

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

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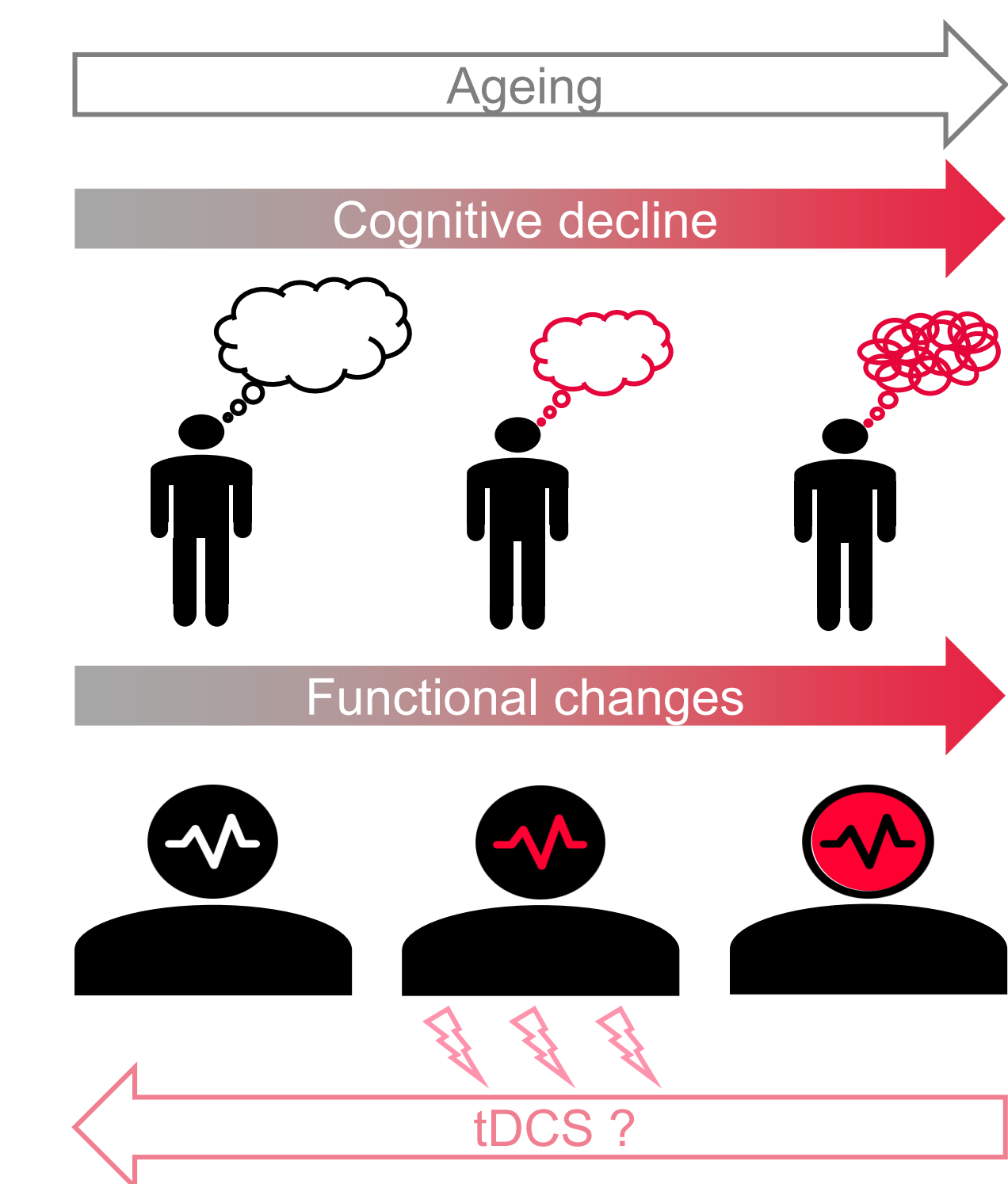
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## Background

