Sustained clinical and neurophysiological effects of cerebellar transcranial Direct Current Stimulation in patients with neurodegenerative ataxia

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BACKGROUND AND OBJECTIVE

Cerebellar ataxias represent a group of disabling disorders for which we currently lack effective therapies. Cerebellar tDCS is a non-invasive technique, which has been previously demonstrated to be able to modulate cerebellar excitability and improve symptoms in patients with cerebellar ataxias.

The present study investigated whether a prolonged session of cerebellar anodal transcranial direct current stimulation (tDCS) could improve symptoms in patients with ataxia at short and long term.

METHODS

We performed a prolonged double-blind, randomized, sham or real anodal tDCS (2 mA, 20 minutes, 5 days/week for 2 weeks; see **figure 1**) in 20 patients with ataxia (five SCA 2, two SCA 38, one SCA 14, one Friedreich's ataxia, one AOA type 2, four MSA-C, one FXTAS, five SOAO). At baseline (T0), each patient underwent a clinical evaluation with SARA (Scale for the Assessment and Rating of Ataxia), ICARS (International Cooperative Ataxia Rating Scale), 9-hole peg test and 8-meter walking time and a neurophysiological evaluation with Transcranial Magnetic Stimulation (TMS) performed with Cerebellar Brain Inhibition (CBI) protocol. The same work-up was carried out immediately after either sham or anodal tDCS (T1), at 1 month (T2) and at 3-months follow-up (T3).

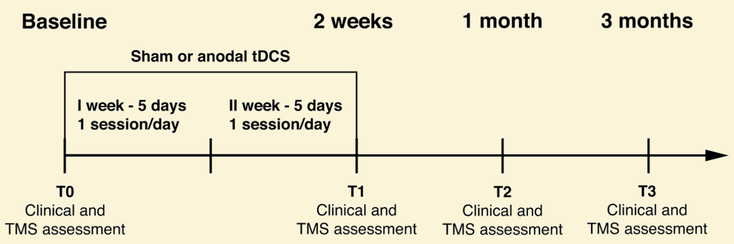

Fig 1. Study design

RESULTS

Significant differences were not identified in clinical or demographic characteristics between patients who received sham or anodal tDCS (see **Table 1**).

	Real	Sham	*p*-value*
Patients, n	8	12	
Age, years	49.8±16.7	55.2±18.2	0.514
Age at onset, years	35.8±20.6	41.4±20.9	0.568
Disease duration	14.0±12.9	13.8±8.6	0.973
MMSE score	28.2±2.6	25.5±7.3	0.674
BADL lost	0.7±1.4	1.0±1.8	0.712
IADL lost	1.7±1.9	2.0±1.9	0.328

Table 1. Demographic and clinical characteristics of included patients.
Demographic characteristics expressed as mean ± SD

As shown in **Table 2**, at baseline, SARA, ICARS scores, 8MWT and 9HPT were not significantly different in the sham trial compared to the intervention trial at the beginning (pre-) of the trials.

Sham tDCS	T0	T1	T2	T3
SARA	17.6±7.9	17.4±8.0	17.5±7.8	17.6±7.9
ICARS	48.3±19.6	47.7±19.8	47.6±19.4	47.1±19.0
9HPT-D(sec)	50.8±37.3	53.1±44.6	49.2±31.7	48.7±31.3
9HPT-nD(sec)	48.6±29.6	50.6±34.4	49.3±29.6	48.7±30.4
8MWT (sec)	9.1±2.8	9.4±2.9	9.5±3.5	9.6±3.0
Real tDCS	T0	T1	T2	T3
SARA	16.1±5.2	13.3±6.1*	12.7±5.9*	13.3±5.7*
ICARS	44.2±13.7	35.2±15.8*	33.7±16.6*	35.3±16.0*
9HPT-D (sec)	41.8±14.9	39.2±13.2	38.3±13.3*	40.1±14.6
9HPT-nD(sec)	45.0±16.5	41.9±16.0*	41.3±15.1*	41.2±13.0
8MWT(sec)	8.5±5.4	7.7±5.4	7.5±4.5	6.2±2.0

Table 2. SARA, ICARS, 9-hole peg test and 8-meter walking time scores, pre and post real/sham stimulation. Values expressed as mean ± SD. * significant difference from baseline-T0

RESULTS

There was a statistically significant interaction between treatment and time on SARA ($F_{(3,54)}$=15.36, p<0.01, partial η^2=0.46) and ICARS scores ($F_{(3,54)}$=18.04, p<0.01, partial η^2=0.50) (see **table 2** and **figure 2**).

SARA and ICARS scores were significantly different in the sham trial compared to the intervention trial at the end of the trial (T1) and after 1 and 3 months (T2, T3).

Regarding 9HPT, we observed a significant TIME×TREATMENT interaction in the non-dominant hand ($F_{(3,51)}$=2.823 p=0.05, partial η^2=0.14), but not in the dominant hand ($F_{(3,51)}$=1.14, p=0.34, partial η^2=0.06).

