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Magnetic resonance spectroscopy study of proton metabolite level changes in sensorimotor cortex after upper limb replantation–revascularization

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Abstract

We aimed to investigate the changes in proton metabolite levels at the motor and somatosensory cortex by magnetic resonance spectroscopy (MRS) after upper extremity replantation or revascularization. Nine patients who referred to our clinic suffering from major total (two) and subtotal (seven) amputation of the upper extremity were enrolled in this study. Mean time value between the injury and operation was 5.1 h. Mean follow-up period or mean time between the injury and MRS analysis was 26.2 months (ranging from 7 to 41 months). Voxels (TR: 2000; TE: 136 ms) were placed onto locations in the bilateral precentral and postcentral cortex area of the cerebral hemispheres that represent the upper extremity. Contralateral sides of the brain hemisphere that represent the injured extremity were accounted as control groups. Metabolite ratios [NAA (*N*-acetyl aspartate)/Cr (creatine) and Cho (choline)/Cr] of the motor and somatosensory cortex were calculated. The NAA/Cr and Cho/Cr metabolite ratios between the two groups were found to be insignificant, and these results may indicate that there is no remarkable somatosensorial cortex disruption or demyelination in these patients. Fifty-six percent of patients were found as functional according to Chen's scale.

Keywords: Replantation; Revascularization; Magnetic resonance spectroscopy

1. Introduction

In the past decade, with the developments of noninvasive imaging techniques such as magnetoencephalogram (MEG), functional MRI and SPECT analysis, some complicated changes in limb amputation and peripheral nerve injury and phantom pain could be explained. Hence, the knowledge gathered with experimental and clinical studies helped us explore brain plasticity [1–5].

Magnetic resonance spectroscopy (MRS) is a rather new noninvasive, imaging modality used to investigate changes in tissue metabolite composition in different brain diseases. In this study, we aimed to investigate the changes in the metabolic response of the motor and somatosensory cortex after upper and lower limb revascularization and replantation by MRS.

2. Materials and methods

We evaluated the MRS analysis of nine patients treated by revascularization or replantation of the upper extremities between October 1999 and August 2002. Mean age was 33.5 (ranging from 6 to 61 years, 7 males and 2 females). Mean follow-up period was 26.2 months (ranging from 7 to 41 months). The ethics committee of our institution approved the study protocol and informed consent was obtained from each patient. None of the patients had any major systemic or cerebrovascular disease, head trauma history or overt cognitive dysfunction. There was gunshot injury in three patients, traffic accident in one, tractor axle

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injury in three, large saw injury in one and train accident in one. In five cases, the right extremities were injured. The level of the injuries in revascularized patients were 1/3 proximal of arm in three, 1/3 distal of arm in two and arm–forearm double-level injury in two patients. Mean time between the injury and operation was 5.1 h. Two patients underwent replantation, and seven patients were treated with revascularization. All of the fractures were treated by open reduction and internal fixation using plate and screw except one (a 6-year-old child) who was treated by K-wire fixation. Median and ulnar nerve injuries in two patients were encountered; median, ulnar and radial nerve injury in four; median, radial, ulnar, musculocutaneus nerve injury in one; median, musculocutaneus, ulnar nerve injury in one; radial nerve injury in one. In five patients, secondary reconstructive procedures such as wrist arthrodesis, tendon transfer, shoulder arthrodesis, free muscle transfer were performed. Functional evaluations of the patients were performed according to Chen's scale [6].

