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Is there training-dependent reorganization of digit representations in area 3b of string players?

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Abstract

Objective: The digit representations in area 3b were studied to examine whether there is training-dependent reorganization in string players.

Methods: Somatosensory evoked magnetic fields were recorded following electrical stimulation of digits 1 (D1), 2 (D2) and 5 (D5) of both hands in 8 string players and of the left hand in 12 control subjects. The N20m and P30m responses, and high-frequency oscillations (HFOs) were separated by 3–300 Hz and 300–900 Hz bandpass filtering.

Results: The dipole locations on the coronal plane and strengths of D1, D2 and D5, and D1-D5 cortical distance estimated at the peak of N20m or P30m did not differ between left and right hand in string players or between left hand in string players and controls. On the other hand, the dipole locations of D2 estimated from N20m and P30m and of D1 from N20m were significantly anterior, the D2-D5 distance from P30m longer, and the number of HFO peaks larger for D5 in string players than controls.

Conclusions/Significance: With strong mutual competition among the fingering digits, the scale of reorganization should be much smaller as compared with the competition-free denervation-induced reorganizations. Taken together, the training-dependent reorganization of somatosensory cortex in string players is manifest not only in the enlarged cortical representation but also in the enhanced HFOs presumably representing activity of the fast-spiking interneurons.

Keywords: Somatosensory evoked field; String players; Area 3b; Digit representation; High frequency oscillation; Fast spiking inhibitory interneuron; Training dependent reorganization

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1. Introduction

It has become increasingly clear over the past two decades that the cortical map in the somatosensory system of adult animals and humans is not fixed but is continuously modified by experiences throughout life. Diverse and manifold descriptions of plasticity and reorganizations in the somatosensory system come mainly from deafferentation studies, where peripheral afferents are either silenced or eliminated (see for review Buonomano and Merzenich, 1998; Jones, 1993, 2000; Florence, 2002; Kaas, 2002). In fact, the vast majority of literature has provided strong evidence for reorganization of adult brain after peripheral denervation. The same principles presumably apply to reorganization induced by behavioral training or sensory experience, because the increase or decrease of sensory inputs is the other side of the coin, resulting in either the representational expansion or shrinkage. However, the studies on the use- and experience-dependent cortical plasticity are extremely few as compared with a large number of reports on the denervation-induced plasticity.

In a microelectrode mapping study, Jenkins et al. (1990) demonstrated plastic changes of the map in monkey

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somatosensory area 3b after prolonged, intense stimulation of fingertips. In more detailed behavioral-neural correlation studies, Recanzone et al. (1992a,b,c) showed an enlarged map for area 3b finger representation after a period of behaviorally controlled tactile stimulation of the fingers in monkeys. Motivated by these pioneering animal experiments and using a noninvasive technique of magnetoencephalography (MEG), Elbert et al. (1995) have shown use-dependent plasticity in humans that somatosensory representations of the fingering digits of the left hand in string players are larger in comparison with those of their opposite hand or with the fingers of the left hand of control subjects. This study has been continuously cited as a typical example of use-dependent cortical plasticity in humans, supporting in general the microelectrode studies in monkey area 3b (Jenkins et al., 1990; Recanzone et al., 1992a,b,c). It is surprising, however, that no single follow-up study has been conducted so far to examine one of the most crucial findings in the neuroscience of human cortical plasticity.

In the present experiment, we studied cortical representations of digits 1 (D1), 2 (D2) and 5 (D5) of both hands in area 3b somatosensory cortex in string players and of the left hand of control subjects by analyzing N20m and P30m components of somatosensory evoked magnetic fields (SEFs) to electrical stimulation of each digit. In addition, we analyzed high-frequency oscillations (HFOs) superimposed on N20m.

2. Methods

Eight string players consisting of 6 violinists, one violist, and one guitarist (one female, 7 males, age 18–29 years, mean 22 years) were studied. They began musical practice at a mean age of 7 years (range 3–15 years) and had played the instruments for a mean period of 13.5 years (range 9–25 years). The mean amount of time spent for practicing the musical instruments during a year prior to the test was 15.1 h per week (range 4.5–25 h per week). Twelve nonmusicians (two females, 10 males, age 22–33 years, mean 25.9 years) served as controls. The occupation or status of control subjects was college students or researchers of our group. As for their ‘manual training’ such as operating a keyboard or using a cellular phone, all the subjects used a personal computer and a cellular phone daily. Otherwise no regular activities of manual training were reported. All subjects were right-handed according to the Edinburgh inventory: the laterality quotient was 97.2 ± 4.8 (mean ± SD) for string players and 94.9 ± 7.8 for controls (Oldfield, 1971). Written informed consent was obtained from all participants. All experimental protocols were conducted in accordance with the Declaration of Helsinki and were approved by the Institutional Bioethics Committee of Tokyo Institute of Psychiatry.

