Intracerebral Hemorrhage and Head Trauma
Common Effects and Common Mechanisms of Injury

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Abstract—Nontraumatic intracerebral hemorrhage (ICH) remains a devastating condition with 30-day mortality rates of 35% to 52%. Until the pathophysiology of this condition is better understood, it will not be possible to develop effective therapies. Studies of cerebral blood flow and metabolism in patients with acute ICH show similar abnormalities to those that occur in patients with traumatic brain injury, thus raising the question of whether there are common mechanisms of injury shared by the 2 conditions. In both ICH and traumatic brain injury, there is an early reduction in the cerebral metabolic rate of oxygen without ischemia, mitochondrial dysfunction, and transient focal increases in regional glucose metabolism that occur after a few days. ICH and traumatic brain injury share barotrauma from pressure waves that propagate through the intracranial contents as a common mechanism of brain injury. Recent data demonstrating contralateral hemispheric damage in patients with acute ICH provide further support for this theory of common injury mechanisms. (Stroke. 2010;41[suppl 1]:S107-S110.)

Key Words: intracerebral hemorrhage ■ traumatic brain injury ■ cerebral oxygen metabolism ■ cerebral glucose metabolism

Nontraumatic intracerebral hemorrhage (ICH) remains a devastating condition with 30-day mortality rates of 35% to 52%.1 In the 2007 American Heart Association/American Stroke Association management guidelines, there is not a single treatment shown to be effective by level A evidence.2 Until the pathophysiology of this condition is better understood, it will not be possible to develop effective therapies. In a series of studies of cerebral blood flow (CBF) and metabolism in patients with acute ICH, I was struck by the similarity of the abnormalities to those that occur in patients with traumatic brain injury (TBI), thus raising the question of whether there are common mechanisms of injury shared by the 2 conditions. Recent data demonstrating contralateral hemispheric damage in patients with acute ICH provide further support for this theory.

Methods and Results

We measured CBF and cerebral metabolic rate of oxygen (CMRO2) with positron emission tomography (PET) in 19 patients 5 to 22 hours after ICH onset (Figure 1).3 CBF and CMRO2 were determined in a 1-cm–wide perihematomal area. In the 16 patients without midline shift, perihematomal data were compared with mirror contralateral regions. All of the PET measurements were corrected for partial volume effect because of clot and ventricles. Both perihematomal CBF and CMRO2 were significantly reduced compared with contralateral values (CBF: 20.9±7.6 versus 37.0±13.9 mL·100 g⁻¹·min⁻¹ [P=0.0004]; CMRO2: 1.4±0.5 versus 2.9±0.9 mL·100 g⁻¹·min⁻¹ [P=0.00001]). The ratio of oxygen delivery (CBF×arterial oxygen content) to CMRO2 was increased in the perihematomal region. This is the opposite of what occurs in acute ischemia when oxygen delivery is reduced relative to CMRO2. These findings of reduced CBF and CMRO2 with a adequate oxygen delivery are consistent with primary metabolic depression of CMRO2.3,4

In 2 PET studies of CBF and CMRO2 following nonpenetrating TBI, we found results strikingly similar to those in ICH. In 9 patients studied 8 to 14 hours after TBI, hemispheric values for CMRO2 were reduced, and O2 delivery/CMRO2 was increased compared with 10 age-matched healthy volunteers.5 In a subsequent study that added 4 additional patients studied within 5 days of injury, regional measurements of CMRO2 were reduced in the areas with the lowest CBF, and oxygen delivery was increased relative to oxygen demand (Figure 1).6 Similar findings after TBI have been reported by others.7 As with ICH, these data are most consistent with primary metabolic depression of CMRO2.

The pathophysiologic link between these 2 conditions may be found in studies of mitochondrial function (Figure 2). Kim-Han et al8 measured mitochondrial oxygen consumption in brain tissue adjacent to the hematoma from 6 patients with acute spontaneous ICH and 6 control patients undergoing brain resection for management of seizures. The mean state 3 (active) O2 consumption for mitochondria from ICH patients was ~40% lower than that of control patients. Verweij et al9...
isolated living mitochondria from brain tissue therapeutically removed at the time of surgery in 16 patients with head injury (Glasgow Coma Scale scores 3 to 14) and 2 patients without head injury. State 3 (active) O₂ consumption in head-injured patient mitochondrial function was impaired (Figure 2). Thus, in both conditions, mitochondrial dysfunction was responsible for reduced CMRO₂.