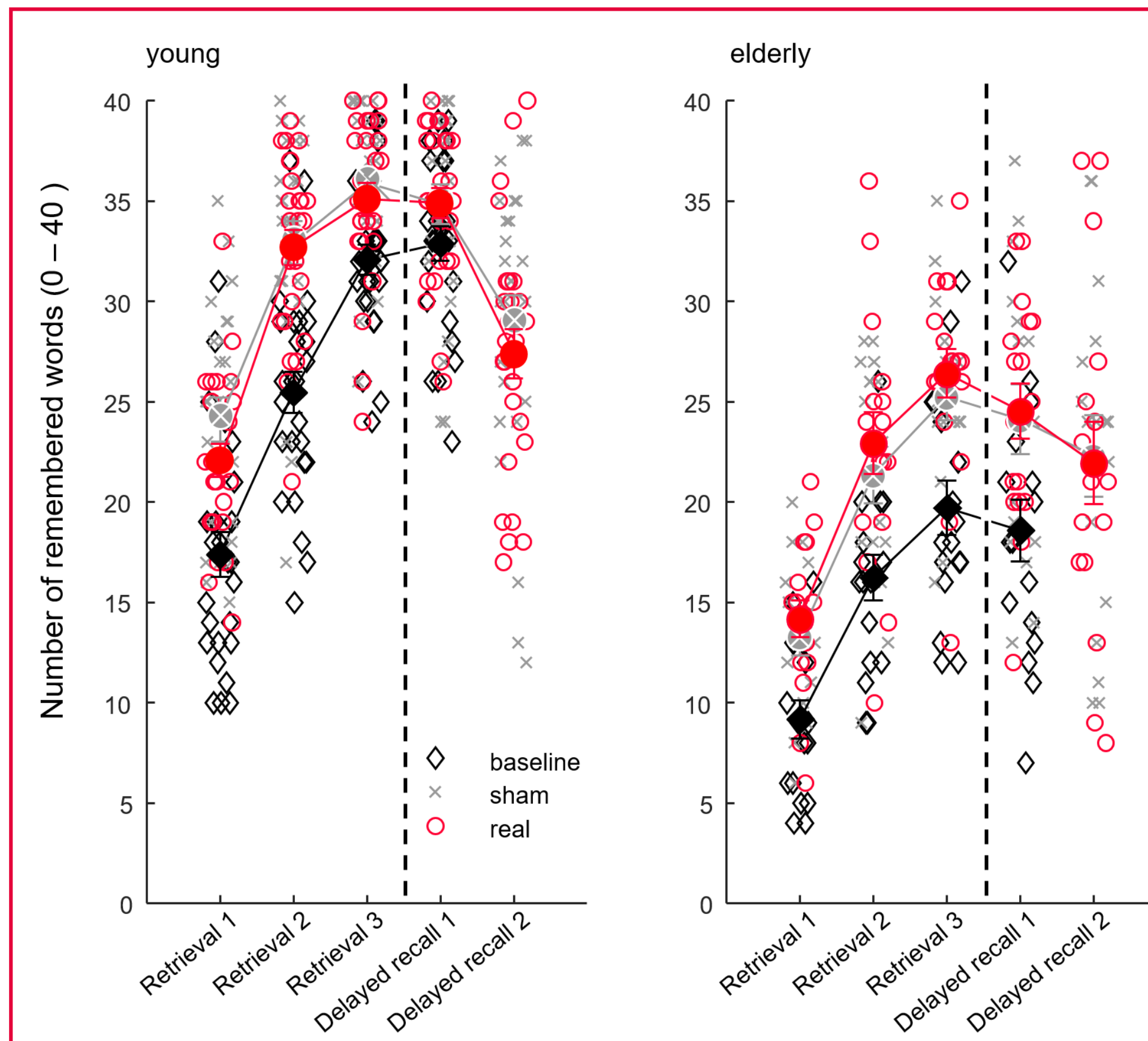
Cognitive decline, which is observed in healthy and pathological ageing [1], is linked to a disrupted excitation/inhibition (E/I) balance, manifesting in the form of hypoexcitability [2]. Increasing the excitability of functionally relevant brain regions, like the dorsolateral prefrontal cortex (DLPFC), 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].



