Spadin and its analogs improve recovery after stroke by preventing post-stroke depression

Mariel Pietri
University of Nice Sophia Antipolis, France

Stroke is a major disease associated with high mortality and serious long-term disability. Unfortunately, usual treatments fail to improve long-term recovery and thrombolysis, which is the unique short-term treatment, is efficient only on 10% of patients. Consequently, developing new treatments is necessary. The TREK-1 channel represents an interesting target since its activity has recently been shown to be protective against stroke. We have identified a short molecule (spadin or PE 12-28) derived from a larger endogenous peptide, which is a potent antidepressant and is able to specifically inhibit TREK-1, as a potential new treatment. Using the in vivo model of MCAO in mice, we demonstrated that chronic treatment with spadin or a shorter analog (PE 22-28) improved the post stoke recovery from days to months after the ischemia. The protocol we used was designed thanks to electrophysiology studies and consisted in a two phase treatment, a low dose for one week followed by a high dose treatment for several weeks. Treated mice showed a significant reduction of the immobility time in the Forced Swimming Test. The eat latency in the Novelty Suppressed Feeding test was significantly reduced. The learning capacity was increased in the Morris Water Maze and the motor coordination was improved in both rotarod and pole test. The increase in neurogenesis, measured by BrdU incorporation was still present even at 10 weeks post trauma. Taken together our results suggest that spadin or its analog are very potent candidates for the development of new treatments improving stroke recovery.

Biography

Mariel Pietri is currently a PhD student at the University of Nice Sophia Antipolis, France, under the guidance of the Drs Catherine Heurteaux and Marc Borsotto. Her work mainly focuses is the development of new treatment for stroke and depression, targeting the TREK-1 channel. She works on the development of spadin and its analogs as a new medicine and her thesis project focuses more specifically on the protection against stroke. She has her expertise in surgery of small animal, behavioural mouse models, immunochemistry and biochemical analyses.

m Pietri@ipmc.cnrs.fr