Local modulation of GABA concentration in human sensorimotor cortex during motor learning

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Introduction

A number of studies have shown that the cortical representation of movement within the human primary motor and somatosensory areas can be changed by motor learning [1,2]. It has been proposed that decreases in local concentration of γ-aminobutyric acid (GABA, a major inhibitory neurotransmitter) and its release may facilitate this plasticity [3]. It was shown in an earlier study [4], that thirty minutes of motor sequence learning reduced the mean GABA concentration within an 8 ml voxel in a brain region that includes the primary sensorimotor cortex contralateral to the hand used in the learning task. These changes were seen over a large spectroscopic voxel, suggesting involvement of a rather wide cortical area.

The purpose of this study was to extend the previous study [4] and to confirm that these rapid GABA changes were regionally specific by monitoring the GABA levels in the primary sensorimotor cortex both contralateral and ipsilateral to the hand used for learning.

Methods

Motor learning task

The motor learning task has been described in detail previously [2]. In summary, two vertical bars were shown on a screen: one-indicated the (varying) target force, the second gave a continuous measure of the subject response. Subjects were required to track the target force by maintaining the two bars at the same height. Root mean square (RMS) tracking error was measured throughout the experiment. All subjects performed the task for thirty minutes during which time the GABA levels were measured continuously. Eight healthy right-hand dominant subjects participated in this study (mean age 25 years).

MR experiments

All MR experiments were performed using a 3T Varian Inova scanner fitted with a standard transmit/receive birdcage RF coil. GABA detection was achieved by using the MEGA-PRESS editing sequence [5] for simultaneous 3D voxel localization, water suppression and editing. Spectra were acquired from 8 ml volumes of interest (VOIs) centered in an alternating way on either the contralateral cortex (hand region in the left hemisphere primary motor cortex) and the ipsilateral cortex (homogolous VOI in the right hemisphere). VOIs were identified on T1 weighted scout images as shown in Fig.1. In order to enable rapid change between two VOIs, separate shim settings together with other acquisition parameters were optimised before the experiment began and values were changed dynamically as acquisitions from the two VOIs alternated.

Analysis

The spectra were analysed using the Linear Combination Model (LCM) [6] using a library of model spectra obtained with the editing sequence. In order to account for the expected contribution from mobile brain macromolecules (MM), the parameterized MM spectrum was included in the basis set of modelled spectra. The parameters for the MM spectrum were derived from metabolite-nulled spectra (obtained by adding a pre-inversion pulse and recovery delay before the editing sequence).

Results

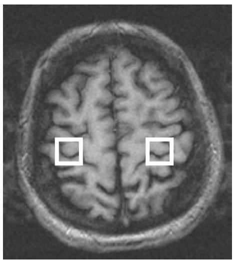

FIG.1.

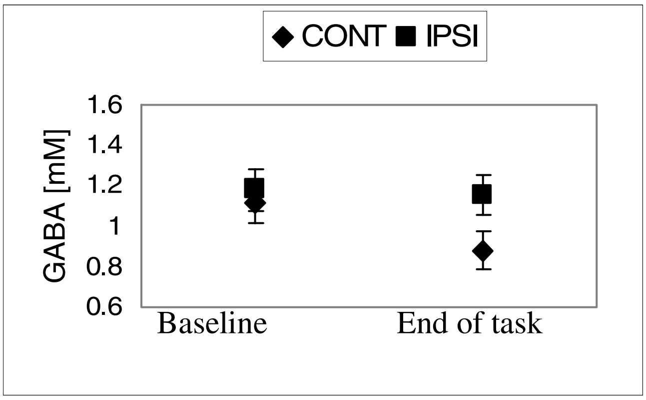

FIG. 2

There was a significant reduction in tracking error over the thirty minute task period as the motor skill was acquired (p=0.05).

The baseline GABA concentrations were (1.11 mM +/-0.04) and (1.14 mM+/- 0.04) for contra and ipsilateral cortices, respectively, and were similar to the values published elsewhere [5]. The GABA concentration measured by MRS decreased in the left (contralateral) hemisphere during sequence learning by ~22% ,(F=6.46, p=0.035) as compared with the baseline value, while GABA in the ipsilateral hemisphere did not show significant change (F=0.113, n.s.) (see Fig. 2).

Conclusions

We reproduced the earlier observation that thirty minutes of motor learning reduced GABA concentration within an 8 ml VOI contralateral to the hand used for the learned task. However, no significant changes were found in the ipsilateral motor cortex. We conclude that these results support the hypothesis that GABA is one of the important and facilitating elements contributing to local cortical changes during fast motor learning. More studies are still needed to relate the observed GABA changes to other mechanisms involved in rapid motor learning.

References:1. Karni, et al., Nature 377:155-158,1995; 2. Floyer et al., J. Neurophysiol. 92:2405-2412, 2004; 3. Castro-Alamancos et al., Proc. Natl. Acad. Sci USA 93:1335-1339, 1996; 4. Floyer et al., J. Neurophysiol. in press, 2005. 5. Mescher et al., NMR Biomed 11:266-271, 1998. 6. Provencher, Magn. Reson. Med. 30:672-679, 1993