Mean time between the injury and MRS was 26 months. The MRI examination consisted of routine imaging and single voxel spectroscopy. Magnetic resonance imaging was performed on a 1.5-T system (Philips, Gyroscan Intera Master, Best, the Netherlands). T1-weighted images (TR: 560; TE: 15) were obtained in the axial and sagittal planes. T2-weighted images (TR: 4530; TE: 100) were obtained in the axial and coronal planes. Single voxel spectroscopy (SVS) was performed in all patients by using a point-resolved spectroscopy sequence (PRESS) (TR: 2000; TE: 136 ms) with 128 average; voxel sizes of 15×15×15 mm were used. Voxels were placed onto locations in the bilateral precentral and postcentral cortex area of the cerebral hemispheres that represent the related upper extremity illustrated in Figs. 1 and 2. Prior to MRS, shimming was performed to optimize field homogeneity, and water suppression was optimized using automated routines provided by the manufacturer. A chemical-shift selective saturation pulse suppressed the water signal. A spectral sweep width of 1000 Hz was used with data size of 1024 points. The magnitude spectra were processed automatically using baseline correction and curve-fitting procedures to determine the resonance areas of *N*-acetyl aspartate (NAA), creatine (Cr) and choline (Cho). Analysis of the spectra was performed by the spectroscopy software package of the MR system. Resonances were assigned as follows: NAA, 2.0 ppm; Cr, 3.02 ppm; Cho, 3.2 ppm (Fig. 2). The peak areas of the metabolite ratios (NAA/Cr and Cho/Cr) were calculated. For each patient, two authors (AA, KS) assessed whether the spectra were diagnostic.

All statistical analyses were performed with the SPSS software package (release 10.0, SPSS, Chicago, IL). That was the rationale for the application of the nonparametric Mann–Whitney U test to assess the differences among these groups. $P<.05$ was considered to be significant.

3. Results

No statistically significant difference was found in the NAA/Cr and Cho/Cr metabolite ratios between the lesion

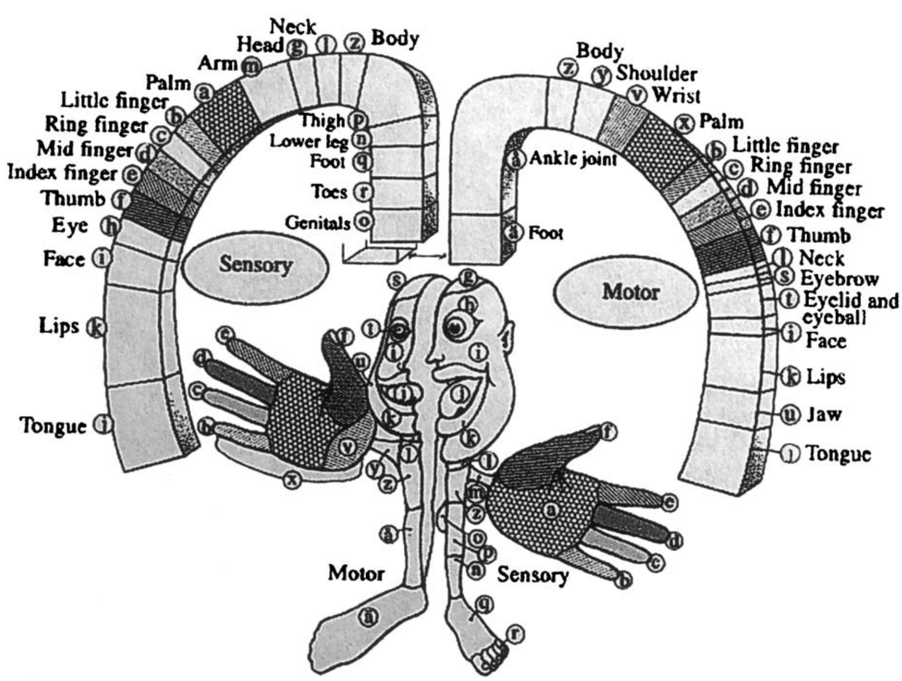

Fig. 1. The cortical body map with reference to sensory (posterior to central sulcus) and motor (anterior to central sulcus) functions. Transverse sections through sensory cortex (upper left) and motor cortex (upper right) illustrate the somatotropic organization of the body parts. The homunculus figure comprises body parts in sizes proportional to their areas in the brain. The hand and face areas are very close and together occupy a substantial part of the sensory cortex. (From Ref. [7] with permission.)

and unaffected sides of the somatosensory cortex detected by MRS in replantation–revascularisation patients (Table 1).

