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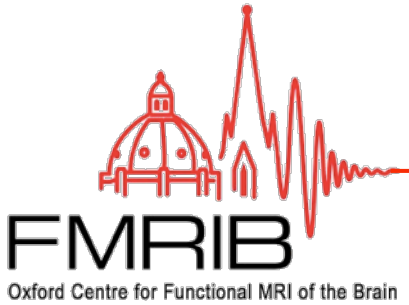
tDCS and MRS for Learning and Recovery



Dr Charlie Stagg

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Wellcome Trust / Royal Society Sir Henry Dale Fellow
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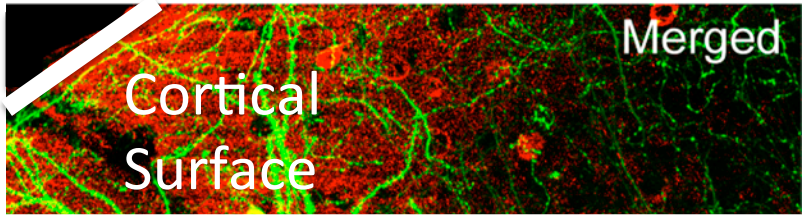
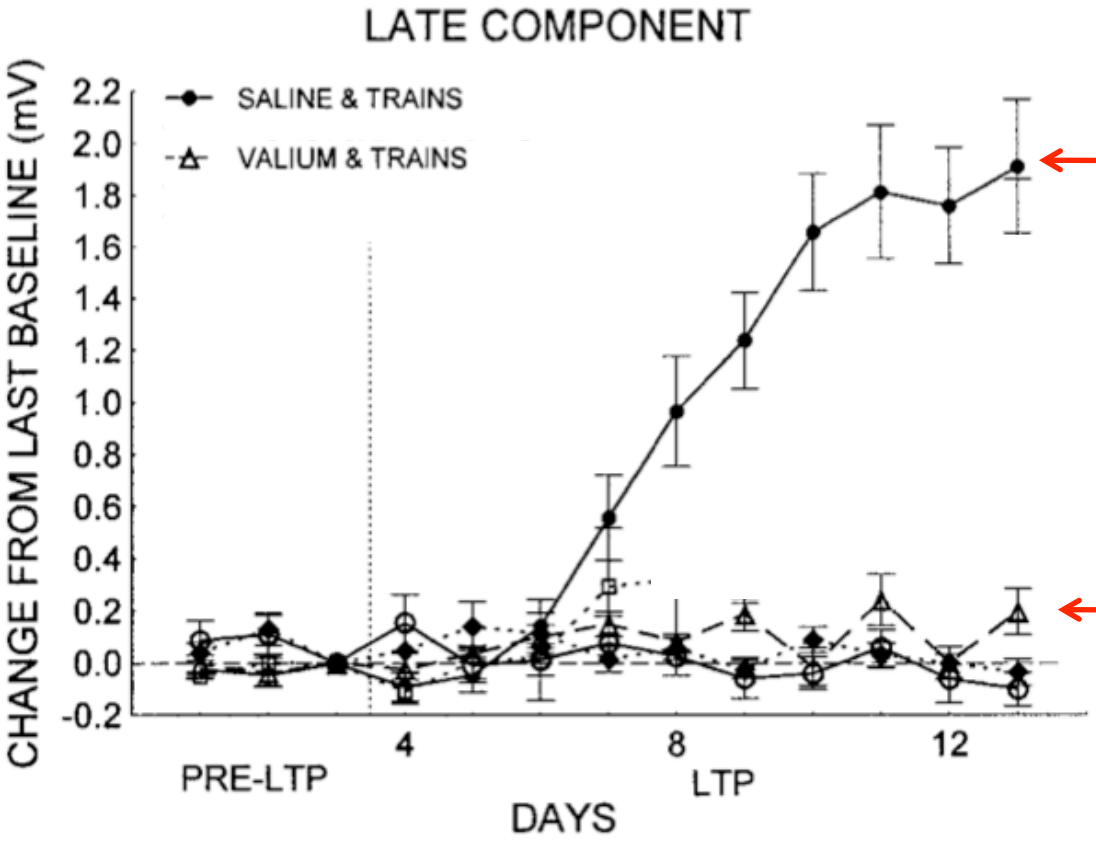
Oxford Radcliffe Hospitals NHS
NHS Trust

NHS
National Institute for Health Research

Motor Cortical plasticity is dependent on changes in GABA





Normal LTP Induction

LTP Induction with GABA agonist

Trepel & Racine, 2000; Lee et al., 2006

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The Larmor Equation

States that the resonant frequency of an atom depends on the magnetic field it is exposed to:

$$\omega = \gamma B$$

- ω Angular Frequency
- γ Gyromagnetic Ratio (constant for a given atom)
- B Strength of Magnetic Field.

Frequency $\propto$ Field strength

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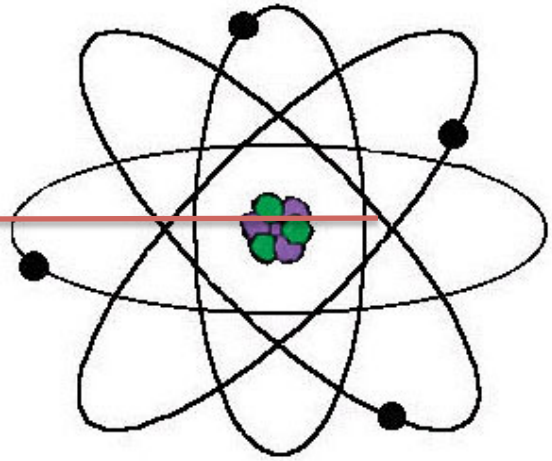
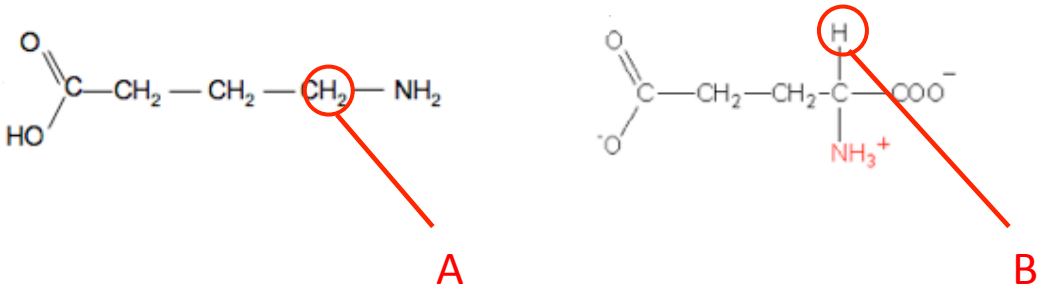
MR Spectroscopy



- An atom is shielded from the magnetic field by circling electrons.
- In a molecule, the degree of shielding is proportional to the number of electrons around the nucleus, which in turn is related to the structure of the overall molecule.
- Therefore atom A will resonate at a slightly different frequency to atom B because of their surrounding molecular structure.



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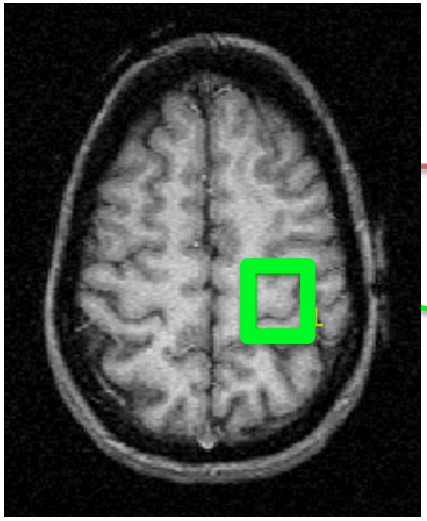
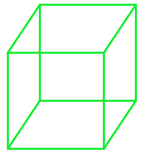
MR Spectroscopy provides *in vivo* measures of neurotransmitters