## 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.

Marked ceiling effects in free recall performances in young participants.

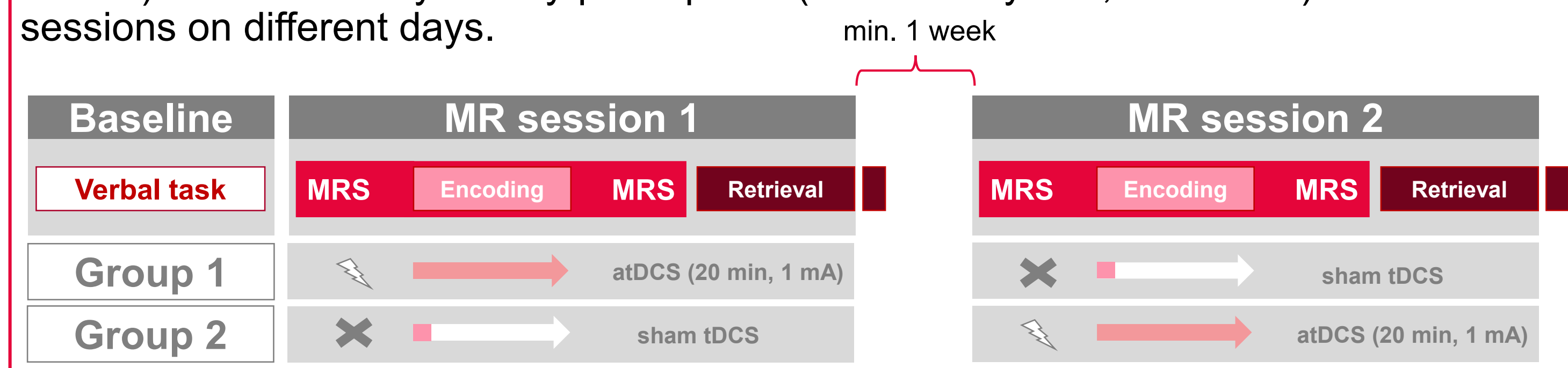