Brief electrical stimuli with 0.2 ms duration were delivered via a pair of ring electrodes (cathode proximal) to D1, and in separate runs to D2, and to D5, and the order of digit stimulation was random within the hand. The digits of the left hand were stimulated first, and then of the opposite hand in string players. For control subjects, only the digits of the left hand were stimulated. For D1 stimulation, the cathode and anode were placed at the metacarpophalangeal and interphalangeal joint, respectively. For D2 and D5 stimulation, the cathode and anode were placed at the proximal interphalangeal and distal interphalangeal joint. We first measured subjective sensory thresholds of D1, D2 and D5 of both hands individually in string players and controls, and then we adjusted the stimulus intensity so that it was 3 mA higher than the maximum sensory threshold among all digits of both hands. The mean stimulus intensity was 5.8 mA (range 5.3–6.8 mA) for string players and 6.0 mA (range 5.3–6.8 mA) for controls. The stimuli were delivered at regular intervals with a repetition rate of 2 Hz. All experiments were conducted during wakefulness.

Magnetic recordings (bandpass 3–2000 Hz) were conducted in a magnetically shielded room using a 160-channel whole-head type gradiometer system (Yokogawa MEGVISION, Yokogawa Electric Corp., Tokyo). The detection coils of the gradiometer are arranged in a uniform array on a helmet-shaped surface of the bottom of the dewar, and the distance between the centers of two adjacent coils is 25 mm; each coil measures 15.5 mm in diameter. The sensors are configured as first-order axial gradiometers with a baseline of 50 mm. The field sensitivities of the sensors were 5 $\mathrm{fT}/\sqrt{Hz}$ or better. An epoch of 200 ms duration (100 ms pre- and 100 ms post-stimulus) was digitized at a 10 kHz/channel sampling rate and 2000 responses were averaged on-line. DC offset was based on the pre-stimulus period. In order to separate HFOs from the underlying N20m and P30m, the wide-band recorded responses were digitally filtered with a bandpass of 300–900 Hz and 3–300 Hz, respectively.

Magnetic resonance imaging (MRI) scans (Magnetom System, Symphony 1.5 T, Siemens, 1.0 mm thickness) were acquired with spherical lipid markers placed on the 5 MEG fiduciary points to allow superposition of magnetic dipole source locations onto the MRI slices. The MRI head shape data were used to determine the best-fit sphere for each subject’s head. The center of the sphere was defined as the midpoint between the pre-auricular points. The x axis passed from the center of the sphere to the nasion. The y axis was adjusted to be perpendicular to the x axis on the plane made by the nasion and pre-auricular points, with positive direction to the left. The z axis pointed to the vertex in a direction perpendicular to the x-y plane. In order to minimize error in the equivalent current dipole (ECD) locations due to variability of head size across subjects, the individual head coordinate system was translated into a standard coordinate system averaged for all subjects in the present study. The fiducial points for this translation were the nasion, left preauricular point and Cz of the International 10–20 system (see Iguchi et al., 2001).

We employed a single ECD model for identifying sources of magnetic signals. Using SEF data from about

30 channels over the response area, the locations, strengths and orientations of the ECDs for N20m and P30m were calculated by the least-squares method. Goodness-of-fit (GOF) of the model was calculated to ascertain what percentage of the measured signal variance was accounted for by the dipole. ECDs with GOF of greater than 90% were accepted for further analysis. For HFOs, only the field strength of the maximum peak-to-peak amplitude (from the maximum to minimum) among the oscillation peaks and the number of peaks within the burst were analyzed because of their lower signal-to-noise ratio. The HFOs with the signal-to-noise ratio higher than 2 were accepted for further analysis. For fair comparison of the dipole locations and moments, we selected the root mean square (rms) peak of N20m and P30m, because it was found recently that the N20m dipole moves dynamically toward anterolateral direction for a distance of 7–9 mm in area 3b around the N20m peak (Hashimoto et al., 2000, 2001; Kimura and Hashimoto, 2001).

The ECD parameters of N20m and P30m were subjected to a parametric two-way analysis of variance (ANOVA). Two factors tested were the Digit (D1, D2 and D5) and the Hand in string players (left and right) or the Group (left hand of string players and controls). In the post hoc analysis, we used a paired *t* test first to assess the statistical significance of difference between the two populations in string players and a two-sample *t* test to evaluate the difference between the left hand of string players and controls. In view of two outliers found in one of the ECD parameters for two control subjects, we considered that a non-parametric test should be used for statistical analysis of this parameter. Therefore we reanalyzed the data using Mann-Whitney test. The maximum field strength of HFOs to stimulation of a digit of the left hand in string players with those of a corresponding digit of the opposite hand in string players or of the left hand in control subjects were compared using a non-parametric Wilcoxon rank sum test or Mann-Whitney test, respectively. We also performed Pearson's correlation coefficient test on the dependence of dipole strength of N20m and P30m ECDs on age of inception of musical practice. For the dependence of the number of HFOs on the age, Rank-order correlation (Spearman) test was performed. The level of probability selected as significant was a value of $P < 0.05$ (two-tailed test).

3. Results

In wide-band recordings, N20m and P30m deflections were clearly identified in SEFs following electrical stimulation of D1, D2 and D5 of both hands in all string players and of the left hand in all control subjects. Fig. 1 shows typical N20m and P30m components after the low-pass filtering (3–300 Hz) of SEFs for stimulation of the D1, D2 and D5 of the left hand in a string player (SP-L). For comparison, the N20m and P30m from the right hand of the same string player (SP-R) and from the left hand of a representative control subject (C-L) were also presented. The isofield contour maps for N20m and P30m demonstrated clear polarity reversal over the contralateral 3b hand area, indicating independent single dipole sources for the two components (Fig. 2, left column). The source localizations of the two peaks for D1, D2 and D5 stimulations overlaid on the subject's MRI showed that they were both in area 3b but were opposite in the dipole direction (Fig. 2, right column).

