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## **Social theatre, Emotions and Parkinson's disease: results from the second pilot study**

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Whether art therapy can be a useful rehabilitative tool is a long standing and debated question. To this aim, we run a randomized, controlled and single-blinded study lasted 3 years, on 20 subjects affected by a moderate form of idiopathic Parkinson's disease (PD), in stable treatment with L-dopa and L-dopa agonists, and without severe sensory deficits (Modugno et al 2010). Half of them were randomly assigned to a "rehabilitative theatre" program, while the other half underwent conventional physiotherapy. Patients of both groups were evaluated at the beginning of each year, using five clinical rating scales. We found that, by the end of the third year, theatre-patients showed greater improvements of motor and non-motor symptoms than those of the control group. Despite the positive results, the study had a number of weakness. Data were collected only on subjective scales, and the benefits appeared only after a long period of time. To overcome these limitations, we run a new project, with 24 PD patients with the same experimental design of the previous one, but i) collecting outputs not only on clinical scales, but also using neuropsychological and psychophysical tests; ii) using a new form of theatre where patients have to undergo to an 'emotional' training. We found that the 'emotional' theatre was extremely effective and allowed to improve mental well-being of patients in only one year's time. Thus, we replicated and extended our previous results showing that theatre, coupled with conventional medical treatments, represents a valid complementary therapeutic interventions for PD treatment.

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## **Increased Blood brain barrier permeability in a transgenic model of Huntington's disease and Motor neuron disease favors increased brain uptake of the complement C5a receptor antagonist PMX205**

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Complement system activation in neurodegenerative diseases such as Huntington's disease (HD) and motor neuron disease (MND) promotes the pathology of neurological conditions, in co-ordination with increased permeability of the blood brain barrier (BBB). We have previously shown that the C5a receptor antagonist, PMX205, reduces brain inflammation and neuronal death in neurodegenerative disease models. The present study investigated the extent and stages of BBB integrity alteration during the progression of neurodegeneration in a model of HD and MND. In addition we examined whether increased BBB permeability, allowed for increased PMX205 entry into the degenerating brain. Transgenic R/61 mice harbouring the human mutant huntingtin gene, transgenic SOD1 mice and age/litter matched control mice at various ages were injected i.v. with sodium fluorescein (Na-FL) to examine BBB permeability. Blood and tissue samples including brain regions (cerebellum, cortex, striatum) and spinal cord were collected after 15 min. Samples were processed for fluorescence determination using a validated quantitative method, and results were expressed as level of Na-FL (ng/g) and % fluorescence uptake. Pharmacokinetic studies were performed by administering PMX205 1 mg/kg i.v., and collecting blood and perfused brain and spinal cord samples after 2.5min. Samples were processed and analysed for PMX205 levels by a validated method using LC-MS/MS. We identified increased BBB permeability in transgenic mice, compared to wild-type littermates. BBB permeability changes occurred early in disease, and increased as neurodegeneration progressed. In line with this, we identified significant changes in PMX205 brain levels, Na-FL levels and fluorescence uptake. In conclusion, these studies demonstrate breakdown of the BBB and blood-spinal cord barrier (BSCB) occurs in the early stages of neurodegeneration in these mouse models. This increased permeability would likely favors effective transport of drugs into degenerating regions of the brain/spinal cord. In this study, we demonstrate increased PMX205 entry, which may assist in the neuroprotective effects of this drug in these neurodegenerative models.

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