

# The cerebellum-periaqueductal gray connectivity: a constrained spherical deconvolution tractography study

Salvatore Bertino<sup>1</sup>, Alberto Cacciola<sup>2</sup>, Gianpaolo Basile<sup>1</sup>, Giuseppe Santoro<sup>1</sup>, Maria Righi<sup>1</sup>, Daniele Bruschetta<sup>1</sup>, Giovanna Vermiglio<sup>1</sup>, Giuseppina Cutroneo<sup>1</sup>

<sup>1</sup> Department of Biomedical, Dental Sciences and Morphological and Functional Images, University of Messina, 98125 Messina, Italy

<sup>2</sup> IRCCS Centro Neurolesi "Bonino Pulejo", Messina, Italy

The periaqueductal gray (PAG) is a relevant neuronal station situated in the mid-brain, which play a pivotal role in triggering behavioral responses to stressful stimuli, such as pain or threat. Current knowledge concerning PAG functions is based on several tract-tracing studies conducted on animals, which unveiled PAG connectivity to both cortical and subcortical areas [1]. Considering that descending projections to spinal cord reach the dorsal horn and connections to motor related cortical areas have never been described yet, the neural structure which best fits PAG modulation of motor behavior is the cerebellum. Direct connections between PAG and cerebellar cortex were firstly described in cats and neurophysiological studies conducted on animals, suggesting either direct or indirect PAG influence to cerebellar activity. In the last decades, the rise of diffusion weighted imaging and tractography have made possible to reliably reconstruct white matter pathways in the human brain. To the best of our knowledge, few tractography studies explored PAG connectivity in humans and the evidences concerning direct or indirect connections with the cerebellar cortex are still sparse. Aimed at investigating PAG connectivity with particular focus on PAG-cerebellum connections, we used high quality diffusion weighted imaging data of thirty healthy subjects from the Human Connectome Project. Fiber tracts have been reconstructed using Spherical Informed Filtering of Tractograms, a novel algorithm improving streamline reconstruction and selection [2]. Connectivity analysis revealed that the PAG is mainly connected with subcortical structures, such as the thalamus and the cerebellum. Taken together our results show a direct interplay between the PAG and the cerebellum, thus suggesting the cerebellum as a likely candidate to modulate complex features of motor behavior in stressful conditions, such as adaptation after social defeat and computing strategies to avoid threatening situations.

## References

- [1] Benarroch (2012) Periaqueductal gray: an interface for behavioral control. *Neurology*. 78: 210-7.
- [2] Smith et al. (2013) SIFT: Spherical-deconvolution informed filtering of tractograms. *Neuroimage*. 67: 298-312.

## Keywords

Periaqueductal gray, cerebellum, MRI, tractography, SIFT