# Neuroplasticity and Disease

https://www.neurodegenerationresearch.eu/survey/neuroplasticity-and-disease/

**Title of project or programme**

Neuroplasticity and Disease

**Principal Investigators of project/programme grant**

| Title | Forname | Surname | Institution | Country |
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| Dr | Vincenzo | De Paola | MRC Clinical Sciences Centre | UK |

**Address of institution of lead PI**

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| Institution | MRC Clinical Sciences Centre |
| Street Address | Faculty of Medicine, Imperial College London, Hammersmith Hospital Campus, Du Cane Road, |
| City | London |
| Postcode | W12 0NN |

**Country**

United Kingdom

**Source of funding information**

Medical Research Council

**Total sum awarded (Euro)**

921420.50

**Start date of award**

01-04-2007

**Total duration of award in months**

36

**The project/programme is most relevant to**

- Alzheimer’s disease and other dementias

**Keywords**

**Research abstract in English**

The goal of our programme is to understand at the molecular and cellular level the mechanisms of synaptic plasticity and their relevance to the proper function and neuropathology of the adult mammalian brain.

Central issues in neuroscience are to define the neural substrates of adaptation to experience, learning and memory and ultimately of common brain disorders. Synapses, microstructures that allow interconnection of neural circuits, play a key role in all these processes. In particular, there is ample evidence that synaptic plasticity underlies cognitive functions such as learning and memory and various neuropathologies including Alzheimer's and stroke.

However, to date, many fundamental questions about synaptic function and plasticity, despite their importance, remain unanswered. In fact, while functional imaging studies can reveal the brain areas involved in disease, cellular events such as modifications of specific neural circuits and synaptic signalling have remained largely inaccessible to existing approaches in intact mammals. For example, are synaptic sites in the adult brain fixed or can learning and memory change them? Which cellular signalling pathways underlie the stability or modification of neuronal connections and how can they be manipulated to design new therapies for neurological diseases?

Given the extraordinarily complex properties of synaptic networks our contribution towards tackling these issues will be interdisciplinary. We will combine behavioural and advanced molecular genetic, optical and anatomical techniques in mice. We plan to investigate the adaptive modifications of neural circuits especially in the context of defined behavioural paradigms and central nervous system dysfunction.

Specifically, one major avenue of research will be to study the dynamics of identified axonal networks in animal models of common brain disorders with in vivo 2-photon microscopy. This optical tool enables the detection of fluorescently-labelled cellular compartments in scattering tissue up to several hundred microns below the surface of the intact brain. We have recently tracked the dynamics of single axons, individual synapses and even synaptic molecule clusters in living animals over a wide range of temporal scales, from seconds to several months.

This provides a novel way of looking at the cellular and synaptic basis of biological processes such as learning and common pathologies such as fragile-X syndrome and brain injury. We hope this approach will lead to the discovery of synaptic and circuit phenotypes at early stages of disease that could be used as therapeutic targets.

**Lay Summary**