Webinar Q&A Report:
An Integrated Understanding of Pressure and Flow – An Essential Partnership

In your stroke model how are you controlling arterial CO2 levels? Have you assessed arterial blood gases during your prep? If not how do you account for potential group differences in CO2?

The short answer is that we don't yet have the ability to monitor or control CO2 in our stroke rats. Most of our data was presented from conscious rats, where it would be extremely difficult to monitor end tidal or arterial CO2 in a meaningful way (would require handing the animals to take a blood sample = stress and breathing changes). We are considering whether to take arterial CO2 samples while our rats are under anesthesia – we are limited in how many samples we could take given the small blood volumes in rodents, but it may be worth doing at least a baseline comparison between groups during the stroke and reperfusion periods.

Does auto regulation take place over longer time i.e. minutes to hours?

We believe that cerebral autoregulation is more effective at preserving CBF over longer time periods. But there may be scenarios and/or pathologies where this is not the case, for example some patients with hypertension appear to have reduced CBF (eg https://pubmed.ncbi.nlm.nih.gov/27672161/)

Did you measure pO2 in the penumbra during general anesthesia?

Yes. Because we use isoflurane anesthesia delivered in 100% O2, we would normally see a quite dramatic increase in tissue oxygenation during general anesthesia, due to the hyperoxia as well as likely direct vasodilatory effects of volatile anesthetic agents. Blood flow to the penumbra is obviously reduced during stroke; as shown in my presentation, penumbra O2 still increases with general anesthesia in Wistar rats, but falls slightly in

hypertensive rats. This suggests that the ability of collateral vasculature to preserve penumbral blood flow may be impaired in hypertensive rats.

Is there any relationship between water intake and blood pressure?

Blood pressure is very well buffered against changes in fluid intake, as long as you are ingesting sensible quantities of water and electrolytes, and avoiding over or underhydration.

Is blood flow in ICA representing CBF?

We believe so. As described in our recent publication (Fong, J App Physiol, 2021), the majority of blood flow in the rat ICA supplies cerebral structures.

What isoflurane concentration do you use? Volatile anesthetics influence vascular regulation, edema formation, etc.

Isoflurane, usually 4-5% to induce and 2% maintenance, in 100% oxygen. Yes, we believe that the profound increase in brain oxygenation seen during GA induction reflects both the hyperoxic delivery, and direct vasodilatory effects of the volatile anesthetic agent itself.

If arterial blood pressure is dropping, that would create an imbalance between mesenteric inflow vs outflow and a net shift of volume out. Is that what is happening such that sympathetic blockade does not compromise volume shift out?

We speculate that when AP pressure drops during volume depletion after ganglionic blockade, this reduces both the arterio-venous pressure gradient and reduces the mesenteric arterial flow coming in, there remains a passive net movement of blood out of the mesentery, most likely due to the resting tension in the mesenteric venous circulation. We can't yet determine the relative contribution of this "passive outflow" vs sympathetic influences on venomotor tone in the baseline state, where volume depletion does not cause a fall in BP. We predict that a more severe hemorrhagic challenge may rely much more heavily on recruiting a sympathetically mediated venomotor response.

The point you made that the finite volume of the brain due to the cranium restricts any ability for vasodilation to actually increase flow (i.e. arteriole dilation means increasing cross sectional area = space taken up). What are the ranges of flow increase that can be evoked by activating dilation? I thought it was substantial in response to hypercapnic challenges?

I wouldn't say that there is no ability for vasodilation to increase flow – certainly during hypercapnia cerebral blood volume increases, resulting in a quite profound increase in intracranial pressure. The increase in CBV is achieved in part by compressing the cerebral veins, and to some extent cerebral structures. But being encased within the cranium does restrict the ability to simply expand to accommodate flow, certainly the vasodilatory capacity is considerably less that the "100-fold" increase possible in skeletal muscle.

Volume loading not increasing mesenteric volume with hexamethonium indicates that without sympathetic tone in mesenteric capacitance, they are already full prior to volume loading?

This is a good question. Recall that the ganglionic blockade is given prior to the volume load, so the "system" will be in a new steady state without SNS influence. Then when we perform the volume load, the mesentery appears to have lost the ability to accommodate the additional volume. We think this suggests that the mesenteric veins must be under tonic SNS control, with the ability to both increase or decrease SNA to permit the fine tuning of capacitance/compliance.

Could you please name the product number of the balloon catheter?

Our silicone atrial balloon catheters are made bespoke by Vesta, which are part of Lubrizl Life Sciences in Franklin, Wisconsin, USA.

Could you clarify the role of tone/compliance in the movement of blood in/out of the splanchnic reservoir - are tone changes required, or is it a purely passive effect?

Our data suggests that different mechanisms may operate with volume increases vs decreases. Certainly, with volume depletion, it appears that neurally-mediated changes in venous tone are not necessary for blood to move out of the mesenteric bed (as this

continues after ganglionic blockade). The ability to accommodate volume expansion does appear to rely on neural input, likely via reduction in tonic sympathetic outflow. This mechanism appears to be disrupted in hypertensive rats.

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