

Supplementary figures and table

Suppl. Fig. 1. Repeatability of the NCE measurement. There was reliable correlation between separate measurements of the NCE taken several weeks apart in both the first cohort (a) and second cohort (b).

Suppl. Fig. 2. Fitted GABA peaks for each individual. Each panel plots the fitted range of the MR spectrum for each participant (x-axis is the MRS chemical shift expressed in parts per million, ppm), showing the experimental data (in black) and the fitted Gaussian model (red; the non-linear least squares optimisation of a single gaussian curve centered between 2.9 and 3.15 ppm, with a baseline that allowed for overall linear trend in the spectra). To quantify GABA concentration, the integral of this fitted function is divided by the integral of the unsuppressed water signal acquired from the same volume, and this measure is normalised to account for differences in the voxel composition of grey/white matter and CSF. The peak will also contain signal from co-edited macromolecules (e.g. cytosol), and this may contribute 30-40% of the integrated area [46]. However, we have no reason to expect that these would differ between individuals or have an influence on sensorimotor behaviour. Confidence that individual differences in our measure reflect actual GABA differences can be drawn from recently reported association of this measurement with gamma frequency, BOLD signal, TMS and sensory tuning, all of which are well modelled by variation in GABA [4, 7, 10-12, 47].

GABA is the only neurotransmitter for which a reliable estimate of individual differences can be obtained using MRS at 3T. Most other neurotransmitters exist in concentrations that are just too small. We can obtain a combined measure of glutamate and glutamine, by fitting the 'glx' peak (see fig 1) with a double Gaussian centered between 3.65-3.85 ppm. We find that the glx concentration does not correlate with either the NCE or with GABA. Arguably the GABA/Glx ratio would be a suitable measure for reflecting the inhibition/excitation ratio in the cortex, and it does correlate with the NCE as we would expect ($r=.51$ and $r=.53$ for the two cohorts). However, glutamate is also a key molecule in cellular metabolism, so in addition to the contamination by glutamine, only a fraction of the glutamate signal relates to neurotransmitter. Further, the glx peak is simply much more noisy than the water peak, so we believe the most robust measure of GABA was obtained by the GABA/water ratio.

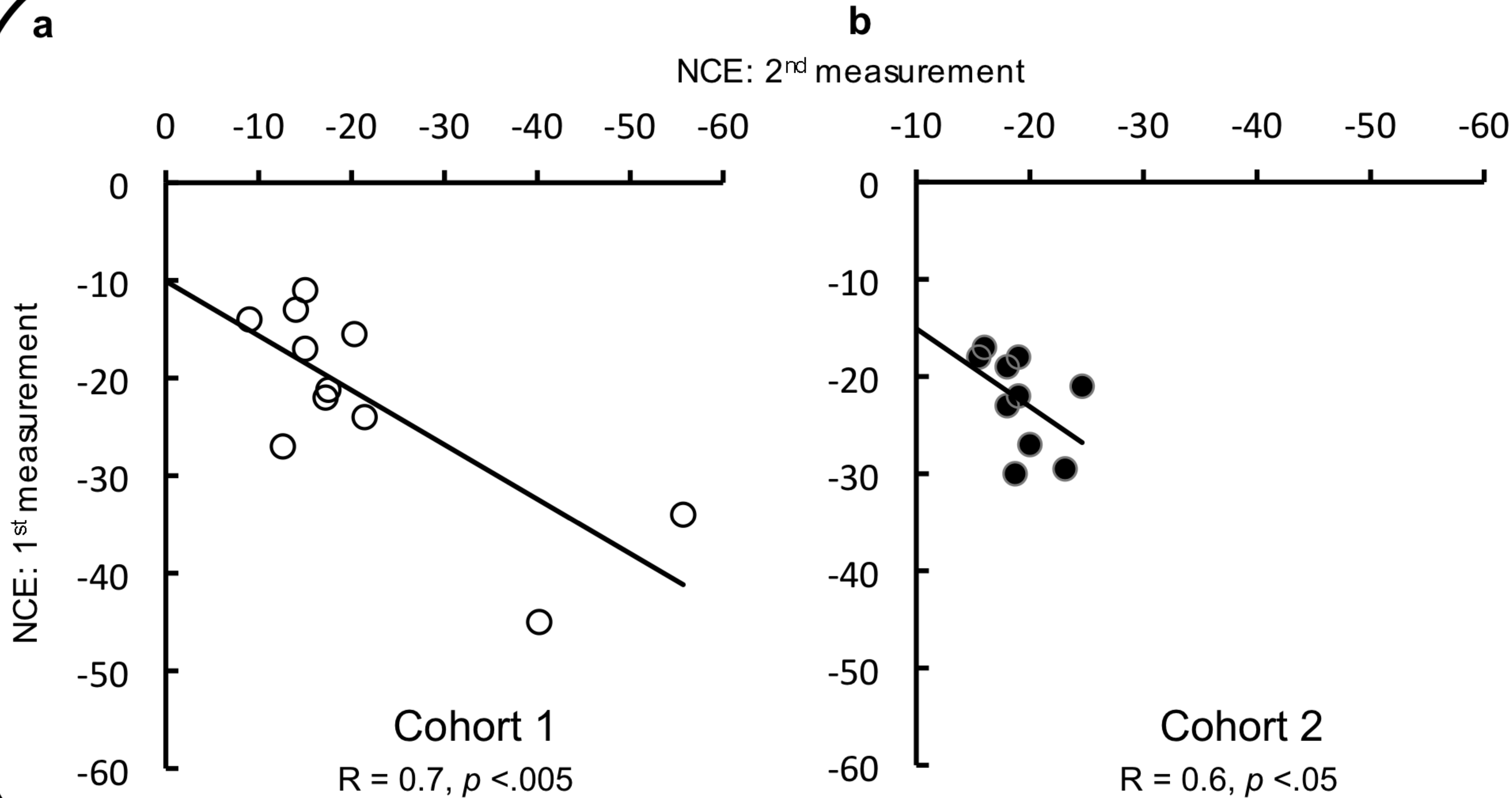