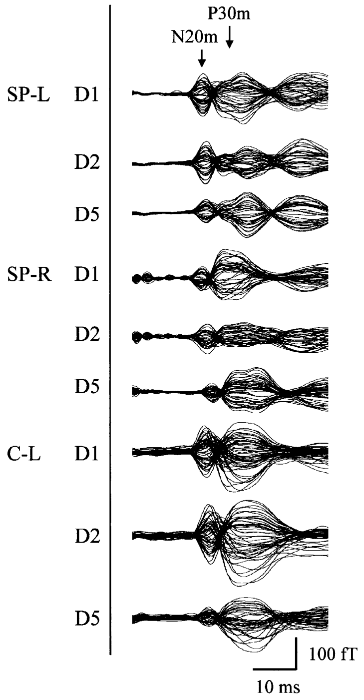

Fig. 1. N20m and P30m for stimulation of the thumb (D1), index (D2) and little (D5) fingers of left hand (SP-L) and of right hand (SP-R) in a string player, and of left hand in a control subject (C-L).

3.1. Comparison of N20m and P30m ECDs for stimulation of digits in string players and controls

For N20m ECD, the ANOVA showed the main effect of the Digit on the *y* and *z* components, and on the dipole strengths (Table 1). However, for P30m, the main effect of the Digit was only found on the *z* component. In addition, the ANOVA showed the main effect of the Group on the *x* component from N20m and P30m and on the N20m latency. There was no interaction between the Digit (D1, D2 and D5) and the Hand in string players (left and right hand) or the Group (left hand of string players and controls). Table 2 summarizes latencies, source localizations and moments as well as GOF values of N20m and P30m peaks for stimulation of different digits in string players and controls. Although there was a main effect of the Group on the N20m peak latency and of the Hand on P30m peak latency (Table 1), the post hoc *t* test was not significant for any of the left digits of the string players as compared with the opposite hand or the left hand of controls (Table 2).

