



Combining transcranial stimulation techniques with magnetic resonance spectroscopy to investigate the motor cortex in health and after stroke



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2009... Bucharest: Dr. Charlotte Stagg



2009... Bucharest



International Brain Research Organization InEurope Grant



FMRI Centre

Nuffield Department of Clinical Neurosciences



One year later... Oxford



Oxford is fantastic!



Oxford is fun!



Oxford is science: John Radcliffe Hospital



Getting Around JR Hospital...



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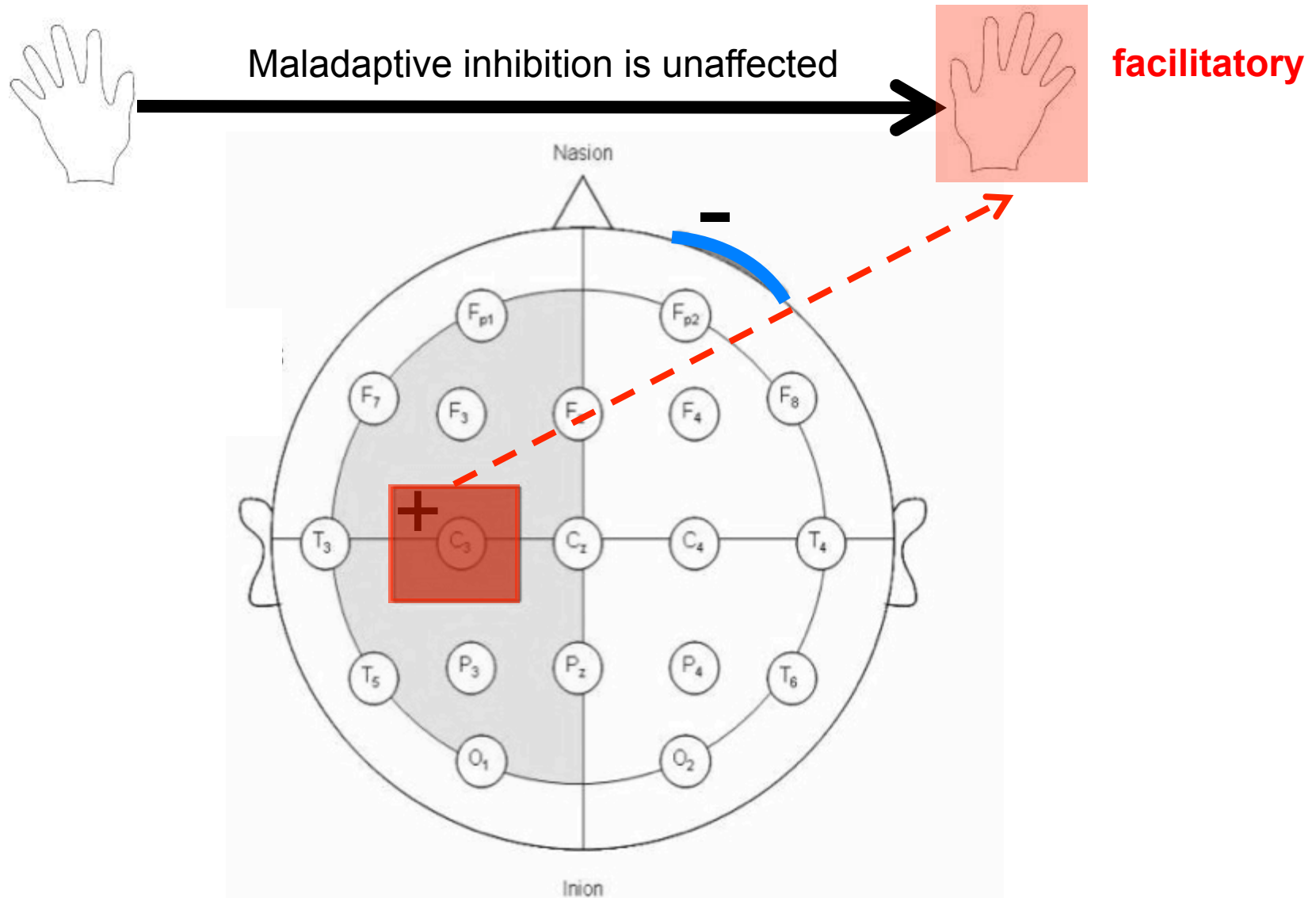
Nuffield Department of Clinical Neurosciences



