Effect of small molecule vasopressin V1a and V2 receptor antagonists on brain edema formation and secondary brain damage following traumatic brain injury in mice.

The attenuation of brain edema is a major therapeutic target after traumatic brain injury (TBI). Vasopressin (AVP) is well known to play a major role in the regulation of brain water content and vasoendothelial functions and to be involved in brain edema formation. Therefore, the aim of the current study was to analyze the antiedematous efficacy of a clinically relevant, nonpeptidic AVP V1a and V2 receptor antagonists. C57Bl6 mice were subjected to controlled cortical impact (CCI) and V1a or V2 receptors were inhibited by using the highly selective antagonists SR-49059 or SR-121463A either by systemic (intraperitoneal, IP) or intracerebroventricular (ICV) application. After 24 h, brain edema, intracranial pressure (ICP), and contusion volume were assessed. Systemically applied AVP receptor antagonists could not reduce secondary lesion growth. In contrast, ICV administration of AVP V1a receptor antagonist decreased brain edema formation by 68%, diminished post-traumatic increase of ICP by 46%, and reduced secondary contusion expansion by 43% 24 h after CCI. The ICV inhibition of V2 receptors resulted in significant reduction of post-traumatic brain edema by 41% 24 h after CCI, but failed to show further influence on ICP and lesion growth. Hence, centrally applied vasopressin V1a receptor antagonists may be used to reduce
brain edema formation after TBI.