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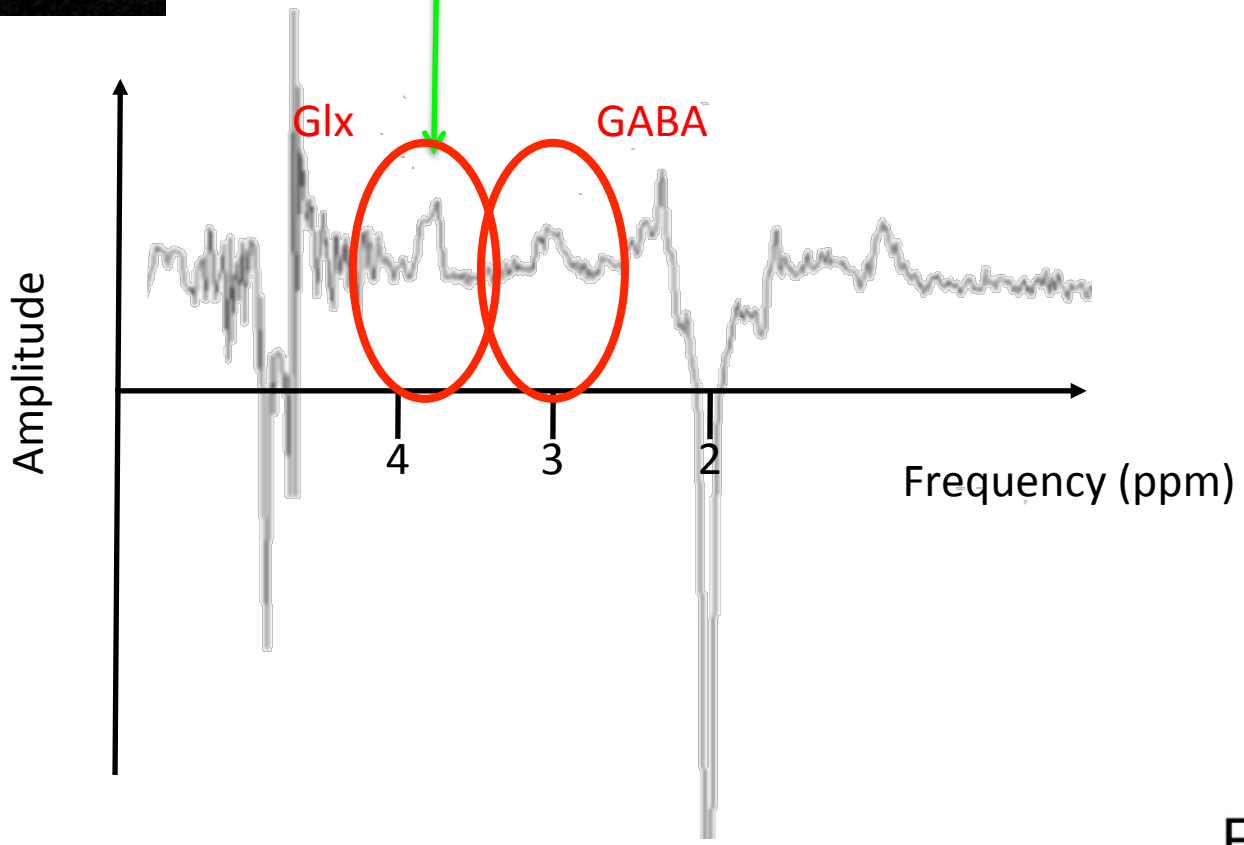

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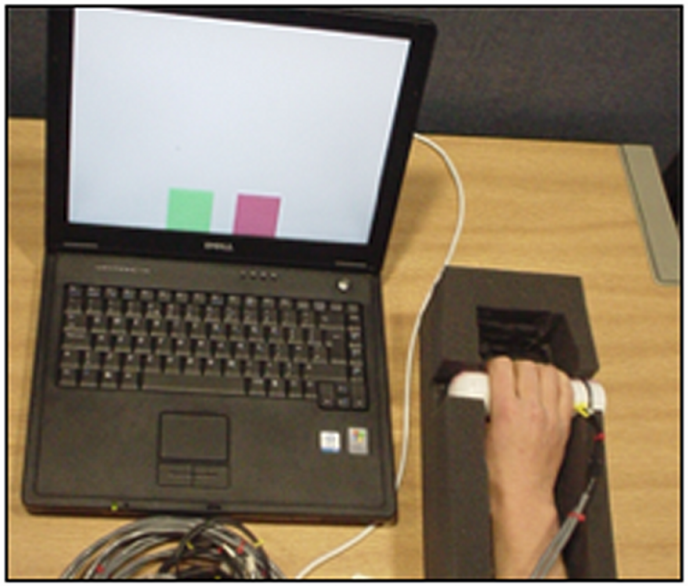
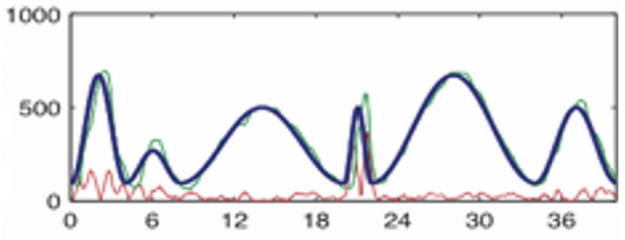
GABA-MRS is sensitive to small changes in neurotransmitters – Decrease in [GABA] during a learning task





Time (s)

Floyer-Lea et al., 2006
(also Gudberg, Stagg, Near & Johansen-Berg, unpublished data)

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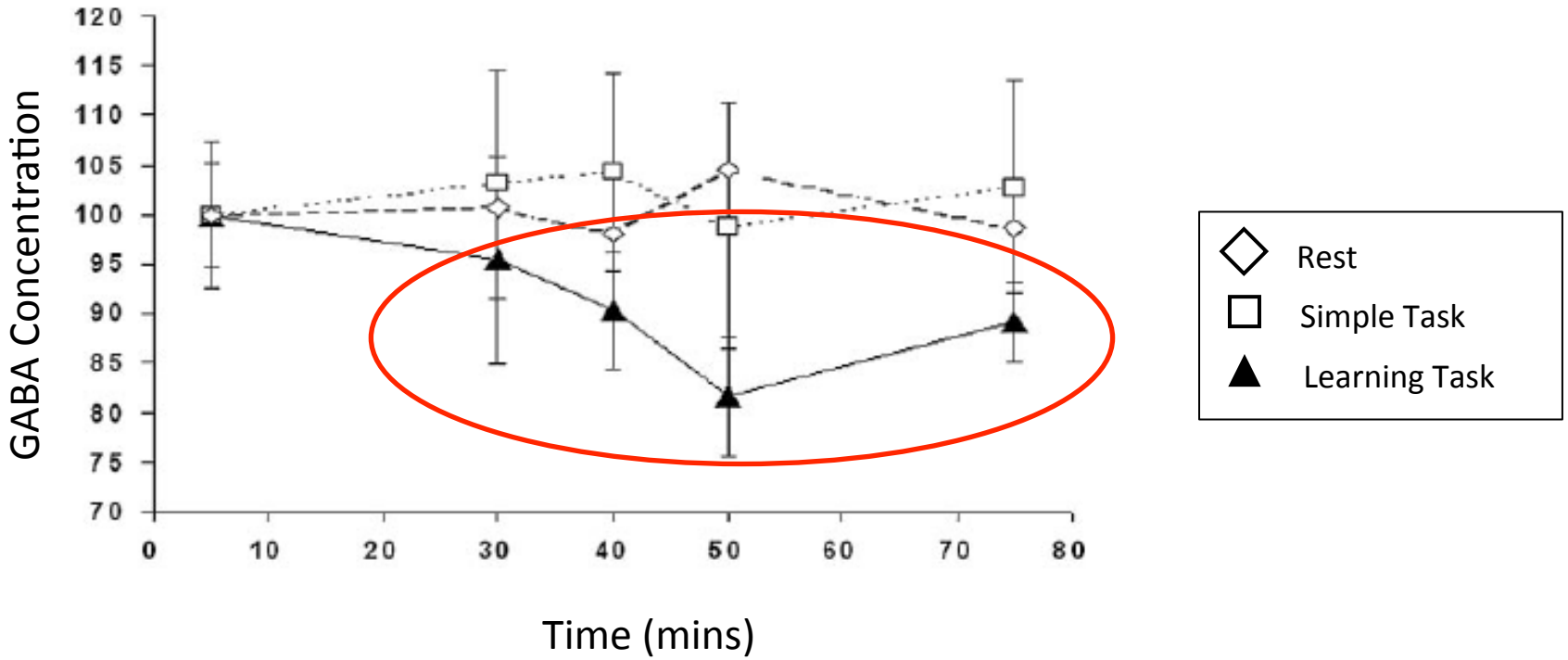
GABA-MRS is sensitive to small changes in neurotransmitters – Decrease in [GABA] during a learning task



