Are we looking in the right place? The Cerebellum as early marker of neurodegenerative disorders

CRUSADE

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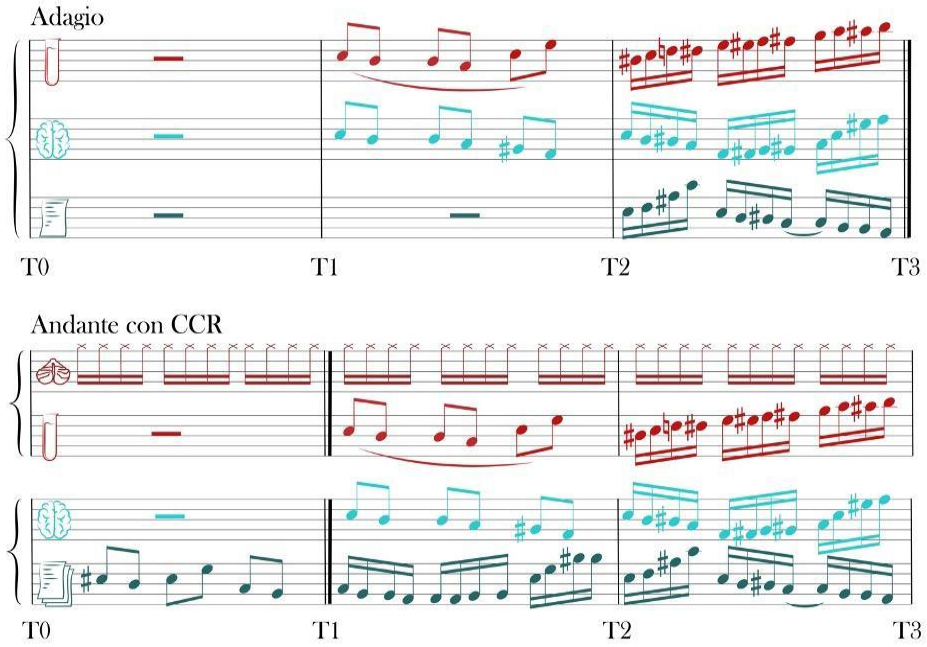

CRUSADE proposes to read the "pentagram" of neurodegenerative disorders (NDD) onset and evolution in cerebellum and cognitive cerebellar reserve (CCR) clef ("Andante con CCR"). Compared to the traditional approach ("Adagio"), according to which bio-humoral and brain macro-evidence of NDD appear only in a clinical, overt phase of disease (T1-T3), CRUSADE aims at longitudinally investigating cerebellar white matter alterations and neuropsychological profile of individuals with subjective cognitive impairment (SCI), compared to those with no referred SCI. By means of Diffusion Tensor Imaging and an ad-hoc set of neuropsychological sensitive tools, CRUSADE goals to move backward in time the known biomarkers cascade, for a very pre-clinical diagnosis of NDD (T0-T1).

For centuries, the role of the cerebellum has been relegated to coordination and control of voluntary movement, gait, and posture. Only recently scientific attention has been directed to the fascinating hypothesis that this organ can play a role in cognition. In particular, it has been hypothesized that cerebellum is involved in neurodegenerative disorders, though how and to what degree remains an intriguing enigma. CRUSADE innovatively proposes the metaphor of the cerebellum as a metronome that beats the time of subjective cognitive impairment (SCI), representing the very earliest marker of neurodegenerative disorders. The provocative, ground-breaking, and ambitious suggestion is: are we looking in the right place? What if the very first warning lights of an incipient neurodegenerative disease derive from the cerebellum rather than from the brain? CRUSADE proposes to read the "pentagram" of neurodegenerative disorders onset and evolution in cerebellum and cognitive cerebellar reserve clef for a very pre-clinical diagnosis. Subtle cerebellar white matter alterations will be longitudinally studied with Diffusion Tensor Imaging techniques in individuals with SCI

compared with individuals with no reported SCI and will be associated with the most known (bio-humoral, imaging, neuropsychological) markers of neurodegeneration. Trajectories of potential onset and kind of neurodegenerative disorders will be then tracked based on micro and macrostructural evidence of disease-specificity. The final aim of CRUSADE is to propose cerebellum, cerebellar cognitive reserve, and an ad-hoc set of neuropsychological investigation as novel means to detect the very earliest and deceiving signs of neurodegenerative processes. Beyond producing frontline research on the unresolved enigma of the cerebellar involvement in dementia, the clinical, social, and economic implications of the novel CRUSADE insights would be aspiringly enormous for the care and cure of neurodegenerative disorders.