Assessing the feasibility, safety and efficacy of cerebello-spinal tDCS in MSA-C

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Objective: Multiple system atrophy (MSA) is a neurodegenerative disorder, that lack of symptomatic treatment, especially for the cerebellar variant (MSA-C). There is preliminary evidence on the efficacy of transcranial direct current stimulation (tDCS) in different ataxia syndromes [1]. We aimed to assess the feasibility, safety and efficacy of tDCS in MSA-C.

Materials: We enrolled 11 consecutive patients with a diagnosis of MSA-C according to the current diagnostic criteria [2] who could still walk unaided as additional inclusion criterion. Patients were evaluated with the Unified Multiple System Atrophy Rating Scale (UMSARS), but also by means of objective measures of gait using wearable sensor (OPAL) during a 2-minute walking test, sway and with the 8 meter walk test (8M-WT).

Methods: The project has been designed as double-blinded, sham-controlled, cross-over trial. Subjects are randomly assigned to one of the two arms to receive either a sham or active stimulation for 5 consecutive days/week (i.e., Monday to Friday) for the first week. The active stimulation consisted of an anodal stimulation over the cerebellum area (2 cm under the inion), with the cathode being applied over the spinal lumbar enlargement (2 cm under T11), using a constant current of 2 mA will be applied for 20 minutes/day.

In the sham condition the electric current is ramped down 5 seconds after the beginning of stimulation. After the first week, groups are crossed to the other stimulation arm for the second week. Before (T0), soon after the first week (T1) and soon after the second week of the protocol (T2), patients have been evaluated as described above. Non-parametric tests for repeated measures were performed.

Results: All patients completed the study protocol and none reported any adverse events. There was a significant difference in the clinical outcome, with an improvement of the UMSARS total score, as well as of both the 8M-WT and many OPAL parameters after the active stimulation ($p<0.05$) which was not observed after the sham stimulation (**fig 1**). For patients receiving the active stimulation first, we observed a carry-over effect at the end of the second week with both clinical and non-clinical outcome being still significant as compared to baseline values (**fig 2)**.

Discussion: Although the current data are preliminary due to the small sample size, they demonstrated the feasibility and safety of cerebello-spinal tDCS in MSA. Moreover, the significant improvement of all outcomes, despite the small sample size, might suggest a reasonable effect size of the observed change.

Conclusions: tDCS appears to be safe and useful in patients with MSA-C. These results should be confirmed in larger trials.

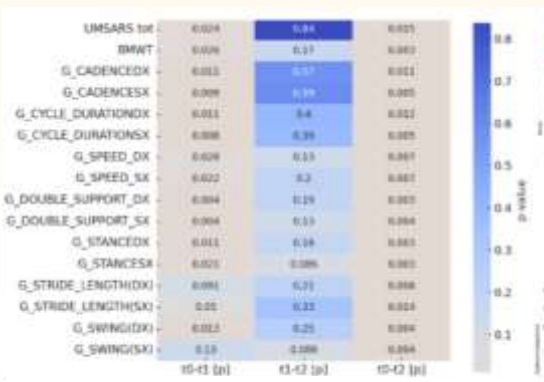

Fig 1. p-value heat map

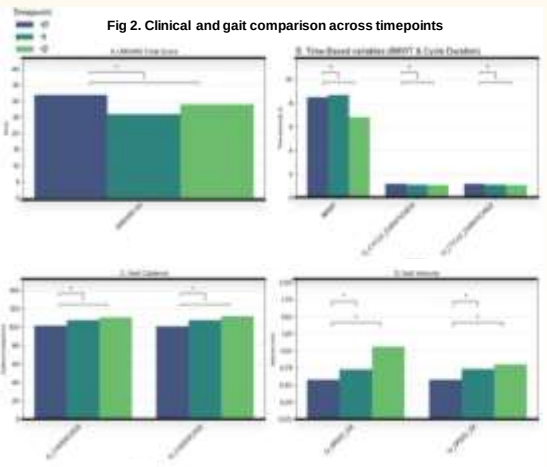

Fig 2. Clinical and gait comparison across timepoints

Benussi A, Pascual-Leone A, Borroni B. Non-Invasive Cerebellar Stimulation in Neurodegenerative Ataxia: A Literature Review. Int J Mol Sci. 2020 Mar

2) Wenning GK et al The Movement Disorder Society Criteria for the Diagnosis of Multiple System Atrophy. Mov Disord. 2022 Jun

3) Benussi A et al Cerebellar transcranial direct current stimulation in patients with ataxia: A double-blind, randomized, sham-controlled study. Mov Disord. 2015 Oct