Floyer-Lea et al., 2006
(also Gudberg, Stagg, Near & Johansen-Berg, unpublished data)

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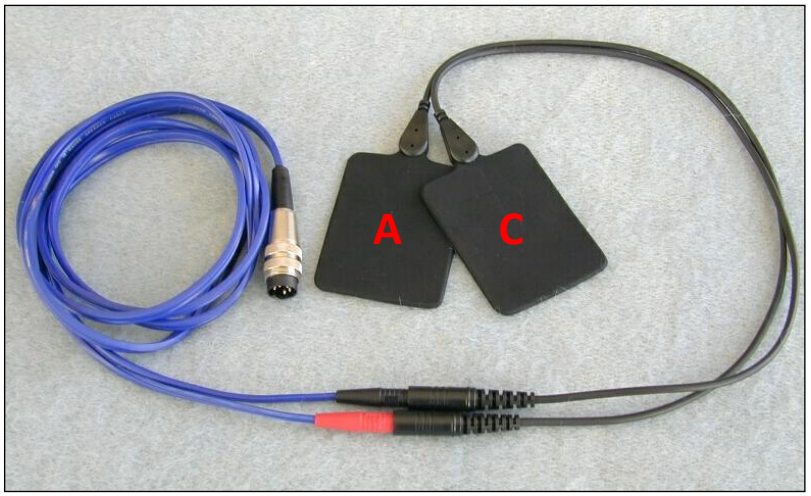
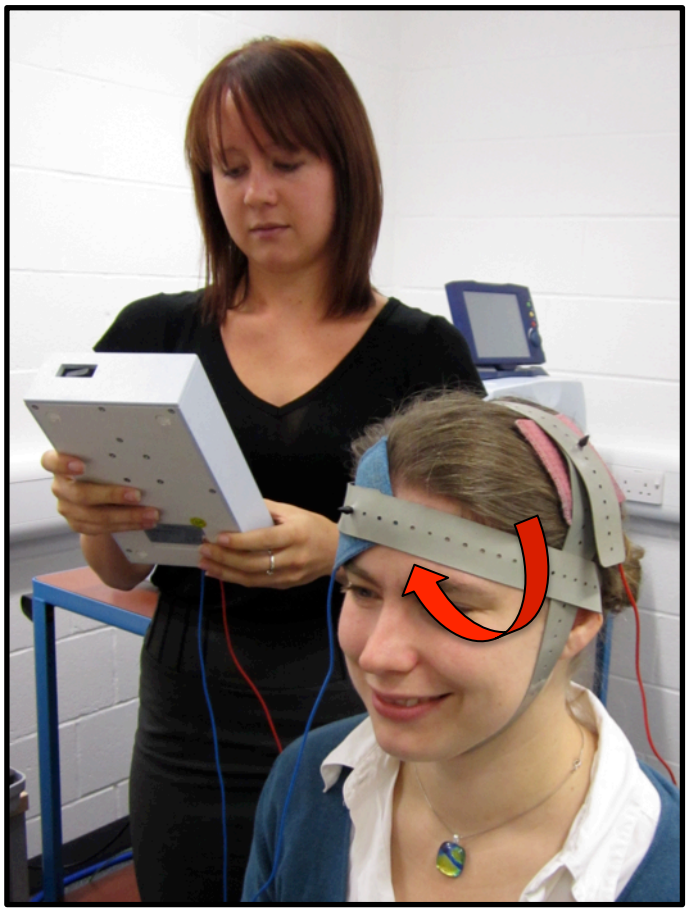
Transcranial Direct Current Stimulation (tDCS)





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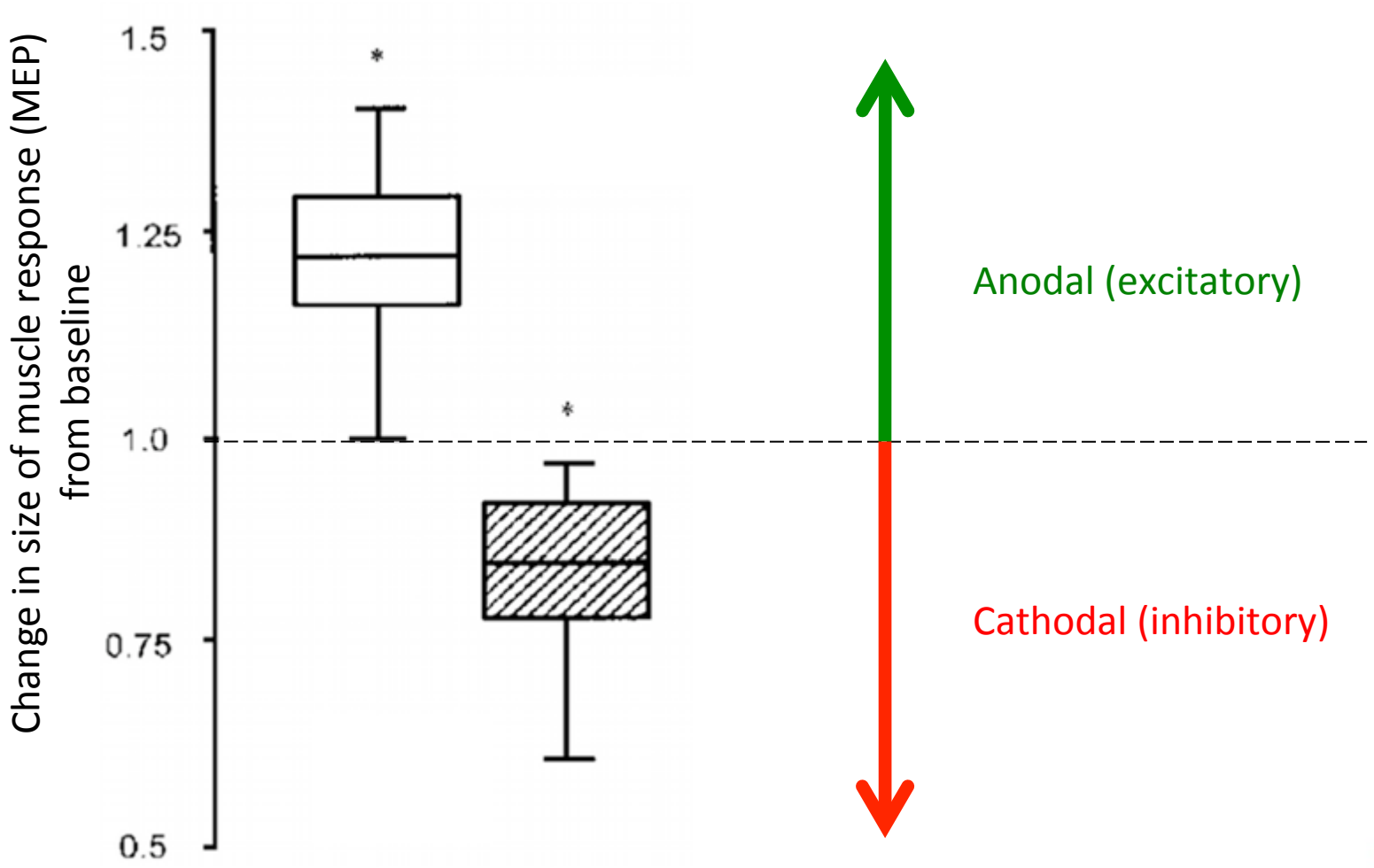
tDCS has polarity-specific effects on cortical excitability



