Cerebellar transcranial direct current stimulation in spinocerebellar ataxia type 3: a randomized, double-blind, sham-controlled trial

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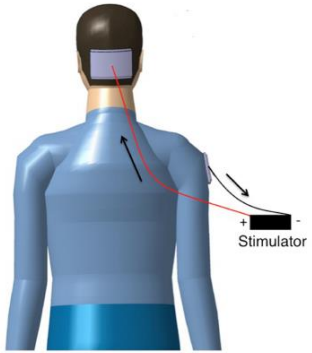
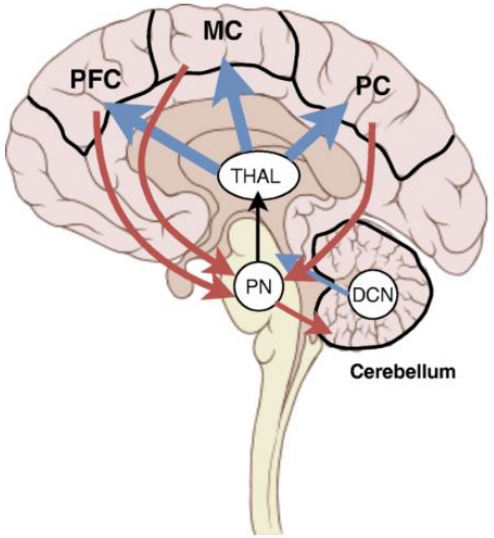
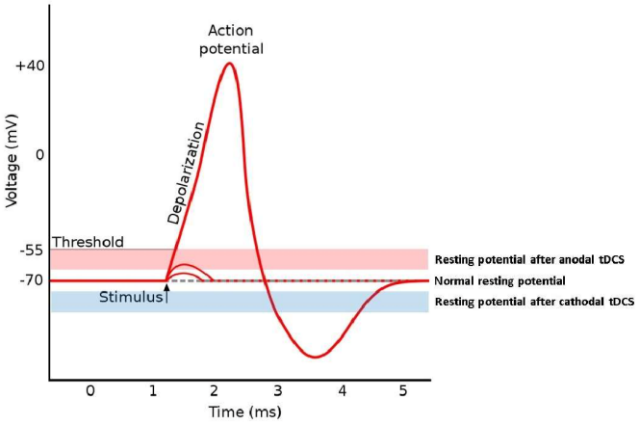
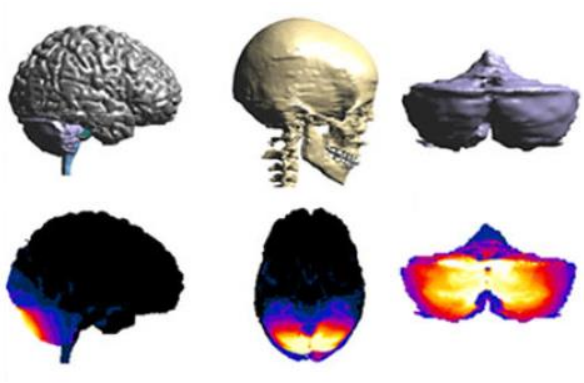
Cerebellar transcranial direct current stimulation









Parazzini et al. *Clin Neurophysiol.* 2014; Van Dun et al. *Front Hum Neurosci.* 2016; Fernandez et al. *Cerebellum* 2020

Cerebellar anodal tDCS in degenerative ataxias

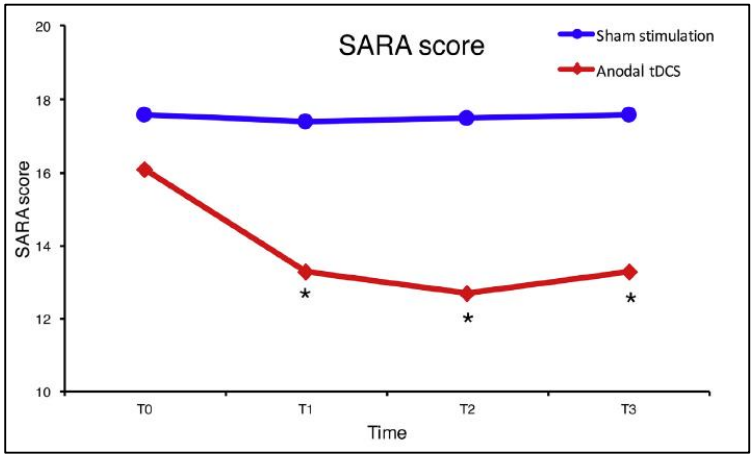
N = 20

- SCA2 (5)
- SCA38 (2)
- SCA14 (1)
- Friedreich ataxia (1)
- AOA type 2 (1)
- FXTAS (1)
- MSA-C (4)
- ILOCA (5)

