

Neurological Disorder, Stroke: Relevance of Preclinical Studies

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Editorial

The neurological disorders and stroke represent the last century's medical challenge. Despite increasing number of elderly people and the subsequent increase of neurological diseases, in so-called industrialized countries, we have no efficacious strategy to fight this plague.

Probably, the more effective method to take on this challenge may be a rigorous prevention and principle risk factors (e.g. high-pressure, stress, obesity, smoke of tobacco and alcohol) elimination. On the other hand, further scientific research in this field could be very useful. This kind of research should be based on the use of animal models to improve current understanding of the pathophysiological features of these diseases and may yield important information on how to improve analysis of the "efficacy" of some possible molecules.

Many authors, in a number of related medical fields, have evaluated the importance of preclinical research and they have written different review articles. However, in these models of disease, we often have some problem to acknowledge a precise human disorder. For instance, an animal model of stroke may use the focal cerebral ischemia. Actually, this model predicts the outcome of an ischemic insult but, it does not reproduce the general background pathophysiological that would cause an endogenous stroke. Therefore, we should accept the limitations inherent in these models and, follow early proof of efficacy studies in "young healthy animals" with more accurate studies in models incorporating age and co-morbidities. Presumably, translational problems may decrease with further improvement in preclinical study design and conduct.

Recent preclinical studies underline the relevance of human cell-based approach to study stroke. Once again, these papers evidenced the crucial role of animal models. Moreover, these models were also appropriate to evaluate the effects of stem cell transplantation in Ischemic Stroke. It is the general opinion that the advantageous clinical translation of cell-based therapy requires the use, in preclinical research, of scientifically appropriate and of reproducible functional neurological result evaluations, which are adequately sensitive to investigate sensor motor asymmetry related to the site of ischemia.

As a relevant outcome of the use of this approach, it should be noted that, regardless of cell type and delivery route, exogenous cells show targeted delivery to the infarct site. These results were obtained after about ten years of research in this field. The use of animals as model of stroke refers to different races, ages, sex and types of ischemia. Therefore, effects of age and sex on stroke incidence, functional neurological recovery and stroke mortality have been demonstrated both in humans and in animal models. In particular, the age-dependent escalation in the advancement of ischemic tissue into infarction, strongly hints that age is a relevant biological parameter for the variability in stroke outcome. Interestingly though, it appears that age plays a significant role in the neurological recovery via recruitment of neighboring neuronal circuitries. This invaluable information may be acquired through animal model studies only. That is due to the fact that, it was regularly observed that neurological recovery is associated with dendritic and synaptic plasticity in the contralesional striatum and with axonal plasticity in contralesional motor cortex. This suggests that a spontaneous post-stroke striatal recovery could also be increased by inputs from contra lateral striatum and could elucidate why patients with sub cortical stroke are more likely to exhibit spontaneous neurological recovery.

A detailed analysis of previous research clearly demonstrates that the contribution of animal model and preclinical studies to understand pathophysiological mechanisms of neurological disorder, stroke and its recovery, represents a pivotal piece of this puzzle. Probably, physicians, specialists (neurologists) and the scientific community (neuroscientists) should collaborate to expand our knowhow regarding these devastating diseases, which represent the second most common cause of death in Europe, and the third most common cause of death in the United States and Canada.