Suppl. Fig. 3. Intercorrelation between GABA concentration (conc.) in different brain regions. (a,b,c) Open symbols and r values in standard text refer to the first cohort, filled symbols and bold text refer to the second cohort. Note that we find no evidence for positive correlation of GABA concentration between brain areas. d) lists R values for all first cohort measurements, which included also voxels for IFG and ACC. Note that for participants with relatively small brains, there was some overlap between IFG and DLPFC voxels (in the white matter), and between ACC and SMA voxels (grey and white matter). For participants with larger brains, there was less or no overlap. Regional specificity in GABA is consistent with a previous study [32] in which MRS measurements were taken from 6 regions, and a significant drop in GABA with age was reported for DLPFC, but not for other regions.

Suppl. Fig. 4. GABA in the SMA does not correlate with Simon task, Eriksen flanker task, or STOP task. a,b) The Simon task [28] consisted of 200 trials (short pauses every 50) in which participants had to respond to letter stimuli (A or H) presented for 100 ms either 4° on the left or on the right of fixation. Participants were instructed to press as fast and accurately as possible the left button when an A was presented and the right button when an H was presented (counterbalanced across participants). RTs are usually faster and more accurate when the stimulus occurs in the same relative spatial location as the response, even though the stimulus location is irrelevant to the task. The Simon effect is the difference between location-compatible and incompatible conditions. c) In the Eriksen flanker task [29, 31] participants were expected to respond to a target arrow flanked by two similar interfering stimuli. The target and the interferers are ‘congruent’ if they all point to the same direction, or ‘incongruent’ if they don’t. RTs to the target tend to be shorter for congruent trials than for incongruent, and the flanker effect is the mean difference between the two. d) For the stop-signal task we used the software provided by [49]. In this task subject are expected to discriminate between a square and a circle stimuli using two button presses presented on a screen and to refrain from responding when an auditory signal is presented (25% of the trials). Participants (12 from cohort 1 and 9 from cohort 2) were given an initial practice block, followed by 3 experimental blocks of 64 trials. The stop-signal RT is the delay between go and stop signals that allows successful stopping in 50% of stop trials.