Although similarities in mitochondrial dysfunction could point toward similar mechanisms of injury in ICH and TBI, this is not very convincing evidence, because abnormalities in mitochondrial function have been described in a wide variety of neurological diseases.10 Some more recent studies of regional cerebral glucose metabolism provide more convincing demonstration of a pathophysiological link between the 2 conditions. We investigated relative changes in the regional cerebral metabolic rate of glucose (CMRglc) with ¹⁸F-fluorodeoxyglucose PET at 1.0±0.3, 2.9±0.8, and 6.7±1.6 days after ICH in 13 subjects. Focal regions of increased perihematomal ¹⁸F-fluorodeoxyglucose uptake appeared transiently in 6 patients 2 to 4 days after acute ICH.11 These findings of focal perihematomal hyperglycolysis 2 to 4 days after ICH are remarkably similar to those reported in human TBI with ¹⁸F-fluorodeoxyglucose PET. Bergsneider et al12 observed focal hyperglycolysis adjacent to focal mass lesions in 5 of 28 patients studied 3 to 14 days after injury. Hattori et al13 reported focal hyperglycolysis by visual inspection in portions of pericontusional regions in 7 of 21 patients with cerebral contusions studied 4.0±3.3 days after onset as compared with 2.6±0.9 days in the 14 without focal hyperglycolysis. Such focal perilesional hyperglycolytic areas have not been seen in acute ischemic stroke or aneurysmal hemorrhage.14–16 Although the underlying cause of these hypermetabolic regions remains to be determined, the similar location, appearance, and time course argue for a common pathophysiology.

The common pathophysiological mechanism of brain injury shared by both of these conditions is barotrauma from pressure waves that propagate through the intracranial contents (Figure 3). With TBI, the barotrauma arises externally from a blow to the head. With ICH, the fluid percussion waves arise from within the cranium because of the sudden expansion of the hematoma under arterial pressure. Because the pressure waves propagate throughout the brain, there should be evidence of diffuse hemispheric damage in both conditions if this is an important pathophysiological mechanism. Bilateral hemispheric damage is a characteristic of human TBI.17 Evidence for diffuse hemispheric damage in humans with ICH was, until recently, inferential based on the fact that severely impaired consciousness is more common with acute supratentorial ICH than with supratentorial infarction ischemic stroke.18 Although commonly invoked, increased intracranial pressure (ICP) is not an adequate explanation for this manifestation of bihemispheric dysfunction, because ICP is only weakly correlated with coma, and the level of consciousness almost never improves with relief of ICP by ventricular drain.19,20 More recently, neuroimaging has provided objective evidence of damage to the contralateral hemisphere in unilateral ICH. Using a very accurate MRI method to determine changes in brain volume, we reported swelling of both ipsilateral and contralateral hemispheres in 15 patients during the first week following acute supratentorial ICH (Figure 4).21 Xing et al22 reported increases in the blood-brain permeability to X-ray contrast within 24 hours of onset in both ipsilateral and contralateral hemispheres in 19 patients with ICH as compared with the contralateral control hemisphere from 5 patients with cortical ischemic stroke (Figure 5). In pilot observations with diffusion tensor imaging, we observed increased fractional anisotropy in the
contralateral periventricular white matter in a 76-year–old
man 7 days after a left occipital ICH compared with age-
matched normal subjects (A Mehrabyan, H An, D Huang, W
Lin, E Bullitt, W Powers, unpublished data; Figure 6). Fractional anisotropy in white matter is increased after mild
TBI.23–25

Conclusions

The effects of cerebral injury attributed to trauma and ICH are
similar. The deleterious effects of ICH are considered to be
because of a combination of primary injury (the local tissue
destruction caused by the hematoma itself and accompanying
increased ICP) and secondary effects produced by the toxic
effects of blood on adjacent tissue.26 To these mechanisms,
we should consider adding the effects of diffuse cerebral fluid
percussion injury caused by internal barotrauma. Such a
mechanism for diffuse brain injury may account for the
alterations in consciousness after ICH that are not always
easily explained by increased ICP, mass effect, or herniation.
Furthermore, the changes described above that occur in the
brain for several days after acute ICH demonstrate that
ongoing processes in response to injury may be indicative of
a prolonged window for intervention to improve neurological
outcome.

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Figure 3. Diagrammatic representation of barotrauma as a mechanism of diffuse
brain injury in TBI and ICH.

Figure 4. Change in hemispheric volume after acute ICH. Data are from Reference 21.

Figure 5. Permeability-surface area (P-S) product reflecting blood-brain barrier per-
meability to X-ray contrast after acute ICH. Contra infarct indicates control data from
the hemispheres contralateral to cerebral infarction. Data from Reference 22.
Figure 6. Fractional anisotropy (FA) in the contralateral periventricular white matter in a 76-year–old man 7 days after acute ICH compared with age-matched normal control subjects.

None.

References


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