Complex models for the complexity of cerebral ischemia

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Abstract

The recent series of articles in the journal devoted to building a dynamic network model of cerebral ischemia provides a refreshing perspective in the field of acute stroke. Several points raised in these articles merit further commentary.

Keywords: Stroke, ischemia, model, collateral circulation, hemodynamics.

Letters to the editor

The recent series of articles in the journal devoted to building a dynamic network model of cerebral ischemia provides a refreshing perspective in the field of acute stroke.(DeGracia 2010a; DeGracia 2010b; DeGracia 2010c; DeGracia 2010d) The complexity of this model may be so advanced that few may appreciate the details yet this conceptual approach is truly innovative, providing a great example of what may be currently lacking in the field. The author takes an introspective viewpoint on the chronicle of colossal efforts that have aimed to extend effective therapies for acute ischemic stroke. Altogether the articles evoke a key question on progress in translating stroke research to the bedside: Are the answers to combating cerebral ischemia buried amidst the tremendous data amassed in prior studies and trials to date, yet we have failed to recognize the solutions?

Several points raised in these articles merit further commentary. The author daringly, yet appropriately questions the concepts of the ischemic cascade suggesting that this approach may be misleading and overly simplistic. The pivotal role of collaterals and hemodynamics as a primary stress response involving various segments of the cerebral circulation are duly accentuated despite little attention to date.(Liebeskind 2003) The concept of vasoprotection and endothelial events is raised, underscoring the impact of ischemia on the entire neurovascular unit beyond neuroprotection. This point should prompt researchers to avoid prior errors in the past where vascular processes and targets such as endothelium have been ignored due to the overwhelming focus on the tissue consequences of ischemia at the neuronal and glial level alone. The proposed integral concept of ischemia may be difficult to follow, but there are clear correlates already recognized such as the compensatory role of collaterals. Collateral circulation is a key element of the vasoprotective stress response operating at the tissue level with influences on numerous facets at the cellular level. This suggested multiscale nature of ischemia overcomes the exclusive focus of the ischemic cascade concept largely limited to intracellular molecular events. A linear concept of time is brain is also appropriately questioned, noting that such a model is implausible from a functional perspective.(Liebeskind 2009) In animals and man, it is well established that arterial occlusion rarely results in the same decrement of downstream perfusion and ischemic severity. The time course of ischemic evolution is also known to be highly variable. This point is important when one considers use of thresholds in imaging analyses of stroke. Heterogeneity in ischemia and perfusion abnormalities and variable topography remain unaccounted in most stroke imaging studies. The dynamic concept proposed in these articles also challenges the use of cerebral blood flow alone, as the sole perfusion parameter of interest. The evolution of ischemia due to hemodynamics driven by venous steal and other mechanisms stresses the potential value of multiparametric perfusion analyses.(Pranevicius and Pranevicius 2002) Multiparametric imaging analyses may also reveal regional gradients or variation in stages of ischemia, providing estimates of potential vulnerability to lesion expansion. Such embedded temporal and spatial data are important as they provide the basis for understanding a variety of post-ischemic state spaces and potential translational therapies for acute to chronic ischemia. In sum, stroke imaging holds the potential to test the innovative concepts advanced in these articles.(DeGracia 2010a; DeGracia 2010b; DeGracia 2010c; DeGracia 2010d)

The complexity of cerebral ischemia will undoubtedly require use of complex models and detailed imaging approaches to disclose potential breakthroughs. The articles are solely the first steps in re-examining...
some entrenched and unfortunately unfruitful concepts in stroke. The onus now rests with other researchers to test such complex models, yet it is clearly time to move beyond simplistic models of a sequential cascade, rigid thresholds and linear time course of ischemia in the brain.

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Conflict of interest

None

References


