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You say resistance, I say compliance; let's call the whole thing cerebral Windkessel control

William H. Cooke
Department of Health and Kinesiology, University of Texas at San Antonio, San Antonio, TX 78249, USA

Email: william.cooke@utsa.edu

Adequate cerebral perfusion and oxygenation are fundamental requirements for maintenance of normal cerebral function, and ultimately maintenance of consciousness. A clear understanding of processes and mechanisms that regulate cerebral blood flow under a wide range of conditions assumes important clinical significance, but studying blood flow regulation in the human brain is not simple. The cerebrovasculature is complex and not readily accessible, and so it has become convenient in recent years to record flow velocities from large intracranial arteries such as the middle cerebral artery using transcranial Doppler ultrasound (TCD). Velocity will reflect flow faithfully as long as the diameter of the insonated vessel is unchanged; this condition seems to be obtained, at least for the middle cerebral artery (with small errors), under a variety of experimental perturbations.

Direct calculations have largely confirmed the notion that cerebral blood flow is maintained relatively (but not absolutely) constant through dilatation and constriction of cerebral vessels (Heistad & Kontos, 1983). Cerebral autoregulation is driven by both myogenic mechanisms (active responses to changes in transmural pressure) and metabolic mechanisms (changes in concentrations of metabolic vasodilators caused by local changes in flow). Autoregulation may be static or dynamic, with characteristics that are revealed with both time- and frequency-domain techniques that characterize associations among arterial pressures and cerebral velocities.

Two classic studies in particular have provided a foundation for our understanding of both static and dynamic cerebral autoregulation. Giller (1990) reported that patients with cerebrovascular disease demonstrated increased coherence between arterial pressure and cerebral velocity at various oscillatory frequencies as compared with asymptomatic, apparently healthy subjects. Increased coherence implied a greater reliance of cerebral velocity on arterial pressure, and therefore indicated impaired cerebral autoregulation. The study by Giller (1990) was the first to describe the coherence between pressure and velocity over various frequencies. Zhang *et al.* (1998) extended these observations by defining the effective cerebral autoregulatory range (about 0.07 to 0.2 Hz), and by modelling cerebral autoregulatory responses to arterial pressure changes using transfer function analysis.

A paper published in a recent issue of *The Journal of Physiology* adds an additional layer of complexity by suggesting that steady-state Windkessel properties of cerebral vessels, such as resistance and compliance, contribute importantly to frequency-dependent, dynamic cerebral autoregulation (Zhang *et al.* 2009). Increases of arterial pressure with infusions of phenylephrine decreased transfer function gain and phase angle, and Windkessel modelling suggested that these reductions could be due to static increases in cerebrovascular resistance or decreases in compliance. This is important, as it implies that consideration of static Windkessel features are necessary for the accurate interpretation of cerebral autoregulation. This speculation was confirmed recently by Chan *et al.* (2011), who decreased and increased arterial pressure with nitroprusside and phenylephrine. Pressure–flow responses at the low frequency were compared with both a single resistive and a two-element Windkessel model; the authors concluded that mechanical properties of the cerebral vasculature are important elements of low frequency cerebrovascular responses to both transient hypotension and hypertension.

In the current issue of *The Journal of Physiology*, Tzeng and co-workers (2011) have further characterised the influence of Windkessel features of the cerebrovasculature using non-pharmacological manipulations of arterial pressure. With application of oscillatory lower body negative pressure (OLBNP), the influence of both pressure-driven resistive flow and capacitive flow was evaluated using cross-spectral associations among arterial pressure and cerebral blood velocity. In addition, subjects repeated the OLBNP protocol after calcium blockade with 60 mg nimodipine. Oscillations of cerebral velocity reflected both resistive and capacitive flow (as determined by the rate of change in arterial pressure and cerebral compliance). Mechanical properties of the cerebral vessels correlated with metrics derived from cross-spectral analyses, providing the first experimental evidence for the contribution of cerebral Windkessel features to human cerebral autoregulation during physiological arterial pressure perturbations. After calcium blockade, resulting increases in resistive flow fluctuations provides some evidence that mechanical buffering properties of cerebral vessels are not related necessarily to active cerebral autoregulation.

Recent characterisations of Windkessel features in the cerebral vasculature represent important advances in our understanding of dynamic cerebrovascular control. New, intriguing complexities must now be considered; and fundamental questions of cerebral autoregulatory processes and mechanisms under conditions of markedly increased arterial pressure oscillations (such as might occur naturally with dehydration, haemorrhage and/or upright posture, etc.) may now be more accurately addressed. We may now even address a new question, is it still appropriate to term the observation of relatively unchanged (or buffered) cerebral blood flow over a wide range of perfusion pressures 'autoregulation'? Beat-by beat changes in cerebral blood flow in response to either transient increases or transient decreases in arterial pressures, or in response to forced arterial pressure oscillations cannot be explained wholly through myogenic or metabolic mechanisms. Cerebral Windkessel features are prominent in the modulation of cerebral blood velocity. This observation suggests that the more appropriate term is 'cerebrovascular control' – a control that includes, but is not modulated entirely by, active autoregulation.

References

Chan GSH, Ainslie PN, Willie CK, Tahylor CE, Atkinson G, Jones H, Lovell NG & Tzeng Y-C (2011). *J Appl Physiol* **110**, 917–925.

Giller CA (1990). *Neurosurgery* **27**, 362–368.

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Heistad DD & Kontos HA (1983). In *Handbook of Physiology*, section 2, *The Cardiovascular System*, vol. III, *Peripheral Circulation and Organ Blood Flow*, ed. Shepard JT, Abboud FM & Geiger SR, pp. 137–182. American Physiological Society, Bethesda.

Tzeng Y-C, Chan GSH, Willie CK & Ainslie PN (2011). *J Physiol* **589**, 3263–3274.

Zhang R, Behbehani K & Levine BD (2009). *J Physiol* **587**, 2567–2577.

Zhang R, Zuckerman JH, Giller CA & Levine BD (1998). *Am J Physiol Heart Circ Physiol* **274**, H233–H241.