Transcranial direct current stimulation (tDCS) in the primary motor cortex (M1) in humans



Anodal tDCS of the M1 after stroke



(adapted from Constantinescu et al, Rom. J. Neurol. 2010)

TRANS-CRANIAL DIRECT CURRENT STIMULATION (tDCS): A PROMISING NEW TOOL TO FACILITATE REHABILITATION OF MANUAL DEXTERITY AFTER STROKE

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Anodal tDCS tips the balance between excitation and inhibition

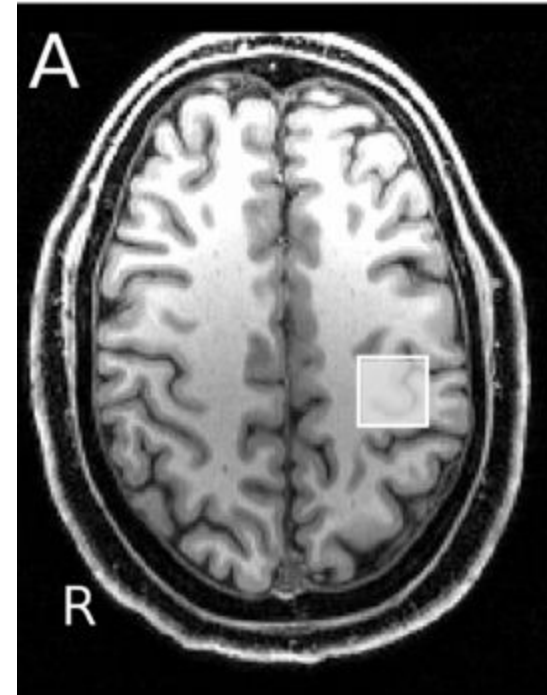
What are the chief excitatory and inhibitory neurotransmitters?