The functional results according to Chen's scale [6] were as follows: grade 1 (excellent) in one (11%) patient, grade 2 (good) in two (22%), grade 3 (moderate) in two (22%), grade 4 (bad) in four (44%) patients. In the follow-up period, humerus nonunion developed in one patient and was treated by autogenous iliac bone graft using plate and screw fixation. Humeral osteomyelitis in another patient was also encountered and treated by debridement and drainage of the infected bone and soft tissues.

4. Discussion

The brain is a complicated neural network that continuously remodels itself as a result of changes in sensory

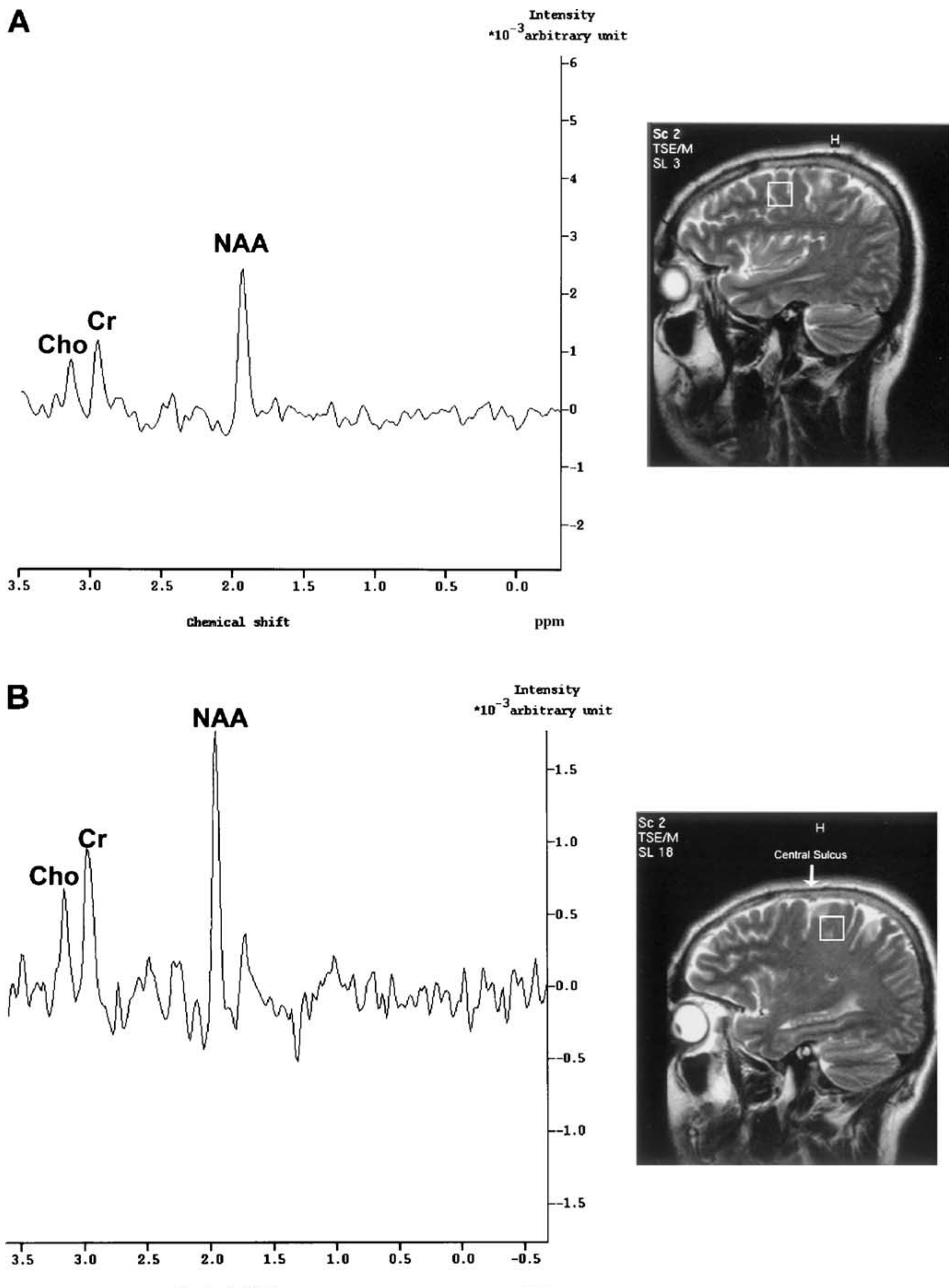

Fig. 2. Images obtained in a 32-year-old man treated with replantation for subtotal amputation at proximal right-arm level 18 months later. (A) MR spectrum (TR: 2000; TE: 136 ms) from obtained right precentral cortices shown as normal NAA/Cr and Cho/Cr ratios. (B) MR spectrum (TR: 2000; TE: 136 ms) from obtained right postcentral cortices shown as normal NAA/Cr and Cho/Cr ratios. (C) MR spectrum (TR: 2000; TE: 136 ms) from obtained left precentral cortices shown as a mild decrease for NAA/Cr, but the Cho/Cr ratios were normal. (D) MR spectrum (TR: 2000; TE: 136 ms) from obtained left precentral cortices shown as normal for NAA/Cr and Cho/Cr ratios.

