



Effect of Hypertension Treatment on Regional Cerebral Blood Flow in Older Adults

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Background:

Hypertension is a well-established risk factor for cardiovascular disease, stroke, and Alzheimer’s disease and related dementias (ADRD) (1). The HIPAC Trial (Hypertension, Intracranial Pulsatility and Brain Amyloid-beta Accumulation in Older Adults) (NCT03354143) aims to determine if lowering blood pressure (BP) using antihypertensive drugs alters brain pulsatility and reduces brain amyloid beta protein accumulation in older adults. In this study, we aim to understand the relationships between BP and regional cerebral blood flow (CBF), as well as the treatment effect of BP medication on CBF.

Methods:

In the HIPAC trial, we obtained high-quality baseline MRI data from 85 subjects (65 ± 6 years old, 37 male). 59 subjects had normal BP (n = 41) or had high BP but without prior BP medication treatment (n = 18). Over the 12 months of intervention,14 subjects were randomized into the standard care arm, and 21 subjects were randomized into the intensive treatment arm with BP lowering medication. 24-hour systolic blood pressure (SBP) and diastolic blood pressure (DBP) were collected during the intervention period. All subjects were scanned on a GE Discovery 3T MR750W MRI scanner with a 48-channel head-neck coil with a comprehensive neuroimaging protocol at baseline and 12 months after the intervention. The protocol included a 3D pseudo-continuous arterial spin-labeled (3D pCASL) pulse sequence to quantify regional CBF. The key parameters were recommended by the ISMRM Perfusion Study Group (2). The sequence parameters were: fast spiral acquisition, 32 4-mm axial slices, TE = 9.83 ms, TR = 4.81 s, 8 spiral arms with 512 sampling points per arm, effective resolution = 3.22 mm × 3.22 mm, reconstructed matrix size = 128 × 128, number of excitation (number of label-control pairs) = 3, FOV = 22 cm × 22 cm, receiver bandwidth = ± 62.5 kHz, labeling duration = 1.45 s, saturation time = 2 s, and post labeling delay time = 2.025 s. CBF maps were generated based on the equation proposed by the ISMRM Perfusion Study Group (2), and based on sequence-specific information provided by the vendor. The CBF maps were aligned to the 3D T1-weighted MPRAGE images. The mean CBF values were calculated in all regions segmented by FreeSurfer (3). Pearson correlations were calculated between SBP/DBP and CBF at gray matter. Pair *t* tests were carried out on the mean CBF at the different brain regions segmented with FreeSurfer between the two time points for each group (standard care and intensive BP medication treatment).

Discussion:

The negative correlation between high blood pressure in cross-sectional study and increase in CBF after intensive BP lowering for 12 months in our randomized trial is consistent with previous studies (4). The increases in gray matter CBF with intensive antihypertensive treatment provide a biological mechanism in support of clinical studies that treatment of hypertension reduced the risks of developing ADRD (5).

Conclusion:

In older adults, high BP leads to a decrease of CBF in gray matter. Intensive BP treatment increases the CBF.

References:

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Results:

Among the 59 subjects with normal BP and high BP but without prior BP medication treatment, the global CBF in gray matter was found significantly correlated with DBP ($r = -0.279$, $P = 0.0326$) (Figure 1) but only a trend on SBP ($r = -0.220$, $P = 0.0945$). The BP was reduced from 134±9.8/76±5.0 to 112±7.2/65±6.5 mmHg in the intensive treatment group and from 139±11.4/76±12.0 to 122±8.0/67±7.9 mmHg in the standard group. The standard care did not show a significant effect on the overall CBF in gray matter (45.7±4.9 before and 46.3±8.5 ml blood/100g tissue/min after, 1.19% increase, $P = 0.797$), but the intensive BP medication treatment showed a significant effect (46.2±7.1 before and 50.2±10.3 ml blood/100g tissue/min after, 8.84% increase, $P = 0.0245$) (Figure 2). The effect of the intensive BP treatment is global, affecting 70% ($P < 0.05$, uncorrected) of the gray-matter regions segmented with FreeSurfer, including the right hippocampus (9.71% increase, $P = 0.00972$) and left hippocampus (9.84% increase, $P = 0.0203$).

