**Evaluation of cerebellar gray matter damage in Huntington's disease: a voxel based morphometry study**

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**Introduction:** In the last years, the cerebellar role in neurodegenerative diseases has been extensively studied[1]. However, few research related cerebellum and Huntington disease (HD)[2]. This is not only due to cerebellar contribution on motor refinement, but mainly by the discovery of its non-motor functions. The aim of our study is detail the cerebellar gray matter (GM) alterations in HD using the tool "spatially unbiased template atlas" (SUIT) for Voxel based morphometry (VBM) on magnetic resonance imaging (MRI).

**Materials and Methods:** We compared 26 patients matched in gender and age with 26 healthy controls. They underwent neurological (Unified Huntington’s disease rating scale – UHDRS) and cognitive (Montreal cognitive assessment - MOCA) evaluations. SUIT was used to analyze GM alterations. We created a two-sample test to analyze GM differences between both groups and another to correlate the cerebellar GM alterations with UHDRS (mood and motor) and MOCA scores, corrected for age, cytosine-adenine-guanine (CAG) repeats and disease duration.

**Results:** While most previous studies found cerebellar atrophy in HD, we observed mostly increased GM density at the anterior cerebellum (*p*<0.05 FWE corrected and *k*>100 voxels), compared to controls. We only observed atrophy with a less restrictive analysis (*p*<0.001 uncorrected and *k*>100 voxels) at the postero-superior cerebellar lobes. Higher GM density in the postero-superior lobe was associated with mood disorders symptoms; worse motor function correlated with GM density alterations in the central portion of the postero-inferior lobe and lateral portion of the postero-superior lobe on the right; and better cognitive function with higher GM density in the left side of the postero-inferior lobe.

**Discussion:** This study is the first to provide a detailed assessment of the cerebellum in HD. Even those that exclusively evaluated the cerebellum, only observed white matter changes, using a volumetric approach, rather than a voxel-by-voxel comparison. The SUIT tool isolates the cerebellum from other brain structures, providing a topographic detailing of each cerebellar lobe, and assessing both GM increases and reductions. We interpreted our GM excess results as a compensatory mechanism or as a structural anatomical breakdown caused by the disease, these findings may also have been influenced by reduced mean time of disease duration in our sample[3].

**Conclusion:** The listed areas are responsible for sensorimotor integration, motor planning, visuospatial function and emotional processing. We believe these findings may contribute to a better understanding of the neuropathological process of HD.

**References:** [1] Guimarães RP et al., Mov Disord 2013, 28(8): 1125-32; [2] Rees EM et al., Mov Disord 2014, 29(13): 1648-54; [3] Piccinin CC et al., Front Neurol. 2015 Jan 8;5:283.