Nitsche & Paulus, J Physiol 2000

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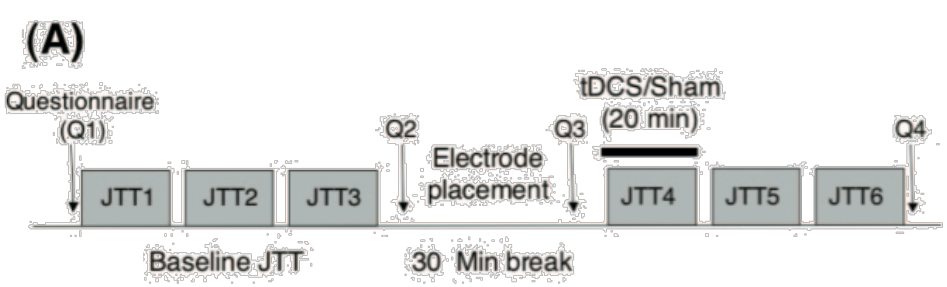
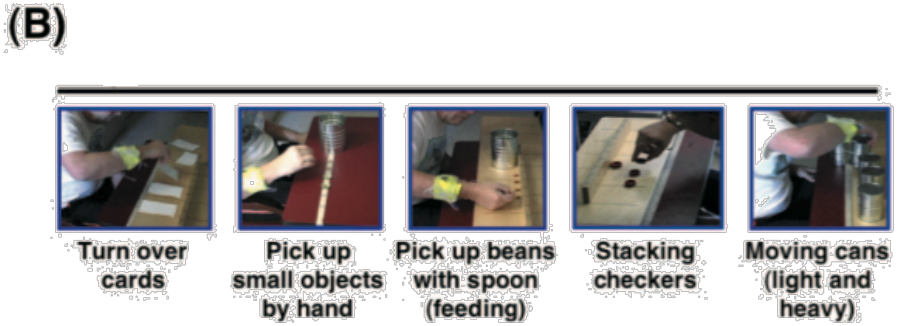
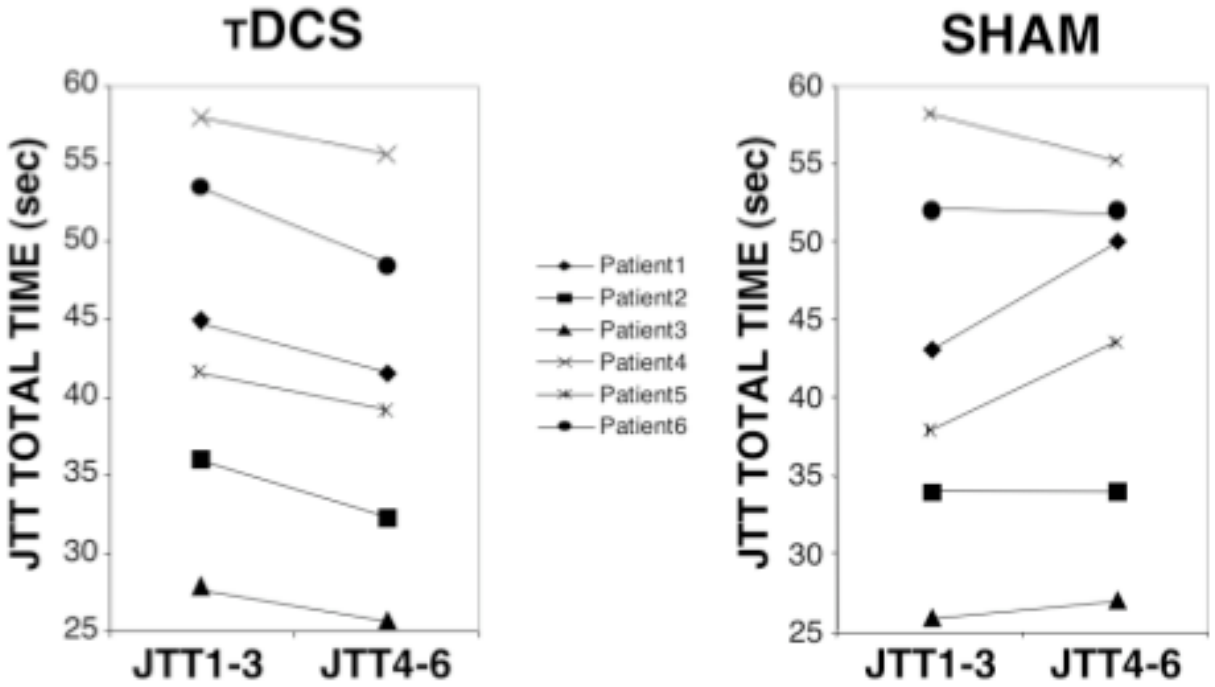
Anodal (facilitatory) tDCS to the ipsilesional hemisphere improves motor function in chronic stroke







Hummel et al., Brain 2005

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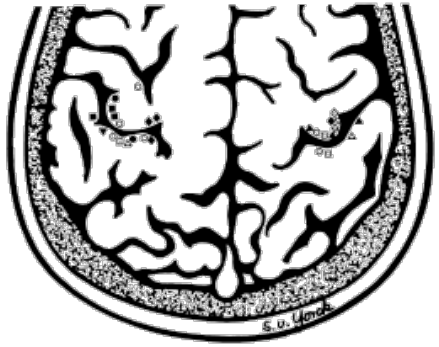
Studying neurotransmitter changes following tDCS

tDCS Pre

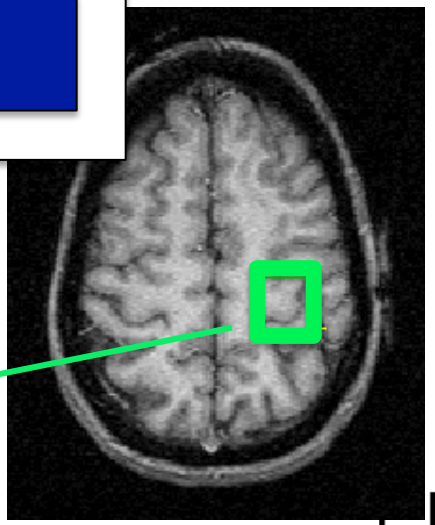
tDCS Post

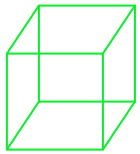
Sham Pre

Sham Post



Yousry et al., 1997





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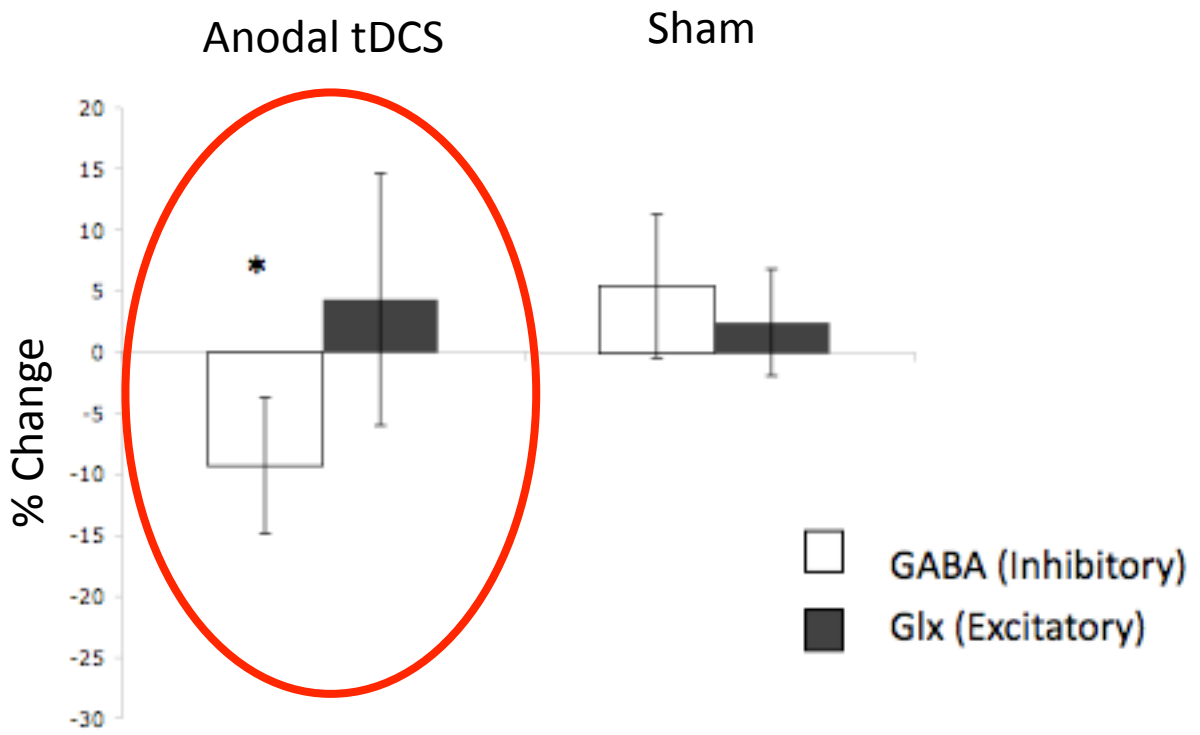
Anodal tDCS decreases [GABA] in stimulated motor cortex