Treatment

- Anodal tDCS vs.
- Sham stimulation

✓ Anode: 2 cm below inion
✓ Cathode: right deltoid
✓ 2 mA, 20 min
✓ 5 days per week for 2 weeks

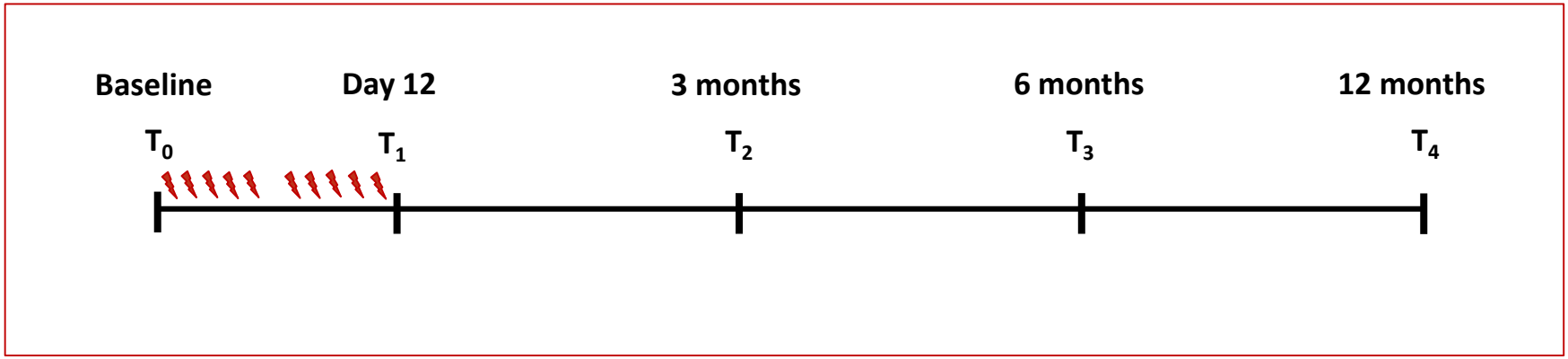


Important issues

- Etiological heterogeneity
- Duration of effects?
- Effects on cerebellar non-motor functions?

Benussi et al. *Brain Stimul.* 2017

SCA3-tDCS study



Inclusion criteria

- Age ≥ 16 years
- *ATXN3* gene mutation
- 3 ≤ SARA score ≤ 20

Exclusion criteria

- Epilepsy
- History of brain surgery
- Metallic implants in or near the skull
- Pacemaker
- Pregnancy
- Severe skin disease affecting electrode location
- Significant comorbidities that interfere with ADL

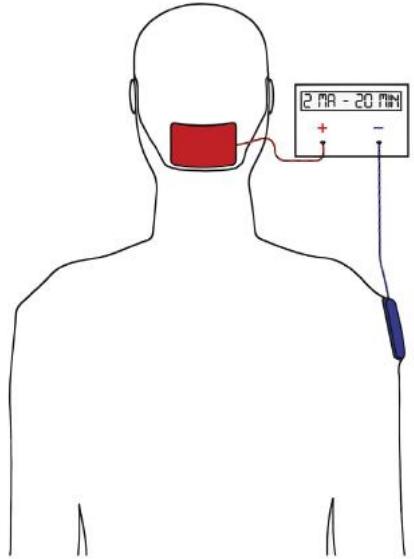
Protocol

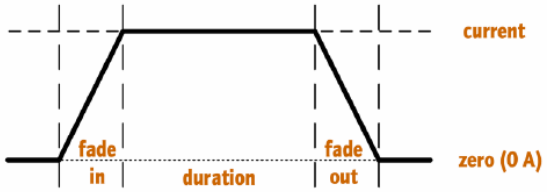
Randomization and blinding

- Block randomization (1:1) with randomly selected variable block sizes
- SARA score as stratification variable
- Patients and investigators blinded

Intervention

- NeuroConn constant current stimulator
- Two 7 x 5 cm rubber electrodes
- 30 s ramp-up, 20 min stimulation at 2 mA, 30 s ramp-down





Outcome measures

Motor

- SARA score
- 8 m walk test
- 9-hole peg test
- PATA repetition rate

Patient-reported

- Patient Global Impression of Change Scale
- EQ-5D-5L
- Patient Health Questionnaire-9
- Profile of Mood States
- Friedreich Ataxia Rating Scale ADL score

Cognitive

- Cerebellar cognitive affective syndrome scale
  - Total score
  - Number of failed tests

Neurophysiological

- Cerebellar brain inhibition
- Static posturography
- Delay eyeblink conditioning

