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Gray matter volume in relation to cardio-vascular stiffness

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ABSTRACT

Background: Hemodynamic disturbances are associated with aging as well as the chronic process of left ventricular and arterial stiffening. This process can influence gray matter volume and thereby contribute to brain atrophy. We performed a comprehensive assessment of left ventricular and arterial function as well as central hemodynamics. These data were correlated with gray matter volume (GMV) as evaluated by magnetic resonance imaging (MRI).
Methods: GMV and aortic stiffness were estimated using MRI. Left ventricular end-systolic elastance or stiffness (Ees), arterial elastance (Ea) and total arterial compliance (TAC) were determined by echocardiography. Central hemodynamics were assessed using pulse wave analysis.
Results: Seventy-five healthy subjects (42 women, 33 men, mean age of 58 years) were recruited. The clinical analyses showed that GMV correlates significantly and inversely with age ($r = -0.37$, $P = 0.001$), end-systolic LV stiffness ($r = -0.39$, $P = 0.0009$), augmentation pressure ($r = -0.48$, $P < 0.0001$), arterial elastance ($r = -0.27$, $P = 0.02$) and aortic stiffness ($r = -0.23$, $P = 0.04$), as determined by aortic pulse wave velocity (aPWV). GMV correlated significantly with total arterial compliance ($r = 0.23$, $P = 0.04$). Stepwise forward multiple regression analysis revealed that 35% of variance ($P < 0.0001$) in GMV is attributed to aPWV, Ees and AP.
Conclusions: Left ventricular end-systolic stiffness, augmentation of central arterial pressure and aortic stiffness are associated independently and negatively with GMV. These associations suggested that brain atrophy is influenced by hemodynamic factors.

1. Introduction

Mismatches between the characteristics of compliant and stiff vessels can result in increased arterial pulsatility that is transmitted to organs with high blood flow such as the brain [1–3]. This phenomenon mediates the structural damage that results in brain atrophy, vascular mediated dementia or stroke [4–6]. Heart failure could also contribute to structural brain damage. Recent studies performed in subjects with impaired left ventricular function showed that a low left ventricular ejection fraction correlates with gray matter volume (GMV) [7]. Moreover, blood pressure (BP) and cardiac function might have independent and interactive effects on brain volume in subjects with heart failure [8]. Some of these observations were performed in studies without appropriate controls, such as healthy age-matched subjects.

Several sets of data suggest that arterial stiffness and left ventricular (LV) stiffness are associated with normal aging [9,10]. Moreover, this process contributes to cardiovascular diseases including heart failure, hypertension and stroke [5,11,12]. Increased arterial stiffness has thus been associated with vascular-mediated dementia and brain atrophy; however, we propose that hemodynamic disturbances associated with aging as well as the chronic process of LV and arterial stiffening could influence GMV independently of heart failure or hypertension. Accordingly, we performed a comprehensive assessment of LV and arterial function as well as central hemodynamics, and correlated the data with GMV as evaluated by magnetic resonance imaging (MRI), in a cohort of healthy subjects.

2. Materials and methods

2.1. Characteristics of subjects

Seventy-five consecutive healthy subjects (42 women, 33 men, mean age of 58 years) were recruited through local advertisement.

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The study subjects were examined physically and their medical history was taken. The baseline clinical characteristics of the patients are given in Table 1. None of the subjects were taking any medication and their resting ECG values were completely normal, although patients with a single measurement of BP > 140/90 were not excluded from the study. Individuals with a history of hypertension, diabetes or any form of chronic medication were excluded from the study. The Poznan University Ethics Committee approved the study protocol and written informed consent was obtained from all participants.

2.2. Brain magnetic resonance imaging

MRI scans of the brains of all subjects were processed on a Siemens Magnetom Avanto 1.5T scanner (45 mT/m @ 200 T/m/s, Siemens, Erlangen, Germany) with 12-channel head RF coils. All patients underwent the same brain MRI protocol consisting of transaxial and sagittal T1-w, T2-w, PD, FLAIR and DWI scans. All scans were performed with a 4-mm slice thickness, no slice gap, 38 slices, covering the entire brain, a 230 × 230 mm field-of-view and 256 × 256 scan matrix. The individual scan parameters were: T1-w: repetition time (TR)/echo time (TE) 480/8 ms, PD: TR/TE 4200/22 ms, T2-w: TR/TE 4250/88 ms and FLAIR: TR/TI/TE 9000/2500/111 ms.

Three-dimensional high-resolution T1-weighted images (MPRGE — Magnetization Prepared Rapid Gradient-Echo): TR 2400/TI 1000/TE 3.6 and slice thickness of 1.2 mm were obtained to calculate white matter (WM) and gray matter (GM) brain volumes.

Morphometric analysis of brain structures (WM and GM volumes) was completed with MRIcro Version 1.35 software (www.sph.s.edu/comb/rorden/mricro.html).

2.3. MRI assessment of aortic pulse wave velocity

MRI examinations were performed on a 1.5 T scanner (Siemens Magnetom Avanto, PA, USA) with the use of a 6-channel phased-array body coil combined with a 6-channel spine matrix coil. The study protocol consisted of the following sequence: scout images to deliver precisely targeted three-plane images involving the ascending aorta, aortic arch and descending thoracic aorta. Steady State Free Precession (SSFP) cine imaging was performed for a candy cane view with appropriately positioned phase contrast sequences.

The aPWV was measured in the aortic arch and phase contrast sequences were acquired at two levels: the ascending aorta 1 cm above the bulb, and the descending aorta at the level of pulmonary bifurcation.

Table 1
Left ventricular morphology and function, gray matter volume and aortic stiffness.