Stagg, Best, Stephenson, O'Shea, Arridge, Kincses, Morris, Matthews & Johansen-Berg *J Neurosci* 2009

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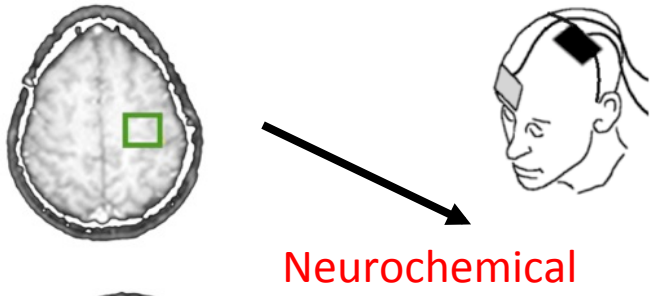
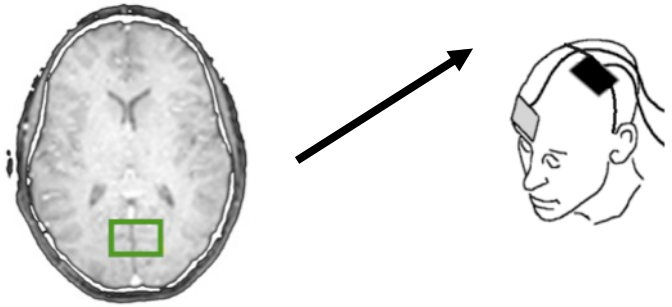
Study Design

1 M1 GABA pre and post anodal tDCS to M1

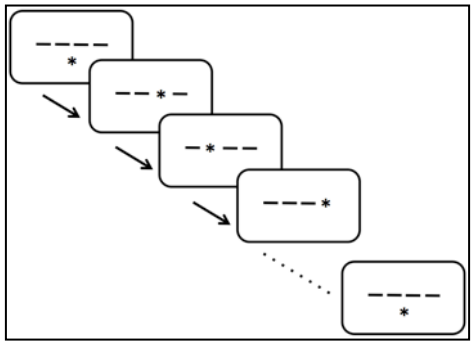


Neurochemical

2 V1 GABA pre and post anodal tDCS to M1



3 fMRI during Motor Learning



Physiological

Behavioural

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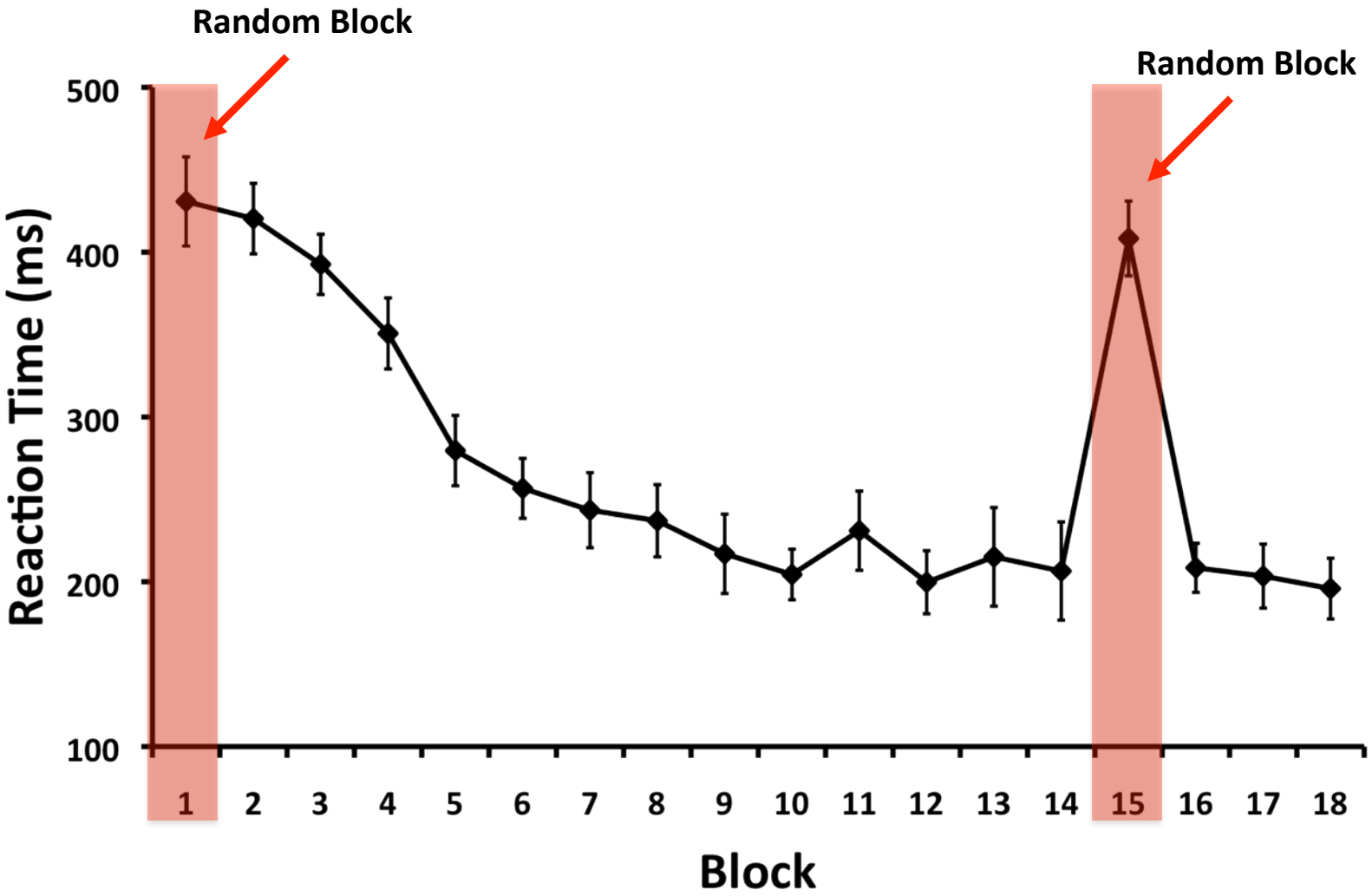
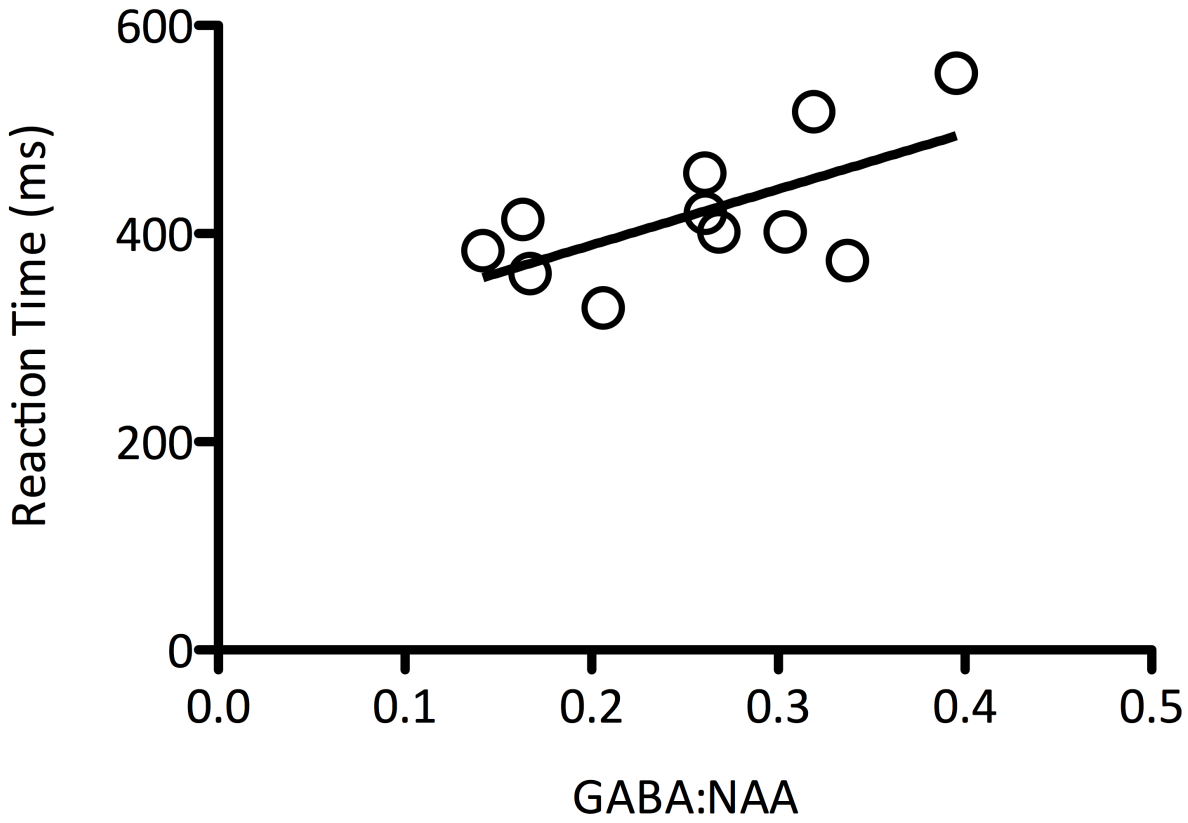
Stagg, Bachtiar & Johansen-Berg; *Current Biology 2011*

