Effect of hyperinsulinemia on cerebral autoregulation

Iman N. Lloyd[1], B Shariffi[1], JL Harper[1], JA Smith[1], CM Manrique-Acevedo[2,3,4], J Padilla[1,4], JK Limberg[1]

[1]Department of Nutrition & Exercise Physiology, University of Missouri [2]Division of Endocrinology, Diabetes & Metabolism, Department of Medicine, University of Missouri; [3]Research Services, Harry S. Truman Memorial Veterans Hospital; [4]Dalton Cardiovascular Research Center, University of Missouri

BACKGROUND

- Hyperinsulinemia has profound vasodilatory effects within the skeletal muscle vasculature in healthy young adults.
- We recently showed hyperinsulinemia in healthy young adults has no effect on cerebrovascular vasodilation.
- We postulate a lack of change in cerebral blood flow during hyperinsulinemia may be due to the importance of autoregulation in the cerebral circulation (*i.e.,* the ability of the cerebral circulation to maintain a constant level of blood flow).

AIM

We sought to examine the acute impact of hyperinsulinemia on cerebral autoregulation.

HYPOTHESIS

We hypothesized cerebral autoregulatory gain in the low (0.07 – 0.20 Hz) frequency range will be greater during hyperinsulinemia when compared to baseline.

METHODS

- **Participants:** 11 healthy young adults (5 men, 6 women; 25±2 yrs, 24±1 kg/m^2)
- **Instrumentation:** Middle cerebral artery velocity (MCAv) was measured with transcranial Doppler ultrasound. Mean arterial blood pressure (MABP) was measured continuously by finger photoplethysmography. Cerebrovascular conductance index (CVCi = MCAv/MABP x 100) was calculated.
- **Infusion:** Insulin was infused intravenously for 60 minutes (40 mU/m^2 body surface area/min) during which time exogenous glucose was infused to maintain euglycemia.

Fig 1: Study set-up, including transcranial Doppler ultrasound, intravenous infusions, and non-invasive finger blood pressure monitoring (finger photoplethysmography.)

METHODS

- **Transfer Function Analysis:** Mean values of blood pressure and cerebral blood flow velocity were obtained for each cardiac cycle. A spectral analysis algorithm (Fast Fourier Transform) was used to obtain spectral estimates in the frequency domain. Auto- and cross-spectrum were used to obtain estimates of coherence function, amplitude (gain), and phase frequency responses.