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Supplementary figure 1

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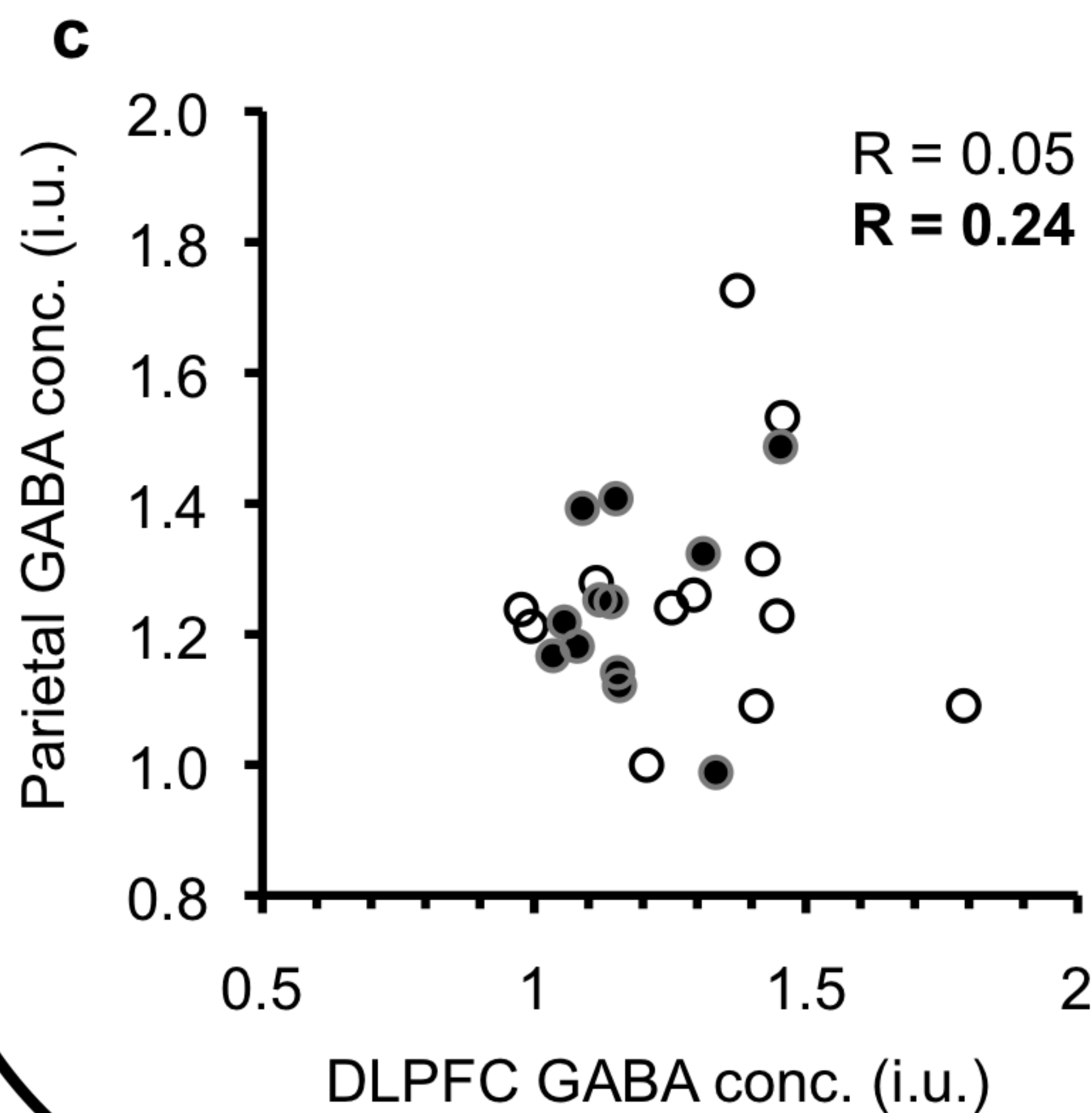