Behavioural Data : Baseline Reaction Times



Stagg, Bachtiar & Johansen-Berg; *Current Biology 2011*

Higher resting [GABA] is correlated with slower reaction times in healthy controls



Stagg, Bachtiar & Johansen-Berg; *Current Biology 2011*

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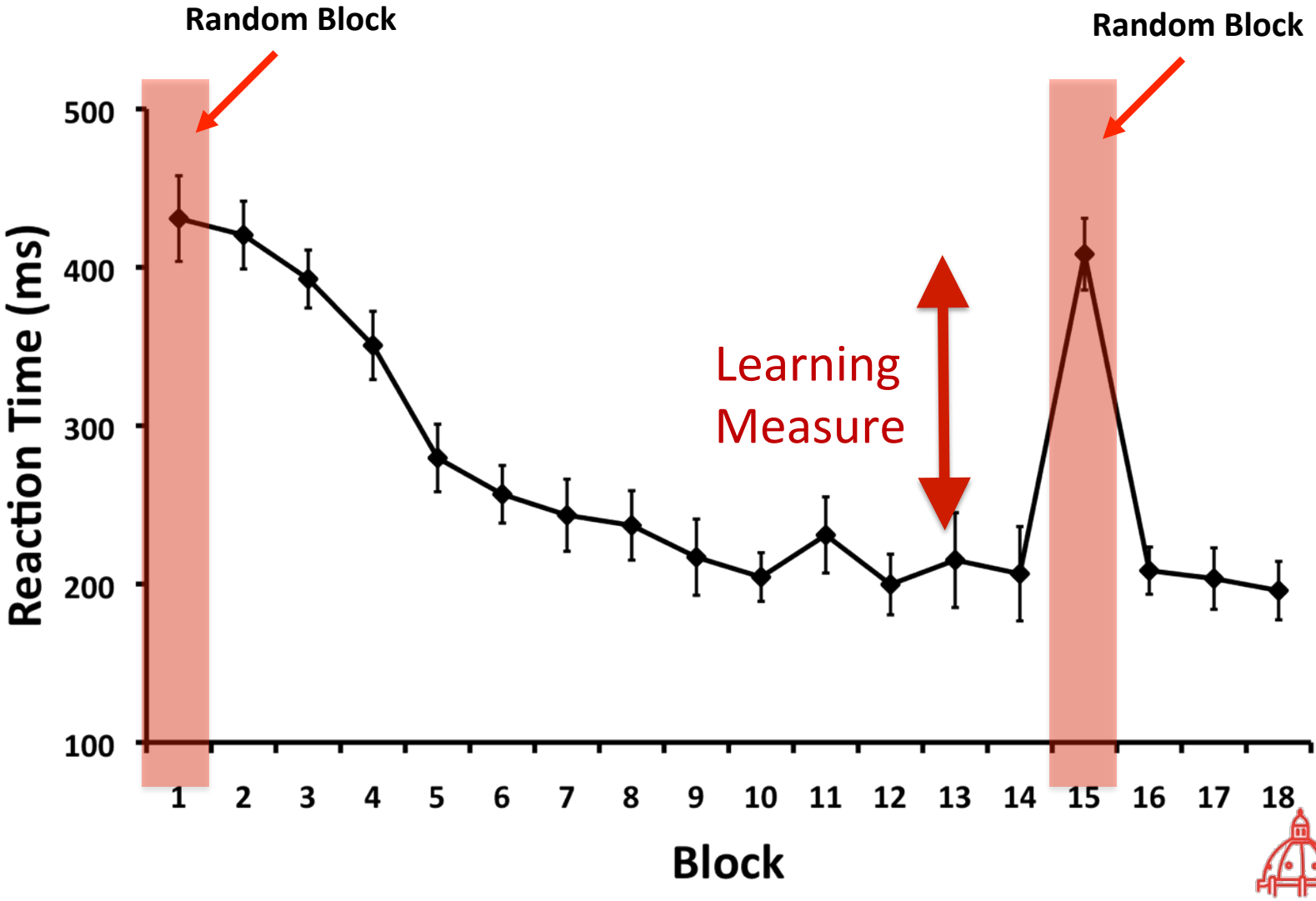
Behavioural Data : Learning Reaction Times



Stagg, Bachtiar & Johansen-Berg; *Current Biology 2011*

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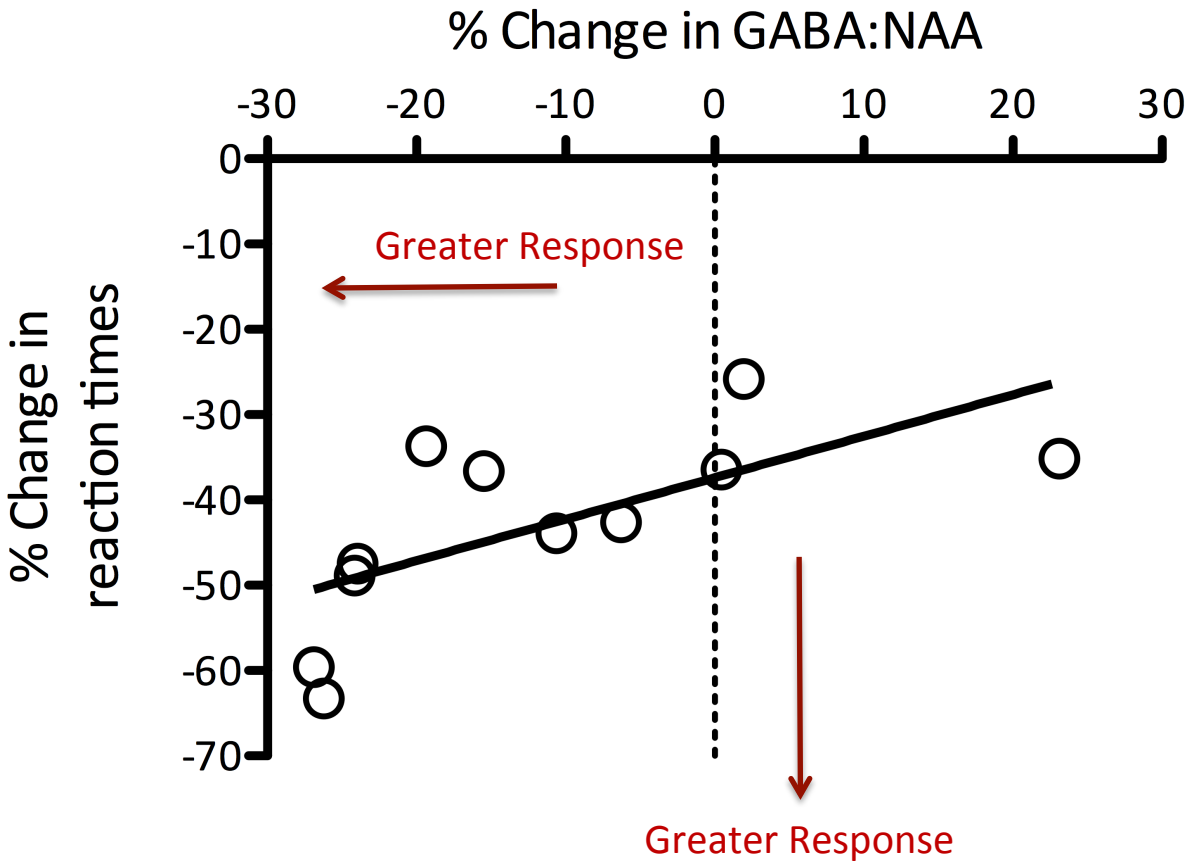
Subjects who show greater decrease in [GABA] due to tDCS also learn more