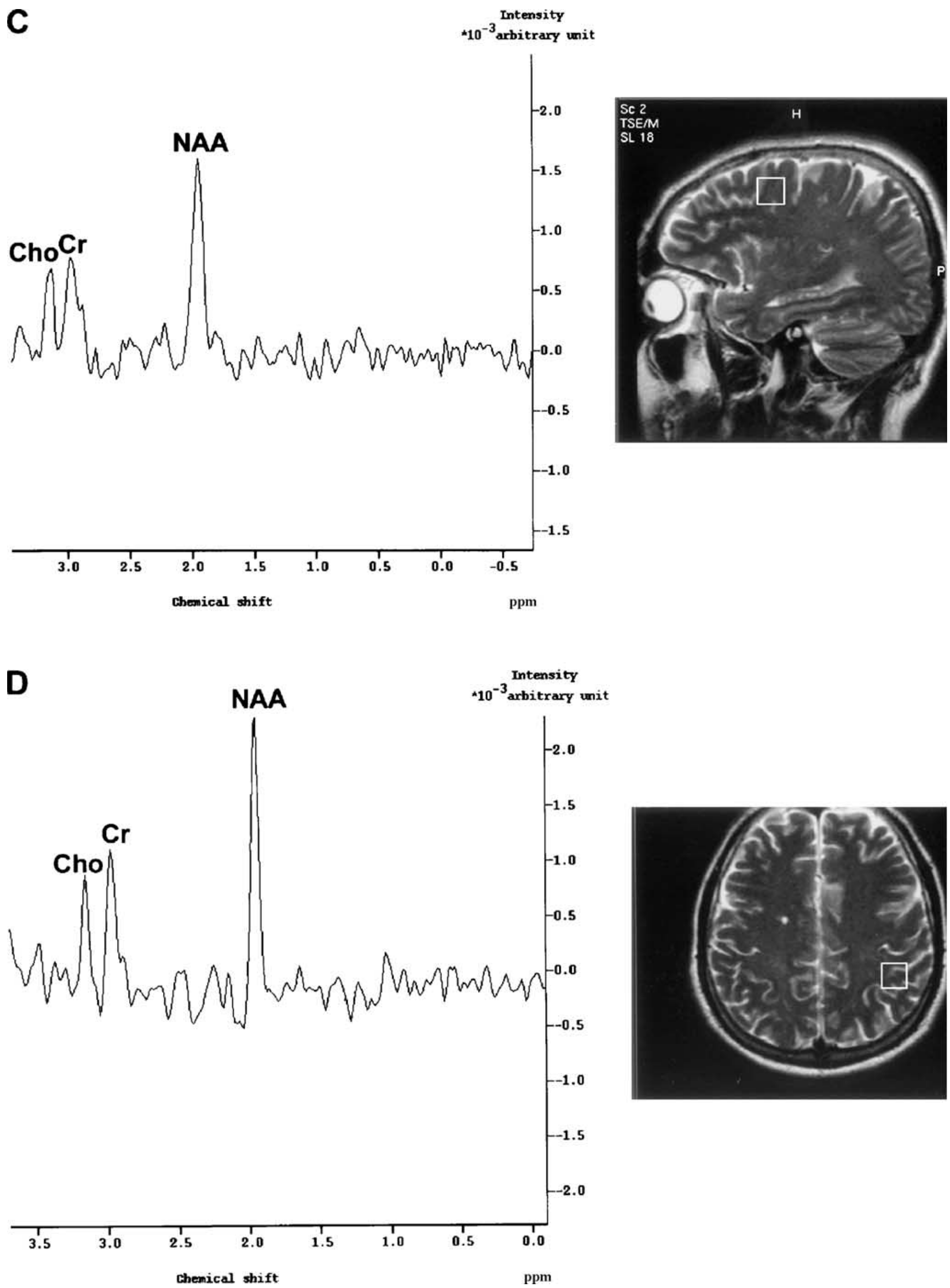

Fig. 2. continued

input. Several experiments on the effects of deafferentation (or amputation) on somatosensory maps in adult primates and other mammals suggest that we may need to revise this conception of the nervous system [7–10]. In a study with monkeys investigating the consequences of long-standing limb amputation and amputation at different ages, regardless of the age of injury, the deprived cortex does not remain nonfunctional, and it takes on new roles and triggers movements in new target muscles [11]. Elbert et al. [12] revealed that any amputation of an upper extremity results in alterations of the homuncular organization as cortical plasticity. In one study, they showed that plasticity occurs after a period of extensive training by activating repetitively a certain receptive field in the cortex of musicians. In the case of such repetitive activity, the size of the activated area was found to be enlarged [12].

The functional results that we obtained were as follows: grade 1 in one (11%) patient, grade 2 in two (22%) patients, grade 3 in two (22%) patients and grade 4 in four (44%) patients. In the study of Berger et al. [13], they found grade 1 in 10 (71.6%) patients, grade 2 in three (21.4%) patients, grade 3 in one (7.2%) patient, grade 4 in none. In another

Table 1
Metabolite ratios found by proton MR spectroscopic imaging obtained from motor and somatosensory cortex of patients

Metabolite ratios	Replantation/ revascularization side		Unaffected side	
	Precentral	Postcentral	Precentral	Postcentral
NAA/Cr	1.81±0.18	1.69±0.13	2.07±0.13	1.75±0.16
Cho/Cr	0.98±0.09	0.72±0.07	1.17±0.10	0.89±0.13

study, Chen and Han [14] found grade 1 in eight (34.8%) patients, grade 2 in 11 (47.8%) patients, grade 3 in four (17.4%) patients and grade 4 in none. In this regard, our results on extremity function, which revealed 33% good results, were found to be in discordance with those of Chen and Han [14] and Berger et al. [13], which yielded 82.6% and 92.8% good results, respectively.

