Cerebellar inhibition disrupts prism adaptation by impairing feedforward error correction

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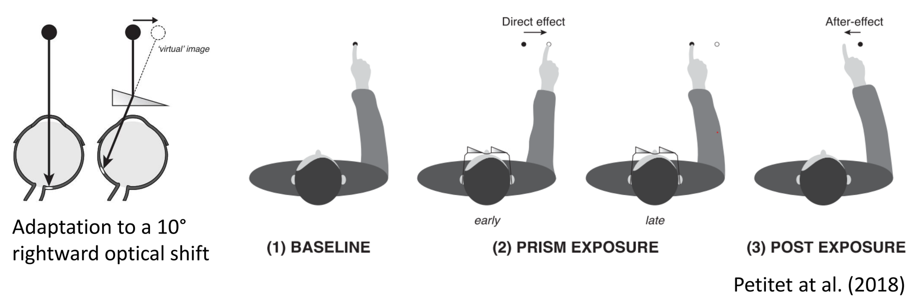
What is the role of the cerebellum in visuo-motor adaptation?

Visuo-motor perturbation: Prism adaptation



Petitet at al. (2018)

How does the brain adapt to perturbations?

Adaptation → Error correction / After-effects

The aim of the study was to investigate the role of the cerebellum by combining:

- **transcranial direct current stimulation (tDCS)** to modulate the excitability of the cerebellum[1]
  → test for causal involvement
- analysis of the whole **movement trajectory**: kinematic markers have been suggested to dissociate different learning processes[2]
  - initial direction → error correction
  - terminal direction → after-effects
- **state-space modelling** which can be used to analyse the temporal dynamics of different processes underlying adaptation[3]

Methods

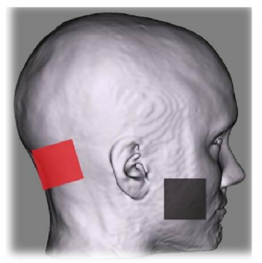
Design:
- sample: n = 9 healthy participants (mean age: 35 ± 9 years)
- within-subject design: anodal, cathodal and sham stimulation in counter-balanced order
- double-blinded tDCS

Recordings of trajectories:
- ultrasound emission device (Zebris)

Stimulation:
- 2mA, 25cm^2 electrodes, 20min (adaptation phase)

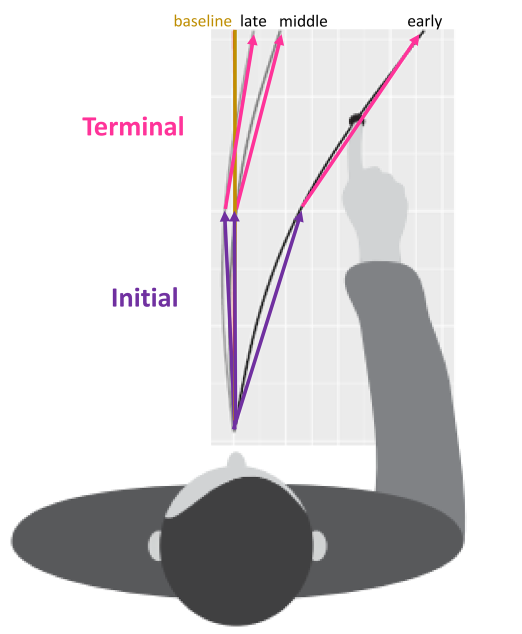
Protocol (Prism adaptation): **CLP**: Closed-loop pointing (visual error feedback) **OLP**: Open-loop pointing (no error feedback)

Training	Base-line	Adaptation	Deadaptation	Rest	Retention
Pointing error (Right / Left)					
40 trials (CLP and OLP)	15 OLP trials	PRISM GLASSES tDCS (20min) 190 trials 6 CLP and 6 OLP blocks in alternating order	150 trials 6 CLP and 6 OLP blocks in alternating order	*10 min*	45 OLP trials


Grimaldi et al. (2016)

Analysis

1. **Analysis of endpoint errors:**
   - repeated-measures ANOVAs of block averages
2. **Analysis of kinematic markers :**
   - extraction based on velocity profile[2]
   - repeated-measures ANOVAs of block averages