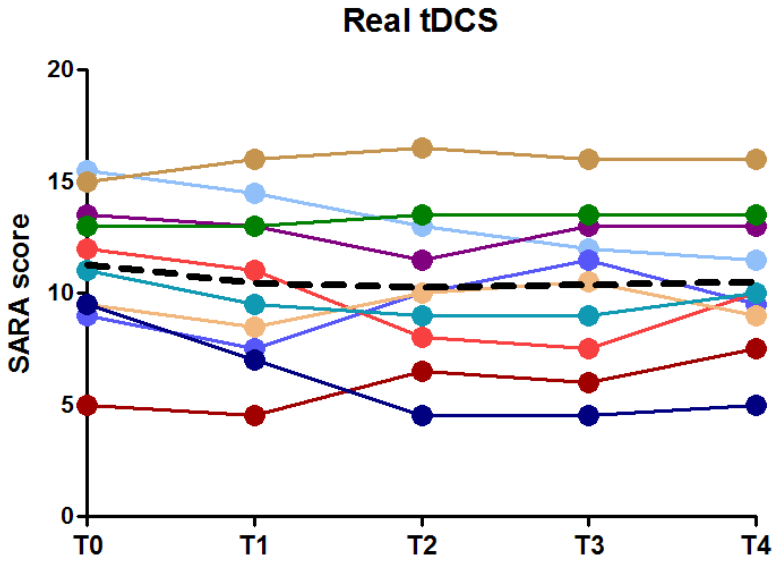
Baseline clinical and demographic characteristics

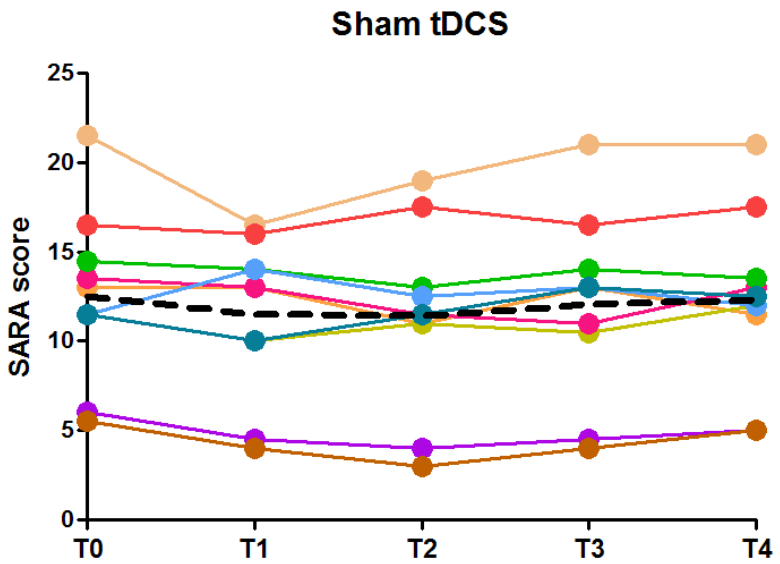
	Sham tDCS (n = 10)	Real tDCS (n = 10)

Baseline clinical and demographic characteristics

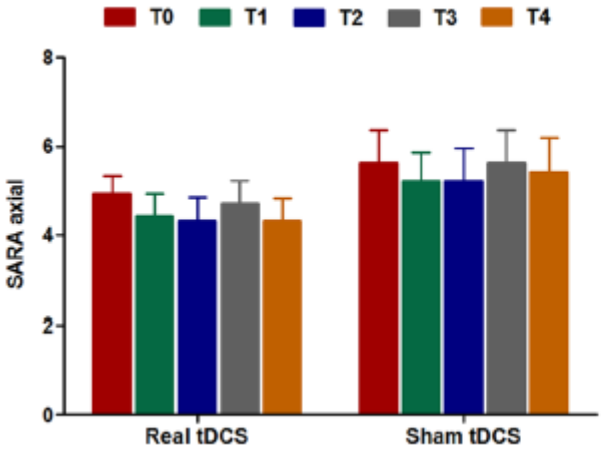
	Sham tDCS (n = 10)	Real tDCS (n = 10)
Age (y)	51.4 ± 9.8	52.4 ± 10.8
Age of onset (y)	42.6 ± 8.8	45.2 ± 9.9
Disease duration (y)	8.8 ± 6.2	7.2 ± 4.7
CAG repeat length	67.3 ± 3.1	67.8 ± 3.8
Sex (% male)	5 (50)	7 (70)
SARA score	12.5 ± 4.7	11.3 ± 3.2
8MWT (s)	6.8 ± 2.8	5.7 ± 0.9
9HPT dominant hand (s)	31.1 ± 9.5	32.1 ± 7.4
9HPT non-dominant hand (s)	33.9 ± 7.8	33.3 ± 5.0
FARS ADL score	11.9 ± 3.5	12.6 ± 4.1
CCAS-S score	83.4 ± 11.2	80.3 ± 7.0