## Hypotheses

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

## Methods

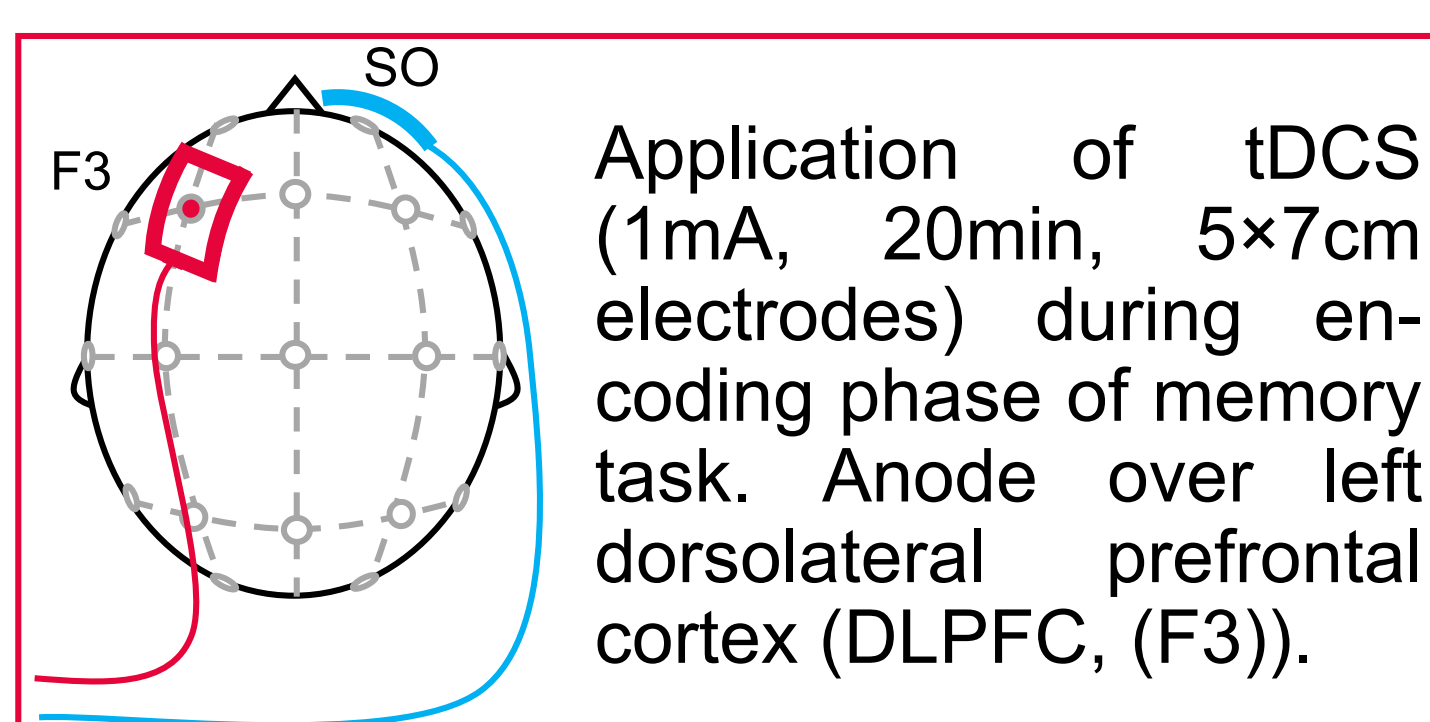
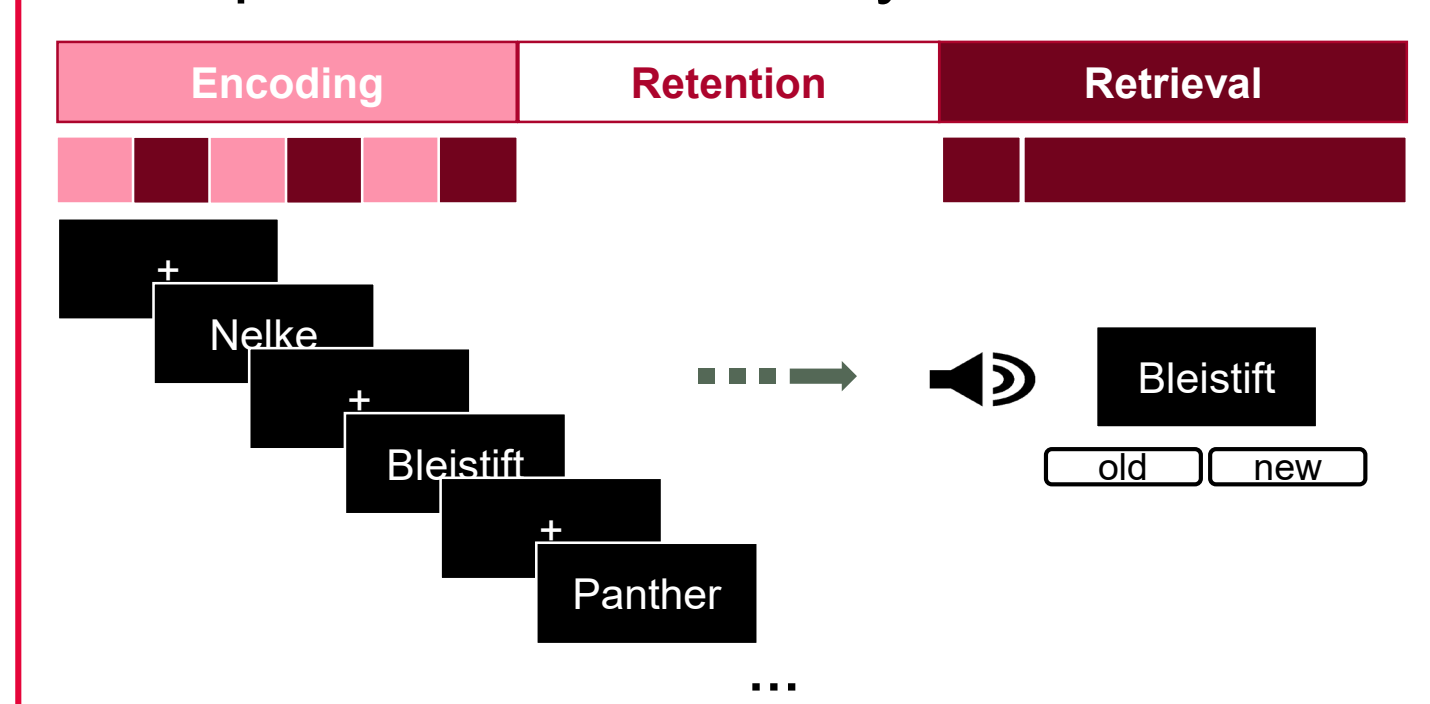
### Study procedure

