

Multidisciplinary morphological approaches to the intrinsic human cerebellar dopaminergic system, its projection and clinical role

Paolo Flace¹, Demetrio Milardi², Alberto Cacciola³, Gianpaolo Basile⁴

¹ Società Italiana di Anatomia e Istologia, Università degli Studi di Bari 'Aldo Moro' - Dipartimento di Scienze Mediche di Base, Neuroscienze e Organi di Senso, Bari, Italia

² Società Italiana di Anatomia e Istologia, Università degli Studi di Messina - Dipartimento di Scienze biomediche, odontoiatriche e delle immagini morfologiche e funzionali, Messina, Italia

³ Società Italiana di Anatomia e Istologia, IRCCS Centro Neurolesi "Bonino Pulejo", Messina, Italy, Messina, Italia

⁴ Università degli Studi di Bari 'Aldo Moro', Università degli Studi di Bari di Messina - Dipartimento di Scienze biomediche, odontoiatriche e delle immagini morfologiche e funzionali, Messina, Italia

Introduction. Studies suggest that the cerebellum plays a role in dopaminergic disorders, such as Parkinson's disease (PD) and Schizophrenia (SCZ). Data on an intrinsic human cerebellar dopaminergic system and on a connection of the cerebellum with basal ganglia and the dopaminergic midbrain area are lacking. Studies demonstrate mainly in rodents an extrinsic dopaminergic fiber system in the cerebellum, originating from the A10 dopaminergic area, and few dopaminergic neurons composed by Purkinje neurons of the cerebellar cortex and by neurons of the deep cerebellar nuclei. Studies on the connection of the cerebellum with the brain area involved in PD and in SCZ are also lacking.

Aim. The aim of this study is to make an immunohistochemical investigation of the presence of an intrinsic human cerebellar dopaminergic system. Recent developments in Diffusion Magnetic Resonance Tractography (DMRT) may allow in vivo studies of the cerebellar connections with basal ganglia and the midbrain traditional dopaminergic area. **Material and Methods.** Autoptic fragments of human cerebellum were fixed in an aldehyde picric acid solution, embedded in paraffin, cut into 5µm sections and subjected to light microscopic immunohistochemistry with rabbit polyclonal antibodies for dopamine transporter (DAT) or dopamine type 2 receptor (DRD2).

A 3T Achieva Philips scanner was used; a SENSE 8 channels head coil, acquiring T1 weighted 3D TFE, DTI sequences: data were analyzed using the contrastained spherical deconvolution technique (CDS). **Results.** DAT and DRD2 positivity was observed in the cerebellar cortex in Purkinje neurons, granules and in some non-traditional neuron types. In the dentate nucleus positivity was observed in large and small neuron types. We demonstrated with CSD cerebellar-subcortical connections. In particular, we found a direct route linking the dentate nucleus to the substantia nigra as well as to the ventro tegmental area.

Conclusions. This study demonstrates for the first time, the existence of an intrinsic human cerebellar dopaminergic system and a cortico-dentate and direct dentate nucleus connection with the substantia nigra and with the ventro tegmental area. Finally, we suggest that the cerebellum may be involved in dopaminergic brain disorders.

Key words

Cerebellum, substantia nigra, ventro tegmental area, dopamine, connectivity, tractography, immunohistochemistry.