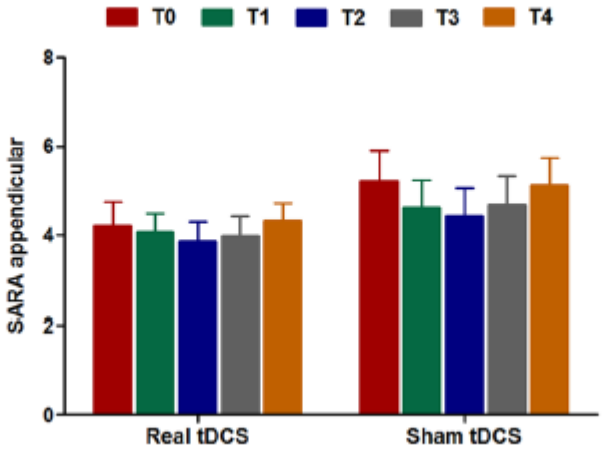
Primary endpoint – SARA score

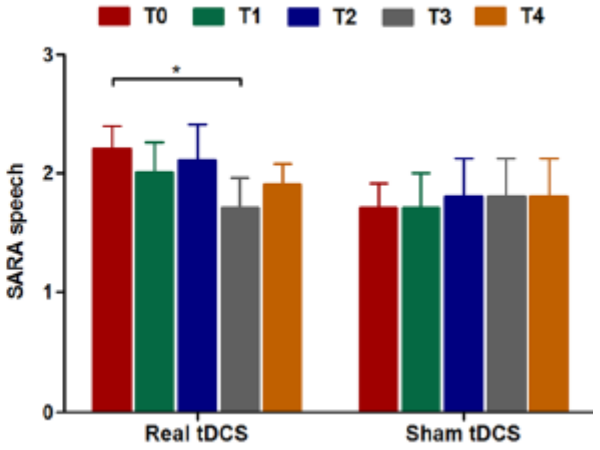




SARA subscores



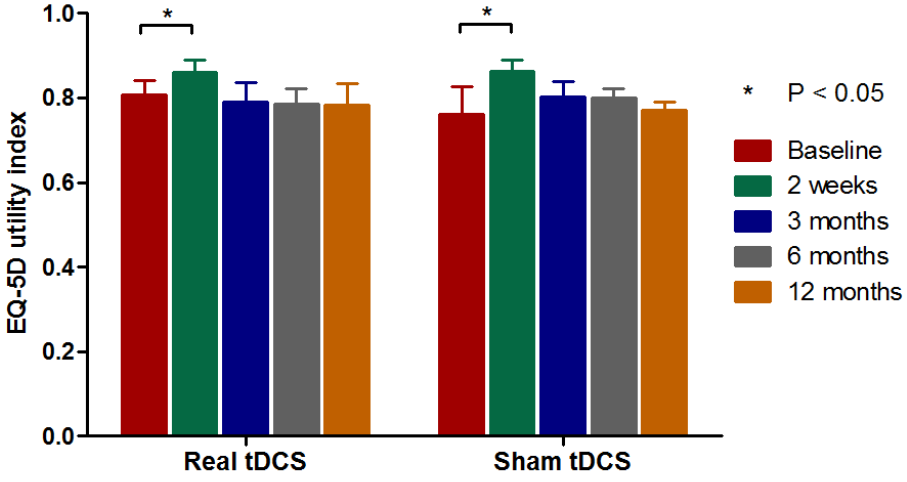


