The combination of two proteins exerts a regenerating effect in Parkinson's disease

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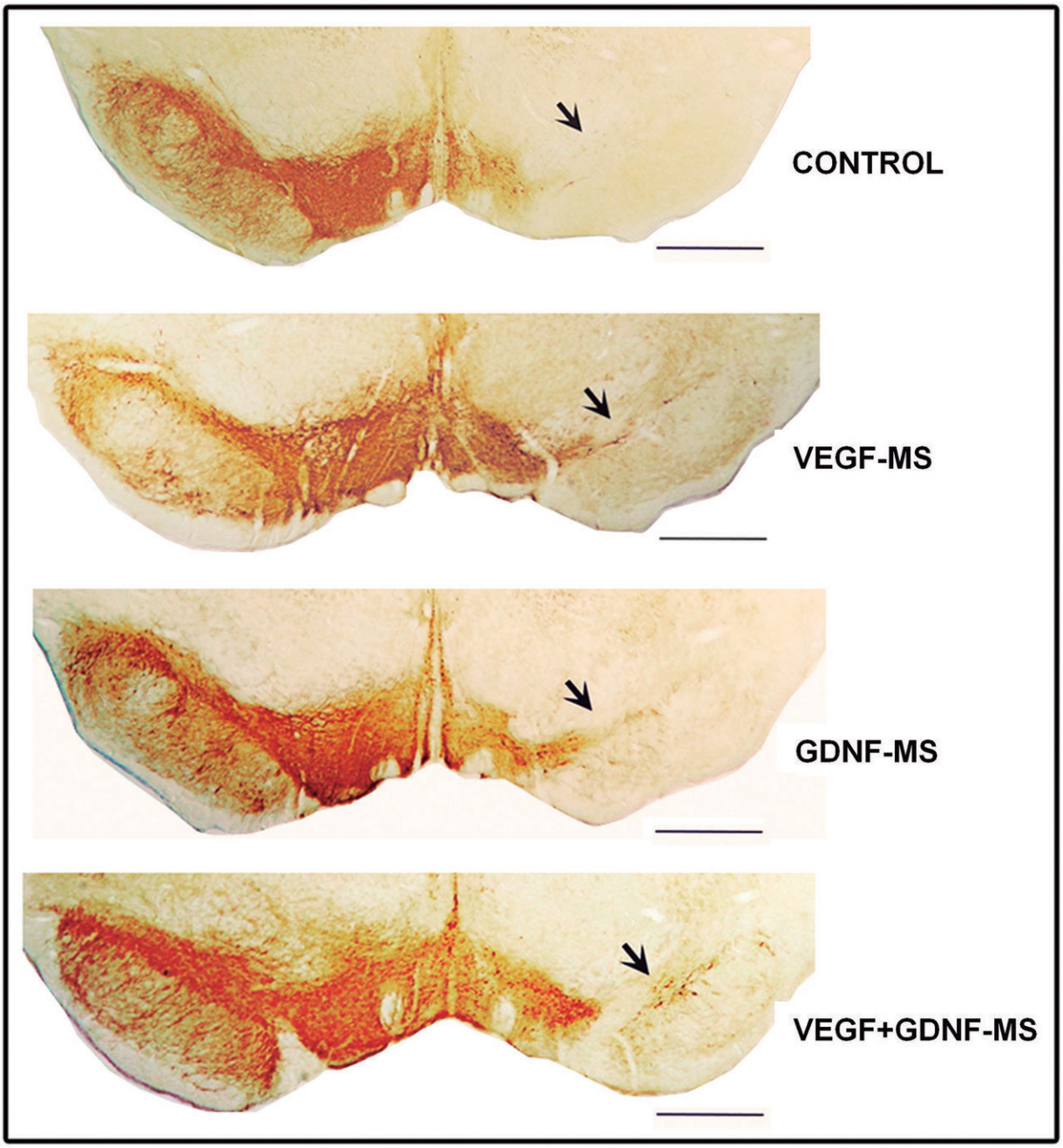

The histological sections show different degrees of impairment or recuperation of the black substance. This formation is dyed to highlight the enzyme tyrosine hydroxylase (precursor of dopamine) in groups treated with empty microspheres (control group), with microspheres loaded with VEGF (VEGF-MS), with microspheres loaded with GDNF (GDNF-MS) and with microspheres loaded with VEGF and GDNF in a combined way (VEGF+GDNF-MS). The arrow

indicates the area of the black substance where there is greater regeneration (greater positivity, browner making). It corresponds to the group treated with microspheres loaded with VEGF and GDNF. Scale bar= 1 mm. Credit: UPV/EHU

Parkinson's disease is currently the second-most widespread neurogenerative pathology. It is a motor disorder caused by the loss of dopaminergic neurons in the gray matter of the brain. These neurons produce dopamine, a neurotransmitter that plays a key role in the modulation of involuntary movements.

The research carried out at the UPV/EHU was developed in an experimental model that reproduces different stages of Parkinson's disease. The results showed that the changes caused by the condition were not homogeneous between different parts of the brain. "The impairment is correlated with the specific anatomic distribution of the dopaminergic neurons and their terminals," said researcher Catalina Requejo. In other words, those areas in which the dopaminergic neurons have more connections with regions that remain whole were found to be less affected.

After confirming that the experimental model could be used to explore the morphological and functional changes caused by the disease, therapeutic strategies based on the release of neurotrophic factors were applied. These factors are proteins that encourage cell growth, plasticity and survival, and therefore play an essential role in controlling neuronal function.

Specifically, the researchers applied vascular endothelial growth factor (VEGF) and glial cell-derived neurotrophic factor (GDNF). These molecules were delivered encapsulated in microspheres or in

nanospheres, comprising a biocompatible, biodegradable polymer: poly lactic-co-glycolic acid (PLGA), which is released continuously and gradually. Furthermore, the factors were administered in a combined way to determine whether they induced a synergistic effect.

The results were encouraging in both the early and severe phase of the model. The combining of the VEGF and GDNF not only significantly reduced the degeneration of the dopaminergic neurons of gray matter, it also induced the formation of new cells and cellular differentiation. The researchers were also able to confirm that there had been an improvement in the areas where the nerve fibres in this region were projected. To confirm the synergistic, neurogenerative effect of the two factors, they administered a molecule that inhibits the receptors of the two neurotrophic factors they were studying. "The consequences for the dopaminergic system were even worse, which supports the beneficial synergistic effects exerted by the VEFG and the GDNF in Parkinson's," concluded the researcher.

Finally, it is worth highlighting that the best results were obtained when the factors were delivered encapsulated in nanospheres during the early phase of the disease replicated in the model. This reinforces the importance of early diagnosis, and that "nanotechnology could be a very useful tool when it comes to administering neurotrophic factors," she said.

More information: Jose V. Lafuente et al, Nanoformulation: A Useful Therapeutic Strategy for Improving Neuroprotection and the Neurorestorative Potential in Experimental Models of Parkinson's Disease, *Nanomedicine in Central Nervous System Injury and Repair* (2017). DOI: 10.1016/bs.irn.2017.09.003