Image obtained by confocal microscopy 3-D showing nerve endings
Positive (green fluorescence) for endothelin-1 in remodeled basilar artery of an adult capybara *(FMVZ / USP)* 23/01/2014 - Special

Scientists propose using capybara as a natural model for the study of stroke By Karina Toledo

Agência FAPESP - Besides being the world's largest rodent, the capybara *(Hydrochaeris Hydrochoerus)* has another peculiar anatomical feature. When it reaches sexual maturity, around one year old, one of two major arteries supplying your brain shuts. The other simultaneously doubles in size and undergoes a remodeling process to meet demand brain with oxygen and nutrients.

A sudden but more and more potentially disastrous outcome, similar obstructive process can occur in patients of human atherosclerosis or coagulopathies. Because of this similarity, in an **article** published in the journal *Cells Tissues Organs*, scientists at the University of São Paulo (USP) and the University College London (UCL), UK, propose using the capybara as study of ischemic stroke type (ischemic stroke) model - that caused by occlusion of a major artery to the brain vasculature.

"The capybara would be better than the rat animal model by having the mean body weight (between 20 and 40 pounds) and longevity (10-14 years) more comparable to the human species. This could be an area multidisciplinary study, with participation of the pharmaceutical industry to test new drugs, "opined the veterinarian and professor Augusto Coppi, head of the Laboratory of Stereology Stochastic and Chemical Anatomy (LSSCA) Department of Surgery, Faculty of Veterinary Medicine and Animal Science (FMVZ) USP and coordinator of the **research supported** by FAPESP.

Both in man and in the capybara as well as in other mammals, the two main carrier of blood to the brain are the internal carotid artery and the basilar artery. "The carotid arteries leaving the heart, passing one on each side of the neck, and at the time when they reach the ears fall into the external carotid artery and internal carotid artery (which causes most of the cerebral arteries). Have the basilar artery is formed by the junction of the vertebral arteries in the nape. This system is also called the vertebral-basilar "said Coppi.

In capybaras, around six months of age, the internal carotid artery naturally begins to undergo a process of fibrosis and at 12 months, is completely blocked by connective tissue, resembling a fibrous cord. Concomitantly, the basilar artery passes through a structural retrofit to become the main supplier of blood to the brain.

"This is a physiological process and not know for sure why it occurs. Formulate some hypotheses on previous published studies by our group and the more likely it is that the basilar artery assume the role of principal vascularization of the entire brain in capybaras. The internal carotid loses its function after sexual maturation, "said Coppi.

In the case of humans, however, the internal carotid and basilar arteries share the task of brain vasculature. "However, the internal carotid is more susceptible to being obstructed by atherosclerotic plaque (consisting of cholesterol and calcium) of the basilar. And unfortunately, unlike what happens with the capybara, the process is sudden and no time to refashion the other system to meet the demand of the brain, "he said.

Nerve impulses

In research published in the journal *Cells Tissues Organs* researchers analyzed tissue samples from adult capybara basilar artery and nerves surrounding it. "Our goal was to figure out how to behave nerves supplying this artery, which are essential to ensure the motility of the vessel and consequently the proper conduct of blood and nutrients to the brain. Not enough to simply increase the caliber of the artery. If blood flow is not regular and constant by vertebrobasilar system, brain tissue can be injured, "said Coppi.

With the aid of immuno-cytochemistry (which use antibodies to identify molecules at the subcellular level), transmission electron microscopy techniques (which allows visualization of structures at the subcellular level) and stereology (Microscopy in 3-D), scientists have confirmed the existence of active synapses and nerve endings in the basilar artery remodeled, ie, communication between nerve fibers and modified in adult capybara basilar artery.

It confirmed the presence of two vasoactive substances (which stimulate contraction of blood vessels) endothelin-1 and its receptor, endothelin A. "Not all vessels have endothelin - important substance in maintaining cerebral hemodynamic balance. There are other vasoactive substances such as norepinephrine, for example. But endothelin offers finer control and a driving more regular blood. Able to confirm that, following the closing of the internal carotid artery during puberty, the basilar artery of adult capybaras takes control, doubles its diameter, becoming thus able to provide a regular blood supply to the entire brain, "explained Coppi.

According to the researcher, the presence of endothelin both in the internal carotid artery or the basilar artery has been described in humans and mice. This, however, is the first time in the literature that confirms the existence of the vasoactive substance in the basilar artery (and its associated nerves) in capybaras.

"Future studies may confirm if there is the presence of other vasoactive substances in the basilar artery of the capybara. We also suggest the study of new drugs that may act on that site. The idea is to think of new biochemical markers that can signal and induce in humans a quick and effective angiogenesis in carotid system and at the same time, activate the mechanism of remodeling of the basilar artery similar to what occurs in the form capybara, promoting Alternatively circulation of blood to the brain, "Coppi said.

The partnership with researchers from the University College London has spanned more than a decade and resulted in three previous publications that complement each other. In 2004, the *Anatomy, Histology, Embryologia* magazine, the **group described** structurally the obstruction of the internal carotid artery and the basilar artery remodeling of capybaras.

In 2005, in the ***Journal of Molecular Histology,*** the authors discussed the possible presence of endothelin-1 and its receptor in the basilar artery of the capybara.

The **work published** in 2006 in the journal *Cell and Tissue Research* described in greater detail the structural changes in the obstructed carotid artery and the increase in size and structural remodeling of the basilar artery.

"It's a series of studies in which we were investigating an integrated and multidisciplinary process, aiming to understand it ever more deeply and holistically. In the latter, we arrive at the level of molecular biology and subsidies have robust to propose the use of this animal as a study of ischemic stroke model.

According to the Brazilian Society of Cardiology (SBC) leads stroke deaths from circulatory diseases in the country. The projection for 2014 is that the problem affects 350,000 Brazilians.

Article *immunoreactive Endothelin-1 and Endothelin A Receptor in Basilar Artery Perivascular Nerves of Young and Adult Capybaras (doi: 10.1159/000348617),* can be read in **http:www.karger.com/Article/FullText/348617.**

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