
BIOGRAPHICAL SKETCH

NAME: **FEDERICO MORO**

POSITION TITLE: Head of the Unit of Pathophysiology and Neuroimaging

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of Milan, Italy	Five years master's degree in Pharm. Chem. and Tech	2005-11	Pharmacology
Open University, Milton Keynes, U.K.	PhD	2012-17	Neuroscience
Imperial College of London, London, U.K.	Visiting Res	2017	Neuroimaging
Mario Negri Institute, Milan, Italy	Post-doc	2017-present	Traumatic Brain Injury

A. Personal Statement

During my research activity I favor non-invasive techniques such as behavioral, in vivo MRI and circulating biomarkers analysis since these technique techniques can be applied in humans in the clinical setting and fulfill the goal of implementing translational research. I have more than 10 years of experience in neuroscience and neuropharmacology research. During my PhD I investigated the effect of glutamatergic therapies acting on astrocytic glutamate transporters for threatening nicotine addiction. I then continued with a postdoctoral fellowship at the Policlinico of Milan where I was collaborating in a European multi-centers study where I was using advance MRI techniques as biomarker for evaluating patients long term consequences of traumatic brain injury (TBI). To this regard I received a specific training at the Imperial College of London, in the laboratory of Computational, Cognitive and Clinical Neuroimaging lead by Prof David J Sharp, on diffusion MRI analysis to evaluate axonal injury after TBI. During the same period, I had the chance of working on preclinical models of TBI at the Mario Negri Institute (IRFMN) in the laboratory of Acute Brain Injury and Therapeutic Strategies lead by Dr Elisa R Zanier where I investigated secondary injury processes in several experimental models of TBI. As a senior post-hoc at IRFMN in Dr Zanier's laboratory my studies included the evaluation of therapeutic strategies for TBI and the characterization of rodent models for studying acute and delayed consequences of acute brain injury. From 2023 I am a junior group leader at IRFMN. My research interests include (1) understanding the mechanisms transforming an initial acute biomechanical injury into a chronic and progressive pathology; (2) understanding the heterogeneity of traumatic brain injury (TBI) and the identification of brain imaging and circulating biomarkers of injury evolution and repair; (3) development of therapeutic strategies.

As part of this work, we have generated an optimized, clinically relevant mouse model of post-traumatic epilepsy (PTE), where epilepsy with frequent generalized seizures occurs in ~50% of mice at 3-5 months post-TBI. More recently we have characterized an acute EEG signature that allows the identification of high- and low-risk mice before seizure onset at 10 days post TBI. This is a unique model not yet available in the current literature; therefore, our laboratories are the only ones able to use it at the present time. The high PTE rate and

the identification of an early PTE biomarkers makes our model highly convenient for discovery mechanisms of epileptogenesis.

In the currently proposed project, I expect to provide an in-depth characterization of early changes underpinning epilepsy development after TBI.

My expertise in animal modelling, my knowledge of cellular biology, my understanding of the pathological sequelae of TBI, and my experience with imaging technique will equip me with the necessary tools to successfully conduct the proposed research.

B. Positions and Honors

Positions and Employment

<i>Years</i>	<i>Position, Place</i>
2023 – 2025	Head of the Unit of Pathobiology and Neuroimaging, laboratory of Traumatic Brain Injury and Neuroprotection, Department of Acute Brain and Cardiovascular Injury, <i>Mario Negri Institute for Pharmacological Research</i> , Milan, Italy.
2021 – 2022	Post-doctoral fellow, <i>Mario Negri Institute for Pharmacological Research</i> , laboratory of Acute Brain Injury and Therapeutic Strategies, Milan, Italy.
2017-2020	Guest scientist, <i>Mario Negri Institute for Pharmacological Research</i> , laboratory of Acute Brain Injury and Therapeutic Strategies, Milan, Italy.
2017-2020	Post-doctoral fellow, <i>Fondazione Ca'Granda – Ospedale Maggiore Policlinico</i> , Department of Anesthesiology and Intensive Care
2017	Visiting Res, <i>Imperial College of London</i> , laboratory of Computational, Cognitive and Clinical Neuroimaging, London, UK.
2012-2016	PhD student, <i>Mario Negri Institute for Pharmacological Research</i> , Laboratory of Experimental Psychopharmacology, Milan, Italy.
2011	Visiting Res, Cardiff University, Neuroscience division, Cardiff, UK.

Honors

<i>Years</i>	<i>Title</i>
2024	Grant award, Fondazione Roche.
2023	Grant award, OU-ARC Research Catalyst Fund, Open University, UK.
2019	Best poster presentation ERA-NET NEURON symposium, Bonn, Germany.
2018	Stipend for attending 11 th FENS Forum of Neuroscience, Berlin, Germany.
2016	Best oral presentation at 3 rd PhD student meeting, Mario Negri institute, Milan Italy.
2016	Travel grants for attending 10 th FENS Forum of Neuroscience, Copenhagen, Denmark.
2015	Travel grants for attending NEURONUS IBRO & IRUN Neuroscience Forum, Krakow, Poland.
2012	Stipend for attending 2 nd neurobiology summer school “The Invertebrate Brain: from Neurons to Behavior”, Trieste, Italy.