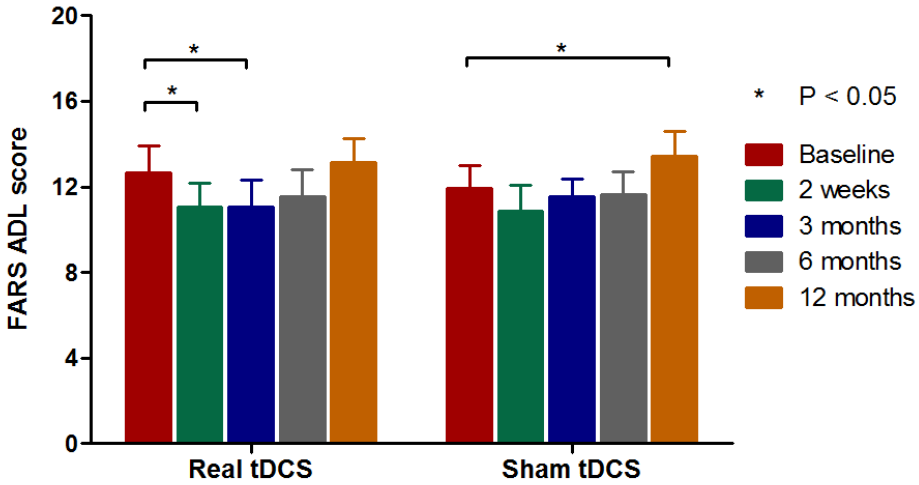


SARA axial = gait + stance + sitting

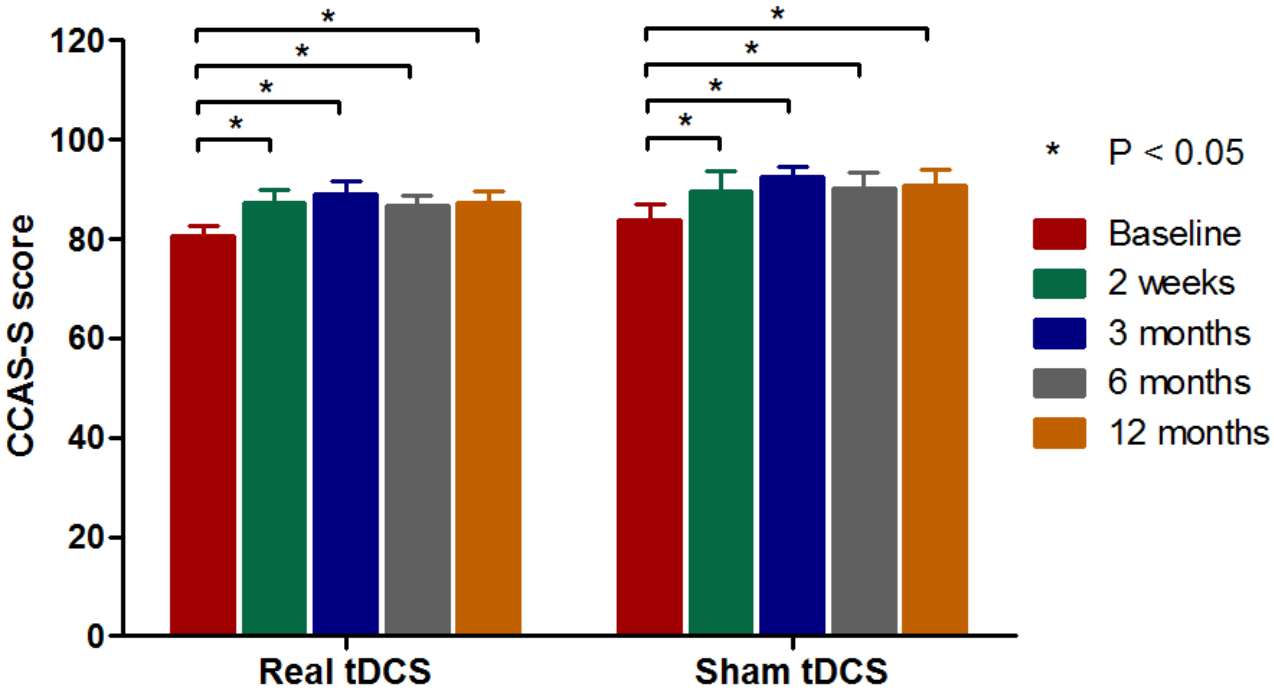
SARA appendicular = finger chase + nose-finger test + diadochokinesis + heel-shin slide

