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Time to Refocus the Target in Stroke Therapy Again?



Stroke treatment has made enormous advances during the past decades. While initial research was focused on the brain parenchyma and its eventual demise, it was actually the arrival of treatments of clot that completely changed the game. Indeed, while from a basic point of view, the pathophysiology of stroke is well-investigated and partly understood enough to develop a pharmaceutical agent,^{1,2} these approaches have, until now, failed. Indeed, while the animal models were very often able to create an ideal model of stroke, the translation into the clinical setting has not met with great success for neuroprotection. However, now that imaging and revascularization have made great progress, it may be time to reassess if neuroprotection could be possible. Indeed, whether by using CT³ or MR imaging⁴ or even DSA-based techniques⁵ or even bypassing these and going directly into the catheter lab, it is possible to obtain imaging of the brain that will diagnose an ischemic event with high certitude and a short time interval. This fast and improved global brain imaging approach, together with the recent successes of interventional revascularization, shows increased rates of recovery⁶⁻⁹ within a longer therapeutic window than previously achievable.¹⁰

The combination of improved diagnostics and interventional measures could make us reassess whether the era of neuroprotective agents may come again. Indeed, while revascularization itself by interventional techniques is now the standard, the results, on the one hand, may be improved if the drugs can now be given directly into the target zone,¹¹ which could lead to new therapeutic drug trials. This means that we also have to reassess the way we conceive the penumbra or the tissue at risk.^{12,13} Indeed, from being at the beginning a metabolic event that was supposed to become the therapeutic target, the penumbral model evolved into a hemodynamically based one with new imaging technologies. This evolution coincided with the initial thrombolysis trials and led to the initial successes against the disease. However, now that we see that not just collaterals play a role in maintaining tissue vitality, we may need to additionally assess the topics of tissular fragility more with advanced imaging techniques and possibly artificial intelligence algorithms to demonstrate the potential ac-

tivity of pharmaceutical treatment. This assessment could, in the end, also facilitate treatment by offering additional therapies with wider access than is currently available to patients who have an ischemic event and do not live close to an integrated stroke center.

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