Priority of Experimental Evidence

To the Editor:

The authors of a recent article that appeared in *Circulation Research* described that “there is no information available regarding the mechanism by which SAH activates the Rho/Rho kinase or PKC pathways” (page 810). I would like to say that such a description is incorrect. There is a history of experiments to identify the relationship between the roles of protein kinase C (PKC) and the mechanism of vasospasm after subarachnoid hemorrhage (SAH). In particular, we have extensively investigated the roles of PKC in the development and maintenance of vasospasm after SAH, as listed in the References. Wickman et al should have discussed the history of the experiments regarding “the mechanism by which SAH activates PKC pathways.” Since we clarified the roles of PKC in the mechanism of vasospasm, we carefully examined which PKC isoforms are expressed in canine basilar artery and which ones are involved in the development and maintenance of vasospasm with Western blotting analysis, just as the authors did. We detected four PKC isoforms in canine basilar artery (PKCα, δ, ζ, η). Among these four PKC isoforms, PKCδ is closely related with the initiation and PKCα with the maintenance of vasospasm in a “two-hemorrhage” canine model (in situ 1-week study). Because the antibodies for PKC isoforms are derived from a different space (rat brain), we showed the specificity of the bands expressed in Western blotting by elimination of these bands using antibody-specific synthetic peptides. I believe that it is not good enough to show the positive control using rat brain, but rather to show the elimination of bands, just as we did, in order to say it is specific. From these points of view, I think that Wickman et al should have discussed the priority of experimental evidence regarding the role of PKC isoforms in the mechanism of vasospasm after SAH by citing previously published studies. Wickman et al emphasized the roles of PKCe and PKCα in the mechanism of vasospasm. The authors should also have discussed the reasons why they obtained such different experimental evidence from ours. The authors’ experimental periods were 1.5 hours in the isometric tension study and 60 minutes in cultured smooth muscles cells. The period of clinical vasospasm lasts for 1 or 2 weeks. In addition, it is not deniable that multiple substances could be candidates to induce vasospasm besides oxyhemoglobin. The authors’ explanation based on their evidence for the mechanism of vasospasm might be a mechanism of the initiation of vasospasm, and a property of rabbit basilar artery to only oxyhemoglobin. However, it cannot be relevant for a mechanism of the sustained cerebral arterial contraction like vasospasm after SAH.

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Circ Res. 2003;93:e25
doi: 10.1161/01.RES.0000087334.44183.A6

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