In contrast to conventional MRI, MRS could provide information on neuronal/axonal viability, cellular energetic and cellular membrane status. With increasing use and application in different diseases of the central nervous system (CNS), MRS could aid in the diagnosis and clinical management of various pathologic processes. Prominent resonances detected on MRS in normal brains include NAA, Cho and Cr. NAA is the most sensitive CNS metabolite. Since it is a neuroaxonal marker, abnormalities of neuronal structures, like reduced neuronal density or viability, lead to reductions in NAA [15]. Therefore, it is an important predictor of neuronal dysfunction. In this study, there was no significant difference in NAA/Cr metabolite ratios between the lesion side and unaffected side of the precentral cortex in replantation–revascularization patients. These findings may be associated with the absence of significant neuro-axonal myelination loss. Major components of the Cho resonance are choline-containing compounds with small molecular weight, such as phosphocholine and glycerophosphocholine, that form a pool involved in membrane synthesis and degradation. The increase in Cho/Cr ratio might point out an inability to properly incorporate Cho-containing molecules into myelin. Loss or disruption of normal myelin also increases the availability of Cho-containing compounds. Thus increase in Cho/Cr ratio could indicate demyelination [15]. In our study, there was no statistically significant difference in Cho/Cr metabolite ratios between the lesion side and unaffected side of the somatosensorial cortex in replantation–revascularization patients that may indicate absence of demyelination. However, we found diminished NAA/Cr ratios, especially at the precentral motor cortex of the lesion side (Table 1).

