University Medicine Essen

Center for Translational Neuro- and Behavioral Sciences

Klinik für Neurologie

Treatment Expectation TRR 289

Cerebellar degeneration and cerebellar-cortical interactions associated with placebo-nocebo effects: a pilot study

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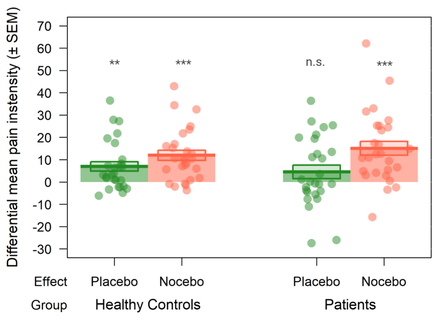
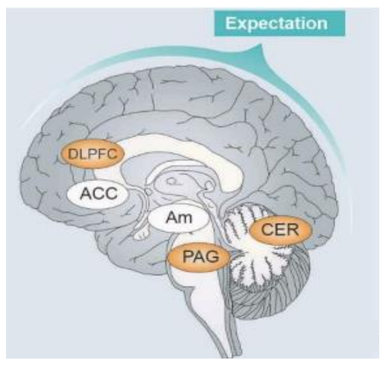
1 Introduction

The contribution of the cerebellum to placebo and nocebo effects has rarely been studied. The aim of the present study is to show that placebo and nocebo effects are reduced in patients with cerebellar disease and that the cerebellum contributes to treatment expectations via its connections with cortical areas including the DLPFC. Interactions will be tested using EEG recording and structural MRI.



Reduced placebo and preserved nocebo effects in patients with cerebellar degeneration
Patients n = 27; Controls n = 27.
Schlitt-Nguyen et al., in preparation.



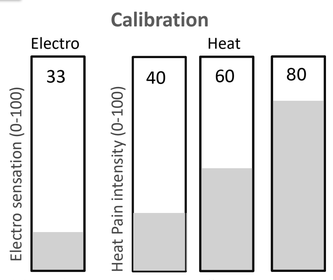
Top down pain modulatory network (DLPFC, ACC, Thalamus and PAG) [modified from Enck et al. 2013].

Pilot study aims:

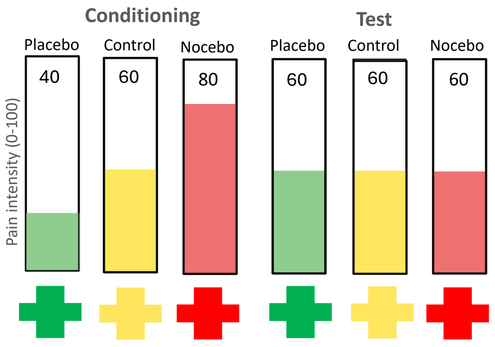
- Test placebo-nocebo paradigm adapted for EEG in young and healthy participants.
- Initial testing of patients with cerebellar degeneration.

2 Methods

Paradigm used in previous studies



Electrical „treatment“ stimulation: to be just felt (33 on a VAS 0-100).
Heat stimuli induced by a thermode: pain intensity of 40, 60 and 80 on a VAS 0-100.

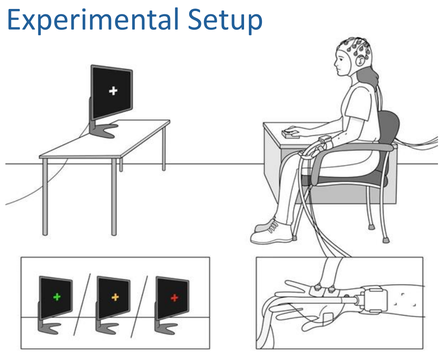


10 Trials each

30 Trials + 10 Movement control trials each

Conditioning session: Positive and negative treatment expectations induced by combining an electrical „treatment“ stimulus with instructed modulation (green: less pain; red: more pain; no influence: yellow)
Test session: Assessment of positive and negative expectations on heat pain [adapted from Colloca et al., 2010 and Kunkel, Schmidt et al. 2025].