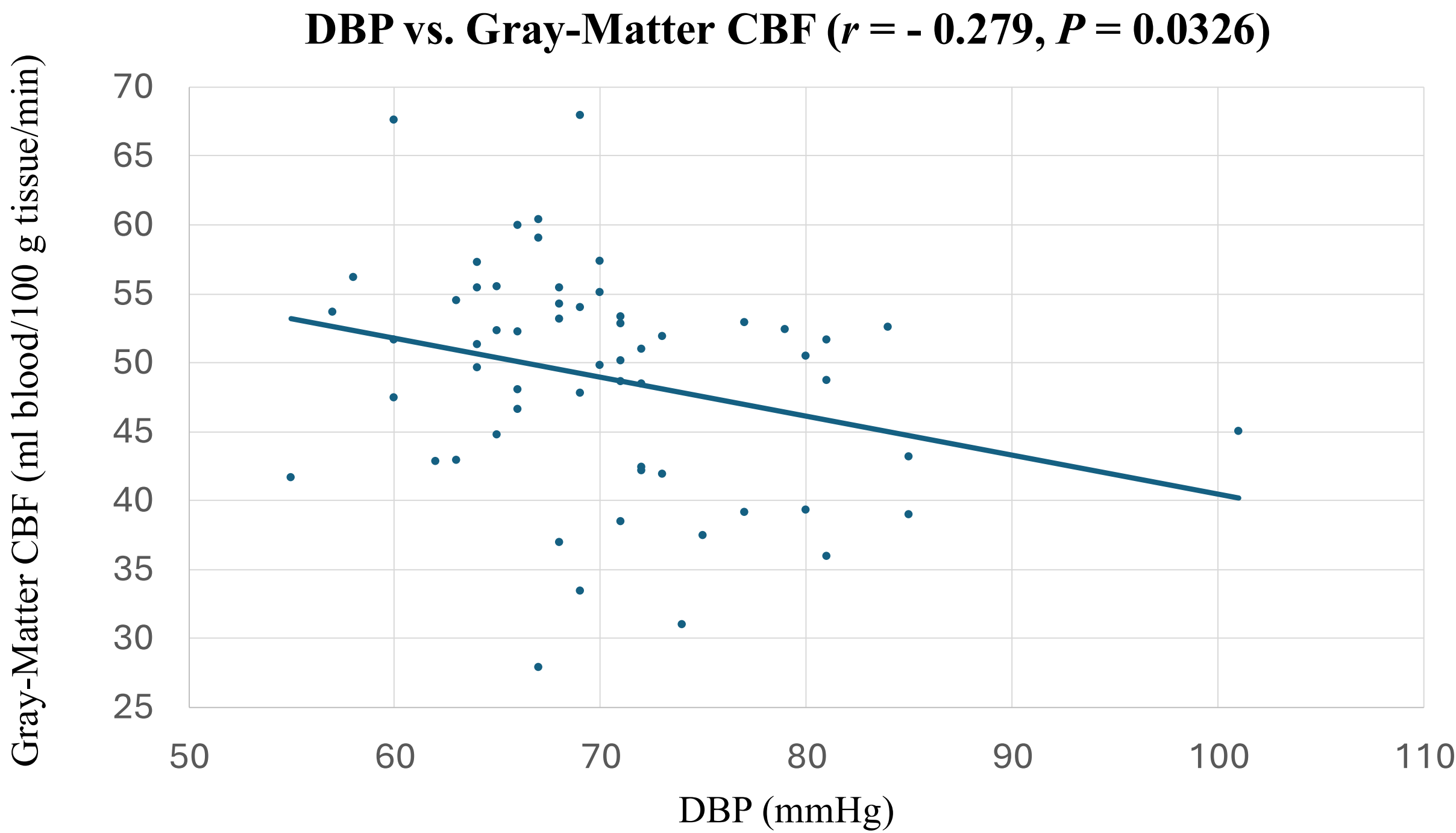


Figure 1. The global CBF in gray matter was found significantly correlated with diastolic blood pressure (DBP). (n = 59)