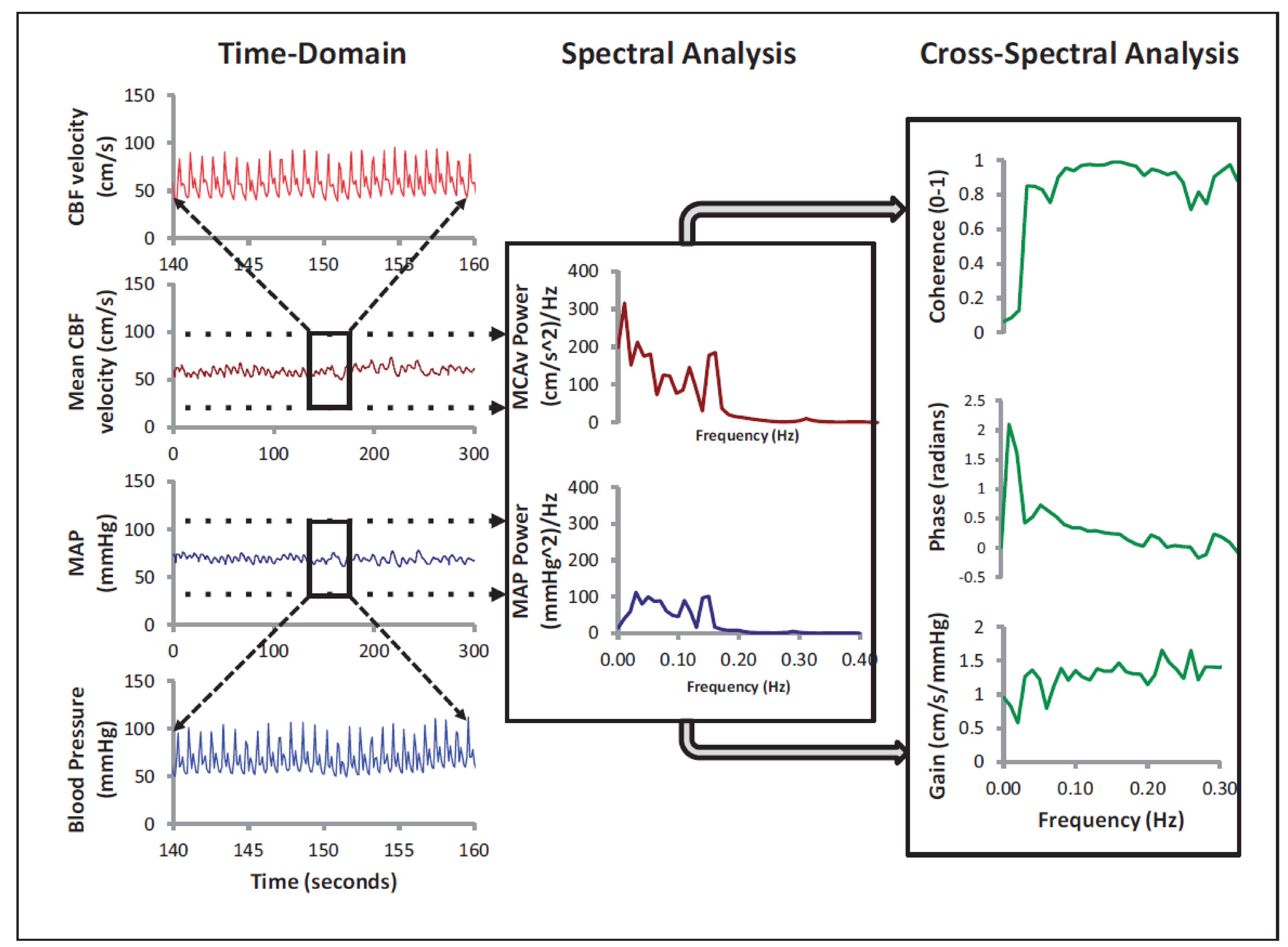


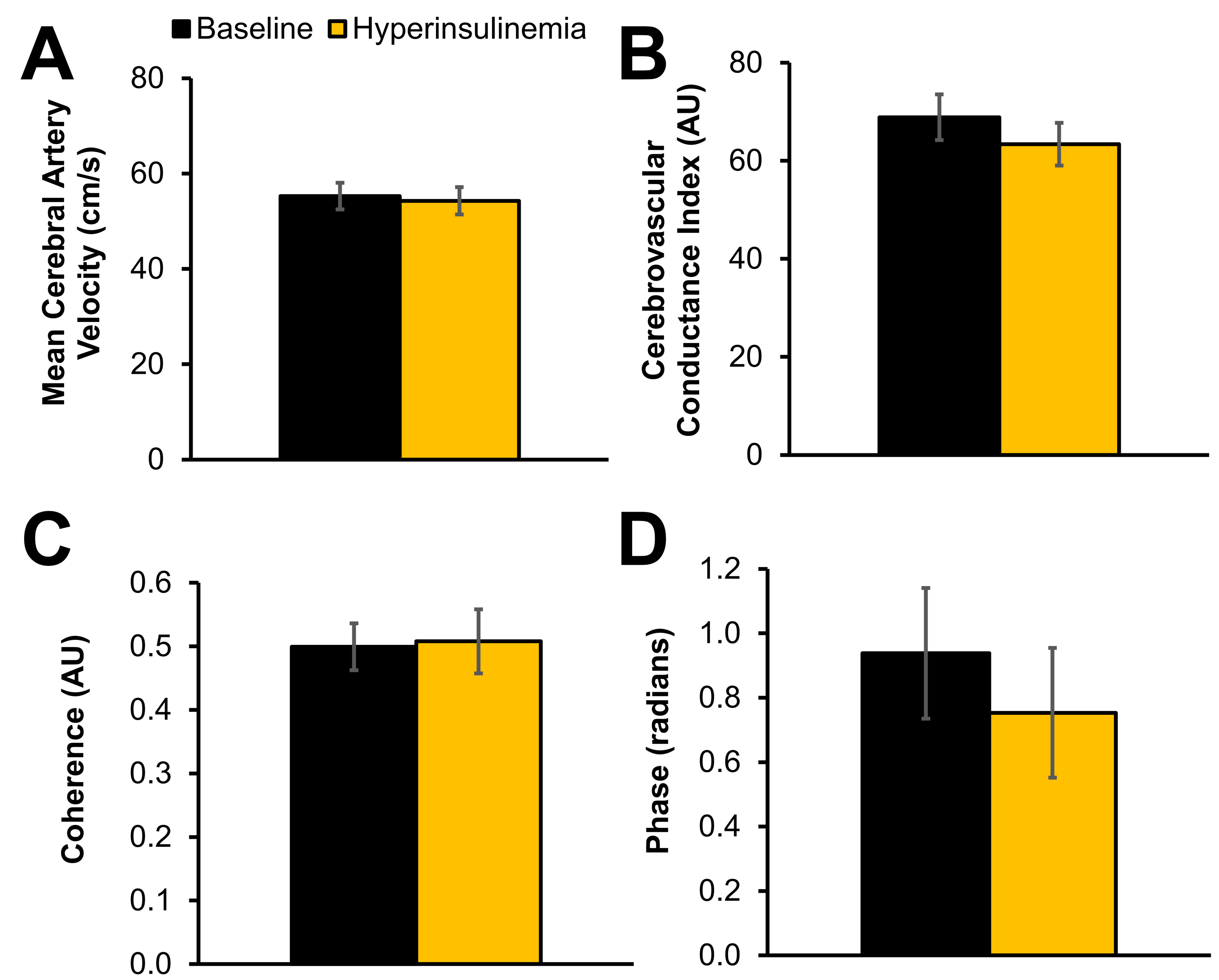
Fig 2: Cerebral Autoregulation Analysis. Transfer function gain, phase, and coherence function between changes in mean arterial blood pressure (MAP) and middle cerebral artery blood flow (CBF) velocity (MCAv) were estimated using the Welch method. Main outcomes were determined in the low (0.07-0.20 Hz) frequency range. Figure adapted from Claassen J, et al. *JCBFM*, 2016.