Patient-reported outcome measures

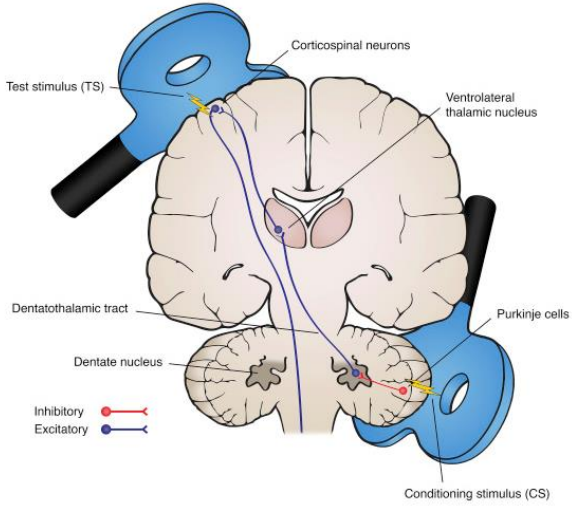


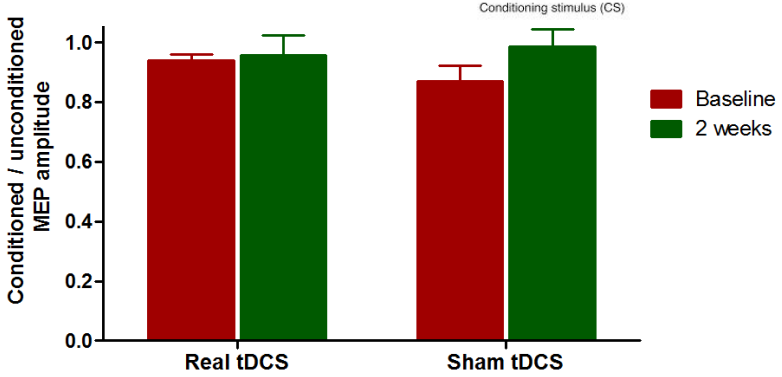


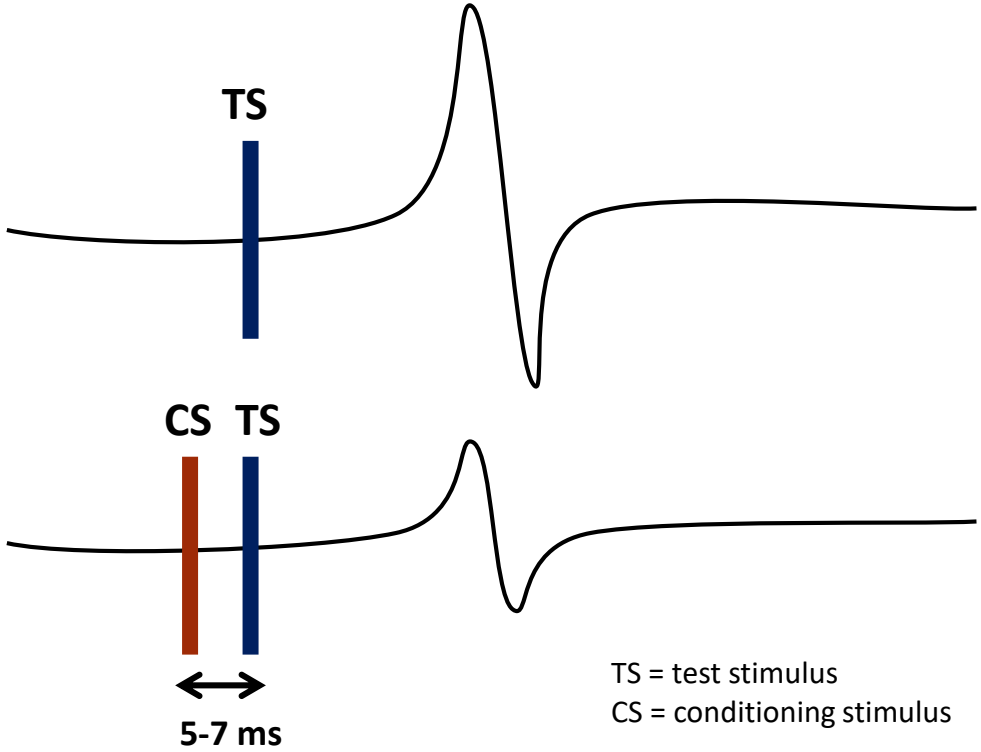
Cognitive outcomes – CCAS-S



Neurophysiological outcome measures – cerebellar brain inhibition (CBI)







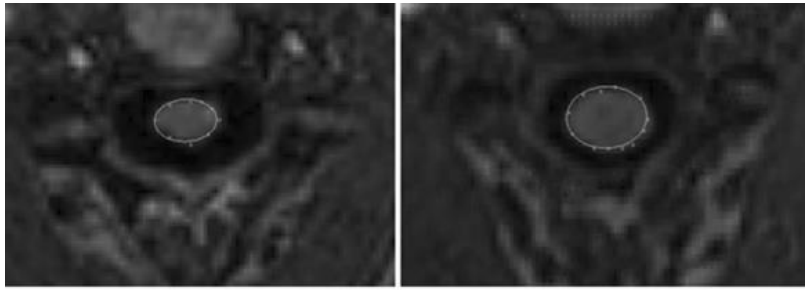
TS = test stimulus
CS = conditioning stimulus

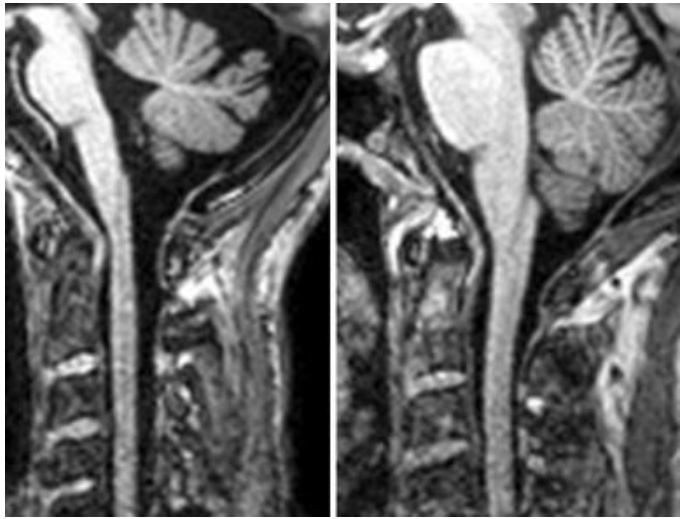
Benussi et al. *Brain Stimul. 2019*; Maas et al. *Mov Disord. 2020*

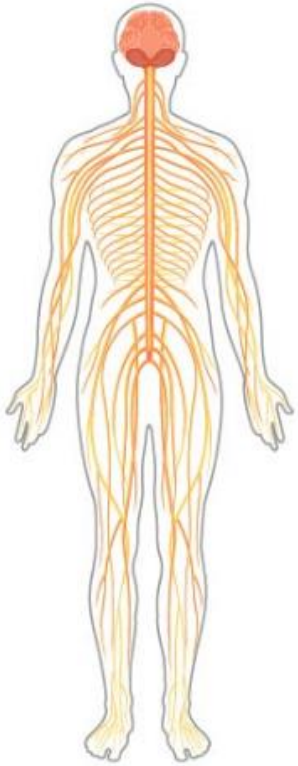
Discrepancies between trials: Patient-related factors?

