tDCS and MRS for Learning and Recovery

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Motor Cortical plasticity is dependent on changes in GABA

Trepel & Racine, 2000; Lee et al., 2006
The Larmor Equation

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

\[ \omega = \gamma B \]

- \(\omega\) Angular Frequency
- \(\gamma\) Gyromagnetic Ratio
  (constant for a given atom)
- \(B\) Strength of Magnetic Field.

Frequency \(\propto\) Field strength
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.
MR Spectroscopy provides *in vivo* measures of neurotransmitters.
GABA-MRS is sensitive to small changes in neurotransmitters – Decrease in \([\text{GABA}]\) during a learning task

Floyer-Lea et al., 2006
(also Gudberg, Stagg, Near & Johansen-Berg, unpublished data)
GABA-MRS is sensitive to small changes in neurotransmitters – Decrease in [GABA] during a learning task

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Transcranial Direct Current Stimulation (tDCS)
tDCS has polarity-specific effects on cortical excitability

Change in size of muscle response (MEP) from baseline

Anodal (excitatory)

Cathodal (inhibitory)

Nitsche & Paulus, J Physiol 2000
Anodal (facilitatory) tDCS to the ipsilesional hemisphere improves motor function in chronic stroke

Hummel et al., Brain 2005
Studying neurotransmitter changes following tDCS

Yousry et al., 1997

Sham Pre  tDCS Pre  Sham Post

Sham Pre  tDCS Post

2x2x2cm
Anodal tDCS decreases [GABA] in stimulated motor cortex

Study Design

1. M1 GABA pre and post anodal tDCS to M1
2. V1 GABA pre and post anodal tDCS to M1
3. fMRI during Motor Learning

Physiological

Behavioural

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
Behavioural Data: Learning Reaction Times

Stagg, Bachtiar & Johansen-Berg; Current Biology 2011
Subjects who show greater decrease in [GABA] due to tDCS also learn more.

Stagg, Bachtiar & Johansen-Berg; Current Biology 2011
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
GABA is decreased in ipsilesional M1 in chronic stroke patients

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*
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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