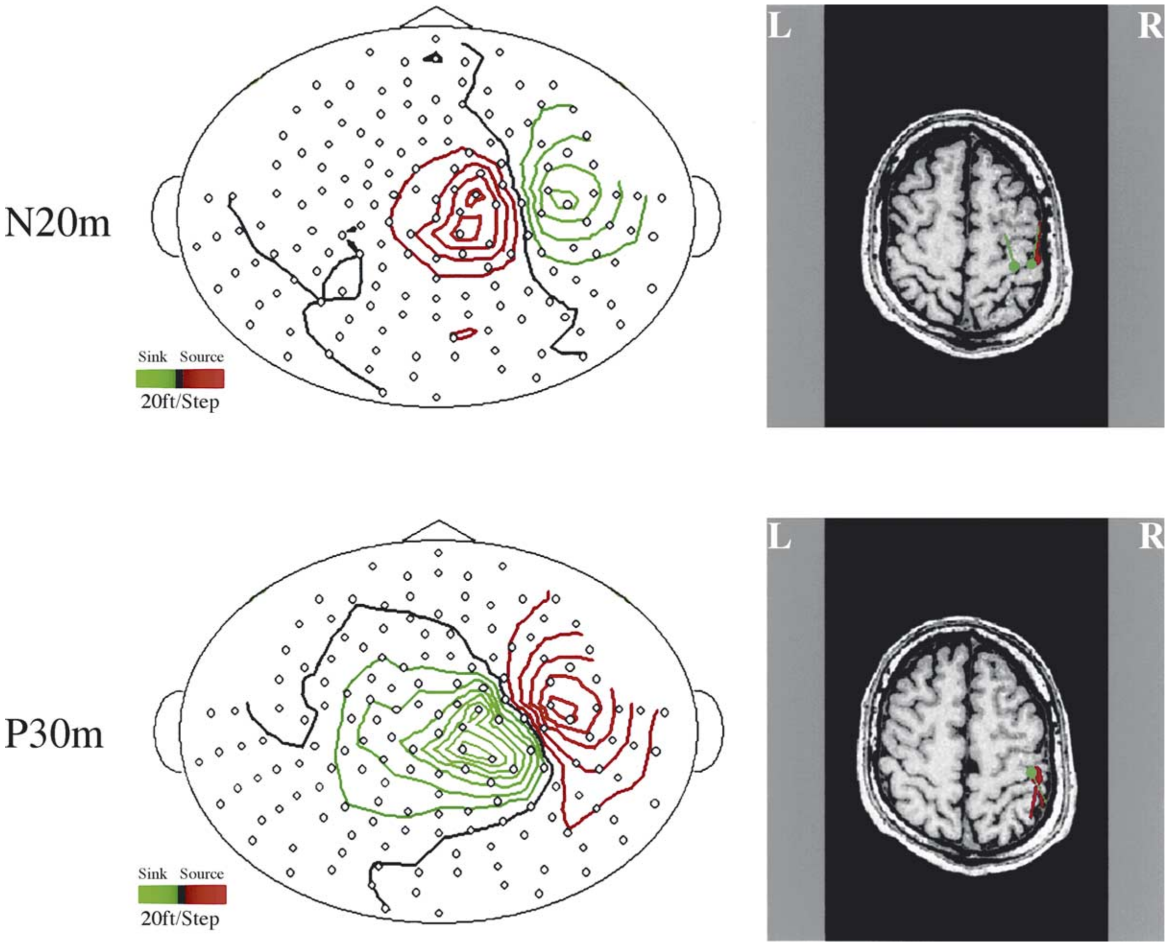

Fig. 2. The isofield contour maps for N20m and P30m for stimulation of the left index finger in a normal control were illustrated on the left. The maps show clear polarity reversal over the contralateral 3b hand area. The source localizations of the N20m and P30m peaks for stimulation of D1, D2 and D5 of left hand in a control subject were overlaid on the subject's MRI. N20m (upper right) and P30m ECDs (lower right) were both in area 3b but were opposite in the dipole direction. Note mediolateral arrangement of D5, D2 and D1 in area 3b along the central sulcus. Red circle signifies D2, medial green circle, D5 and lateral green circle, D1. Bars denote direction of the dipoles.

3.1.1. N20m ECDs

The ECD localizations of N20m peak for stimulation of D1, D2 and D5 were systematically arranged from the lateral-inferior (D1) to medial-superior (D5) direction in area 3b along the central sulcus in each hand tested (Fig. 2, right column). The difference in the localizations was largest for the vertical *z* axis. The ECD moment was largest for D1 and smallest for D5 in string players and controls in accordance with the size of their cortical representations (Table 2, upper panel). There were no significant differences in the ECD locations for *y* and *z* axes in the coronal plane, which is approximately parallel to the central sulcus, and in the moments between the corresponding digits of the left and right hand in string players or between the digits of the left hand in string players and controls (Table 2, upper panel). However, there were significant differences in the ECD locations for anterior-posterior *x* axis between the corresponding D1 and D2 of the left hand of string players and controls. We initially considered that these differences reflect the extremely small values in the *x* axis for two control subjects in the study, which results from a greater variability across subjects in the location of central sulcus for the anterior-posterior axis with respect to the preauricular points. Even if individual head coordinate system was translated into a standard coordinate system in the present study, this type of variability could not be eliminated. Therefore, we reanalyzed the ECD locations for the *x* axis using a non-parametric Mann-Whitney test. The result showed that differences in the ECD locations for the *x* axis between the digits of the left hand in string players and controls failed to reach significance by a margin (D1, $P = 0.054$; D2, $P = 0.064$). Although insignificant in the non-parametric test, the differences in *t* test cannot be ignored and may indicate genuine differences in ECD locations between the string players and controls.

There was no tendency for the ECD locations of D1, D2 and D5 to be shifted medially or for their moments to be larger in the left hand of string players. Fig. 3 illustrates the magnitude of the dipole moment for each digit of both hands as a function of the age of inception for musical practice

Table 1
Summary of the two-way analysis of variance

			Factor	F value	
A. Group (SP-L and C-L) vs. Digit (D1, D2 and D5)					
N20m	Latency		Group	$F(1,53) = 4.15$	$P < 0.05$
	Coordinate	x	Group	$F(1,53) = 10.44$	$P < 0.005$
		y	Digit	$F(2,53) = 8.01$	$P < 0.001$
		z	Digit	$F(2,53) = 14.09$	$P < 0.0001$
	Moment		Digit	$F(2,53) = 19.98$	$P < 0.0001$
P30m	Latency		–	–	–
	Coordinate	x	Group	$F(1,46) = 13.18$	$P < 0.001$
		y	–	–	–
		z	Digit	$F(2,46) = 11.88$	$P < 0.0001$
	Moment		–	–	–
B. Hand (SP-L and SP-R) vs. Digit (D1, D2 and D5)					
N20m	Latency		–	–	–
	Coordinate	x	–	–	–
		y	Digit	$F(2,42) = 3.81$	$P < 0.05$
		z	Digit	$F(2,42) = 26.91$	$P < 0.0001$
	Moment		Digit	$F(2,42) = 20.91$	$P < 0.0001$
P30m	Latency		Hand	$F(1,46) = 7.21$	$P < 0.05$
	Coordinate	x	–	–	–
		y	–	–	–
		z	Digit	$F(2,41) = 17.57$	$P < 0.0001$
	Moment		–	–	–

(Fig. 3, left column). The dipole strengths for digits of left hand in string players are indicated by filled circles, and those of right hand by open circles and of control subjects by shaded circles. In string players, the dipole moments tended to be larger in all digits of both hands for individuals beginning musical practice before the age of 5 years. However, these values were well within the range for control subjects. Comparing the scatterplots of D5 dipole strength versus age at the beginning of musical practice in the previous and present studies, it is clear that the dipole

Table 2
N20m and P30m ECDs for stimulation of digits 1 (D1), 2 (D2) and 5 (D5) (Mean ± SD)