Functional extremity value of only 33% in our cases did not show a satisfactory correlation with MRS results. The metabolite ratios found by MRS of replanted or revascularized patients may support the conclusion that there was no remarkable somatosensorial cortex disruption or demyelination in these patients. Fifty-six percent of patients were found as functional according to Chen's scale.

References

[1] Schwenkreis P, Wýtscher K, Janssen F, Pleger B, Dertwinkel R, Zenk M, et al. Assessment of reorganization in the sensorimotor cortex after upper limb amputation. Clin Neurophysiol 2001;112(4):627–35.
[2] Condes-Lara M, Barrýos FA, Romo JR, Rojas R, Salgado P, Sanchez-Cortazar J. Brain somatic representation of phantom and intact limb: a fMRI study case report. Eur J Pain 2000;4(3):239–245.
[3] Moore CE, Schady W. Investigation of the functional correlates of reorganization within the human somatosensory cortex. Brain 2000;123(9):1883–95.
[4] Rasmusson D. Changes in the organization of the ventroposterior lateral thalamic nucleus after digit removal in adult raccoon. J Comp Neurol 1996;364(1):92–103.
[5] Wiech K, Preissl H, Lutzenberger W, Kiefer RT, Topfner S, Haerle M, et al. Cortical reorganization after digit-to-hand replantation. J Neurosurg 2000;93(5):876–83.
[6] Chen ZW, Meyer VE, Kleinert HE, Beasley RW. Present indication and contraindications for replantation as reflected by long-term functional results. Orthop Clin North Am 1981;12:849–70.
[7] Lundborg G. Brain plasticity and hand surgery: an overview. J Hand Surg [Br] 2000;25(3):242–52.
[8] Florence SL, Kaas JH. Large-scale reorganization at multiple levels of the somatosensory pathway follows therapeutic amputation of the hand in monkeys. J Neurosci 1995;15(12):8083–95.
[9] Hung GU, Tan TS, Kao CH, Wang SJ. Focal cerebral hyper-perfusion in phantom limbs: assessed by Tc-99m HMPAO SPECT. Kaohsiung J Med Sci 2000;16(8):429–31.
[10] Ramachanran VS, Hirstein W. The perception of phantom limbs. Brain 1998;121(9):1603–30.
[11] Qi HX, Stepniewska I, Kaas JH. Reorganization of primary cortex in adult macaque monkeys with long-standing amputations. J Neurophysiol 2000;84(4):2133–47.
[12] Elbert T, Pantev C, Wienbruch C, Rockstroh B, Taub E. Increased use of the left hand in string players associated with increased cortical representation of the fingers. Science 1995;270:305–7.
[13] Berger A, Hierner R, Becker MH-J, Rieck B, Lassner F. Replantationschirurgie. Unfallchirurg 1997;100:694–704.
[14] Chen ZW, Han YL. Major limb replantation. In: Urbaniak JR, editor. Microsurgery for major limb reconstruction. St Louis (Mo): Mosby; 1987. p. 22–6.
[15] Alkan A, Sarac K, Kutlu R, Yakinci C, Sigirci A, Aslan M, et al. Early and late state subacute sclerosing panencephalitis: chemical shift imaging and single voxel MR spectroscopy. AJNR Am J Neuroradiol 2003;24(3):501–6.