

Traumatic brain injury and the subsequent risk of stroke

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EDITORIAL

Both traumatic brain injury and stroke are common disorders and amongst the largest causes of long-term disability. Traumatic brain injury causes diverse neural pathology that not only drives acute and chronic symptoms, but also may convey an increased risk of cerebrovascular accidents. There are many risk factors for stroke and cerebral vascular disease, but TBI may have been previously overlooked as a risk factor. Some very large empirical studies have demonstrated a significant risk for stroke after TBI. In 2011, a study (1) compared 213,199 people in Taiwan who had suffered a TBI with 69,597 who had not and they found that stroke risk increases tenfold in the three months after a traumatic brain injury. Other large studies also show increased risk, however of a much smaller magnitude. In 2016, and even larger study (2) on this issue was published involving 435,630 people with traumatic brain injury and 736,723 people with trauma with no brain injury. Individuals were followed an average of 28 months following the injury, 11,229 people, or 1 percent, had an ischemic stroke. A total of 1.1 percent of those with TBI suffered a stroke, compared to 0.9 percent of those with trauma with no brain injury. Though the findings of these two study vary widely, taken together they make a strong case for at least some increased likelihood of ischemic stroke after TBI. This is not yet a widely researched topic, but given the significant public health implications of these disorders, more research is warranted.

PATHOPHYSIOLOGICAL CONNECTION BETWEEN TBI AND STROKE

After reviewing this research, a compelling clinical question concerns how TBI increases stroke risk. What still remains unclear is what the exact mechanism or residual TBI pathophysiology that increases stroke risk. Some research suggests that perhaps microvascular pathology is the link.

A small body of research suggests that traumatic cerebral vascular injury (TCVI) is a frequent, if not universal, feature after traumatic brain injury (3). TBI often results in various types of hemorrhage including subdural, subarachnoid, and intraparenchymal. Even more frequent is the microvascular pathology. The microvascular network regulates blood flow, vascular permeability and angiogenesis in the central nervous system and this system has been coined the neurovascular unit (NVU). Pathology in the NVU is thought to be at least in part, responsible for functional deficits and TBI-related chronic disability. Pathology in the NVU is involved in the pathogenesis of many brain disorders including vascular dementia, Alzheimer's Dementia, Parkinson's Disease, and others. However, the role of the NVU issues is unclear since it is not clear if the NVU pathology is a cause or consequence of these disorders (4). It is unclear if the vascular damage results in vasospasms, turbulent blood flow causing thrombotic or embolic potential, or risk of vessel rupture.

Traumatic neurovascular injury can result from both primary and secondary injury (e.g. blood brain barrier (BBB) disruption, increased intracellular calcium, mitochondrial dysfunction, neuroinflammation (5,6). After TBI, the

changes in the BBB are thought to be caused by direct damage to endothelial cells followed by changes from secondary injuries in other elements of the NVU (neurons, astrocytes, microglia and the extracellular matrix) (7). Diminished CBF and focal tissue hypoxia is a common precipitant of NVU pathophysiology and is mediated through multiple pathophysiologic cascades (e.g. BBB disruption, edema, focal ischemia). When injured, the NVU rapidly increases blood flow and oxygen supply and induces factors that promote angiogenesis (8), however it is thought that attempts at self-repair may have potential deleterious consequences.

CONCLUSION

Stroke is a significant public health issue. Large empirical studies suggest that traumatic brain injury significantly increases risk of subsequent ischemic stroke. The relative increase in risk varies greatly between studies, but all suggest increased risk. Though conventional brain imaging does not show the microvascular pathology in a sufficiently definitive manner, new brain imaging techniques appear to have some promise in further delineating these issues. From a public health perspective once could ask how should these finding change future TBI follow up care and public education. Clearly more research is needed to understand what subgroups of individuals who have suffered TBI are at most risk for stroke.

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