Digit	Hand	Latency (ms)	Coordinate (mm)*			Moment (nAm)	GOF (%)
			x	y	z		
N20m ECDs							
D1	SP-L	21.5 ± 0.6	28.8 ± 5.3	−47.8 ± 6.5	88.6 ± 5.2	12.0 ± 3.4	97.6 ± 1.4
	SP-R	21.5 ± 0.7	26.3 ± 7.7	48.1 ± 6.3	87.4 ± 4.8	10.4 ± 3.7	97.7 ± 1.4
	C-L	22.4 ± 1.5	20.4 ± 8.3**	−49.2 ± 5.6	92.0 ± 7.1	9.3 ± 3.9	96.9 ± 2.5
D2	SP-L	22.1 ± 0.9	29.7 ± 6.6	−48.0 ± 7.3	91.5 ± 7.0	7.8 ± 1.9	97.1 ± 2.3
	SP-R	22.2 ± 0.7	27.0 ± 8.0	49.6 ± 8.6	92.0 ± 5.2	7.8 ± 3.0	97.2 ± 1.6
	C-L	23.0 ± 1.6	22.6 ± 6.9**	−47.6 ± 5.1	96.5 ± 4.5	8.3 ± 2.8	96.9 ± 2.8
D5	SP-L	22.3 ± 1.7	23.2 ± 9.0	−40.5 ± 7.6	101.8 ± 5.7	4.7 ± 1.6	96.1 ± 1.7
	SP-R	22.2 ± 0.7	28.0 ± 7.6	43.0 ± 7.6	103.2 ± 4.2	4.3 ± 2.0	96.7 ± 1.9
	C-L	22.8 ± 1.5	19.7 ± 9.9	−38.8 ± 8.6	101.4 ± 8.6	4.9 ± 2.0	95.0 ± 2.8
P30m ECDs							
D1	SP-L	29.4 ± 2.0	25.2 ± 10.9	−43.4 ± 7.8	91.5 ± 7.4	13.2 ± 8.2	96.4 ± 2.0
	SP-R	30.2 ± 2.1	26.3 ± 9.1	47.2 ± 5.1	89.6 ± 5.6	10.1 ± 4.6	96.5 ± 2.6
	C-L	33.0 ± 5.1	16.7 ± 10.3	−41.9 ± 6.2	93.2 ± 8.1	11.7 ± 6.6	96.7 ± 2.6
D2	SP-L	30.8 ± 2.6	30.5 ± 9.3	−44.5 ± 5.3	93.8 ± 4.5	9.8 ± 5.9	95.7 ± 2.7
	SP-R	30.9 ± 1.1	27.3 ± 7.6	48.3 ± 4.9	94.9 ± 2.7	9.2 ± 4.7	96.1 ± 2.7
	C-L	33.5 ± 3.9	18.0 ± 8.5***	−46.8 ± 3.9	99.1 ± 8.8	10.2 ± 5.9	97.4 ± 2.2
D5	SP-L	29.9 ± 2.3	24.8 ± 9.0	−43.3 ± 8.5	103.8 ± 7.3	9.1 ± 3.9	97.2 ± 0.9
	SP-R	30.0 ± 2.1	25.4 ± 9.3	45.9 ± 5.3	101.4 ± 4.5	7.7 ± 4.4	94.7 ± 3.6
	C-L	32.4 ± 4.4	15.8 ± 9.4	−45.6 ± 4.9	106.6 ± 8.4	6.6 ± 3.4	96.2 ± 2.7

GOF, goodness of fit. The standardized coordinate values were presented. **$P < 0.05$ (t test); these differences in x axis between SP-L and C-L were insignificant by Mann-Whitney test. ***$P < 0.01$ (t test); the difference in x axis between SP-L and C-L was also significant by Mann-Whitney test ($P = 0.01$).