Glutamate

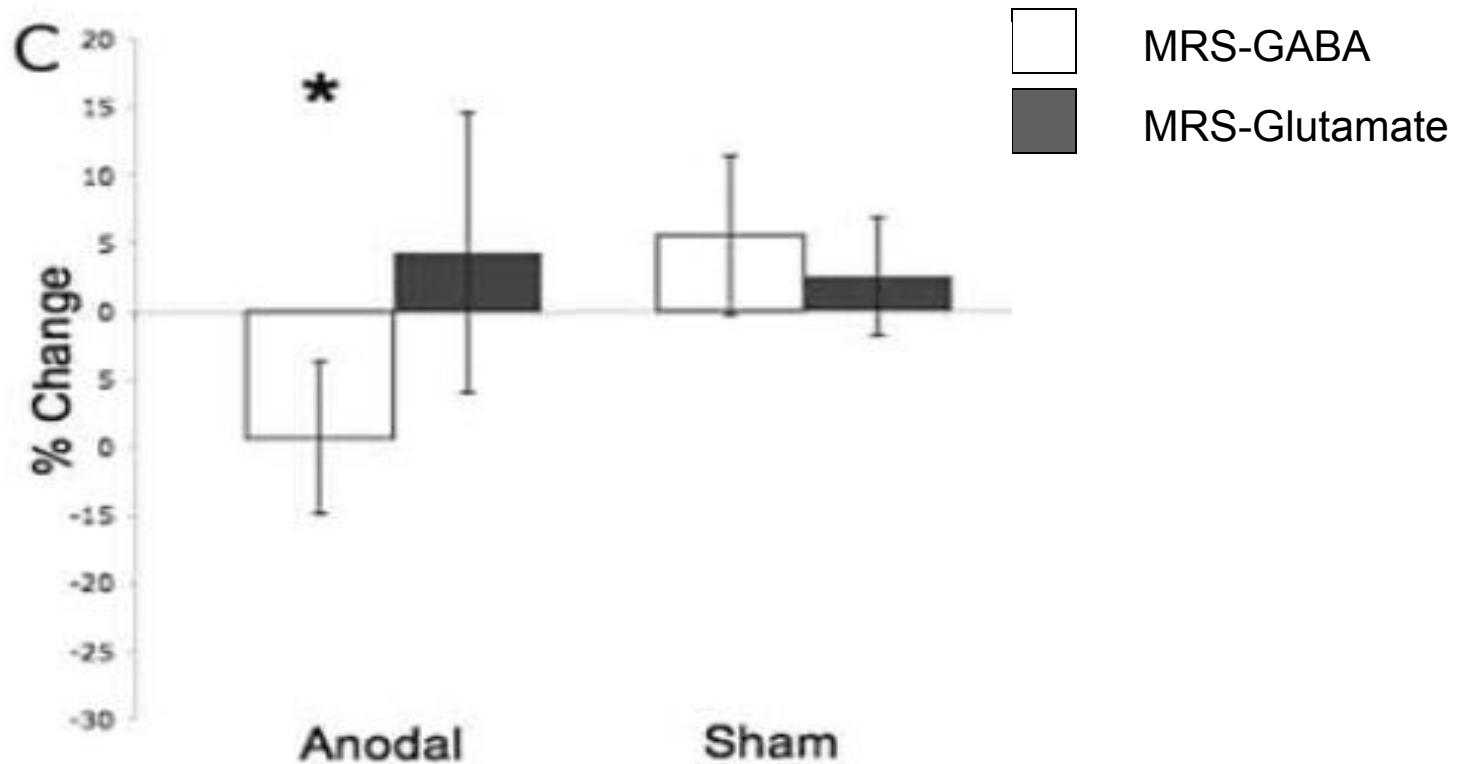
GABA

How can we measure GABA and Glutamate?



**Magnetic resonance spectroscopy
(MRS)**

How does anodal tDCS modulate GABA and Glutamate?



