Low Glx:GABA ratio at baseline predicts greater tDCS gains in verbal episodic memory

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Background
Cognitive decline, which is observed in healthy and pathological ageing [1], is linked to a disrupted excitation/inhibition (E/I) balance, manifesting in the form of hypoexcitability [2]. Increasing the excitability of functionally relevant brain regions, like the dorsolateral prefrontal cortex (DLPFC), via the application of anodal transcranial direct current stimulation (tDCS) may counteract this cognitive deterioration [3]. Behavioural studies, however, show that the responsiveness to tDCS is highly variable between individuals, with low performers experiencing the greatest benefits [4]. To increase the reliability of tDCS as an intervention, its underlying neurophysiological mechanisms need to be understood. In this context, the levels of glutamatergic metabolites (Glx) and GABA as well as their respective ratio, present themselves as potential biomarkers for tDCS-induced gains [5].

Methods

Study procedure
In this double-blind, sham-controlled, cross-over study, 32 young (24.5 ± 2.6 years, 20 female) and 21 healthy elderly participants (67.3 ± 4.4 years, 11 female) attended three sessions on different days.

Baseline MR session 1 new atDCS (20 min, 1 mA) MRS 
MRS Retrieval MRS Retrieval MRS Retrieval 

MR spectroscopy

Voxel (2x2x2 cm) placed in left DLPFC. Acquisition of glutamatergic metabolites and GABA spectra pre- and post-tDCS.

Results

Performance in verbal memory task

Absence of overall stimulation effect in the encoding phase as well as during the delayed recalls in young and elderly participants.

Behaviour ~ Neurometabolites

Differential benefit in delayed recall from tDCS depends on E/I ratio prior to stimulation:
E/I ratio high: sham > real
E/I ratio low: real > sham

Conclusions

The potential of tDCS to improve cognition is limited [6], even in elderly whose cognitive abilities have dwindled. Further, this study could not determine the effects of anodal tDCS on neurotransmitter levels or E/I balance. Nevertheless, the moderating effect of the latter on behavioural gains suggests that future tDCS studies should not neglect the state of the non-quietest targeted system, which operates within homeostatic limits. Thus, tDCS needs to be finely tuned to increase excitability, and thus behavioural performance, without overdriving the system.

References
[6] Habich A et al., No effect of anodal tDCS on verbal episodic memory performance and neurotransmitter levels in young and elderly participants. Neural Plasticity, (accepted)

Hypotheses
1) Differential impact of anodal tDCS on verbal episodic memory with greater benefits in young low performers and elderly.
2) Increased Glx:GABA ratio after anodal tDCS
3) Low initial cognitive capacity and low Glx:GABA ratio at baseline predict greater benefits from anodal tDCS.

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