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.



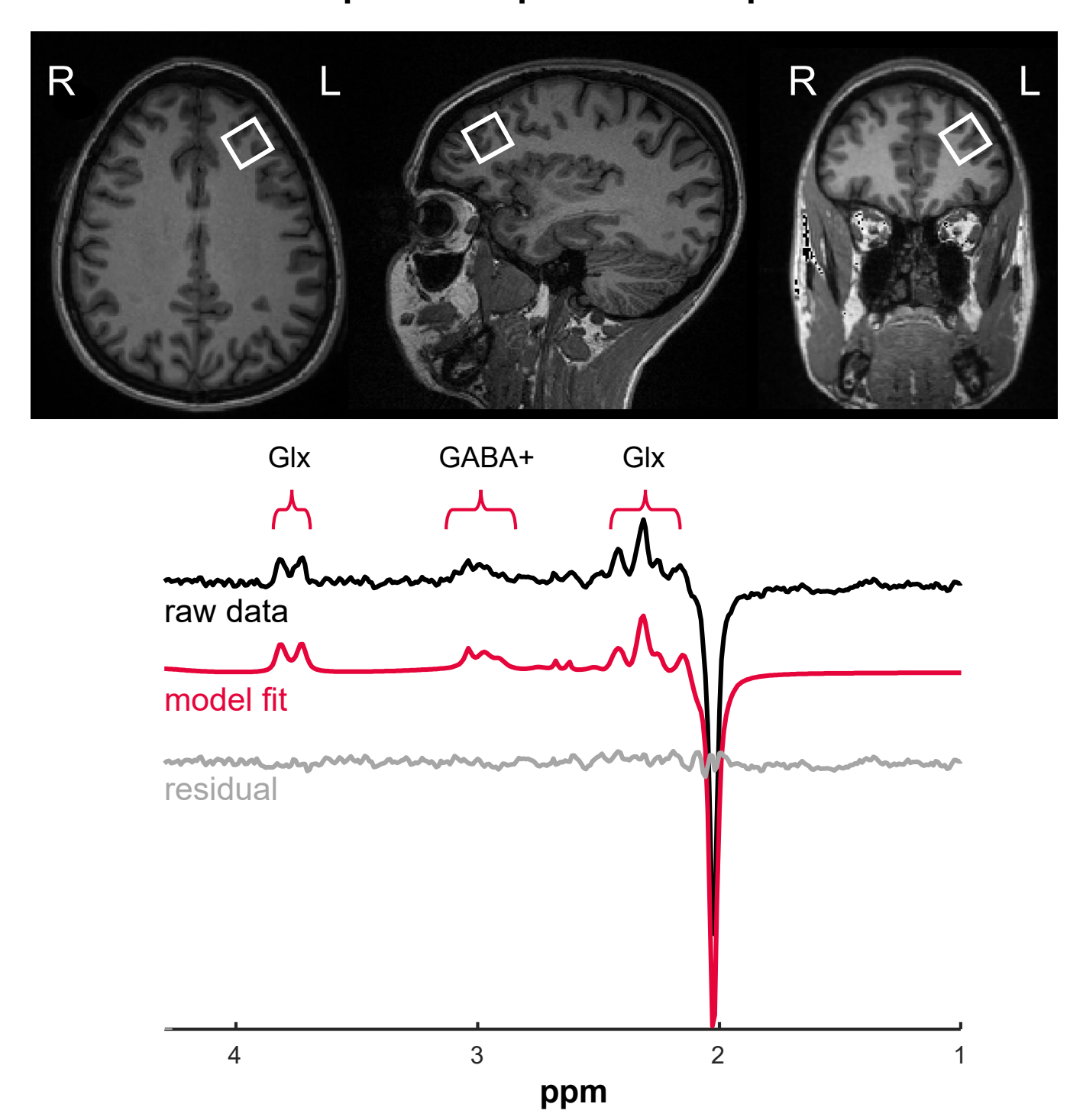
### Verbal memory task & tDCS

Visual presentation of 40 nouns in 3 encoding blocks. Free recall after each block plus additional delayed recall.