Anodal tDCS decreases **MRS-GABA** (inhibitory) in M1 → facilitatory

(Stagg et al, J. Neurosci. 2009)

What are we really measuring with MRS-GABA?

Aim

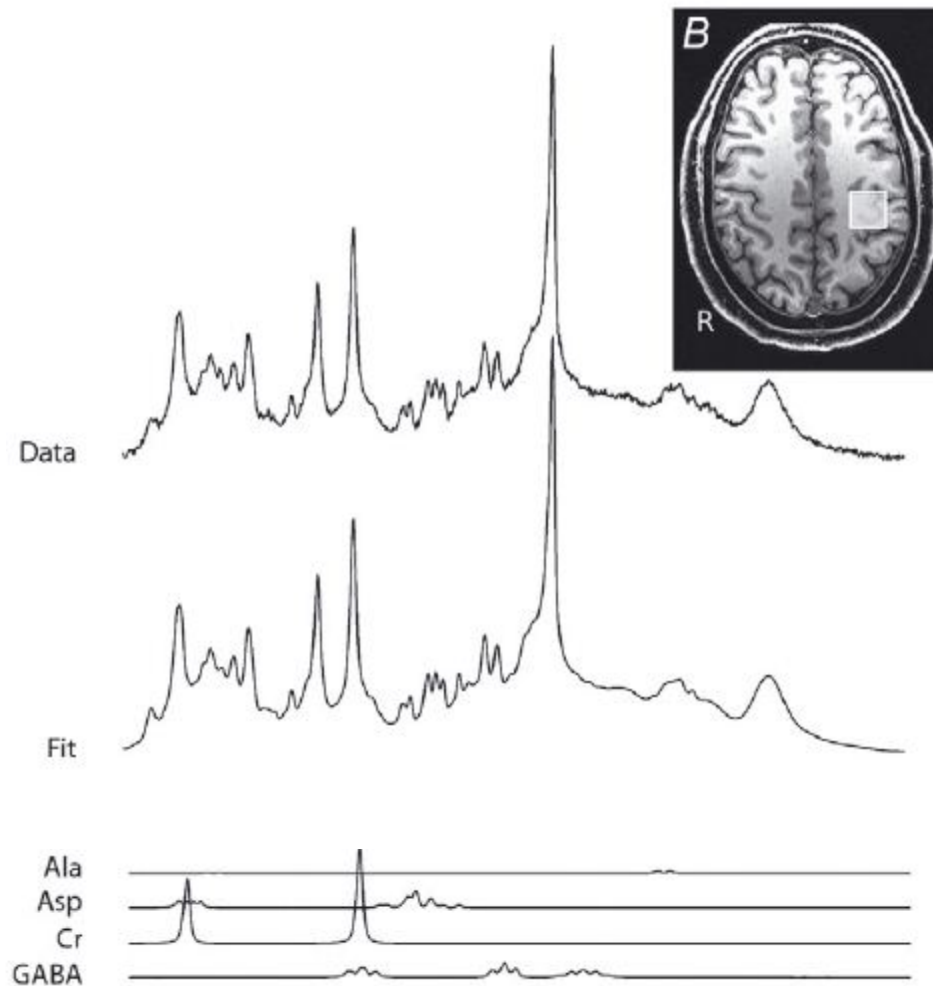
To investigate how MRS-GABA relates to GABA-ergic synaptic activity