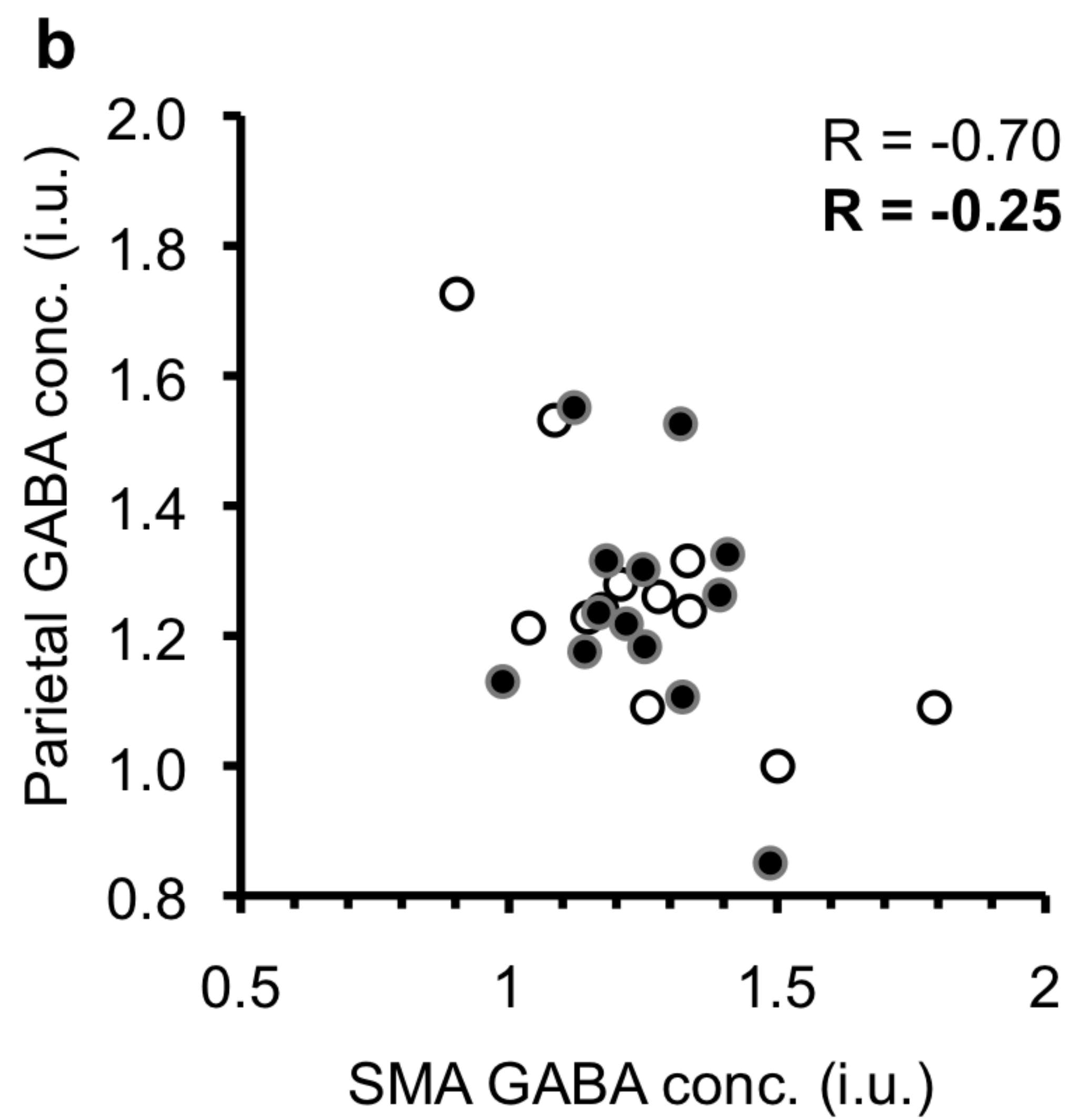
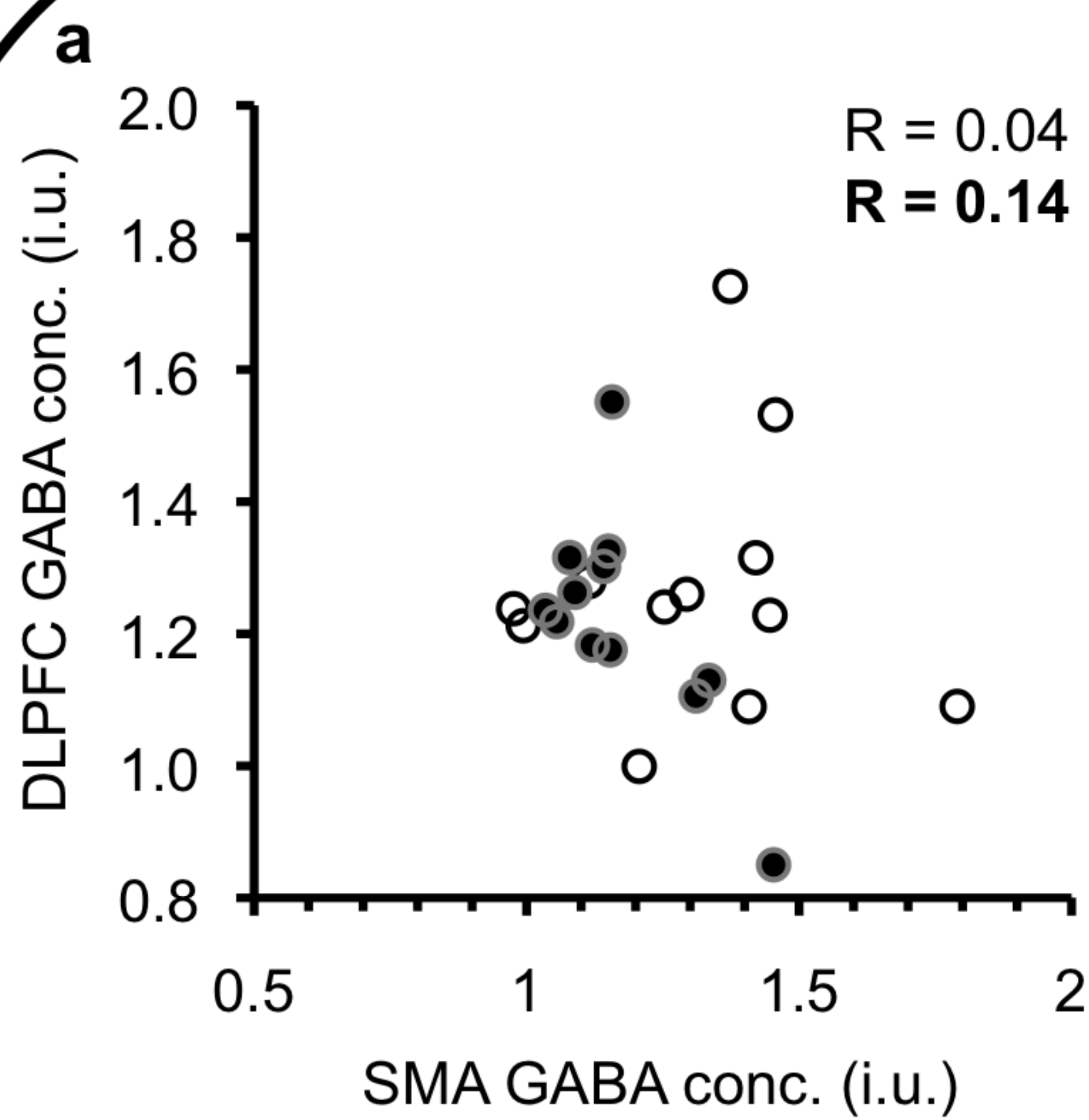
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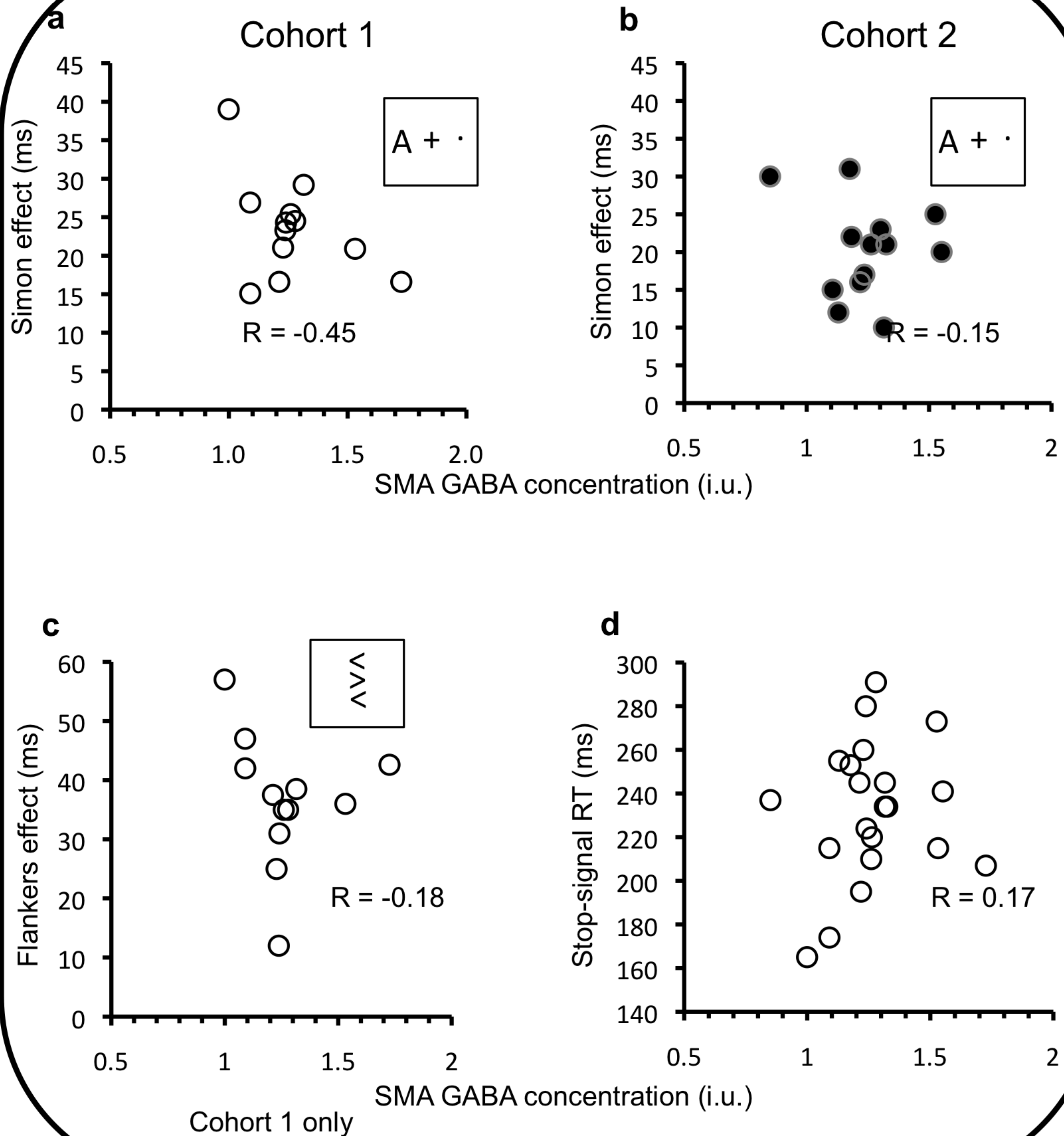
| | SMA region | DLPFC | Parietal | ACC |
|----------|------------|-------|----------|------|
| DLPFC | 0.04 | 1 | | |
| Parietal | -0.70 | 0.05 | 1 | |
| ACC | -0.21 | 0.38 | -0.11 | 1 |
| IFG | 0.32 | 0.41 | -0.45 | 0.53 |

Supplementary figure 3

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Supplementary figure 4