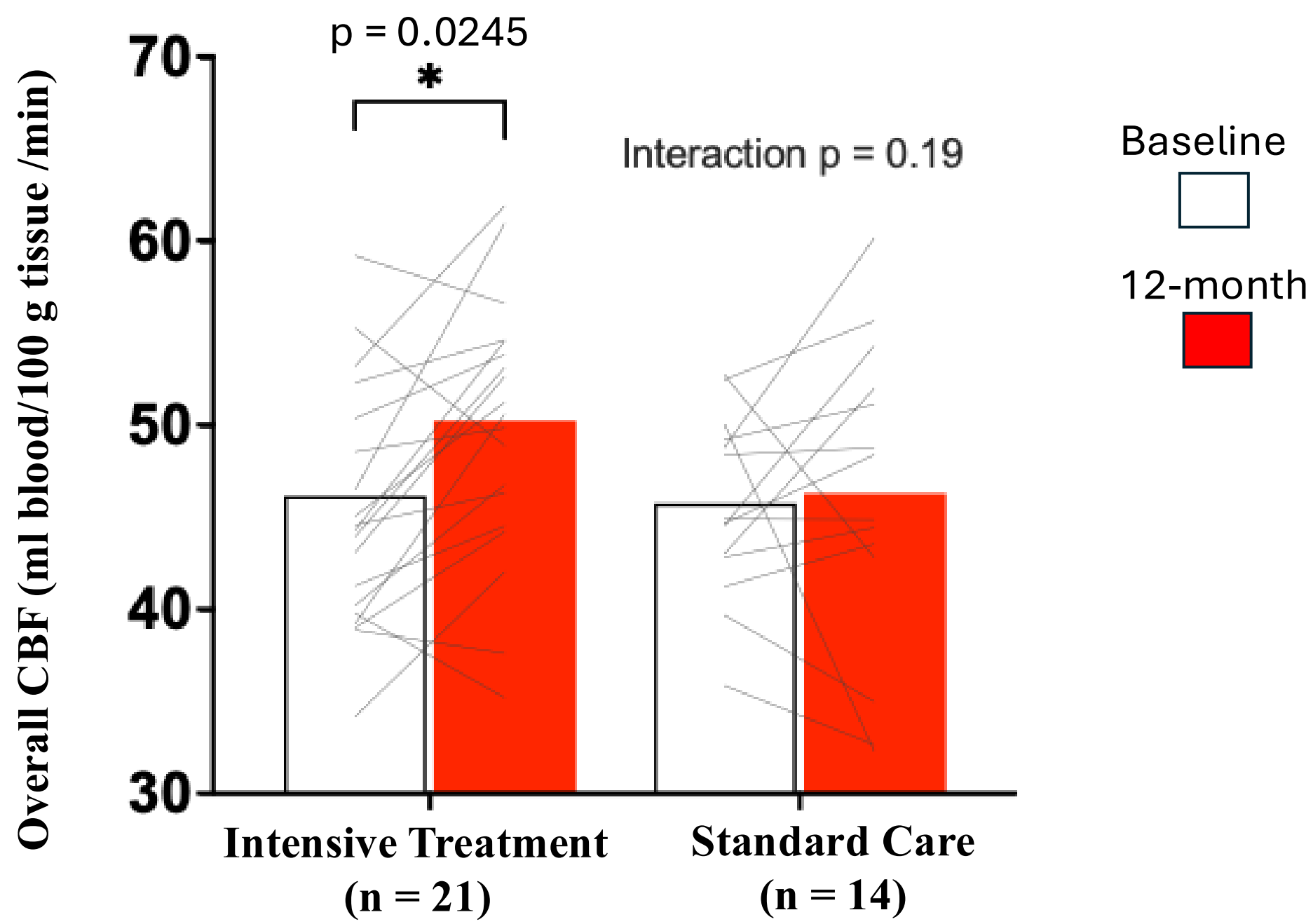


Figure 2. The effect of BP medication treatment on overall CBF in gray matter.