THE ROLE OF SUBSTANCE P IN CEREBRAL EDEMA ASSOCIATED WITH RAT AND HUMAN INFACTION AND CONTUSION

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A Thesis Submitted to the University of Adelaide in Fulfillment of the Requirements for the Degree of Master of Medical Science

August 2006
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Abstract

Cerebrovascular stroke is the third commonest cause of death in industrialized countries while traumatic brain injury (TBI) is the leading cause of mortality and disability in individuals below 40 years of age. An important influence on the severity of both TBI and stroke is cerebral edema. The mechanism of cerebral edema in both is poorly understood.

Recent evidence suggests that substance P (SP) plays a role in this edema and, specifically, that injured SP-containing perivascular nerve fibers are involved.

The present study examined tissue obtained from rat models of infarction and contusion as well as human post mortem infarct and contusion tissue at several timepoints. Immunohistochemistry was used to characterize and correlate, in the cores of the lesions and their margins, the presence and distribution of SP and extravascular albumin, an indicator of vasogenic edema. In addition, the tissues were examined to identify injured perivascular SP-containing nerve fibers using amyloid precursor protein (APP) as an indicator of axonal injury.

Our results demonstrated, in all examined rat and human tissue, that perivascular SP-iR was present in astrocytic processes rather than in nerve fibers. Furthermore, no APP-immunoreactive perivascular nerve fibers were observed. This implies that perivascular astrocytic processes might be more
important than perivascular nerve fibers in any effect that SP may have on the blood-brain barrier (BBB) in the settings of infarction and contusion. In addition, the results generally showed, in rat infarcts and contusions, an increase in SP-immunoreactivity (SP-IR) and albumin-immunoreactivity (albumin-IR). This suggests that, in the rat, increased SP in the setting of infarction and contusion might contribute to vasogenic edema. Human tissue, however, showed no increase in SP-IR following infarction or contusion in spite of the presence of albumin-IR. These observations in human tissue might be related to the unavailability of tissue for examination at earlier timepoints post-insult and further investigation is warranted to provide greater detail on any possible involvement of SP with edema in these settings.