Stagg, Bachtiar & Johansen-Berg; Current Biology 2011

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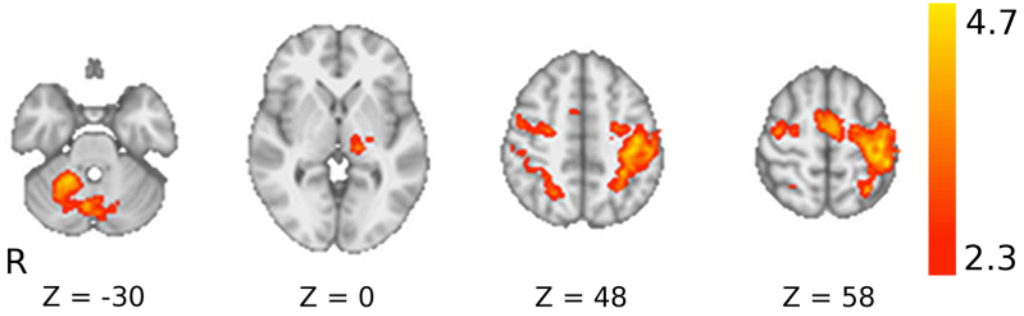
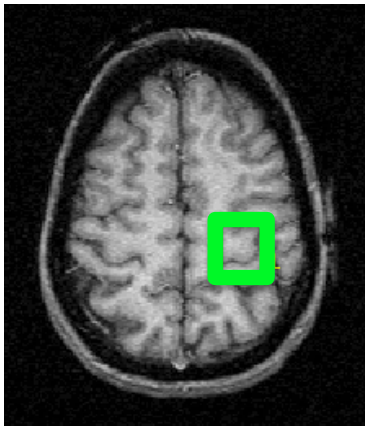
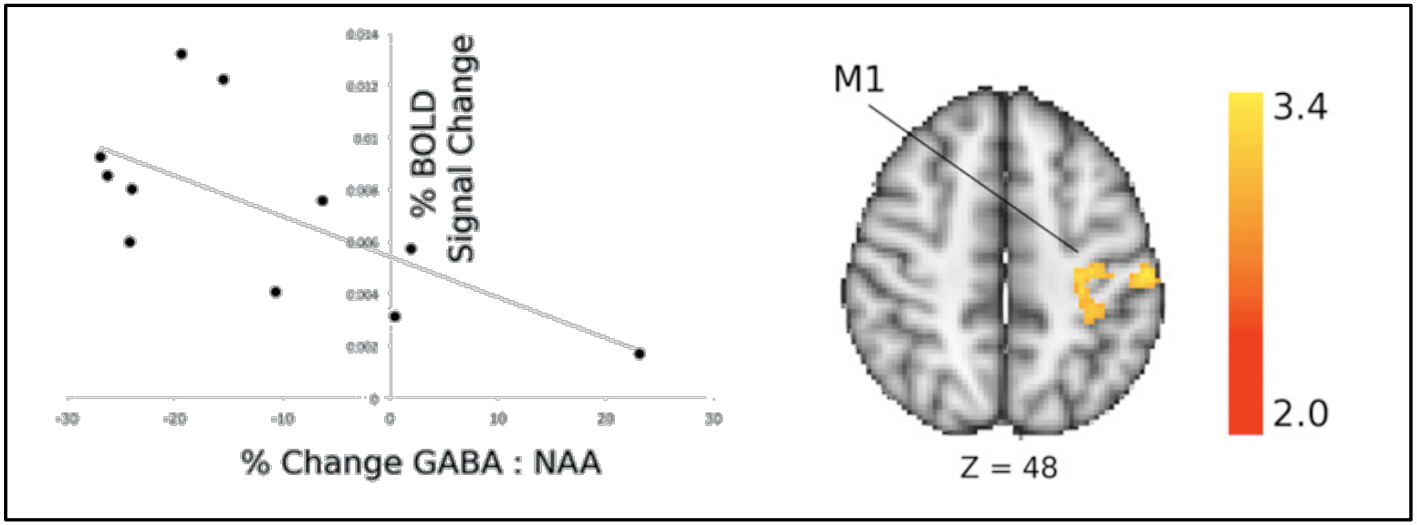
Subjects who show greater decrease in [GABA] due to tDCS also show a greater learning-related fMRI signal







Stagg, Bachtiar & Johansen-Berg; *Current Biology 2011*

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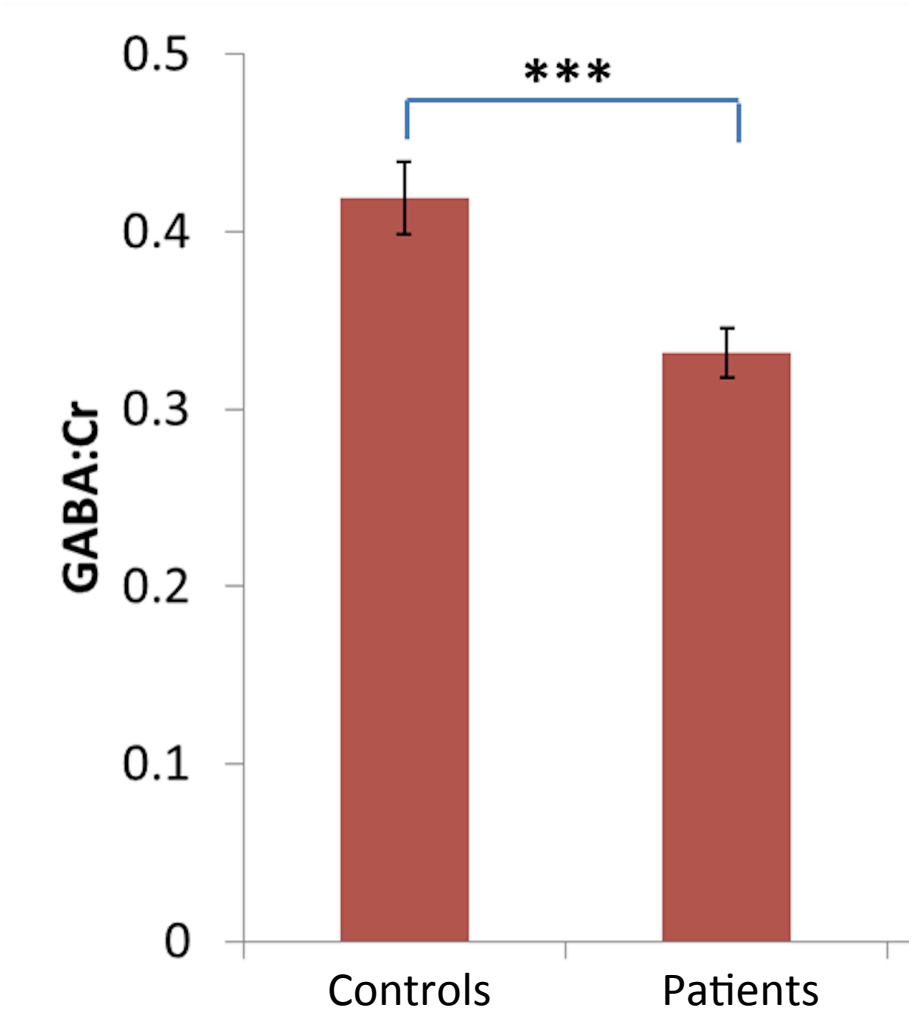
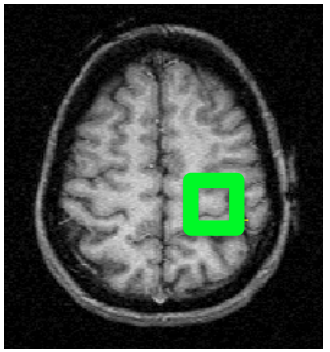
GABA is decreased in ipsilesional M1 in chronic stroke patients