Experimental Setup



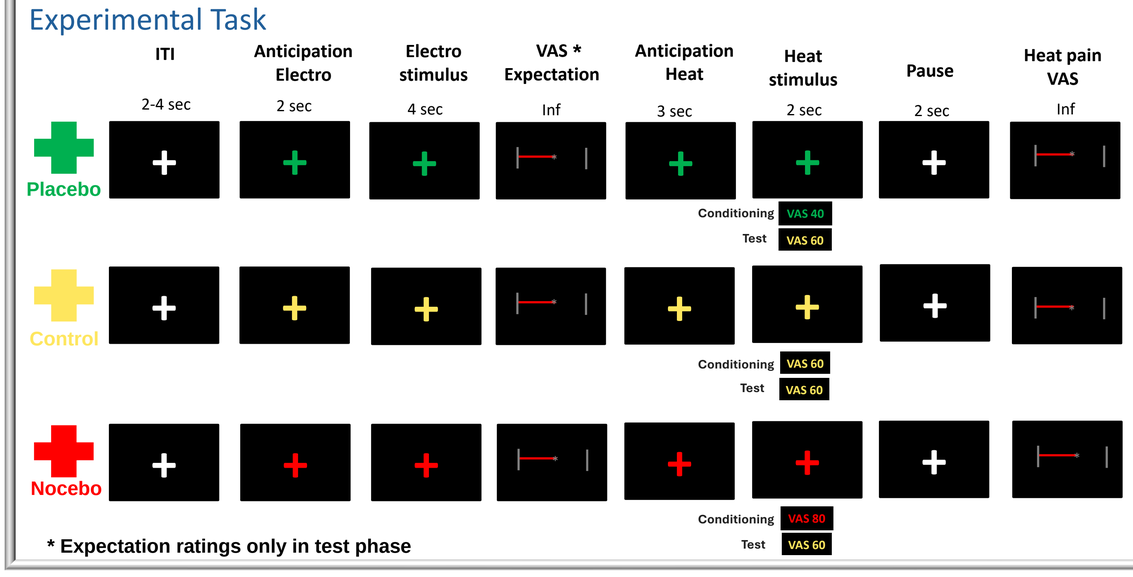
Implementation of EEG

- Short time intervals (e.g. heat stimulation)
- High number of trials
- Movement control trials
- Expectation ratings in each trial

Pilot (healthy) Participants

Group	*N*	*Mean* Age	*SD* Age
Total	20	25.55	4.21
Male	10	27.20	4.54
female	10	23.90	3.28

