Mapping plasticity in the forepaw digit barrel subfield of rat brain using functional MRI

J-C. Weng[1,2], K-H. Chuang[1], A. Goloshevsky[1], S. Dodd[1], J-H. Chen[2], and A. P. Koretsky[1]

[1]Laboratory of Functional and Molecular Imaging, NINDS, National Institutes of Health, Bethesda, MD, United States, [2]Interdisciplinary MRI/MRS Lab, Dept. of Electrical Engineering, National Taiwan University, Taipei, Taiwan

Introduction

In 1970, Woolsey and Van deer Loos described an organization of cell aggregates in layer IV of mouse and rat somatosensory (SI) cortex [1]. In 1976, Welker extended the study by demonstrating the presence of barrels and barrel-like structures in certain regions of rat SI cortex which were termed barrel subfields [2]. They noted that neurons in these barrel subfields could be driven by stimulation of skin as opposed to those neurons in the face-related barrels. She also noted the forepaw representation was topographically organized and was related to the barrel subfield in layer IV. In 1995, Waters et al. extended these works by describing the details of the relationship between the representation of the forepaw and forepaw barrel subfield in rat SI cortex by using the mitochondrial marker cytochrome oxidase [3].

This well-defined relationship between the cortical barrels and the forepaw digit makes this system a good model for the study of neuronal function and plasticity. Although the representation of digit columns has been previously investigated by optical imaging of intrinsic signal [4], mapping this topographically organized representation non-invasively remains challenging. Functional MRI (fMRI) has been shown to map columns in cat visual [5] as well as in rodent whisker barrels [6]. The goal of this study was to test the feasibility of and to optimize fMRI to map the forepaw digit representations in the SI of the rat. Further, this technique was applied for mapping brain plasticity after digit amputation.

Materials and Methods

All experiments were approved by the Animal Care and Use Committee of the NINDS, NIH. Adult male Sprague Dawley rats (~250g) were divided into the control (n=5) and amputated (n=5) groups. In the amputated group, the 3rd digit (D3) of baby rats were cut and the rat was allowed to grow for an additional 2.5-month. For fMRI experiment, rats were orally intubated and anesthetized with constant infusion ofα-chloralose (27 mg/kg/hr). A block-design paradigm was used to stimulate the rat's 2nd (D2) or 4th (D4) digit. It consisted of 10 cycles of 15 s digit stimulation and 75 s resting. Only one digit was stimulated at a time and each digit was stimulated alternatively. The experiment time of each run was 465 s. At least 6 runs of the experiment were conducted in each rat. For electrical stimulation, two ring pairs were attached on the D2/D4 and serial rectangular pulses with 2 mA current, 0.33 ms duration, and 3 Hz were used.

Images were acquired using an 11.7 T/31 cm horizontal bore magnet, interfaced to an AVANCE console (Bruker BioSpin, Billerica, MA). A home-made 10-mm-diameter receiving surface coil and a 90-mm-diameter birdcage transmitter coil were used. Gradient echo, 3D EPI images were obtained with the following parameters: effective echo time = 30 ms, effective repetition time = 1.5 s, matrix size = 64 x 64 x 32, field of view = 19.2 x 19.2 x 9.6 mm^3, yielding a 300 μm isotropic voxel size.

Data analyses were performed using SPM5 and in-house written software in MATLAB. Linear baseline drift was corrected and data of different runs were averaged to improve SNR. The activation threshold was set at a correlation coefficient of 0.2 and with a minimum cluster size of 3 voxels. Correlation analysis was conducted with two kinds of boxcar waveforms: in the regular analysis, a digit stimulation was compared with resting (i.e., D2 vs. rest or D4 vs. rest); in the differential analysis, stimulation of one digit was compared with the other (i.e., D2 vs. D4 or D4 vs. D2).

Results and Discussions

With signal averaging of at least 6 runs, sufficient SNR was achieved. Significant and focal activations were observed (Fig. 1) with D2 activation (in red color) located more anterior and lateral than D4 activation (in green color). This is consistent with the known location of these columns (1, 2). The activation of areas of D2 and D4 were wider and had overlap when each digit was mapped individually. However, the activation areas of the two digits analyzed by differential analysis were narrower, extended deeper into the cortex, and had a gap in between, which may be representation of D3. Therefore differential analysis was used to determine if plasticity in the digit cortex could be detected.

In the amputated group, the activation areas of both digits became wider and the gap between them became narrower (Fig 2b, 3b). Comparing the centers of mass between D2 and D4 activation, the distances between the D2 and D4 representation was wider in the normal rats (1.5±0.3 mm) than in the amputated group (0.9±0.2 mm, $p<0.01$) (Fig. 2, 3).

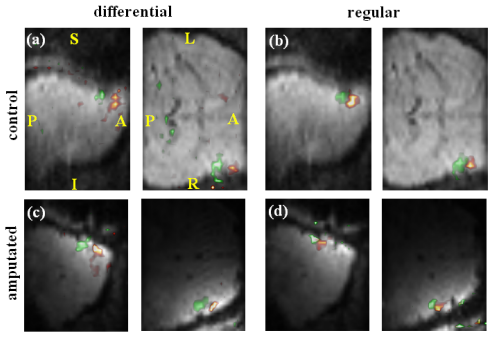

Fig. 1 Functional maps of sagittal and horizontal view of rat in control group using differential (a) and regular (b) analyses, and in amputated group using differential (c) and regular (d) analyses.

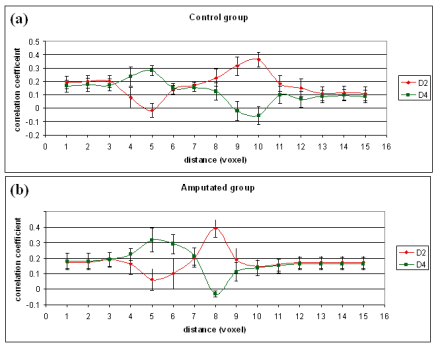

Fig. 2 The averaged signal intensity profiles of correlation coefficient map in control group (a) and amputated group (b) using differential analysis.

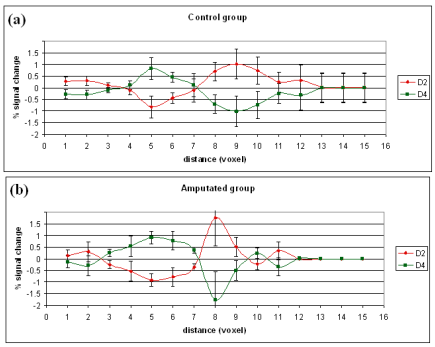

Fig. 3 The averaged signal intensity profiles of percentage signal change map in control group (a) and amputated group (b) using differential analysis.

Conclusions

We have demonstrated that forepaw barrel subfields of single digits can be mapped using fMRI at 11.7T. The patterns could be reproduced over different experiments. This method was useful to study neural plasticity after amputation of a digit. To the best of out knowledge this is the first fMRI demonstration of plasticity in cortical columns by fMRI. The observed distances between the D2 and D4 representations were larger than those reported in electrophysiological studies in the control animal. This could be due to partial volume blurring at the resolution used, which was about the same size of single digit representation area. Future studies will be performed with increased spatial resolution and to verify the identified digit representations using histological staining or manganese enhanced MRI.

References

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