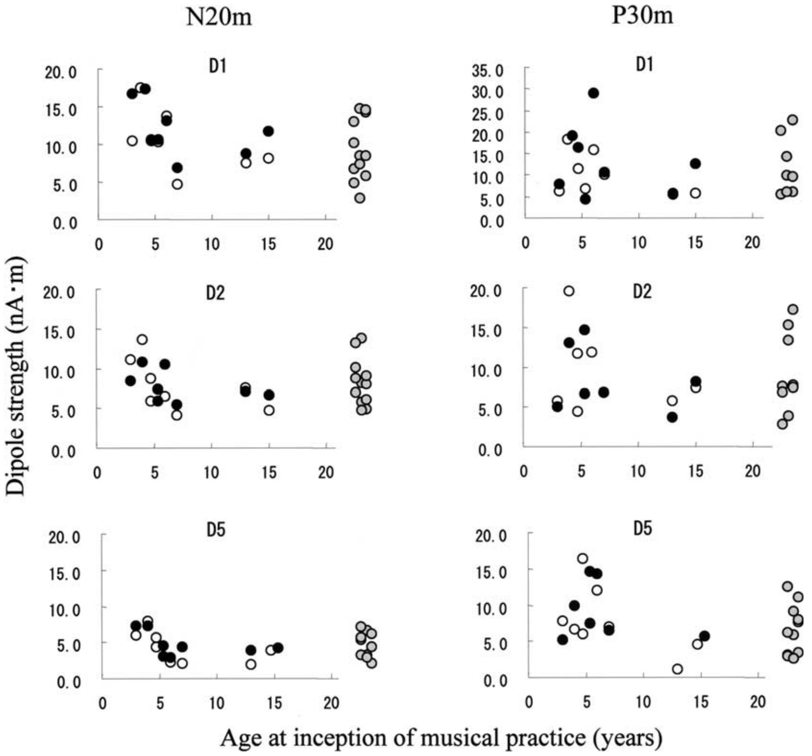

Fig. 3. (Left column) The magnitude of N20m dipole moment for D1, D2 and D5 as a function of the age of inception for musical practice. Filled circles indicate the dipole strengths for digits of left hand in string players, and open circles and shaded circles, those of right hand in string players and of left hand in control subjects. Although there is a tendency that the dipole moments are larger for individuals beginning musical practice before the age of 5, these were within the range for control subjects. (Right column) The magnitude of P30m dipole moment for D1, D2 and D5 as a function of the age of inception for musical practice.

strengths in the musicians are strikingly larger in the previous study, while those in non-musicians are very similar (Elbert et al., 1995). Pearson's correlation coefficient test on the dependence of dipole strength on the age of starting musical training was not significant (Table 3).

3.1.2. P30m ECDs

The ECD localizations of P30m peak for stimulation of D1, D2 and D5 were systematically arranged from the lateral-inferior (D1) to medial-superior (D5) direction in area 3b along the central sulcus in each hand tested similar to those of N20m ECDs. The difference in the localizations was largest for the vertical z axis. The ECD moment was largest for D1 and smallest for D5 in string players and controls (Table 2, lower panel). There were no significant differences in the ECD locations for y and z axes on the coronal plane and in the moments between the corresponding digits of the left and right hand in string players or between the digits of the left hand in string players and controls. However, there was a significant difference in the ECD locations for the x axis between the corresponding D2 of the left hand of string players and controls. We reanalyzed the ECD locations for the x axis using a non-parametric Mann-Whitney test as we have done on N20m. The result showed that there was a significant difference in the ECD locations for the x axis between the D2 of the left hand in string players and controls ($P = 0.01$).

The magnitude of the P30m dipole moment for each digit of both hands was shown as a function of the age of inception for musical training (Fig. 3, right column). Although the P30m dipoles had a tendency for larger moments in all digits for individuals beginning musical practice before the age of 5 years, these were well within the range for control subjects. Comparing the scatterplots of D5 dipole strength versus age at the beginning of musical practice in the previous and present studies, it is clear that the dipole strengths in the musicians are relatively larger in

Table 3
Pearson's correlation coefficient test on the dependence of dipole strength (N20m and P30m ECDs) on age of inception of musical practice

		Digit D1		Digit D2		Digit D5	
		SP-L	SP-R	SP-L	SP-R	SP-L	SP-R
N20m ECDs	r	−0.47	−0.51	−0.39	−0.54	−0.41	−0.54
	P value	0.25	0.21	0.36	0.18	0.33	0.18
P30m ECDs	r	−0.21	−0.48	−0.31	−0.33	−0.29	−0.57
	P value	0.63	0.24	0.47	0.44	0.55	0.15

r signifies correlation coefficient.

the previous study, while those in non-musicians are smaller (Elbert et al., 1995). Pearson's correlation coefficient test on the dependence of the dipole strength on the age of starting musical practice was not significant (Table 3).

3.2. Comparison of Euclidean distances of D1-D5 and D2-D5 from N20m and P30m ECDs in string players and controls

3.2.1. N20m ECDs

As expected from the homuncular organization of the digits in area 3b, the mean Euclidean distance between D1 and D5 from N20m ECDs was greater than that between D2 and D5 within the respective hand (Table 4). The average Euclidean distances from D1 or D2 to D5 were not different between the left and right hand in string players or between the left hand of string players and controls. There was even a tendency toward shorter distances for the left hand in string players as compared with the opposite hand or with the left hand of controls (Table 4). Fig. 4 shows the Euclidean distances for all subjects between D1 and D5, and between D2 and D5, in which ordinate denotes the distance for the left (SP-L) and right hand (SP-R) in each string player and for the left hand in each control subject (C-L) (Fig. 4, upper panel). Overall, the distributions for string players and controls overlapped each other.

3.2.2. P30m ECDs

The average Euclidean distances from D1 to D5 were not different between the left and right hand in string players or between the left hand of string players and controls. However, there was a significantly longer mean distance from D2 to D5 for the left hand in string players as compared with the left hand of controls ($P = 0.049$, t test). Fig. 4 shows the Euclidean distances for all subjects between D1 and D5, and between D2 and D5, in which ordinate denotes the distance for the left (SP-L) and right hand (SP-R) in each string player and for the left hand in each control subject (C-L) (lower panel). Although the distributions for string players and controls overlapped each other for D1-D5 distances, there was an obvious trend toward longer distances for D2-D5 in string players.

Table 4
Euclidean distances (mm) between D1-D5 and D2-D5 (Mean ± SD)

		Hand		
		SP-L	SP-R	C-L
N20m ECDs	D1-D5	17.6 ± 3.6	18.3 ± 5.2	19.4 ± 5.0
	D2-D5	16.1 ± 5.0	15.5 ± 4.8	17.9 ± 5.2
P30m ECDs	D1-D5	14.6 ± 5.0	14.1 ± 3.2	14.3 ± 4.8
	D2-D5	14.7 ± 4.4	10.8 ± 4.3	10.9 ± 3.1*

Euclidean distances were calculated from the standardized values. *$P < 0.05$ (t test). This was not significant by Mann-Whitney test ($P = 0.097$).

