzheimer's disease and vascular diseases such as stroke. Data ladder from molecular mechanisms to clinical symptoms may significantly support everyday clinical practice in geriatrics [1]. Deeper knowledge concerning relationship between aging, cerebral functional connectivity and variability of long-term cognitive performance both in healthy elderly subjects and patients with neurodegenerative disorders may allow for more appropriate selection of predictors, ways of diagnosis and management as far as explaining underlying pathologies and sources of risk (e.g. genetic, environmental, etc.). Altered brain network properties may be associated with pathologic processes such as oxidative stress [2]. Molecular links may be defined between e.g. stroke and Alzheimer's disease in elderly [3].

Aim of this study was assess cerebral blood flow, white matter micro-structures and gray matter function in adult aged 61-81 years.

Patients and Methods

■ Patients

Fifty adult patients aged 61-81 years participated in the study. Table 1 shows patients' overall profile.

■ Methods

Two MRI techniques were applied:

– Arterial Spin Labeling (ASL) – a noninvasive technique using arterial water as an endogenous tracer to measure cerebral blood flow (CBF),

– Diffusion Tensor Imaging (DTI) – a diffusion technique examining the brain's white matter (WM) micro-structures and gray matter (GM) function.

Three main parameters were assessed:

- Fractional Anisotropy (FA) is an index for the amount of diffusion asymmetry within a voxel which describing the degree of anisotropy of a diffusion process i.e. measure of connectivity in the brain derived from the diffusion tensor imaging (DTI) dataset,

- Enhanced Attenuation (EA),

- Anisotropy Index (AI),

Within areas:

- Anterior Commissure (AC),

- Posterior Commissure (PC),

- Projection Fibre Anterior Right (PAR),

- Projection Fibre Anterior Left (PAL),

- Projection Fibre Posterior Right (PPR),

- Projection Fibre Posterior Left (PPL),

- Medulla oblongata (M).

The material for biochemical analysis was venous blood collected in an amount of approx. 8 ml of the antecubital vein into lithium heparin tubes and tubes without anticoagulant. Blood samples were collected at 8.00. Then, collected material was transported to the Department of Biochemistry of Nicolaus Copernicus University Collegium Medicum in Bydgoszcz. Tests were carried out on the same day, within approx. 1 h of material collection. From the blood drawn into tubes without anticoagulant (approx. 3 ml) serum was obtained by centrifugation of the material over 5 min at 5000 × g, then it was transferred to Eppendorf tubes and frozen at -80°C. The prepared serum was stored to determine the activity of the oxidase ceruloplasmin (Cp). Before preparing the hemolysate, 500 µl blood was collected to determine the levels of glutathione (GSH) in the erythrocytes, the remaining aliquot of blood (approx. 5 ml) was centrifuged to obtain plasma, wherein the concentration of nitrate/nitrite was determined. The remaining cells were used for the preparation of the hemolysate, wherein the dialdehyde malonic concentration (MDA) and the activity of the enzymes: glutathione peroxidase (cGPx), glutathione S-transferase (GST) and superoxide dismutase (SOD-1) were determined. MyoD (myogenic determination) protein was also assessed.

Table 1: Patients overall profile.

Parameter	Study group (n=50)
Age (years):	
Mean	68.28
SD	4.79
Min	61
Median	67
Max	81

■ Statistical analysis

All the data in this study were collected and stored using the MS Access 2013 software. The Shapiro-Wilk test was used as a powerful normality test. Where, available mean and standard deviation (SD) were calculated to show the results of this study. Spearman's' rho was used to assess correlations. The strength of the correlation using the following guide for the absolute value of:

- .00-.19: "very weak",
- .20-.39: "weak",
- .40-.59: "moderate",
- .60-.79: "strong",
- .80-1.0: "very strong".

Statistical analysis was performed using Statistica 12 (Statsoft). The difference was statistically significant at $p<0.05$.

■ Ethical issues

This study was conducted in accordance with the Declaration of Helsinki and the guidelines for Good Clinical Practice (GCP). Freely given written informed consent was obtained from every patient prior to the study.

Results

Results are presented in **Tables 2 and 3**. Significant differences of ASL and DTI results between sides were observed **(Table 2)**.

Coefficient of variation (CV) ranged from 6% to 45%.

None correlations among age and ASL parameters were observed. Moderate negative

Table 2: ASL results – cerebral blood flow assessment.

Parameter		Study group (n=50)	
		Mean	SD
ASL			
Hippocampus (R)		44.72	6.79
Hippocampus (L)		42.39	8.06
Thalamus (R)		53.97	9.08
Thalamus (L)		52.07	8.06
Cingulate gyrus (R)		56.45	15.16
Cingulate gyrus (L)		55.20	14.51
Occipital lobe (R)		45.23	12.67
Occipital lobe (L)		44.33	12.48
Cerebellum		43.82	8.29
DTI			
Anterior comissure (AC)	Fractional anisotropy (FA-AC)	0.78	0.05
	Expotential attenuation (EA-AC)	0.44	0.03
	Anisotropy index (AI-AC)	0.47	0.07
Posterior commisure (PC)	Fractional anisotropy (FA-PC)	0.79	0.05
	Expotential attenuation (EA-PC)	0.45	0.03
	Anisotropy index (AI-PC)	0.46	0.08
Projective anterior (PAR)	Fractional anisotropy (FA-PAR)	0.40	0.04
	Expotential attenuation (EA-PAR)	0.45	0.02
	Anisotropy index (AI-PAR)	0.09	0.02
Projective anterior (PAL)	Fractional anisotropy (FA-PAL)	0.37	0.04
	Expotential attenuation (EA-PAL)	0.43	0.02
	Anisotropy index (AI-PAL)	0.08	0.01
Projective posterior (PPR)	Fractional anisotropy (FA-PPR)	0.44	0.05
	Expotential attenuation (EA-PPR)	0.56	0.08
	Anisotropy index (AI-PPR)	0.14	0.06
Projective posterior (PPL)	Fractional anisotropy (FA-PPL)	0.43	0.05
	Expotential attenuation (EA-PPL)	0.44	0.03
	Anisotropy index (AI-PPL)	0.11	0.02
Medulla (M)	Fractional anisotropy (FA-M)	0.43	0.06
	Expotential attenuation (EA-M)	0.46	0.02
	Anisotropy index (AI-M)	0.10	0.04