Characteristic	Total cohort (n = 75)	Women (n = 42)	Men (n = 33)	*P* value*
Age (years)	58 ± 0.7	59 ± 0.9	57 ± 0.9	0.08
LVIDd (cm)	4.3 ± 0.1	4.1 ± 0.1	4.6 ± 0.1	<0.0001
LVIDs (cm)	2.8 ± 0.1	2.7 ± 0.1	3.0 ± 0.1	0.0009
EF (%)	61 ± 1	63 ± 1	59 ± 2	0.11
E/E′ (cm/s)	8.3 ± 0.3	9.0 ± 0.4	7.5 ± 0.4	0.006
SV (mL)	74 ± 2	68 ± 3	82 ± 2	0.0003
CO (mL/min)	3676 ± 127	3115 ± 110	4389 ± 193	<0.0001
Ea (mm Hg/mL)	2.1 ± 0.1	2.3 ± 0.1	1.7 ± 0.1	<0.0001
Ees (mm Hg/mL)	3.6 ± 0.1	4.1 ± 0.1	2.9 ± 0.2	<0.0001
Ea/Ees	0.6 ± 0.02	0.58 ± 0.02	0.62 ± 0.03	0.19
TAC (mL/mm Hg)	1.6 ± 0.1	1.5 ± 0.1	1.6 ± 0.1	0.006
AP (mm Hg)	10.5 ± 0.6	12.4 ± 0.8	8.0 ± 0.6	<0.0001
aPWV (m/s)	6.4 ± 0.1	6.4 ± 0.2	6.5 ± 0.2	0.69
Gray matter volume (mL)	580 ± 4	572 ± 5	591 ± 5	0.01

LVIDd — left ventricular internal diameter in diastole; LVIDs — left ventricular internal diameter in systole; EF — ejection fraction; E/E′ — peak early velocity to peak early annular velocity ratio; CO — cardiac output; Ees — left ventricular end-systolic stiffness (elastance); Ea — arterial elastance; TAC — total arterial compliance; AP — augmentation pressure; aPWV — aortic pulse wave velocity.
* $P < 0.05$ was considered significant.

A simple equation was used to calculate PWV:

$$PWV = \Delta x/\Delta t$$

where,

Δx distance between the two levels of flow;
Δt time displacement of the pulse wave between two points of measurement, calculated as the period between the mid-heights of the pulse wave curves.

The measurements were performed on a dedicated workstation (Siemens Medical Solution, PA, USA).

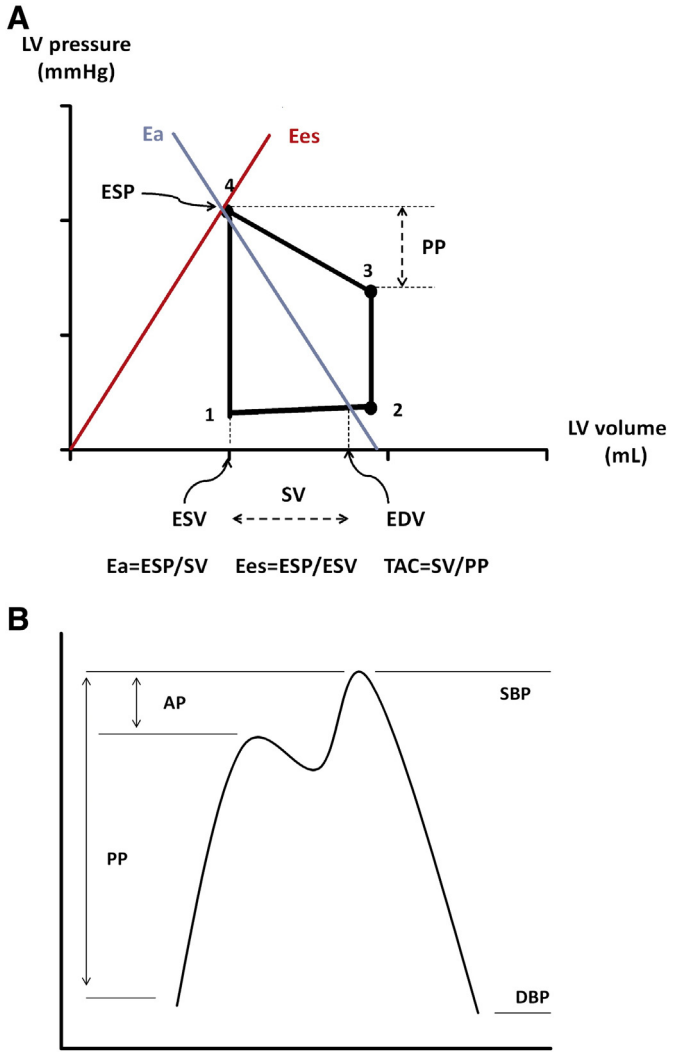

Fig. 1. Schematic representation of pressure–volume loop of the left ventricle (part A) and central blood pressure wave (part B). Part A. The black box represents the pressure volume loop (PVL) of the left ventricle. Points on the loop depict: 1 — mitral valve opening, 2 — mitral valve closure, 3 — aortic valve opening, and 4 — aortic valve closure. Red line represents the end-systolic pressure–volume relationship and the slope of the line is the left ventricular end systolic stiffness (elastance) — Ees. The slope of the blue line represents arterial elastance (Ea). ESP — end systolic pressure; PP — pulse pressure; ESV — end systolic volume; EDV — end diastolic volume; SV — stroke volume; LV — left ventricle; TAC — total arterial compliance. Part B. AP — augmentation pressure; PP — pulse pressure; SBP — systolic blood pressure; DBP — diastolic blood pressure.