GABA concentration predicts perceptual learning ability after repetitive electrical stimulation

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<u>Target audience:</u> Neuroscientists and clinicians with an interest in GABA, GABA-MRS and plasticity as well as scientists and clinicians interested in disorders where sensory processing is altered.

<u>*Purpose*:</u> GABA, the main inhibitory neurotransmitter, is a key molecule in neuronal activity. Individual differences in GABA, as measured by edited magnetic resonance spectroscopy (MRS), have been linked to behavioral and neuroimaging measures and disease[1]. The GABA system is also key to neuronal plasticity and recent studies have linked changes in GABA to motor learning and to plasticity[2-3]. Studies have shown that repetitive electrical stimulation (rES) on the fingers induces short-term cortical reorganisation in the somatosensory cortex by changing excitability and inhibition, resulting in changes in brain response[4] and learning on a tactile 2-point discrimination task[5] (the smallest difference between two points in which two separate points can still be discerned). Although it is widely accepted that rES modulates tactile processing on a neuronal level, the underlying mechanism remains unclear. In this study, GABA concentration and 2-point discrimination were measured before- and after application of 45 min of rES to further investigate the cortical mechanisms underlying short-term plasticity in the somatosensory cortex.

<u>*Methods*:</u> Subject consent was obtained under local IRB approval. *Neuroimaging*: GABA-edited MR spectra were acquired from (3cm)^3 volumes using the MEGA-PRESS J-difference editing method on a 3T Philips 'Achieva' scanner for 19 participants (8 female, all right-handed). Spectra were acquired from left and right sensorimotor regions (see Figure 1). The sensorimotor regions, as seen in Figure 1, were centred on the "hand knob" as identified in axial T1-weighted images and aligned with the cortical surface. Experimental parameters: 32-channel head coil, TE 68ms; TR 2000ms; 320 transients (10 min). Data was analysed using Gannet[7] and corrected for tissue fraction. *Behavioral*: 2-point discrimination data were acquired from the tip of the index fingers for both hands, using a method of constant stimuli[6] and psychometric thresholds were obtained. *Stimulation*: Repetitive Electrical Stimulation (rES) was applied on the dominant hand only for 45 minutes consisting of stimulus trains of 2 s (including 2 x 0.5 s ramp, pulse duration 0.2 ms, 20 Hz) and inter-train intervals of 5 s.

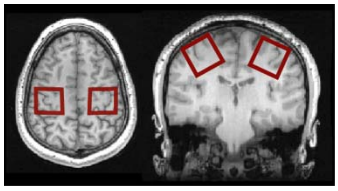

Figure 1. Voxels were placed on left- and right sensorimotor cortices and aligned with the surface of the brain.

<u>*Results*:</u> Average GABA concentrations were not significantly different between pre- and post-rES (Figure 2a), but behavioral performance was, only for the stimulated hand (Figure 2b). For the stimulated side, pre-rES GABA concentration correlated strongly and significantly with the learning-effect between pre- and post 2-point discrimination (Figure 3a) as well as with post-rES performance.

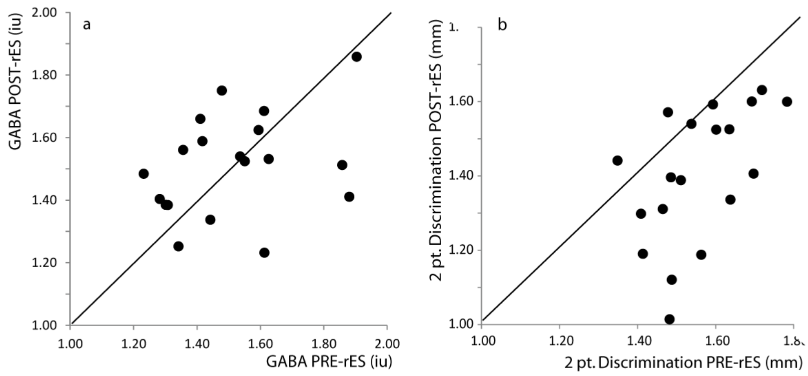

Figure 2. a. GABA concentration did not significantly differ between PRE and POST-rES. b. 2-pt discrimination significantly improved after rES.

<u>*Discussion*:</u> Baseline GABA in the stimulated cortex predicts the amount of learning that participants are capable of as well as performance after rES. rES results in a gain in 2-pt discrimination performance, but not in net changes in GABA concentration. It may be that rES enhances GABAergic efficacy and therefore the homeostatic interaction between excitation and inhibition, which might be of more importance than large changes in GABA concentration per se.

<u>*Conclusion*:</u> We have shown that after short-term plasticity inducing rES, performance is improved and that this improvement is predicted by pre-rES GABA concentration, suggesting that baseline levels of inhibition in particular play an important role in learning/plasticity.

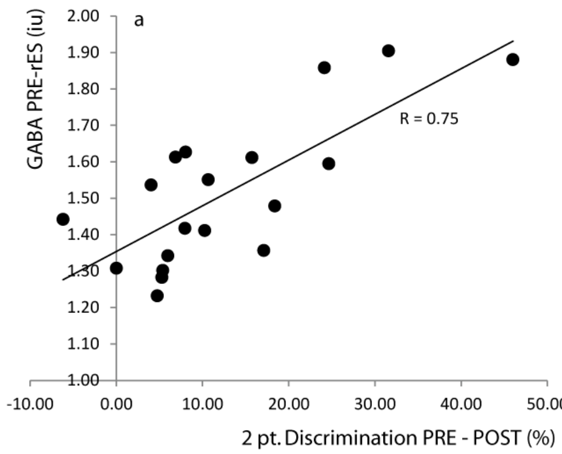

Figure 3. a. PRE-rES GABA concentration predicts gain in 2pt. discrimination performance

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