

A single, clinically relevant dose of baclofen significantly impairs motor sequence learning

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The role of GABA in human motor learning

GABA levels in the primary motor cortex (M1) decrease during motor learning (Kolasinski & Hinson *et al.* 2019).

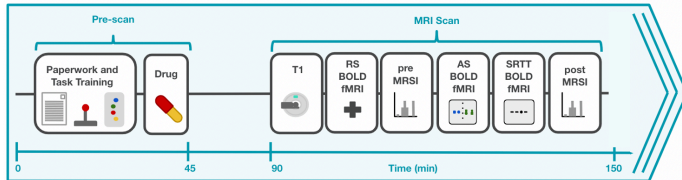
Decreases in GABA levels correlate significantly with better motor learning (Stagg *et al.* 2011), while increasing GABAergic activity is shown to impair the learning of a visuo-motor adaptation task (Willerslev-Olsen *et al.* 2011).



How does pharmacologically modulating GABA activity affect motor learning?

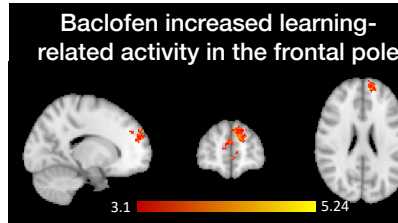
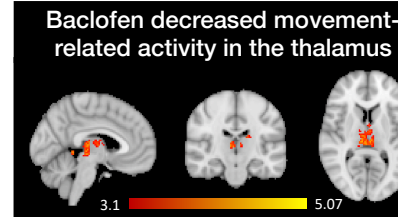
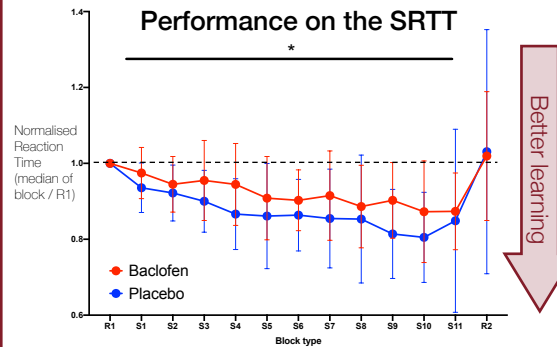
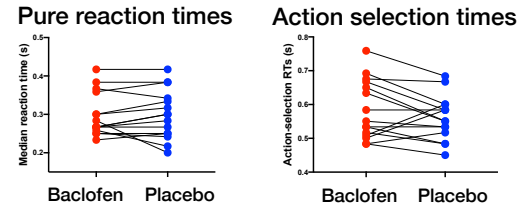
Pharmaco-MRI study design

Baclofen is a GABA_B receptor agonist, which can be prescribed to treat muscle spasticity in stroke survivors.



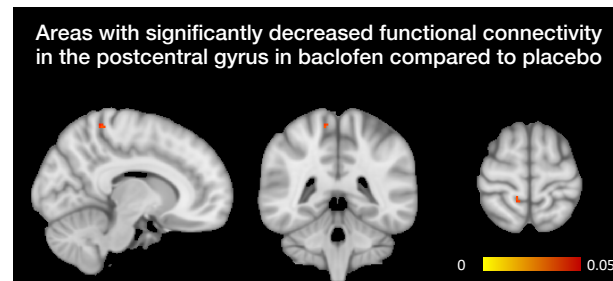
- Within-subject, double-blinded, placebo-controlled
- 18 young, healthy participants x 2 sessions
- Single dose of baclofen (20mg) or placebo
- Motor learning task: Serial Reaction Time Task (SRTT)
- Motor non-learning task: Action Selection (AS)
- Neuroimaging:
 - fMRI: task (SRTT and AS) and resting state
 - Magnetic Resonance Spectroscopic Imaging (MRSI)

Baclofen significantly impairs motor sequence learning



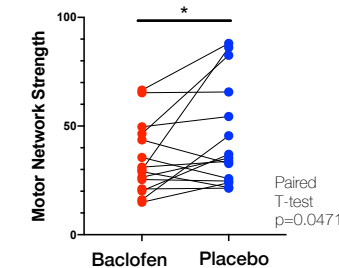
Median reaction times for sequence blocks were compared using two-way RM-ANOVA with factors of block and treatment: significant effect of block ($F(3.218, 41.84)=4.423, p=0.0075$), significant effect of treatment ($F(1,13)=4.606, p=0.0472$), no significant block x treatment interaction ($F(2.390, 31.07)=0.5167, p=0.634$).

Baclofen decreases functional connectivity in the sensorimotor network



Scale represents TFCE corrected p values after paired t-test between baclofen and placebo (5000 permutations).

Sensorimotor network strength decreases with baclofen



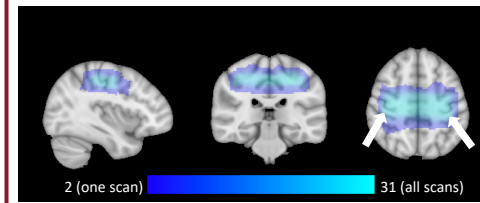
Conclusions

Baclofen impairs motor sequence learning, but not reaction times, action-selection, working memory or alertness.

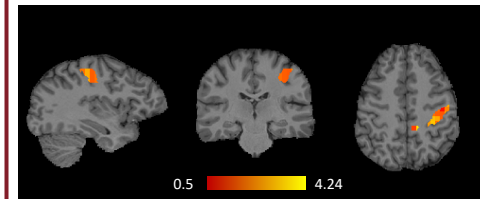
Neuroimaging analysis shows different activation patterns during SRTT task performance, as well as decreased functional connectivity in the sensorimotor network, with baclofen treatment.

Ongoing MRSI analysis will soon provide more details about how baclofen affects GABA levels in M1.

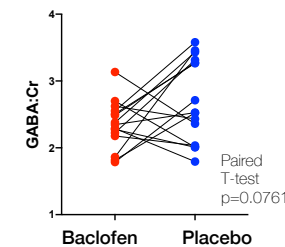
Preliminary results of the MRSI analysis



Overlay of the MRSI region of interest from all scans. Left- and right-hand areas (arrows) are included in all participants.



Example of GABA map in left M1 in one participant. All voxels passed the SNR and CRLB thresholding.



Baclofen does not significantly change baseline GABA levels in the left M1, but there is a trend towards GABA levels being lower with baclofen.

Ongoing analysis will look at how baclofen affects the reported change in GABA after motor learning.