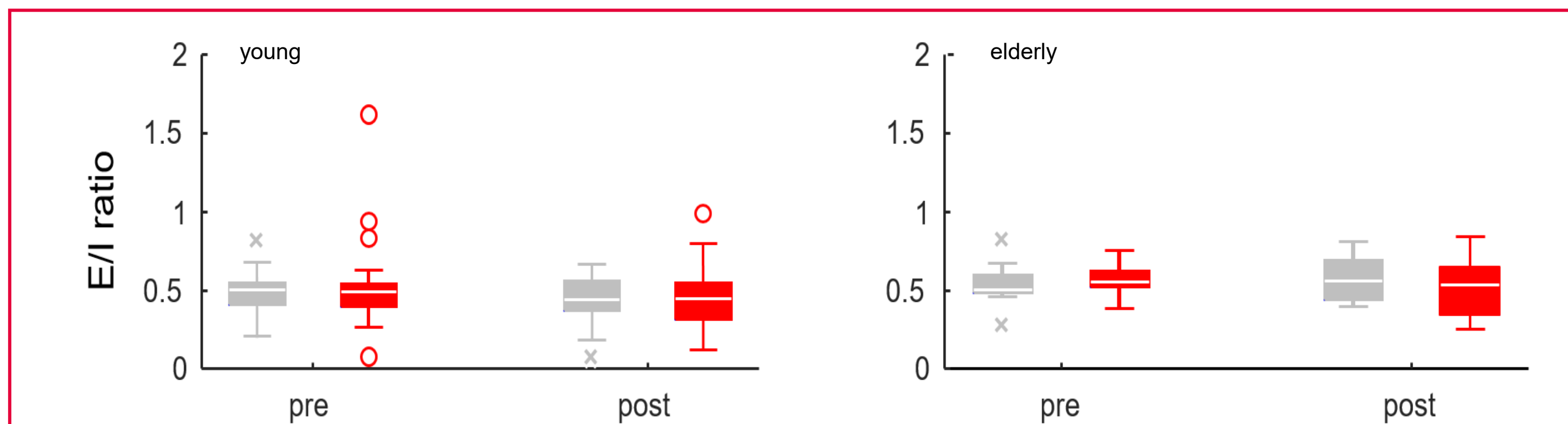


### MR spectroscopy

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

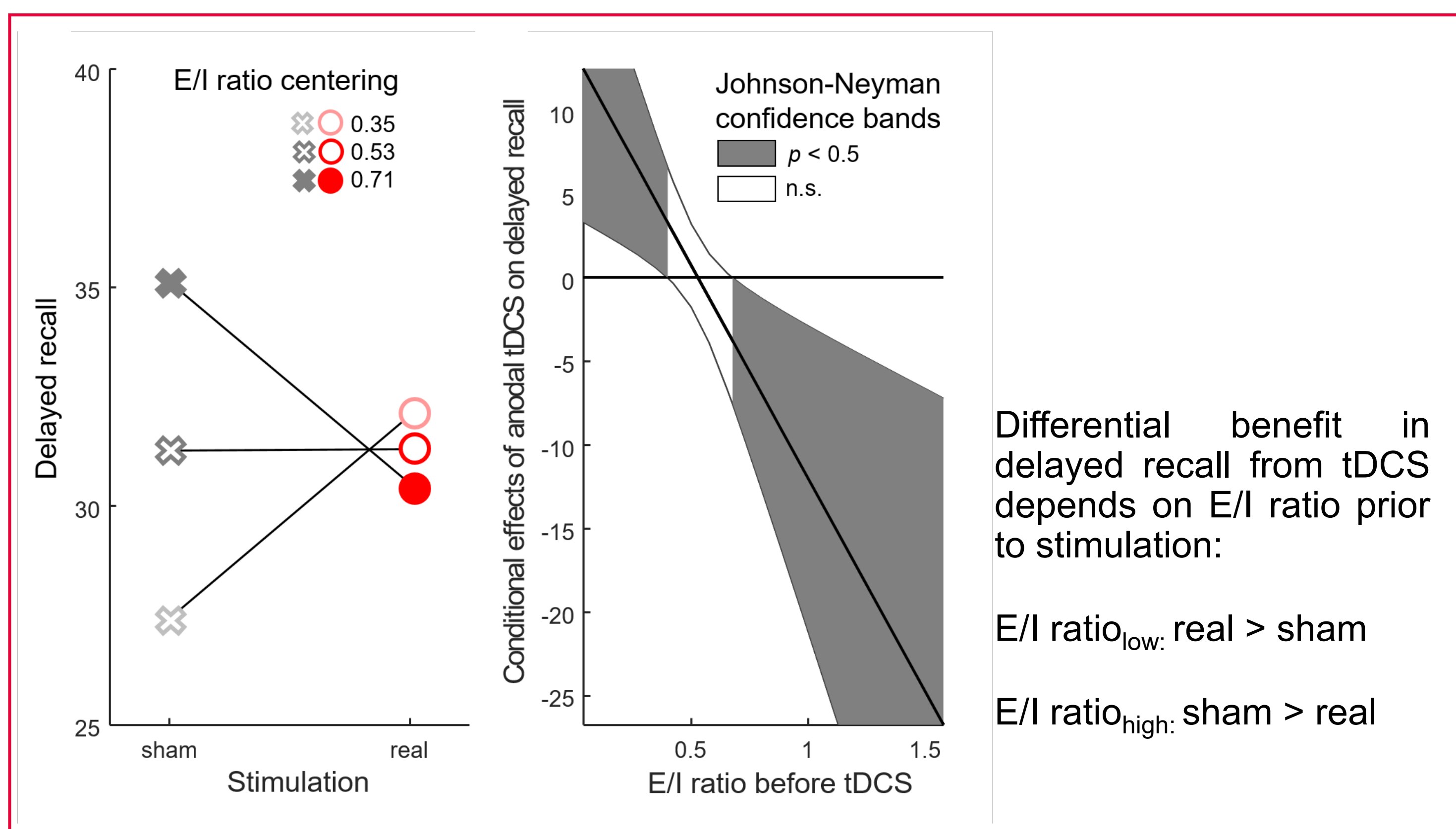


### Neurotransmitters



No tDCS, related increase of E/I ratio (i.e., Glx:GABA ratio) nor on either of the two neurotransmitter levels on their own.

### Behaviour ~ Neurotransmitters



Differential benefit in delayed recall from tDCS depends on E/I ratio prior to stimulation:

E/I ratio<sub>low</sub>: real > sham

E/I ratio<sub>high</sub>: sham > real

## Conclusion

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-quiescent 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.



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### References

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