Editorial

Intracerebral Hematoma
Beyond the Mass Lesion

Raymond A. Swanson, MD

See related article, pages 2457-2462.

The signs and symptoms of acute intracranial hemorrhage are those of a rapidly developing mass lesion, compounded over time by surrounding edema, and sometimes by brain herniation. These are dramatic, debilitating, and often fatal events, but does the pathophysiology of intracranial hemorrhage extend beyond that of mass effect? Blood contains several factors that are potentially, and in some cases definitively, neurotoxic. Chief among these are hemoglobin and its breakdown products, heme and iron, which exhibit neurotoxicity at low micromolar concentrations through mechanisms involving iron-catalyzed production of reactive oxygen species. Brain has a variety of defense mechanisms to prevent the formation of reactive iron from blood hemoglobin, including inducible and constitutive heme oxygenases and iron-binding proteins, but these are easily overwhelmed by frank hemorrhage. Indirect evidence for hematoma toxicity on surrounding brain has come from studies showing reduced extraction of blood oxygen by perihematoma brain tissue. Given that heme and iron are potent mitochondrial toxins, one explanation for reduced oxygen use during production of ATP from ADP, and thus approximates mitochondrial function under normal conditions in situ. State 4 respiration is a measure of oxygen consumption in the absence of ADP substrate, and hence provides a measure of the “leakiness” of mitochondrial membranes, which increases with mitochondrial damage.

Although neither of these measures alone reached a P value of 0.05, the use of tissue from human surgical resections unavoidably introduces variability into the study. The patients were of differing ages and with differing underlying diseases. Mitochondria were taken from several different brain regions, with variable ratios of neuronal and non-neuronal mitochondria. Large changes in neuronal mitochondria may be masked by smaller changes in more resilient glial cells, or by the extended time interval between resection and respiration measurements. All of these factors tend to introduce “noise” into the results, but the key question, not definitively addressed by these studies, is whether the observed mitochondrial dysfunction is attributable primarily to local trauma and mass effect, or is in fact attributable to diffusible factors from the hematoma. The findings by Kim-Han et al set the stage for future work in which interventions that target mitochondrial damage can be assessed to more clearly delineate the cause-effect relationships suggested by this work.

Disclosures

None.

References

4. Keep RF, Xi G, Hua Y, Hoff JT. The deleterious or beneficial effects of different agents in intracerebral hemorrhage: think big, think small, or is hematoma size important? Stroke. 2005;36:1594–1596.

KEY WORDS: intracranial hemorrhage ■ mitochondria

The opinions in this editorial are not necessarily those of the editors or of the American Heart Association. From the Department of Neurology, University of California, San Francisco, and Veterans Affairs Medical Center, San Francisco, Calif. Correspondence to Raymond A. Swanson, Department of Neurology, Veterans Affairs Medical Center, 4150 Clement St, San Francisco, CA 94121. E-mail raymond.swanson@va.gov (Stroke. 2006;37:2445.) © 2006 American Heart Association, Inc. Stroke is available at http://www.strokeaha.org

DOI: 10.1161/01.STR.0000244060.83388.76
Intracerebral Hematoma: Beyond the Mass Lesion
Raymond A. Swanson

Stroke. 2006;37:2445; originally published online September 7, 2006;
doi: 10.1161/01.STR.0000244060.83388.76
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2006 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/37/10/2445

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published
in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office.
Once the online version of the published article for which permission is being requested is located, click
Request Permissions in the middle column of the Web page under Services. Further information about this
process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/