Protecting blood flow to the ‘selfish’ brain in health and disease

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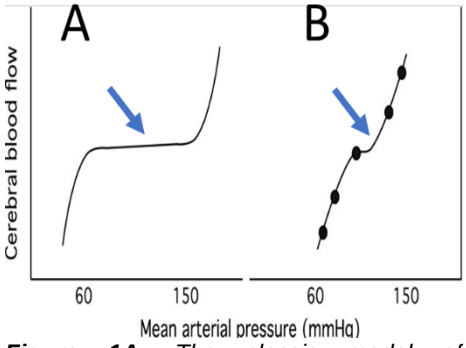

***Figure 1A**: The classic model of autoregulation based on Lassen's 1959[3] meta-analysis, pooling data between-subjects over a range of normal and abnormal resting blood pressure (BP). **1B:** Cerebral blood flow (CBF) as BP is varied within each (healthy) individual subject. Note the narrow plateau (arrowed).*

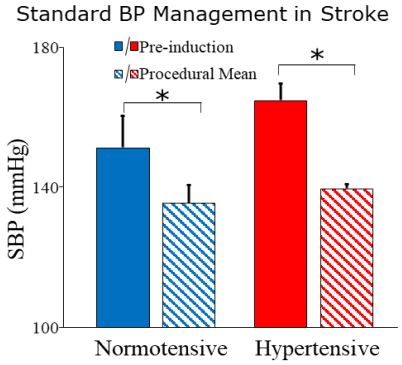

Figure 1: SBP before and during GA for endovascular thrombectomy in large-artery ischemic stroke patients, with (Hypertensive, n=16) or without (Normotensive, n=10) a prior history of hypertension. Note that the procedural mean is significantly lower than the pre-induction SBP in both groups, particularly for Hypertensive patients. *(Zhang, Billing, Campbell & McBryde, unpublished data, 2019).*

The brain is our most energy-expensive organ, with a constant and unrelenting demand for blood flow to meet its metabolic needs. Classic dogma holds that blood flow to the brain is largely protected by an in-built mechanism called "cerebral autoregulation". This states that as perfusion pressure falls, the blood vessels in the brain rapidly and automatically dilate (or constrict with an increase in pressure) to maintain cerebral blood flow. The textbook view is that this powerful mechanism operates to keep cerebral blood flow constant across a wide range of perfusion pressures, termed the 'autoregulatory plateau' (Fig 1A). An important but often overlooked point is that the classic curve shown in Fig 1A is NOT the response to varying pressure within individuals, but represents a mean steady-state measurement from multiple groups of subjects with pathologies resulting in abnormal resting blood pressure. We and others have shown that even in healthy individuals the dynamic relationship between cerebral blood flow and blood pressure has little or no plateau as previously thought (Fig 1B), meaning that moment-to-moment cerebral autoregulation in fact may be highly limited. How then does the brain protect itself from fluctuations in perfusion?

Our ‘selfish brain’ hypothesis predicts that reductions in cerebral perfusion trigger the brain to demand an increase in systemic blood pressure, thereby restoring the supply pressure and hence flow to the brain. This is consistent with observations in ischemic stroke patients, where the vast majority (>80%) show a pronounced increase in blood pressure. A key question is where should blood pressure be set in patients during interventional procedures such as endovascular thrombectomy?

The standard of care in New Zealand is for endovascular thrombectomy to be performed under general anaethesia. Given the prevalence of hypertension as a risk factor for stroke, understanding how different BP targets affect subjects with varying levels of pre-stroke BP is of particular importance. A recent analysis of stroke patients undergoing endovascular thrombectomy at Auckland City Hospital, showed that standard BP management during GA resulted in BP below the pre-induction level even where there was no history of hypertension (ΔSBP: -15±4mmHg); this fall was much greater in patients with known hypertension (ΔSBP: -25±2mmHg). It is not yet known whether this reduction in BP may affect outcome.

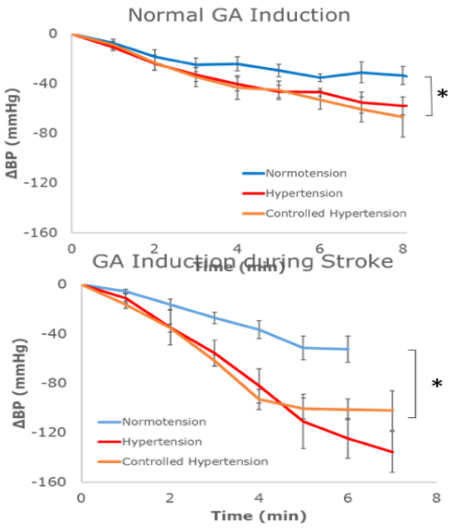

Figure 2: Anaesthetic-induced Hypotension during Stroke. Data shown for rats where baseline BP was normal, high or treated hypertension.

In our preclinical rodent model of stroke, we have observed that inducing GA during occlusive stroke produces hypotension, which is greatly exacerbated in hypertensive rats, regardless of whether or not BP was treated and controlled prior to stroke (Figure 2). Taken together, these data suggest that the administration of anaesthesia during ischemic stroke may require particular care and more precise haemodynamic management than for other procedures.