3. **State-space modelling of endpoint errors[3] / kinematic markers:**
   - fit to group / individual data
   - model comparison based on AIC

$$e(n) = f(n) - x(n)$$
$$x(n) = x_1(n) + x_2(n)$$
$$x_1(n+1) = A_f \cdot x_1(n) + B_f \cdot e(n)$$
$$x_2(n+1) = A_s \cdot x_2(n) + B_s \cdot e(n)$$
$$B_f > B_s, A_s > A_f$$

x(n) – Motor output on trial n
x_1, x_2 – States of the two systems
e(n) – error on trial n
B – Learning rate
A – Retention rate

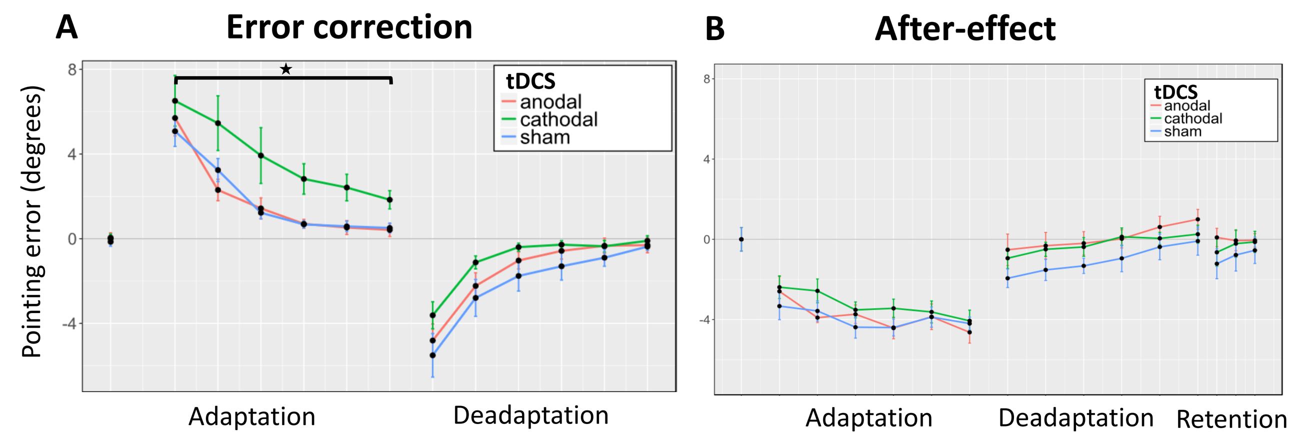
Fast system: high responsitivity to errors, poor retention

