EDITORIAL

Redefining the cerebral autoregulatory range of blood pressures: Not as wide as previously reported

The brain is a highly metabolically active organ that utilizes ~20% of cardiac output at rest. While energy demand is high, overall brain perfusion remains relatively constant. This is thought to occur through modulating vessel diameter and thus, resistance. The classic cerebral autoregulation curve, described by Lassen (1959), showed that cerebral blood flow (CBF) is kept relatively constant at wide ranges of mean arterial pressures (MAP) of ~60–150 mmHg. Paulson later added the upper limit of the autoregulatory curve (Paulson et al., 1990) from animal studies, creating the autoregulatory curve that is widely used and cited in the literature (Figure 1, orange curve and shaded area). In the paper by Brassard et al. (2021) entitled, “Losing the dogmatic view of cerebral autoregulation”, the authors provide compelling evidence for updating the classic cerebral autoregulatory curve.

One of the arguments is that the autoregulatory curve was generated using unique data points (Lassen, 1959) from 376 subjects, obtained over seven different studies that included elevated blood pressures derived from administration of vasoactive drugs and patients with hypertensive disorders. While similar cerebral autoregulatory curves have been reproduced in different species such as rats and non-human primates (Heistad et al., 1980; Hernandez et al., 1978), whether the ranges of cerebral autoregulation demonstrated by Lassen is applicable under non-invasive, physiological circumstances has been disputed. Indeed, Heistad and Kontos (1983) challenged Lassen’s study, highlighting that because some of the points on Lassen’s curve were obtained using vasodilatory drugs known to have direct effects on CBF, one cannot claim that these specific points are representative solely of MAP-dependent changes in CBF. Another concern was that three of the studies included in Lassen’s curve showed increases in CBF with slight MAP changes, challenging whether there is a true plateau of CBF relative to MAP. Furthermore, the authors emphasize that optimally, cerebral perfusion pressure should be monitored in tandem with CBF, given that cerebral perfusion pressure changes with shifts in body position as well as pathologies. Thus, plotting changes in CBF relative to changes in cerebral perfusion pressure may be a better option.

Another key point raised by the authors is that previous work by Tan and colleagues showed that CBF is stable in healthy, non-anesthetized individuals at a much lower range of MAP (~5–10 mmHg) than what was proposed by Lassen (~90 mmHg). To further extrapolate these findings, the authors performed a reanalysis of the dataset originally published by Numan et al. (2014) with the addition of recent papers published from 2012 to 2020. This resulted in a total of 29 papers with increased MAP and 27 papers with decreased MAP included in the analysis. Using a 3rd order polynomial function to maximize goodness of fit to the curve, the reanalysis showed a smaller range of MAP for the CBF plateau. These data were analyzed with the exclusion of pharmacological intervention (Figure 1, blue curve and shaded area), thus removing the data points where vasoactive drugs could have contributed to confounding effects on CBF.

Brassard et al. (2021) also challenged whether a standard lower and upper range of cerebral autoregulation exists on an individual basis. The authors argue that an asymmetry in autoregulation, where the brain is better equipped to respond to increases in MAP but is not as efficient in adjusting to decreases in MAP, places the brain at greater risk of hypoperfusion and subsequent neurological deficits following drops in MAP (Selnes et al., 2012).

Instead of separating cerebral autoregulation into static (steady-state) and dynamic (transient) processes, the authors suggest that the two processes should be viewed as a continuation of each other. They further elaborate that Lassen’s curve reflects steady-state, rather than physiological transient (dynamic) changes that tend to occur clinically. Thus, an important consideration is whether the cerebral autoregulatory curve, derived from observing slow changes in MAP, can and should be used in clinical settings where continuous blood pressure fluctuations are common.

Of course, limitations of available methodologies must also be considered. It is difficult to separate the direct...
As with all challenges to accepted dogma, it may take some time for the concept of a smaller plateau of cerebral autoregulation to be accepted. Studies utilizing dynamic measures of CBF under physiological conditions (within subjects) and with transient changes in MAP will help solidify these findings. Nonetheless, we hope that the publication of this editorial along with the companion paper, will begin the conversation around this topic, and will spark further rigorous experiments in both humans and preclinical animal models.

CONFLICT OF INTEREST
Authors have no conflicts to declare.

AUTHOR CONTRIBUTIONS
Drafting and Writing: MJM; Revision: MJM and JPW; Approval: MJM and JPW.

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