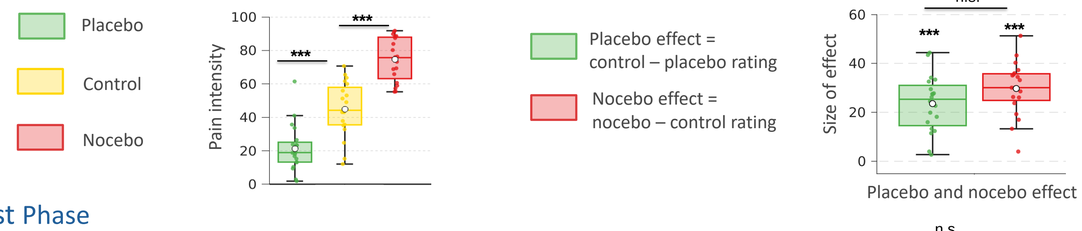
Experimental Task

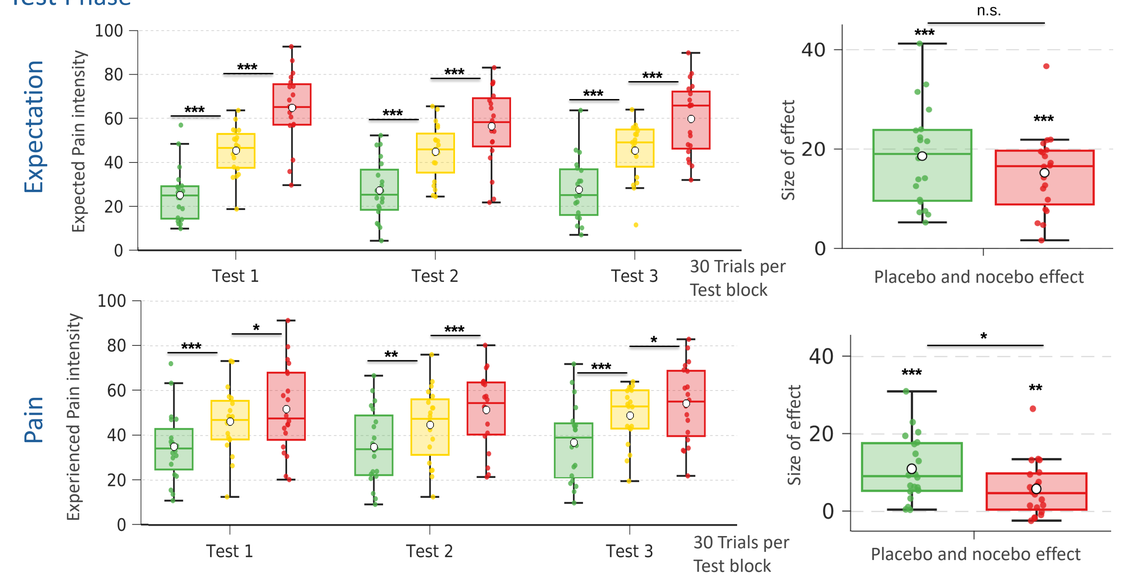


*** Expectation ratings only in test phase**

3 Results

Behavioral findings





EEG findings

↑**power** of **theta, alpha** and **beta** in the **placebo** > **control** condition during heat pain stimulation.

p = 0.0060
Frequency range: 4.03 - 19.04 Hz
Time range: 0.100 - 0.950 s

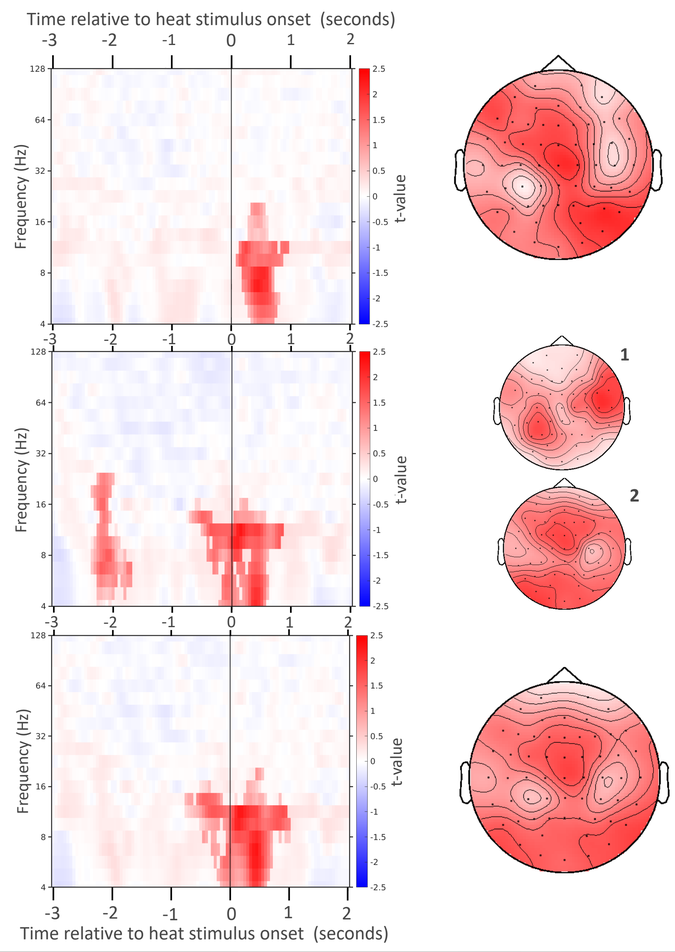
↑**power** of **theta, alpha** and **beta** in the **nocebo** > **control** condition during heat pain anticipation, stimulation.