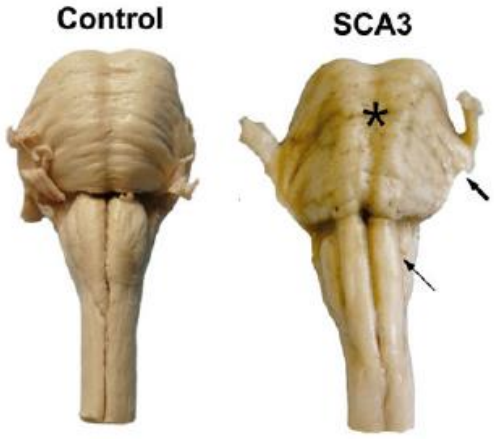
	Present study	Benussi et al. 2017	P value
Age (y)	51.9 ± 10.0	45.3 ± 14.6	0.18
Disease duration	8.0 ± 5.4	16.0 ± 9.4	0.008
SARA score	11.9 ± 3.9	17.9 ± 6.5	0.006
8MWT	6.3 ± 2.1	10.8 ± 6.7	0.011
9HPT dominant hand (s)	31.6 ± 8.3	50.9 ± 23.1	0.003
9HPT non-dominant hand (s)	33.6 ± 6.4	55.0 ± 21.9	< 0.001

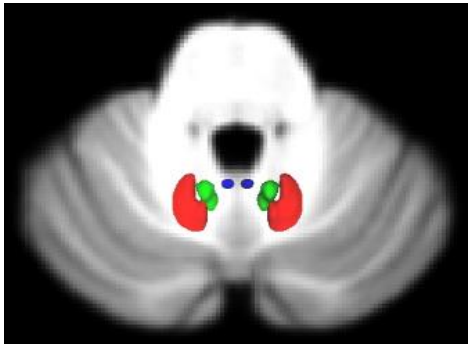
Discrepancies between trials: SCA3-related factors?