RESULTS

	Baseline	Hyperinsulinemia
Heart rate (beats/min)	59±3	64±3*
Mean blood pressure (mmHg)	82±3	87±3*
Cardiac output (L/min)	5.4±0.3	6.2±0.4*
Glucose (mg/dL)	74±2	75±3
Insulin (µIU/L)	6±1	40±2

Table 1: Hemodynamic and humoral responses to acute hyperinsulinemia. Mean ± SEM from n=11, unless noted (Insulin, n=8). Students paired t-test. *$P \le 0.05$ vs Baseline.

RESULTS



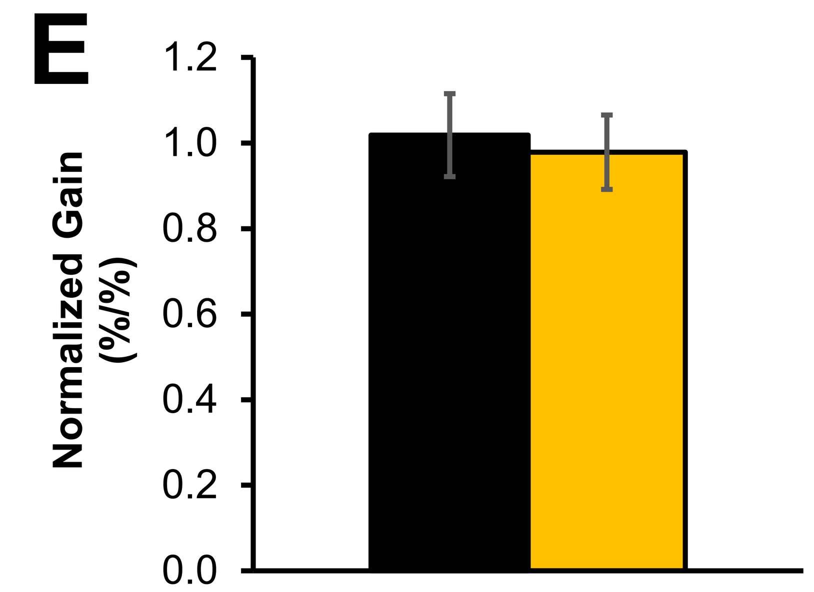


Fig 3 Cerebral autoregulation during hyperinsulinemia. There was no effect of hyperinsulinemia on middle cerebral artery velocity (P=0.73) or cerebrovascular conductance index (P=0.13). There was no effect of hyperinsulinemia on cerebral coherence (P=0.88), phase frequency (P=0.34), or normalized gain (P=0.78).

CONCLUSIONS

- Following a 60-minute systemic insulin infusion there is no change in MCAv or CVCi (**Fig 3A-B**), nor cerebral autoregulatory gain (**Fig 4E**), in healthy young adults.
- These findings indicate that during hyperinsulinemia, sensitivity of the cerebrovascular circulation to changes in blood pressure (*i.e.,* cerebral autoregulation) is unaltered.
- Whether these results translate to disease states and the implications for cerebrovascular health have yet to be explored.

Funding: Margaret W. Mangel Faculty Research Catalyst Fund (JP, JKL), NIH HL137769 (JP). **IRB#** 20166225