A significant TIME×TREATMENT interaction was also found in the 8MWT ($F_{(3,54)}$=18.04, p<0.01, partial η^2=0.50).

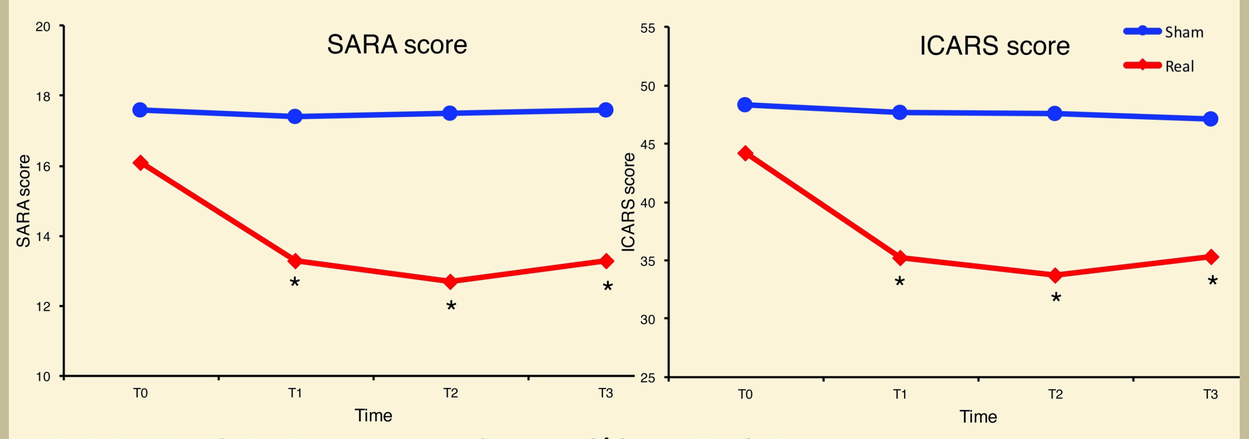

Fig 2. SARA and ICARS scores, pre and post real/sham stimulation.
Results are expressed as mean ± SD; *significant difference from baseline (T0).

In patients treated with anodal tDCS there was a restoration of cerebellar brain inhibition (CBI), which has been shown to be impaired in patients with cerebellar ataxia.

There was a statistically significant three-way interaction between time (T0, T1, T2, T3), ISI (3, 5, 10 ms) and group (sham vs anodal) ($F_{(6,78)}$=2.26, p=0.05, partial η^2=0.15) (see **figure 3**).

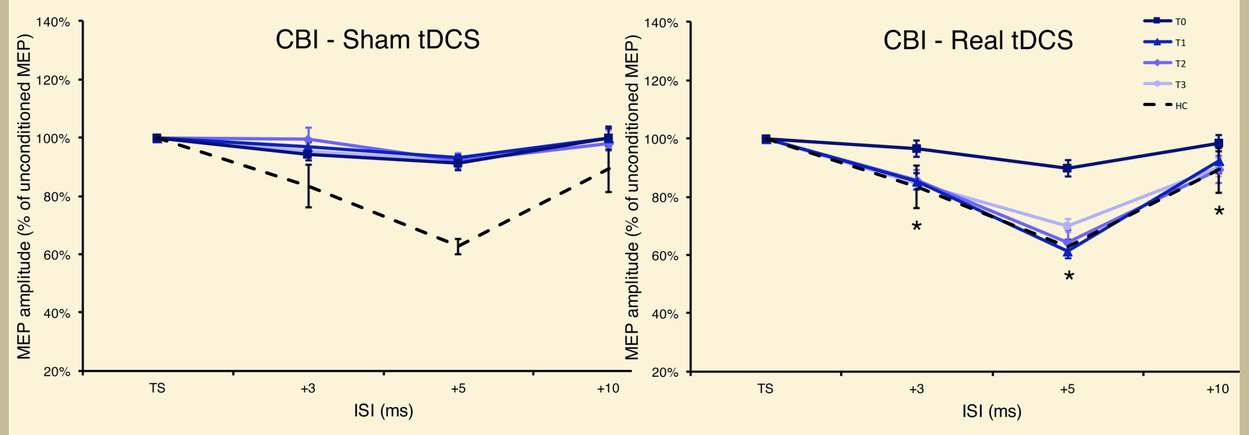

Fig 3. CBI assessed with TMS, pre and post real/sham stimulation.
*significant difference from baseline-T0

CONCLUSIONS

These results suggest that a prolonged session of anodal cerebellar tDCS can improve symptoms in patients with ataxia at long-term, and is able to restore the inhibitory activity of the cerebellum on the primary motor cortex. Based on our results anodal tDCS might represent a promising future therapeutic and rehabilitative approach in patients with neurodegenerative ataxia.

REFERENCES

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