C. Contributions to Science

1. **Biosignatures of network dysfunction to predict post-traumatic epilepsy:** Therapeutic interventions for arresting the late neurological sequelae such as post-traumatic epilepsy (PTE) are still missing and urgently required. The latent period between TBI and PTE onset provides an ideal therapeutic window for interventions apt to prevent PTE. The development of preventive interventions has been hampered however by the limited knowledge of the mechanisms underlying TBI-induced epileptogenesis and by the lack of validated non-invasive biomarkers for identifying patients at-risk for PTE. There is therefore an urgent need for robust preclinical PTE models to discover the molecular mechanisms and biomarkers for

the transition from TBI to PTE. We have recently characterized a mouse model with a high PTE incidence and spontaneous seizures frequency that provide an ideal model for biomarker discovery and for testing new drugs.

- a. Di Sapia R, Rizzi M, **Moro F**, Lisi I, Caccamo A, Ravizza T, Vezzani A, Zanier ER. ECoG spiking activity and signal dimension are early predictive measures of epileptogenesis in a translational mouse model of traumatic brain injury. *Neurobiol Dis.* 2023 Aug 1.
- b. Di Sapia R.*, **Moro F.***, Montanarella M., Iori V., Micotti E., Tolomeo D., Wang K.K.W., Vezzani A., Ravizza T., and Zanier E.R. (2021). In-depth characterization of a mouse model of post-traumatic epilepsy for biomarker and drug discovery. *Acta Neuropathol Commun* 9, 76.

2. **New therapies for TBI:** Supportive treatment for the management of TBI has progressed over the past 20 years, but specific neuroprotective strategies are still lacking.

We have demonstrated that in our murine model of TBI, Argon is effective in accelerating the recovery of sensorimotor and cognitive functions by reducing the area of vasogenic edema- and microglial-mediated neuroinflammation.

We have recently found that A β 1-6A2V(D) treatment in TBI mice improved neurological outcomes and reduced blood markers of axonal damage by impeding tau aggregation but also favors its degradation by tissue proteases.

- a. Diomede L, Zanier ER, **Moro F**, Vegliante G, Colombo L, Russo L, Cagnotto A, Natale C, Xodo FM, De Luigi A, Mosconi M, Beeg M, Catania M, Rossi G, Tagliavini F, Di Fede G, Salmona M. A β 1-6A2V(D) peptide, effective on A β aggregation, inhibits tau misfolding and protects the brain after traumatic brain injury. *Mol Psychiatry.* 2023 May 17
- b. **Moro F.**, Fossi F., Magliocca A., Pascente R., Sammali E., Baldini F., Tolomeo D., Micotti E., Citerio G., Stocchetti N., et al. (2021). Efficacy of acute administration of inhaled argon on traumatic brain injury in mice. *Br J Anaesth* 126, 256–264.

3. **Effect of aging on the consequences of TBI:** Older age is one of the strongest predictors for poor prognosis after brain trauma, a phenomenon driven by the presence of extra-cranial comorbidities as well as pre-existent pathologies. Furthermore, ageing is associated with a dysregulated immune response, leading to chronic inflammatory states. We found a slower and less complete recovery from functional deficits after TBI in aged mice with behavioural differences underpinned, by DTI-MRI abnormalities in white matter structures, and accompanied by a dysregulated systemic, meningeal and brain tissue immune response, as well as widespread reactive astrogliosis with indications for proinflammatory signature.

- a. **Moro F.**, Pischiutta F., Portet A, Needham JE, Norton JE, Ferdinand RJ, Vegliante G, Sammali E, Pascente R, Caruso E, Micotti E, Tolomeo D, Barros RM, Fraunberger E, Wang KKW, Esser M, Menon D, Clatworthy RM, Zanier ER. (2022). Aging is associated to maladaptive immune response and worse outcome after traumatic brain injury. *Brain Commun* 4(2):fcac036.

4. **Developing and validating blood and imaging biomarkers of axonal injury following traumatic brain injury:** Long-term outcomes of TBI are frequently poor, with around half of patients affected by residual disability. Traumatic axonal injury is a key determinant of these clinical outcomes. However, validated methods to quantify the extent of axonal injury are lacking in a clinical context. Our research showed that plasma neurofilament light (NfL) provides a sensitive and clinically meaningful measure of axonal injury produced by TBI, with evidence in the preclinical model showing its utility to monitor brain's susceptibility also to mild TBI. This reflects the extent of underlying damage, validated using advanced MRI, and experimental models, thus supporting the incorporation of NfL sampling subacutely after injury into clinical practice to assist with the diagnosis of axonal injury and to improve prognostication.

