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Commentary on a Non-Human Primate Model of Aneurismal Subarachnoid Hemorrhage

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I and my colleagues recently presented a primate model subarachnoid hemorrhage (SAH) [1] characteristics describing medical, surgical, imagining techniques that had been used at the Surgical Neurology Branch of the National Institute of Neurological Disorders and Stroke from 1989 until 2011 when I left the NIH.

As aneurismal SAH (aSAH) leaves 50% of patients dead and almost 70% of survivors disabled, for years has been an urgent necessity to develop an animal model(s) reliably mimicking pathophysiology and clinical course of this disease. Such an animal model would allow investigation of cause or causes of a poor outcome aSAH rending a possibility for development of a cause-targeted treatment.

We, and several other research groups, quickly realized that the best mimicking clinical situation characterized by a delayed onset of intracranial arterial vasospasm has been a non-human primate model introduced by Espinoza et al. in the Bryce Weir laboratory in 1984 [2]. Over the decades of intensive, multicenter experimental effort using a non-human primate, but also other models, elucidated many mechanisms underlying deleterious effects of aSAH in some people as well as initiated a paradigm shift in goals for adequate treatment development.

For well over a half of century, a delayed intracranial vasospasm has been widely accepted as a central culprit responsible for a poor outcome after SAH due to delayed ischemic neurological deficits also known as delayed cerebral infarcts (DCI) [3]. However, this dogma has been recently challenged and new avenues of SAH-related research, like early brain injury and ultra-early vasospasm, have been pursued [4-6]. This renewed interest in mechanisms contributing to development of DCI with or without delayed intracranial vasospasm, has increased efforts to develop an adequate SAH model(s).

A non-human primate model with a direct surgical placement of blood clot around the middle cerebral artery has proven to be the most consistent and reliable model of delayed intracranial vasospasm after SAH and led to many clinical trials confirming its clinical usefulness. However, this model was inadequate to mimic clinical course of aSAH clinical consequences, as monkeys did not develop DCI. This discrepancy was explained by differences in the brain size and/or development of collateral cerebral blood flow in animals but not in humans after aSAH. However, a Clazosentan study showing a clinical efficacy confirmed that vasospasm [5,6], despite being a tremendous challenge and a possible contributor to a poor outcome, may not be as crucial as it has been thought for years [5,6]. New culprits, including early ischemia, early brain injury, ultra-early vasospasm, inflammation, gene and protein changes, as well as combination of cortical spreading depressions and cortical spreading ischemias [5,6] have been proposed to be responsible for DCI and a poor outcome. This paradigm shift has opened new perspectives for research and new avenues for SAH modeling.

A modified primate model, we developed, incorporated combined advantages of (1) providing superior control of SAH conditions, (2) allowing for repeated cerebral arteriographies, (3) producing reliable and consistent middle cerebral artery spasm, (4) evoking local brain changes but without debilitating neurological deficits and (5) allowing for physical and psychological assessment of animals for prolonged observation, imagining and behavioral testing.

To provide an insight in the SAH-related mechanisms responsible for DCI and delayed cerebral vasospasm, we modified a model, in which after opening the dura matter but before opening the Sylvian fissure's arachnoid to expose he middle cerebral artery, we partially removed arachnoid over the posterior aspect of "clinically silent" inferior and/or middle frontal gyri as well as over the anterior and central part of the temporal lobe. Those areas of the brain depleted of arachnoid were suitable for an easy recognition during autopsy and histopathological studies as well as allowed for a prolonged animal observation and testing.

Another mechanism responsible for DCI could be an early brain injury evoked, among other causes, by a rapid and dramatic increase of ICP after aneurismal rapture.

Since this mechanism is impossible to mimic in an Espinosa's clot model we proposed an additional modification of this non-human primate SAH model involving a surgical implantation of a flat-shaped balloon after removal of arachnoid that could be inflated/deflated h/days later or a controlled SAH with puncturing the right MCA or ICA bifurcation. In the latter, an intracranial bleeding could be stopped by inflation of intra-arterial balloon, which should control a volume of blood accessing subarachnoid space.

The future development and/or natural evolution of a non-human primate model of SAH should address a paradigm shift(s) in our knowledge and better our understanding of brain injury after aSAH and sources of poor outcome.

References

1. Ryszard MP, John B, Boris S, Victoria H (2014) A non-human primate model of aneurismal subarachnoid hemorrhage (SAH). Transl Stroke Res 5: 681-691.
2. Espinosa F, Weir B, Overton T, Castor W, Grace M, et al. (1984) A randomized placebo-controlled double-blind trial of nimodipine after SAH in monkeys. Part I: Clinical and radiological findings. J Neurosurg 60: 1167-1175.
3. Vergouwen MD, Frijns CJ, Roos YB, Rinkel GJ, Baas F, et al. (2004) Plasminogen activator inhibitor-1 4 g allele in the 4 g/5 g promoter polymorphism increases the occurrence of cerebral ischemia after aneurysmal subarachnoid hemorrhage. Stroke 35: 1280-1283.
4. Hansen-Schwartz J, Vajkoczy P, Macdonald RL, Pluta RM, Zhang JH (2007) Cerebral vasospasm: Looking beyond vasoconstriction. Trends Pharmacol Sci 28: 252-256.
5. Macdonald RL, Pluta RM, Zhang JH (2007) Cerebral vasospasm after subarachnoid hemorrhage: The emerging revolution. Nat Clin Pract Neurol 3: 256-263.
6. Pluta RM, Hansen-Schwartz J, Dreier J, Vajkoczy P, Macdonald RL, et al. (2009) Cerebral vasospasm following subarachnoid hemorrhage: Time for a new world of thought. Neurol Res 31: 151-158.

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