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Flow-pressure regulation in cerebrovascular disease

Stroke ranks third among the leading causes of death and is the leading cause of long-term disability in older adults. Adequate perfusion of regions surrounding the ischemic areas is essential for brain tissue recovery and the clinical outcomes after ischemic stroke. Dynamic cerebral autoregulation (dCA) reflects the ability to restore cerebral blood flow (CBF) in the face of sudden changes of perfusion pressure and increased metabolic demands. The efficacy of dCA is critically important during acute ischemia for maintenance of blood flow to ischemic areas and for avoidance of excessive hyperperfusion. In the absence of dCA, elevations of blood pressure (BP) may increase blood volume and lead to brain swelling, while low BP may promote infarct growth and long-term tissue damage.

Autoregulatory mechanisms rapidly adapt perfusion to accommodate variations in intracranial pressure and BP. As a result, beat-to-beat BP and BFV signals are nonstationary and their relationship is nonlinear under clinical conditions. Transcranial Doppler enables assessment of dCA from spontaneous BP and blood flow velocity (BFV) fluctuations and during interventions inducing sudden BP changes induced by the Valsalva maneuver, head-up tilt and sit-to-stand test. Conventional approaches typically model autoregulation using mathematical models that govern the dynamics of BP (as an input to the system) and CBF (as output) that can be approximated by a linear, time-invariant system. Fourier transform-based transfer function and coherence are used analytically to represent the relationship between the input BP and the output BFV. These techniques assume a linear relationship between two stationary signals that can only be met under very limited conditions, where these analyses have shown a significant phase lead of cerebral BFV with respect to systemic BP. These unrealistic requirements of signal properties may significantly limit their utility, even if direct measurements of CBF and intracranial pressure are made. Recently developed nonlinear approach called multimodal pressure-flow analysis (MMPF), to detect instantaneous changes in BP-BFV regulation. Because the MMPF technique does not assume stationarity and linearity of the signals and provides instantaneous BP-BFV phase shift, this technology is suitable for evaluation of autoregulation using the Valsalva maneuver and for continuous monitoring of dCA from spontaneous BP-BFV fluctuations. Therefore, novel modeling approaches that would allow prediction of unknown variables (i.e. intracranial pressure) are need to improve assessment of autoregulation in medical diagnostics.