

PROJECT 1**DoS:** Maria Assunta Rocca**Title:** Differences in brain structure and function in primary headache disorders: a multimodal MRI study**Curriculum:** Neuroscience and Experimental Neurology

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<http://www.hsr.it/research/organization/divisions-centers/division-of-neuroscience/maria-a-rocca/>**Project description** (Number of characters, including spaces: 2.000 - 3.000):

Primary headache disorders, such as migraine and cluster headache, are one of the most common and disabling neurological diseases worldwide. Migraine has a high familiarity and some variants (e.g., familiar hemiplegic migraine) have been associated with some genetic mutations.

Migraine patients usually experience unilateral or bilateral, throbbing pain that may last from 4 to 72 hours, and may be associated with phonophobia, photophobia, nausea and vomiting. The variability in frequency of migraine attacks is related to both the genetic component carried by the individual and environmental triggering factors. Neurological symptoms, defined as aura, can precede the onset of migraine attack in a certain percentage of patients.

Core features of cluster headache attacks are its circadian periodicity, the severe, sharpening, unilateral pain, lasting from 15 to 180 minutes, the autonomic symptoms and the sense of restlessness that patients experience during the attacks. Many clinical features (e.g., unilateral pain, autonomic symptoms, phonophobia, photophobia) are common to these two primary headaches and some patients can experience both types of attacks.

Conventional and advanced MRI techniques have been applied extensively to the study of patients with these conditions, both in the course of an acute attack and during the interictal phase. There is ample evidence that in predisposed migraine and cluster headache patients the activation of different cortical, subcortical and brainstem regions and the subsequent release of key neuropeptides, such as the calcitonin gene-related peptide (CGRP), can contribute to the onset of the disease. Widespread structural and functional MRI abnormalities in brain areas involved in pain and multisensory processing have been shown in both conditions. Whether such alterations represent a predisposing trait or are the consequence of the recurrence of headache attacks is still a matter of debate. Many studies demonstrated that brain regions, like the brainstem, thalamus and hypothalamus, have a pivotal role in triggering the migraine and cluster headache attacks. Other studies have shown that the brain of these patients can be remodeled over time.

Only a few neuroimaging studies have compared migraine and cluster headache patients. Our working hypothesis is that migraine and cluster headache patients might share some structural and functional abnormalities in regions involved in the onset of both type of headache attacks and in pain processing. However, different MRI alterations might explain those clinical features that differed between these two primary headaches.

In this project, using a multimodal MRI approach including different functional and structural MR techniques, we plan to identify an MRI pattern that might help us to distinguish migraine from cluster headache patients and controls.

Project objectives:

- To investigate differences in regional brain activity and morphometry in migraine patients compared to age and sex matched cluster headache patients and controls;

- To investigate whether variants in genes that might contribute to migraine and cluster headache pathophysiology are associated to different MRI patterns.

Skills to be acquired by the student:

- Diagnosis, treatment and monitoring of different headache conditions,
- Expertise in MRI aspects of the main headache conditions,
- Knowledge of MRI techniques and sequences,
- Knowledge of segmentation and registration methods,
- Skill in the use of software for voxel-wise analysis (e.g., SPM, fsl),
- Expertise in the set-up of MRI studies for monitoring of pharmaceutical drugs.

References (max. 3)

1. Messina R, Rocca MA, Colombo B, Valsasina P, Horsfield MA, Copetti M, et al. Cortical abnormalities in patients with migraine: a surface-based analysis. *Radiology*. 2013;268(1):170-80.
2. Rocca MA, Ceccarelli A, Falini A, Colombo B, Tortorella P, Bernasconi L, et al. Brain gray matter changes in migraine patients with T2-visible lesions: a 3-T MRI study. *Stroke*. 2006;37(7):1765-70.
3. Rocca MA, Valsasina P, Absinta M, Colombo B, Barcella V, Falini A, et al. Central nervous system dysregulation extends beyond the pain-matrix network in cluster headache. *Cephalalgia*. 2010;30(11):1383-91.