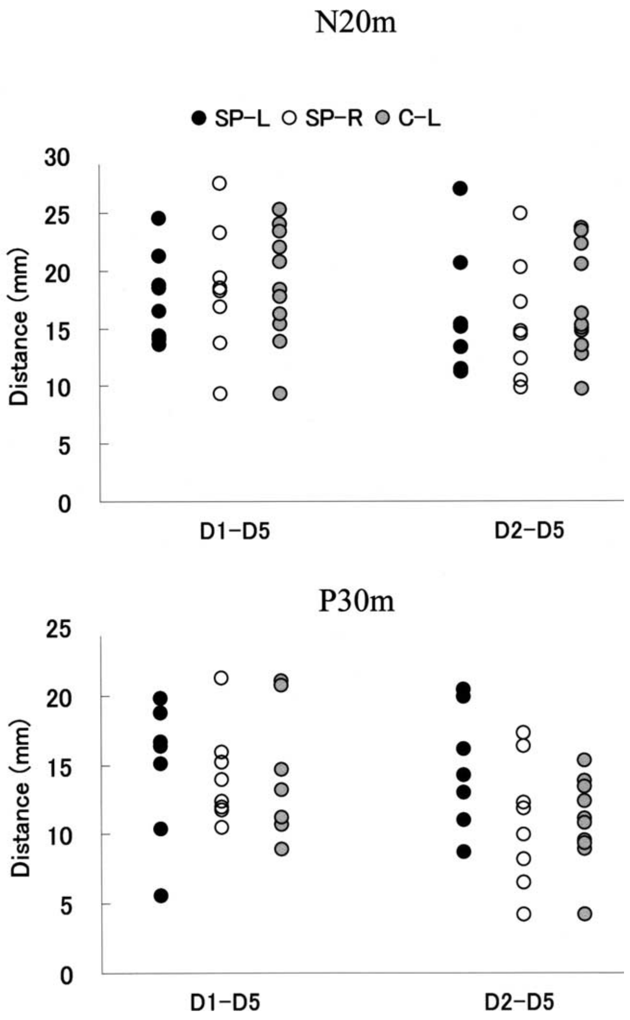

Fig. 4. (Upper diagram) The Euclidean distances for N20m ECDs between the cortical representations of D1 and D5 (D1-D5 distance), and between D2 and D5 (D2-D5 distance). Ordinate denotes the distance for the left (SP-L) and right hand (SP-R) in each string player and for the left hand in each control subject (C-L). Note that the distributions for the string players and controls overlapped each other. (Lower diagram) The Euclidean distances for P30m ECDs between the cortical representations of D1 and D5 (D1-D5 distance), and between D2 and D5 (D2-D5 distance). Note the obvious trend toward longer distances for D2-D5 in string players.

3.3. Comparison of HFOs for stimulation of digits in string players and controls

After the high-pass filtering (300–900 Hz), low amplitude HFOs were isolated from the underlying N20m for stimulation of each digit. For string players, stimulation of each digit of the left hand (SP-L) as well as the right hand (SP-R) elicited the HFOs in almost all subjects (Fig. 5). For the left hand of control subjects, the occurrence ratio of the HFOs was lower than for the left and right hand of string players (Table 5). Notably, the occurrence ratio of the HFOs

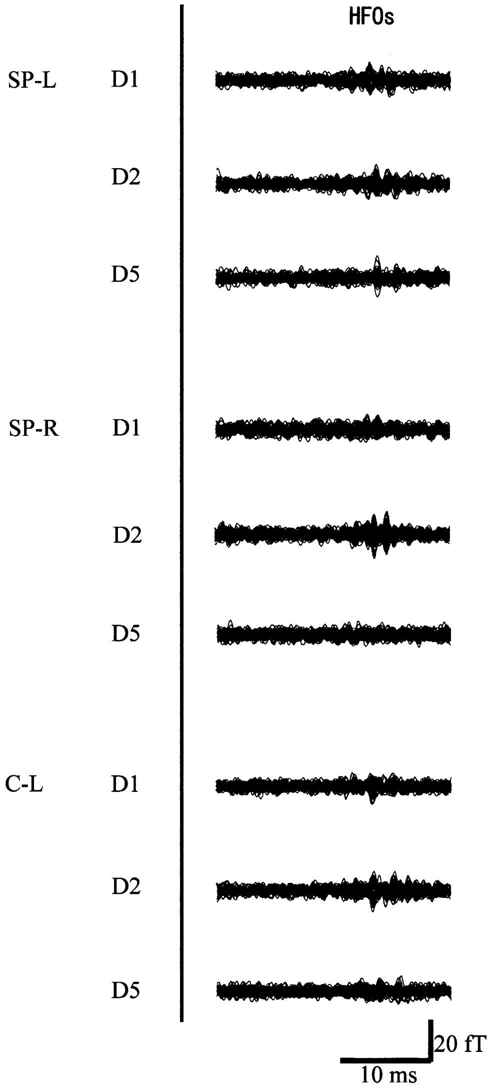

Fig. 5. High-frequency oscillations (HFOs) for stimulation of D1, D2 and D5 of left hand (SP-L) and of right hand (SP-R) in a string player, and of left hand in a control subject (C-L). Note presence of high-frequency oscillations for all the left digits of the string player.

for D5 in controls (5/12) was the lowest. For each digit examined, there was no significant difference in the maximum field strength between the left and right hand in string players or between the left hand of string players and controls.