Table 3: Correlations (Spearmans' rho values) among ASL and DTI parameters.

DTI parameters \ ASL parameters	Hippocampus R	Hippocampus L	Thalamus R	Thalamus L	Cingulate gyrus R	Cingulate gyrus L	Occipital lobe R	Occipital lobe L	Cerebellum
FA-AC	n.s.	n.s.	n.s.	n.s.	n.s.	r=0.506 p=0.000	n.s.	n.s.	n.s.
EA-AC	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
AI-AC	n.s.	n.s.	n.s.	n.s.	n.s.	r=0.370 p=0.008	n.s.	n.s.	n.s.
FA-PC	n.s.	n.s.	n.s.	n.s.	n.s.	r=0.326 p=0.021	n.s.	n.s.	n.s.
EA-PC	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
AI-PC	r=-0.363 p=0.010	r=-0.290 p=0.041	n.s.	n.s.	r=-0.315 p=0.026	r=-0.298 p=0.035	r=-0.367 p=0.009	r=-0.308 p=0.030	r=-0.304 p=0.032
FA-PAR	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EA-PAR	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	r=0.309 p=0.029	n.s.	n.s.
AI-PAR	n.s.	r=-0.311 p=0.028	r=-0.326 p=0.021	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
FA-PAL	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EA-PAL	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
AI-PAL	n.s.	n.s.	r=-0.317 p=0.025	r=-0.348 p=0.013	n.s.	n.s.	n.s.	r=-0.293 p=0.039	r=-0.450 p=0.001
FA-PPR	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EA-PPR	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
AI-PPR	n.s.	-0.330 p=0.019	-0.319 p=0.024	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
FA-PPL	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EA-PPL	n.s.	n.s.	n.s.	n.s.	r=0.284 p=0.045	r=0.327 p=0.020	n.s.	n.s.	r=0.290 p=0.041
AI-PPL	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
FA-M	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
EA-M	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
AI-M	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

correlation (rho=-0.493) between age and DTI parameter (EA-PPR) was observed. Multiple moderate correlations among ASL and DTI parameters were observed **(Table 3)**.

Discussion

ASL offers reliable absolute quantification of CBF with higher spatial and temporal resolution than other techniques, but its routine application is still limited. According to review by Borogovac & Asslani ASL offers several advantages over blood oxygenation level-dependent (BOLD) MRI, especially in applications where slow varying changes in brain function are investigated, such as spatial localization, signal quantification, power spectrum and sensitivity. None statistically significant correlations between ASL and biochemical markers of oxidative stress and DTI and biochemical markers of oxidative stress were observed, despite intensification of the oxidative stress was observed in the course of age-dependent diseases. Relevant moderate correlations among DTI parameters and MyoD - a protein playing a major role in regulating muscle differentiation - were observed for EA-PAR, FA-PAL and EA-PPL [4,5]. ASL is more often used in two cases: normal aging (but also in Alzheimer's disease and shizophrenia) and vascular diseases (stroke, carotid occlusive diseases) [6-11]. In aging people changes in CBF (in time or compared to healthy study group) can occur independently of structural changes in the brain or precede them [5]. Comparison of CBF between young and showed the largest partial volume effects (PVE) contribution in the frontal lobe (additional 10% and 12% increase) in the age-related CBF difference between men and women, respectively [6]. DTI and MRI techniques are used for examining the brain's white matter (WM) micro-structures and gray matter (GM) function [12]. Seed location may affect the ability to detect between-group differences in structural networks, e.g. healthy controls and patients with AD [13]. DTI may help assess microstructural basis of white matter during maturation and

aging: it is regional specific, not uniformal [14]. Associated age-related changes in task switching and performance may be observed [15].

We still look for the objective measure. Perfusion computed tomography (PCT) is regarded minimally invasive and widely available technique for brain blood flow assessment, including calculation of CBF, cerebral blood volume (CBV), time to peak (TTP), and peak enhancement intensity (PEI). From the other side its application may be restricted by large variation of results. PCT, TTP or CBV ratios may be more suitable than CBF values patients with chronic cerebral ischemia. CBF inter- and intraobserver variability is lower (differences between two observations: 30%) [16,17]. Thus estimating of reproducibility of imaging results may constitute a real challenge [18-20].

Limitation of the study is low number of participants, convenience sample, and lack of reference group. This study may be regarded preliminary to bigger comparative research. Factors influencing successful prevention of changes and strengthening the defense system may be a direction of further research.

Conclusions

Statistically significant correlations between ASL and DTI results were observed. This study may be regarded preliminary to bigger comparative research.

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