- a. Lisi I*, **Moro F***, Mazzone E, Marklund N, Pischutta F, Kobeissy F, Mao X, Corrigan F, Helmy A, Nasrallah F, Pietro VD, Ngwenya LB, Portela LV, Semple BD, Schneider ALC, Arrastia RD, Menon DK, Smith DH, Wellington C, Loane DJ, Wang KKW, Zanier ER. Exploiting blood-based biomarkers to align preclinical models with human traumatic brain injury. *Brain*. 2025 Apr 3.
 - b. Li LM, Heslegrave A, Soreq E, Nattino G, Rosnati M, Garbero E, Zimmerman KA, Graham NSN, **Moro F**, Novelli D, Gradisek P, Magnoni S, Glocker B, Zetterberg H, Bertolini G, Sharp DJ. Investigating the characteristics and correlates of systemic inflammation after traumatic brain injury: the TBI-BraINFLAMM study. *BMJ Open*. 2023 May 23;13(5):e069594.
 - c. **Moro F**, Lisi I, Tolomeo D, Vegliante G, Pascente R, Mazzone E, Hussain R, Micotti E, Dallmeier J, Pischutta F, Bianchi E, Chiesa R, Wang KK, Zanier ER. Acute Blood Levels of Neurofilament Light Indicate One-Year White Matter Pathology and Functional Impairment in Repetitive Mild Traumatic Brain Injured Mice. *J Neurotrauma*. 2023 Mar 13.
 - d. 6. Graham NSN, Zimmerman KA, **Moro F**, Heslegrave A, Maillard SA, Bernini A, Miroz JP, Donat CK, Lopez MY, Bourke N, Jolly AE, Mallas EJ, Soreq E, Wilson MH, Fatania G, Roi D, Patel MC, Garbero E, Nattino G, Baciuc C, Fainardi E, Chieragato A, Gradisek P, Magnoni S, Oddo M, Zetterberg H, Bertolini G, Sharp DJ. Axonal marker neurofilament light predicts long-term outcomes and progressive neurodegeneration after traumatic brain injury. *Sci Transl Med*. 2021 Sep 29;13(613).
 - e. Graham NSN, Zimmerman KA, Bertolini G, Magnoni S, Oddo M, Zetterberg H, **Moro F**, Novelli D, Heslegrave A, Chieragato A, Fainardi E, Fleming JM, Garbero E, Abed-Maillard S, Gradisek P, Bernini A, Sharp DJ. Multicentre longitudinal study of fluid and neuroimaging BIOmarkers of AXonal injury after traumatic brain injury: the BIO-AX-TBI study protocol. *BMJ Open*. 2020 Nov 10;10(11):e042093.
5. **Maladaptive changes in the cortico-accumbal glutamate network implicated in drug addiction:** My early publications addressed the neurobiological changes persisting into or occurring during abstinence from use of a drug of abuse to provide targets for developing medications to reduce relapse. Our research lead to the findings that stimulating metabotropic glutamate receptor mGluR2/3 could prevent acute and chronic cue-controlled drug-seeking.
- a. **Moro F.**, Giannotti G., Caffino L., Marzo C.M., Di Clemente A., Fumagalli F., and Cervo L. (2020). Lasting reduction of nicotine-seeking behavior by chronic N-acetylcysteine during experimental cue-exposure therapy. *Addict Biol* 25, e12771.
 - b. **Moro F.**, Orrù A., Marzo C.M., Di Clemente A., and Cervo, L. (2018). mGluR2/3 mediates short-term control of nicotine-seeking by acute systemic N-acetylcysteine: N-acetylcysteine and nicotine-seeking. *Addiction Biology* 23, 28–40.
 - c. Caffino L., Cassina C., Giannotti G., Orrù A., **Moro F.**, Di Clemente A., Racagni G., Fumagalli F., and Cervo L. (2014). Short-term abstinence from cocaine self-administration, but not passive cocaine infusion, elevates α CaMKII autophosphorylation in the rat nucleus accumbens and medial prefrontal cortex. *Int J Neuropsychopharmacol* 17, 323–329.
 - d. Fumagalli F., **Moro F.**, Caffino L., Orrù A., Cassina C., Giannotti G., Di Clemente A., Racagni G., Riva M.A., and Cervo L. (2013). Region-specific effects on BDNF expression after contingent or non-contingent cocaine i.v. self-administration in rats. *Int J Neuropsychopharmacol* 16, 913–918.

[Link to List of Published Works](#)

Full list of publications: <https://www.ncbi.nlm.nih.gov/myncbi/1BUWvL-rMWfkfe/bibliography/public/>
(29 peer reviewed papers; h-index=11)