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Title

Compromised blood brain barrier function in patients with heart failure

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Compromised Blood Brain Barrier Function in Patients with Heart Failure

Heart failure (HF) patients show brain injury, but the underlying cause for this neural damage is unknown. A potential cause for this brain injury is alteration in the blood brain barrier (BBB) function, but BBB changes have not been reported in HF. Therefore, the specific aim of this pilot study was to examine the BBB function in HF compared to healthy controls. **METHODS:** We assessed global brain arterial transit time (ATT) and water exchange rates across the BBB values [indicator of BBB status ($K_w = P_{sw}/V_c$; P_{sw} = capillary permeability surface area product of water, V_c = distribution volume of water tracer in capillary space)] in HF compared to control subjects, using diffusion-weighted pCASL procedures developed by Co-Investigator Dr. Wang and his colleagues.^{28,29,42} We collected diffusion-weighted pCASL data from 3 HF subjects (age, 52 ± 19 years), and 6 control subjects (age, 53 ± 3 years), using a 3.0 Tesla MRI scanner. ATT and

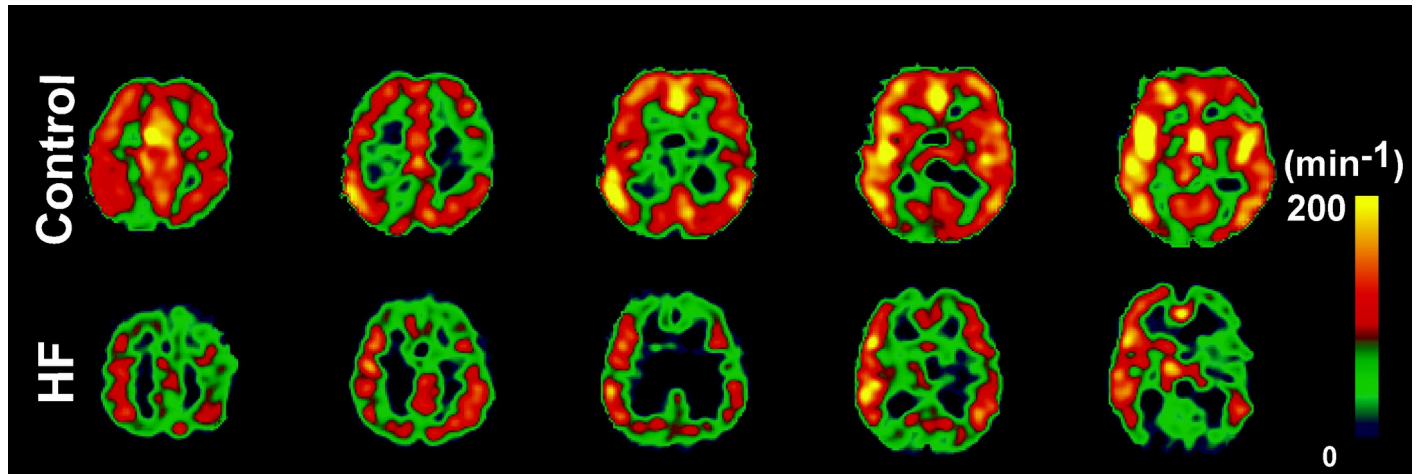


Figure 2. K_w maps (indicator of BBB function) from a control subject and a HF patient. Multiple brain regions in HF subject show reduced K_w values compared with control subject (sites with hot vs. cool color).

K_w maps were calculated from diffusion-weighted pCASL data, as described earlier.²⁸⁻³⁰ Global brain mean ATT and K_w values were calculated and compared between the groups using two-sample t-tests. **RESULTS:** Global brain K_w values were lower in HF (HF vs controls; 87.8 ± 13.5 vs 105.3 ± 21.5 min^{-1} ; $p = 0.2$; effect size = 0.97), suggestive of reduced water exchange rates across the BBB, compared to control subjects, with ATT values (1.81 ± 0.17 vs 1.82 ± 0.12 sec; $p = 0.93$; effect size = 0.07) comparable to controls. A set of K_w maps from a HF and a control subject (Figure 2) are displayed showing global reduction in K_w values in HF subject.

CONCLUSIONS: HF subjects showed lower K_w values over controls, with ATT values equivalent to control values, indicating compromised BBB function with intact large arteries. The compromised BBB function can contribute to damage of neural tissue in HF subjects. The findings suggest a need to repair BBB function, with strategies commonly-used in other fields, to protect neural tissue in the condition.