Slow system: responds weekly to error, retains well

Hypotheses

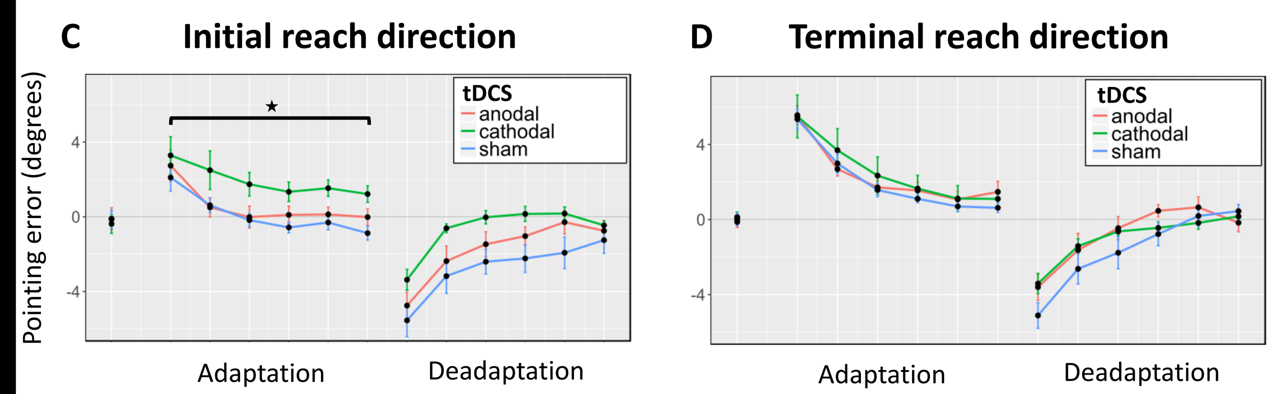
RESULTS

1 Cathodal tDCS will impair error correction, anodal tDCS will enhance.



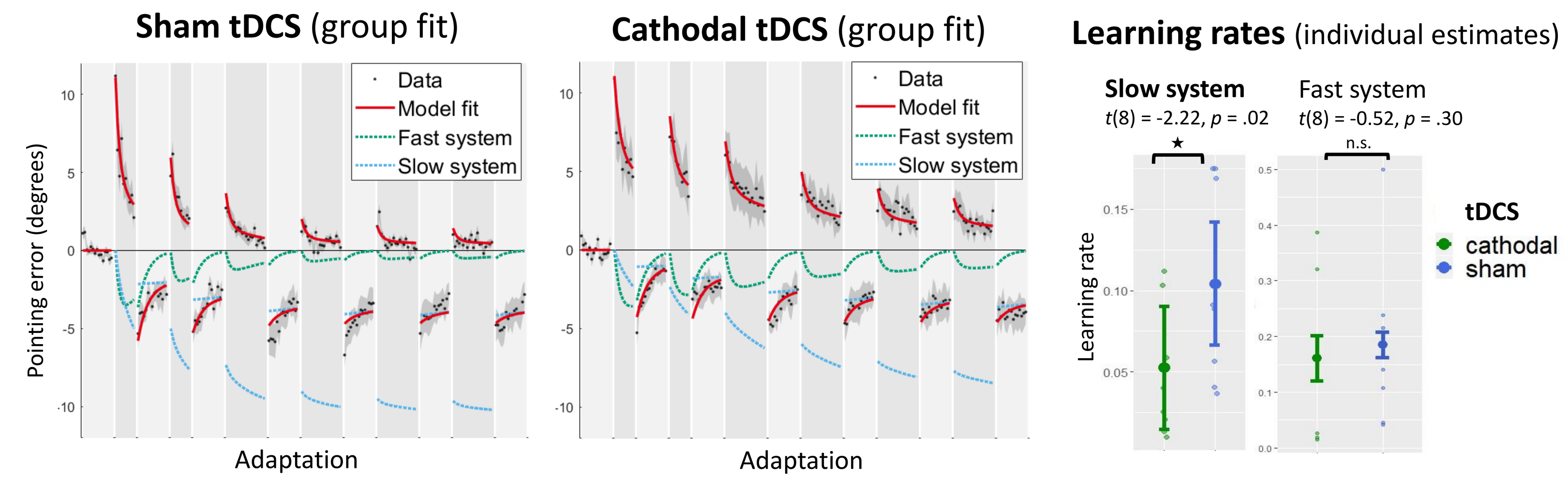
- **cathodal vs. sham tDCS disrupted error reduction specifically during adaptation** (A)($F(1,8) = 5.39$, $p < .05$)
- effect was **functionally specific**: no change in deadaptation (A). No change in after-effect (B)(all p >.05)
- effect was **polarity-specific** (anodal vs. sham tDCS: $F(1,8) = 0.03$, $p = .86$)

2 Cerebellar tDCS will change behaviour by selectively affecting the feedforward phase of the movement (i.e. initial phase of reach direction).