1 *p* = 0.0500
Frequency range: 4.03 - 22.58 Hz
Time range: -2.350 - -1.700 s

2 *p* = 0.0060
Frequency range: 4.03 - 15.99 Hz
Time range: -0.750 - 0.850 s

↑**power** of **theta**, **alpha** and **beta** in the **placebo** as well as **nocebo** > **control** condition during heat pain anticipation and stimulation.

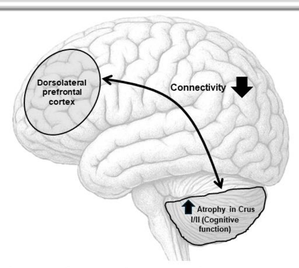
p = 0.0060
Frequency range: 4.03 - 19.04 Hz
Time range: -0.750 - 1.000 s



4 Conclusions

- The placebo nocebo paradigm adapted for EEG induced significant placebo and nocebo effects, and can be applied in cerebellar patients.
- Placebo and nocebo expectations modulated oscillatory activity during heat pain processing, reflected by increased theta, alpha, and beta power compared to the control condition. Nocebo effects emerged already during pain anticipation, whereas placebo-related increases were mainly observed during heat pain stimulation.

5 Patient Study



Hypotheses for patient study:

1. Patients show a reduction in brain oscillations during the anticipation and experience of pain.
2. Reduced placebo and nocebo effects in patients are related to reduced connectivity between the cerebellum and the DLPFC.

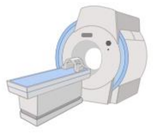
Study Cohort

40 **Patients** with cerebellar degeneration
- SCA27B
- SCA6

40 **Controls**
- healthy
- Age matched
- Sex matched

Study Design

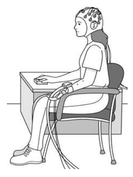
Day 1



3 T-MRI Scan
- MPRAGE
- Resting State
- DWI
- QSM

Neurological examination
- SARA and CCAS scales
- QST

Day 2



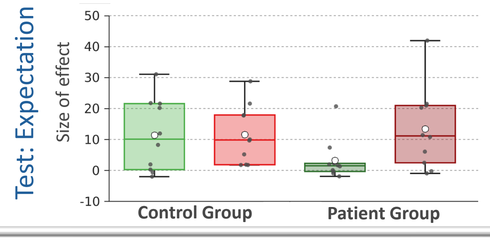
Placebo/ nocebo paradigm

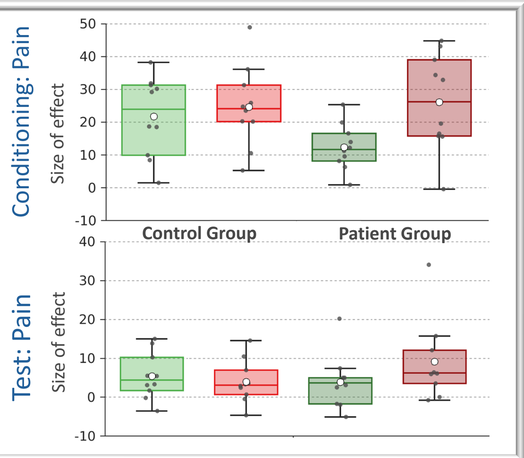
Preliminary Data

Control group *n* = 10
Patient group *n* = 10

Placebo effect = control – placebo rating

Nocebo effect = nocebo – control rating





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Colloca L, Petrovic P, Wager TD, Ingvar M, Benedetti F. How the number of learning trials affects placebo and nocebo responses. Pain 2010 Nov; 151(2):p 430-439. doi: 10.1016/j.pain.2010.08.007
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Abbreviations
EOG = Electrooculography; EMG = Electromyography; VAS = visual analog scale; ITI = inter-trial interval; SD = standard deviation; SCA = spinocerebellar ataxia; DWI = diffusion-weighted imaging; QSM = Quantitative Susceptibility Mapping; QST = quantitaive sensory testing

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