Materials and Methods

- healthy human subjects
- MRS – measure of GABA
- paired-pulse transcranial magnetic stimulation (paired-pulse TMS) – measures of synaptic GABA activity

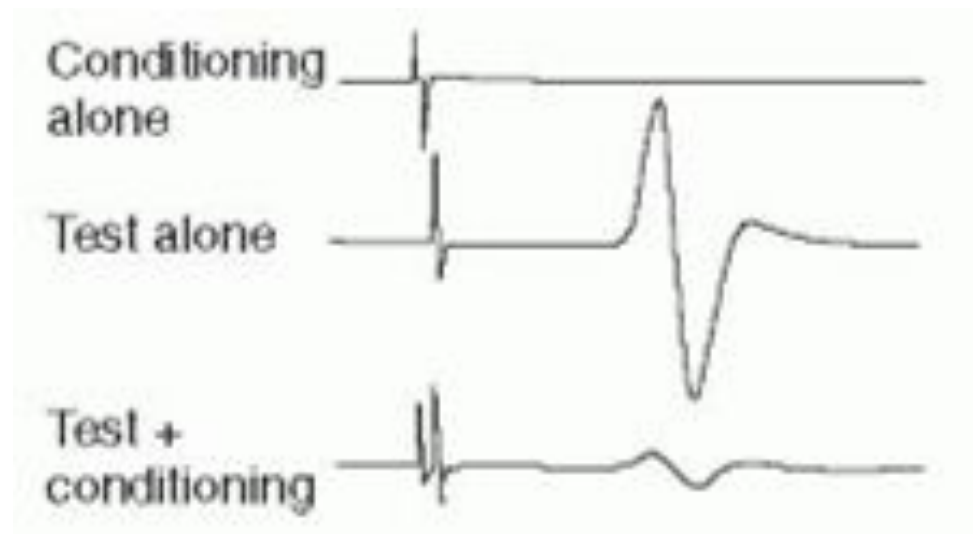
Materials and Methods

MRS

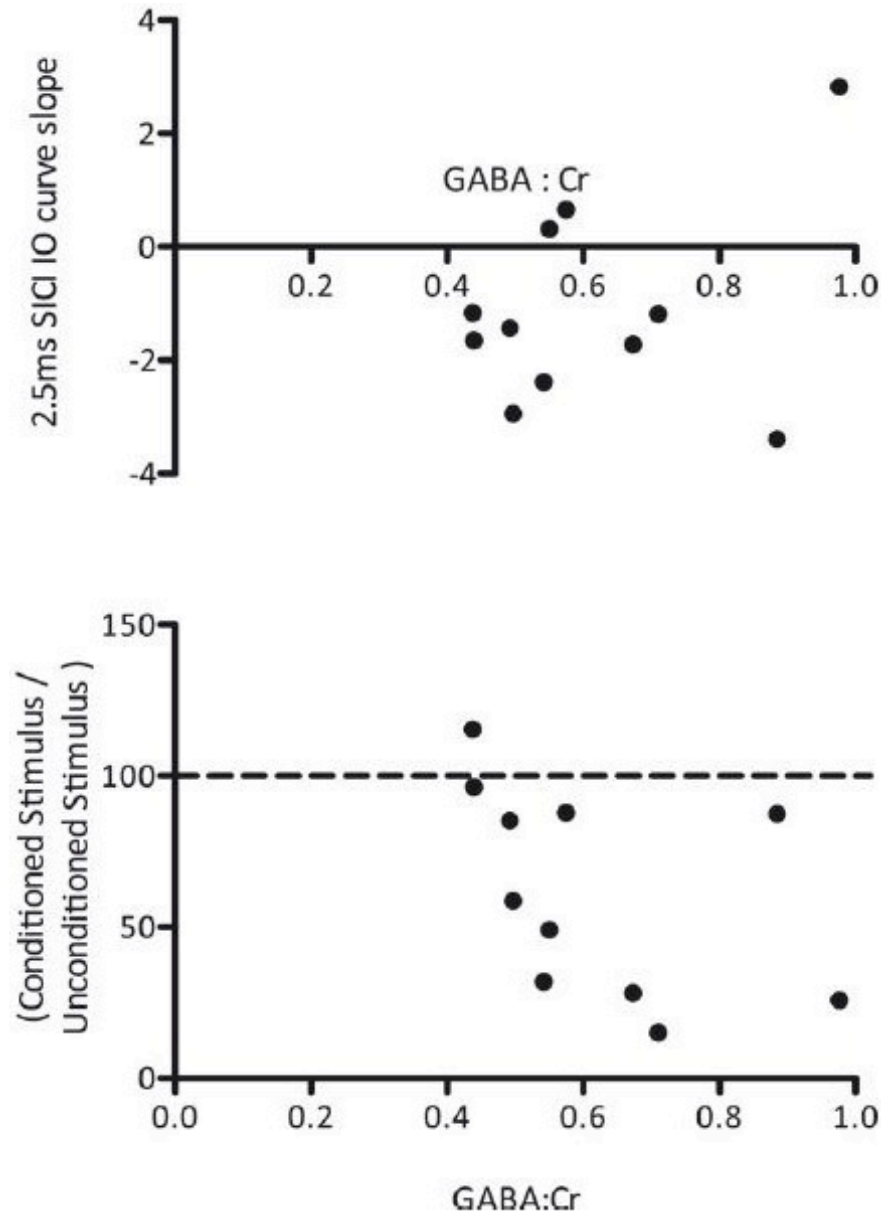


Materials and Methods

Paired-pulse TMS

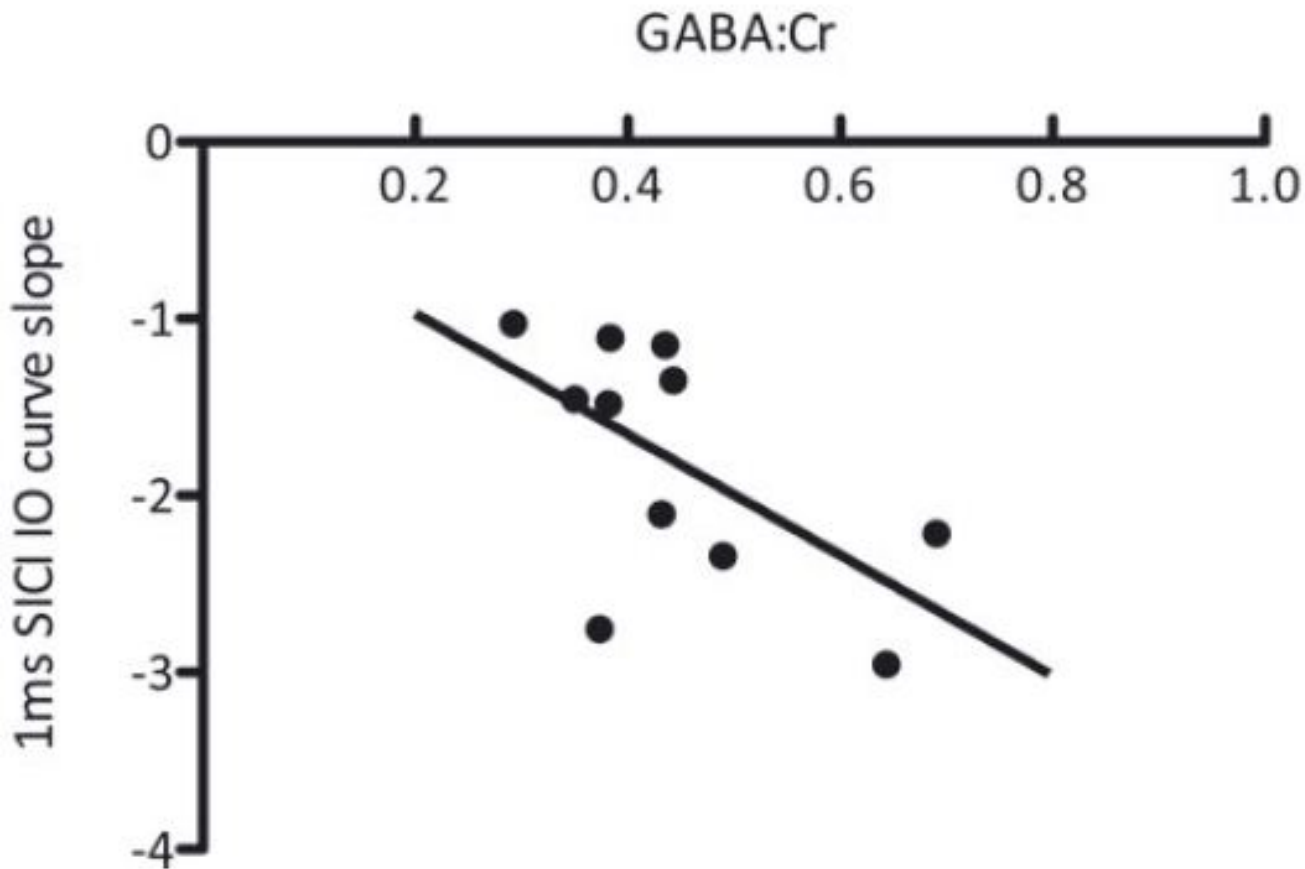


Results



No relationship between TMS measures of synaptic GABA_A and GABA_B activity and MRS measures of GABA

Results



A significant relationship between MRS measures of GABA and TMS measures of extrasynaptic (!) GABA_A activity

Results

- MRS-GABA does not reflect synaptic GABA_A or GABA_B activity
- MRS-GABA most probably reflects tonic extrasynaptic GABA_A activity

Relationship between physiological measures of excitability and levels of glutamate and GABA in the human motor cortex

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Non-technical summary Inter-individual differences in regional GABA as assessed by magnetic resonance spectroscopy (MRS) relate to behavioural variation in humans. However, it is not clear what the relationship is between MRS measures of the concentration of neurotransmitters in a region and synaptic activity. Transcranial magnetic stimulation (TMS) techniques provide physiological measures of cortical excitation or inhibition. Here, we investigated the relationship between MRS and TMS measures of glutamatergic and GABAergic activity within the same individuals. We demonstrated a relationship between MRS-assessed glutamate levels and a TMS measure of global cortical excitability, suggesting that MRS measures of glutamate do reflect glutamatergic activity. However, there was no clear relationship between MRS-assessed GABA

Clinical impact

- importance for interpreting MRS data;
- relevance for understanding the tDCS mechanisms;
- a step forward in the development of tDCS protocols tailored to individual stroke patients

Thank you!

Dr. Charlotte Stagg

Dr. Mihai Moldovan (Copenhagen University)

IBRO In-Europe