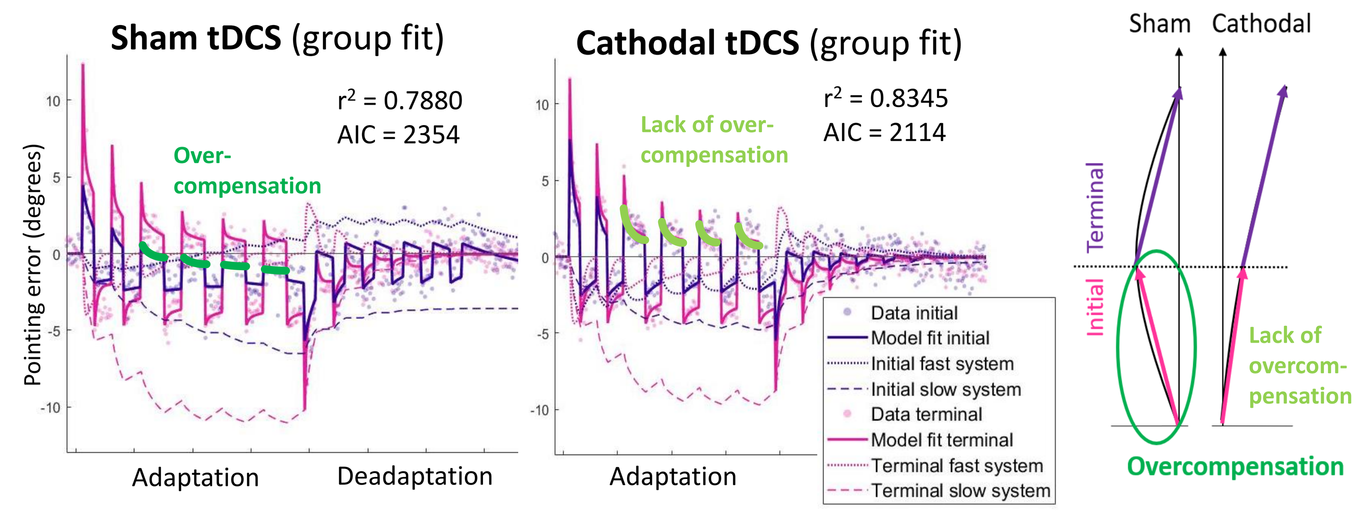
- during adaptation, cathodal tDCS specifically disrupted error reduction during **the initial phase of the reach trajectory** (C)($F(1,7) = 8.66$, $p = .02$)
- there was no effect on the terminal phase (D)($F(2,14) = 3.45$, $p = .06$)

3 Cathodal tDCS will disrupt adaptation by impairing fast learning processes (learning/retention of the fast system).



- the estimated **learning rate of the slow system** was lower for cathodal vs. sham tDCS
- the learning rate of the fast system did not differ between sham and cathodal tDCS

Exploratory analysis: State-space modelling of the kinematic data



- the kinematic data are best described by a model in which the initial reach direction learns from the error in the terminal reach direction
- The model captures the **compensatory leftward shift of the initial direction** observed during later blocks of adaptation (see fig: green)
- this „overcompensation" – exaggerated leftward pointing during the initial reach phase – is how participants normally correct their errors during the late phase of adaptation (fig: sham)
- **cathodal tDCS seems to disrupt this mechanism**

$$X_{i,s}(n+1) = A_{i,s}X_{i,s}(n) + B_{i,s}\, e_i(n) + B_{i,t,s}e_{terminal}(n)$$ → The initial direction of the reach trajectory learns from **terminal error** of previous trial (i: initial, t: terminal, s: slow)

Conclusions

1. **Cathodal cerebellar tDCS impairs error reduction during adaptation**
   - replication of previous findings[4,5]
   - **polarity-specific** (no effect of anodal tDCS[6]) and **functionally-specific**: no effect on the after-effect, deadaptation or retention
2. Cathodal tDCS disrupted adaptation by specifically impairing the correction of the **initial reach direction**
   - causal role of the cerebellum in **feedforward error corrrection**
3. Cathodal tDCS **disrupted slow learning processes** during prism exposure
4. Model fitting shows that cathodal tDCS **disrupts over-compensation of the initial reach direction**
   - this slow learning process normally drives error reduction during later stages of adaptation

References
[1]Galea et al. (2009), *Journal of Neuroscience*
[2]O'Shea et al. (2014), *Neuropsychologia*
[3]Smith et al. (2006), *PLoS Biology*
[4]Herzfeld et al. (2014), *NeuroImage*
[5]Panico et al. (2016), *Brain and Cognition*
[6]Jalali et al. (2017), *Journal of Neurophysiology*

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Grimaldi et al. (2016), *The Neuroscientist*

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