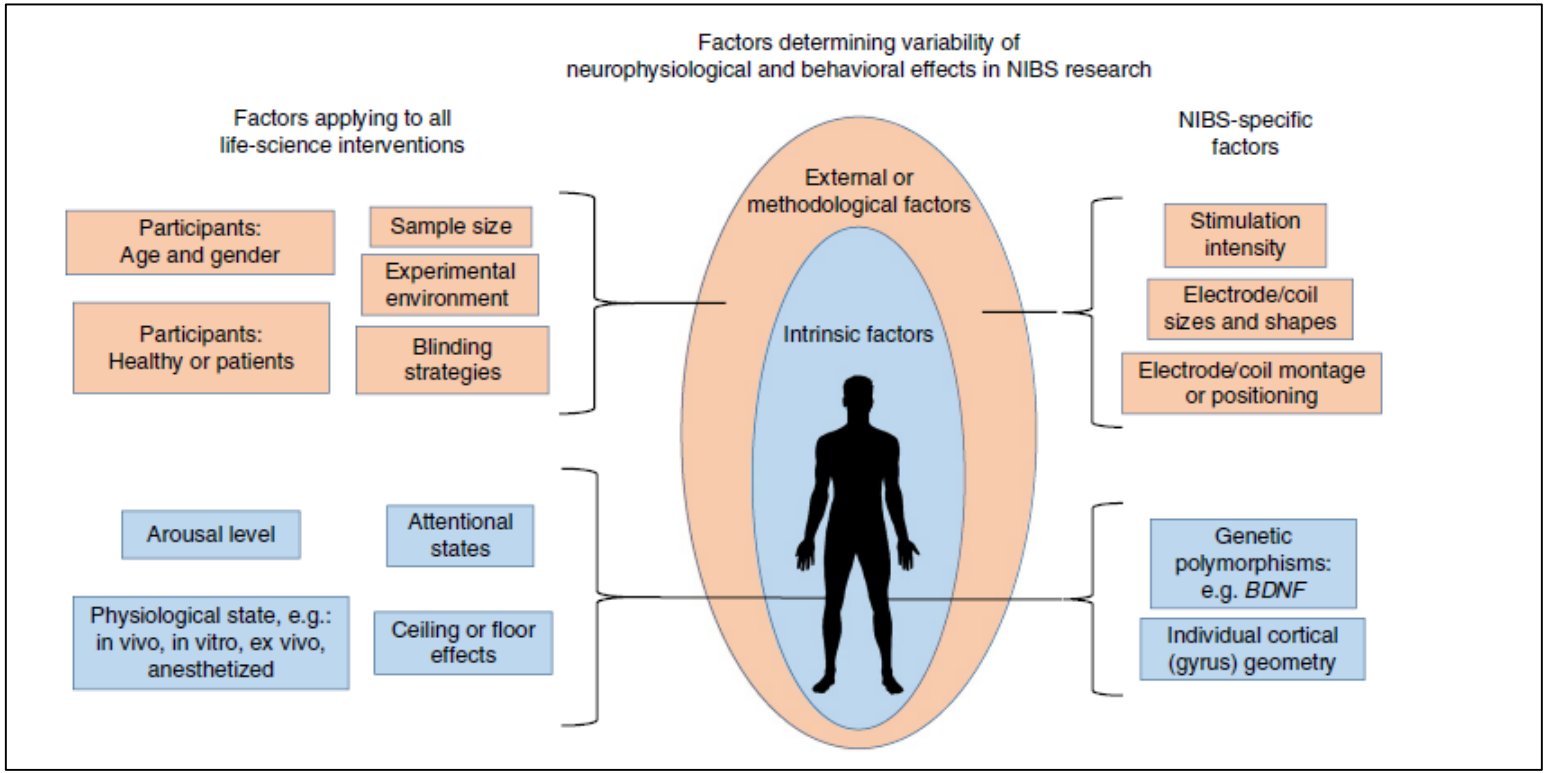






Fahl et al. *Cerebellum* 2015; Seidel et al. *Acta Neuropathol*. 2012

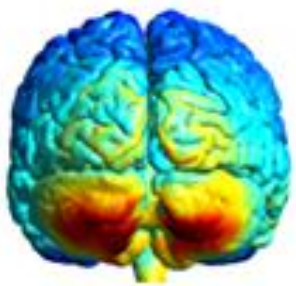
Discrepancies between trials: tDCS-related factors?



Polanía et al. *Nat Neurosci.* 2018

Conclusion

- First cerebellar tDCS study in an etiologically homogeneous group of ataxia patients
- Overall, no motor or cognitive improvement following 10 cerebellar tDCS sessions and no significant modulation of cerebellum-M1 connectivity in SCA3 patients
- Individual predictors of treatment response?



Acknowledgements

Radboud University Medical Center
Steven Teerenstra, PhD
Sven Killaars, BSc
Geert van Bon, MSc
Vivian Weerdesteyn, PhD
Bart van de Warrenburg, MD, PhD

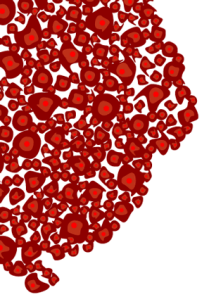
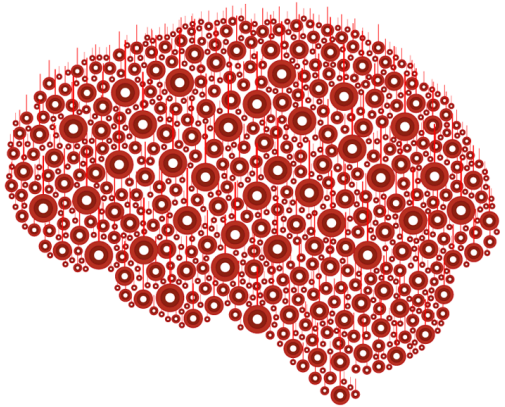
Helmholtz Institute, Utrecht University
Dennis Schutter, PhD

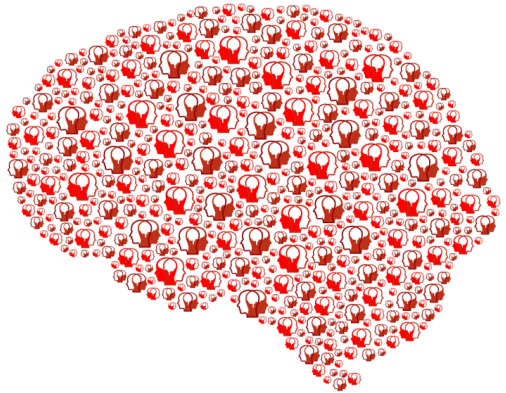
Donders Institute for Brain, Cognition, and Behaviour
Ivan Toni, PhD

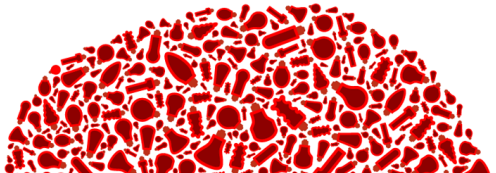
University Hospital Bonn
Thomas Klockgether, MD

University Hospital Essen
Dagmar Timmann, MD

Hersenstichting

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Questions?

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