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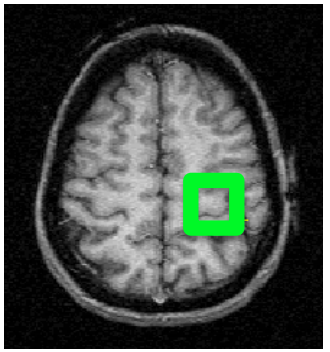
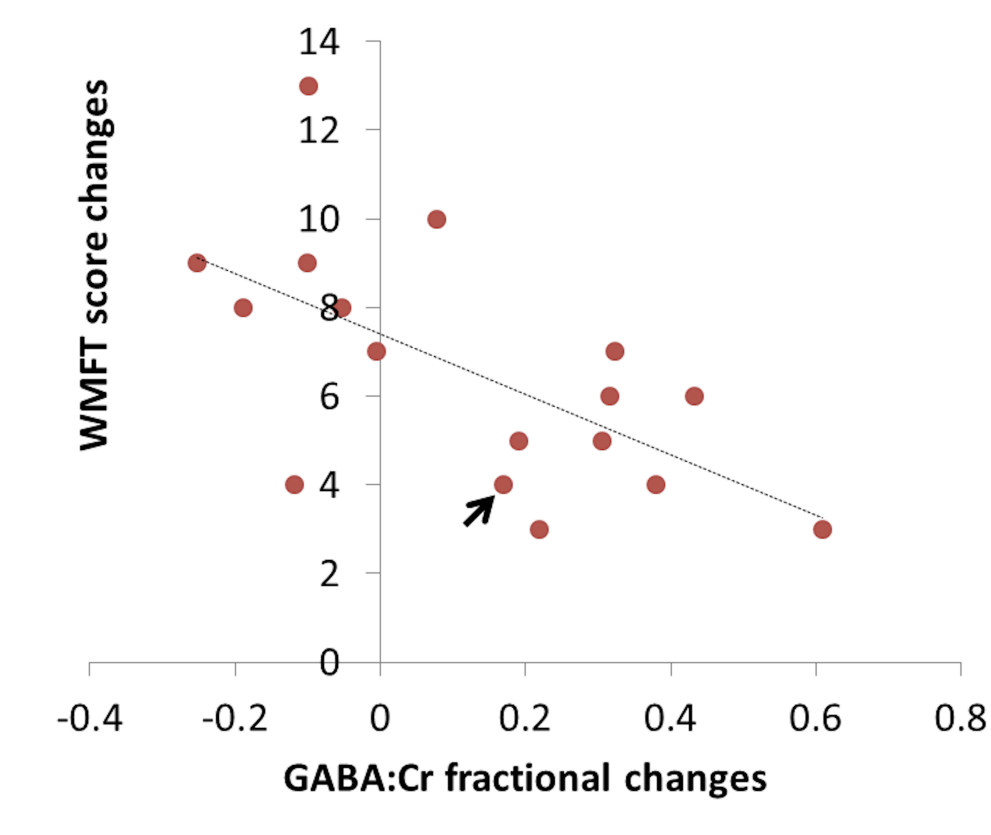
Blicher et al., in revision

GABA change due to training can be related to clinical outcome in chronic stroke patients





Blicher et al., in revision

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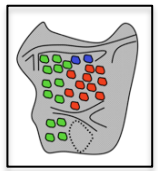
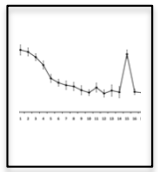
Conclusions and ongoing questions

- A decrease in GABA is necessary for plasticity in the primary motor cortex in animals

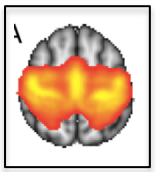


- GABA modulation appears to be behaviourally relevant in motor cortical plasticity in humans

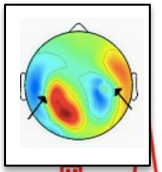


- At baseline, MRS GABA is probably related to extra-synaptic GABA tone (Stagg et al., *J Physiol* 2011) but what changes represent is still unclear

- Ultra-high field (7T) MR will allow better temporal, spatial and frequency resolution



- Combining MRS and tDCS with fMRI and MEG / EEG measures of activity will be the next step in understanding the role of inhibition (and excitation) in plasticity



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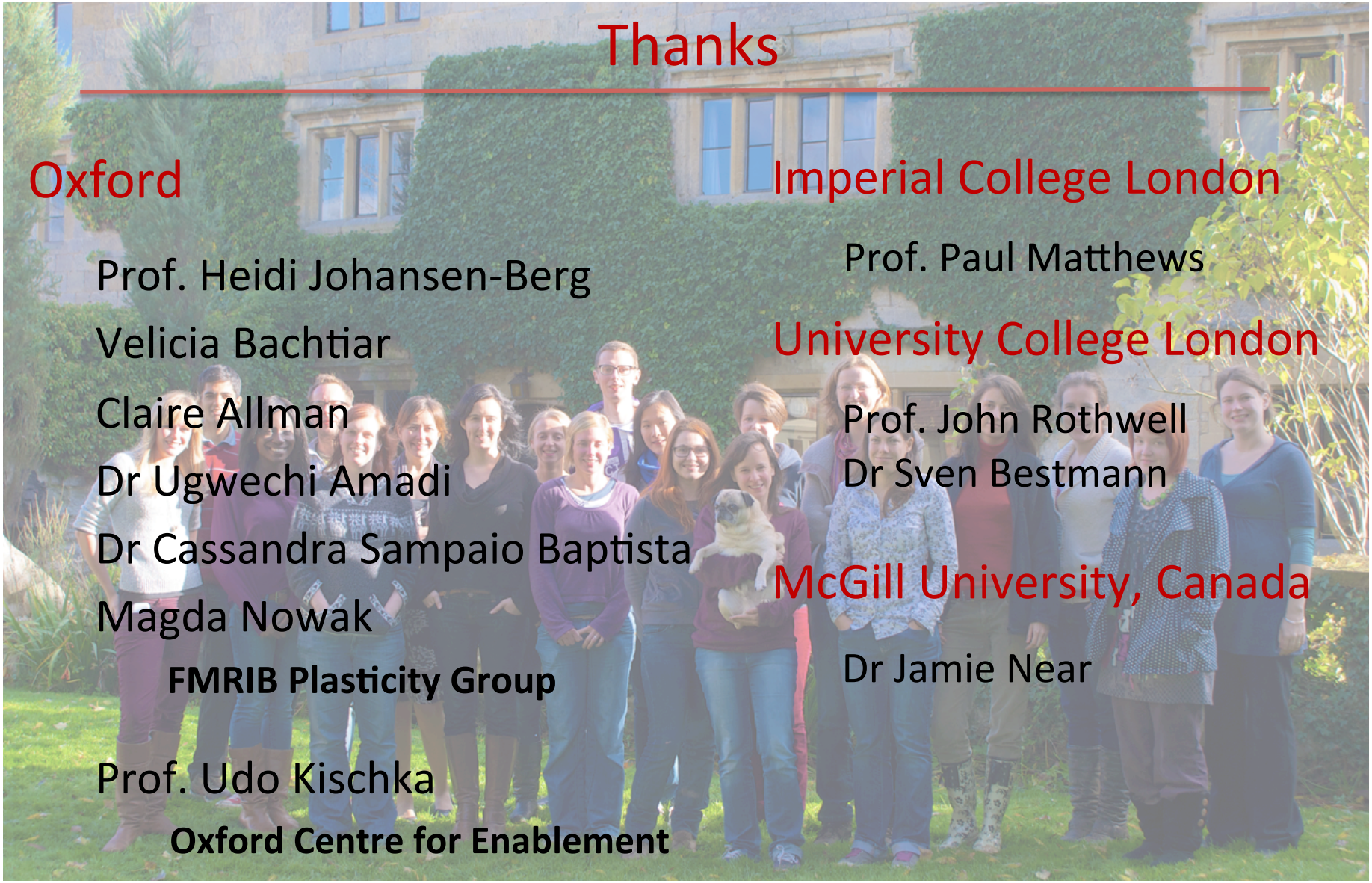
Thanks



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