Hyponatremia means a reduction in the plasma sodium ion (Na^+) concentration from normal level 144 mM to below 135 mM. It is the most common electrolyte abnormality in hospitalized patients. The most frequent cause of hyponatremia is water retention due to the increase in blood levels of antidiuretic hormone, also known as vasopressin (AVP). Hyponatremia is associated with neurological deficits, significant morbidity and mortality. The severity of neurological symptoms in hyponatremia depends on the rate of the decrease in Na^+ concentration. If this decrease occurs in less than 48 hours we are dealing with acute hyponatremia and mild to severe symptoms, if it occurs in more than 48 hours hyponatremia is called chronic and the symptoms are mild or absent. The cause of the adverse effects of hyponatremia in patients remain unclear. Recent studies showed that patients with chronic hyponatremia have attention deficits, cognitive impairments and impaired motor functions. The most likely cause of such abnormalities in hyponatremia is a disturbance in the metabolic regulation of the cerebral circulation. The preliminary studies to this project showed that the increased concentration of AVP in the presence of a decreased sodium concentration (*in vitro* model of AVP-associated hyponatremia) leads to vascular dysfunction such as: constriction and impaired regulation of the tone of small intracerebral blood vessels known as the parenchymal arterioles (PA). Such abnormalities indicate the endothelial dysfunction. Under physiological conditions, cerebral vascular endothelial cells insulate the brain from the blood by forming a blood-brain barrier (BBB) and participate in functional hyperemia (the increase in blood delivery to the activated part of the brain) through the release of vasodilating nitric oxide (NO). The dysfunctional endothelium releases vasoconstrictors, impairs functional hyperemia and leads to the leakage of the BBB. One of the causes of the endothelial dysfunction in AVP-associated hyponatremia may be the oxidative stress and production of reactive oxygen species (ROS). The aim of this project is to elucidate the mechanisms of vascular disorders in hyponatremia in the presence of AVP with regard to the known consequences of oxidative stress. The project traces how changes at the cellular level translate into the dysfunction of the brain in acute and chronic AVP-associated hyponatremia. The specific objectives of this study are to determine whether AVP-associated hyponatremia leads to: 1) the constriction of the isolated PAs via V_{1a} vasopressin receptor; 2) the constriction and disturbed endothelial regulation of the isolated PAs which can be reversed by ROS scavengers and a precursor of NO, namely L-arginine; 3) vascular inflammation; 4) the disruption of the BBB; 5) the impairment of functional hyperemia and microvascular reactivity to the products of cellular metabolism; 6) neurological deficits. All experiments planned in this project will be performed *in vivo* on rats or *in vitro* on tissues collected from them, such as parenchymal arterioles, brain and blood. The *in vitro* experiments on the isolated PAs will be performed in the organ chamber, in which the vessels will be placed in a special buffer, pressurized and perfused. Hyponatremia will be induced by lowering sodium concentration in the buffer from 144 to 121 mM in the presence of 15 pg/ml AVP. With the aid of this model, it will be assessed whether vascular impairment in acute hyponatremia in the presence of AVP is associated with the activation of V_1 vasopressin receptor, with disordered endothelial release of NO and with the generation of ROS. In the *in vivo* studies two models of hyponatremia, namely acute and chronic, will be used. The acute AVP-associated hyponatremia will be induced by subcutaneous injection of AVP in conjunction with intraperitoneal administration of water for injections in a dose of 9-12% body weight. The generation of ROS in the parenchymal arterioles will be detected using special fluorescence staining. The concentration of nitrite in the plasma, which is a marker of NO production, will be measured using nitric oxide analyzer. The gene expression and protein level of the inflammatory mediators as well as proteins of tight junctions of the BBB will be analyzed using real time PCR and Western blot methods. The permeability of the BBB will be assessed using fluorescein-dextran (FITC-dextran) and fluorescence spectrophotometry. To find out whether AVP-associated hyponatremia impairs functional hyperemia, the changes in the microflow in the somato-sensory cortex in response to the stimulation of the front paw will be studied. Under physiological conditions, the increase in microflow during such stimulation is observed. Impairment of this response may result in neurological deficits. The third part of studies will be performed in the *in vivo* model of chronic AVP-associated hyponatremia. In this model, hyponatremia will be induced using AVP-filled ALZET mini-osmotic pump and a rodent liquid diet. In this model of hyponatremia the same experiments as in the *in vivo* model of acute AVP-associated hyponatremia will be performed. In addition, the assessment of cognitive and motor functions will be performed using behavioral tests. The problems addressed in the project are medically important, as they are often raised in the medical literature, but have never been studied before. The studies planned within this project will contribute to a better understanding of the adverse effects of hyponatremia on patients in whom this disorder is associated with high plasma concentration of AVP and will reveal differences between the acute and chronic effects of hyponatremia on the brain vascular system and on the brain function. This knowledge is important not only from a purely scientific point of view, but also, in perspective, for the appropriate treatment of acute and chronic hyponatremia.