In contrast, comparison of the number of peaks in HFOs showed a significant difference between the left hand of string players and controls; the number of peaks was increased for stimulation of D5 in string players ($P = 0.038$, Mann-Whitney test) (Table 5). It should be noted that the difference might be due to the small number of HFOs in the control group. In addition, there was a general trend toward smaller numbers for D5 as compared with D1 or D2 for each hand examined. The D5 digital nerves have a fewer fibers than D1 and D2. As a result, the dipole strengths of N20m for D5 were much smaller than those for D1 or D2 (Table 2). It is possible, therefore, that a lower signal-to-noise ratio with the D5 HFOs reduced their detectability. There was also a general trend toward smaller numbers for D1 and D2 in the controls. The trend toward a larger number of HFO peaks was also seen for the left D1 in the string players, although it did not reach significance by a margin ($P = 0.054$, Mann-Whitney test). It is worthy of note that the number of peaks was also increased significantly for stimulation of D2 in the right hand of string players ($P = 0.028$, Wilcoxon rank sum test).

Rank-order correlation (Spearman) test on the dependence of the number of HFO peaks on age of inception of musical practice was not significant, although the Spearman rank correlation coefficient for the left D1 showed a higher value ($r = 0.62$, $P = 0.10$) (Table 6).

4. Discussion

The present study revealed that the dipole locations and strengths of D1, D2 and D5, and the D1-D5 cortical distance estimated from the N20m and P30m ECDs did not differ between the left and right hand in string players or between the left hand in string players and controls. On the other

Table 5
High-frequency oscillations for stimulation of digits 1 (D1), 2 (D2) and 5 (D5) (Mean ± SD)

		Hand		
		SP-L	SP-R	C-L
Field strength (fT)	D1	18.0 ± 5.3 (8/8)	17.1 ± 4.1 (7/8)	15.8 ± 2.6 (9/12)
	D2	17.2 ± 4.6 (7/8)	17.2 ± 3.5 (8/8)	18.3 ± 5.1 (10/12)
	D5	14.9 ± 3.9 (8/8)	16.5 ± 4.8 (7/8)	15.0 ± 5.1 (5/12)
Number	D1	4.9 ± 2.8	3.8 ± 2.1	2.3 ± 1.7
	D2	3.4 ± 2.0	4.9 ± 2.1*	2.3 ± 1.8
	D5	2.8 ± 2.4	3.1 ± 2.1	0.6 ± 0.9**

In the parentheses are the occurrence ratios of the high-frequency oscillations. *$P < 0.05$, Wilcoxon rank sum test. The difference was significant between SP-L and SP-R. **$P < 0.05$, Mann-Whitney test. The difference was significant between SP-L and C-L.

Table 6
Rank-order correlation (Spearman) test on the dependence of the number of HFO peaks on age of inception of musical practice

	Digit D1		Digit D2		Digit D5	
	SP-L	SP-R	SP-L	SP-R	SP-L	SP-R
r	−0.09	−0.01	−0.35	−0.43	0.62	0.08
P value	0.82	0.98	0.35	0.25	0.10	0.82

r signifies Spearman rank correlation coefficient.

hand, the dipole locations of D2 estimated from N20m and P30m and of D1 from N20m were significantly anterior, the D2-D5 distance from P30m longer, and the number of HFO peaks larger for D5 in string players than controls.

4.1. Methodological considerations

Our finding of an absence of significant group differences in the measured distances between D1 and D5 from N20m or P30m ECDs is congruous with the observations of Elbert et al. (1995). However, there was a significant difference in the D2-D5 distance between the left hand of string players and controls ($P < 0.05$, t test). Thus, there appear to be similarities as well as differences between the present and the previous study. In brief, they found that the cortical representations and the response strengths of the left digits (D1 and D5) increased, and that the dipole locations for the left digits shifted toward medial direction along the central sulcus by 5 mm for D1 and by 7 mm for D5 in string players (Elbert et al., 1995). In that study, they calculated the medians of the dipole location and moment from a selection of points within a 20 ms time segment (11 sampling points) around the maximal rms peak of M50, with the selection of points satisfying their certain predetermined criteria. This means that the rms peak of M50 was not necessarily selected for the ECD analysis in their study. This may or may not be one of the important factors contributing to the conflicting results, because a moving dipole around the M50 peak cannot be ruled out. For fair comparison of the dipole locations and moments, we selected the rms peak of N20m and P30m, because the dipole moves dynamically toward anterolateral direction in area 3b around the N20m peak (Hashimoto et al., 2000, 2001; Kimura and Hashimoto, 2001; Ozaki et al., 2001) and also around the P30m peak in the present study.

There are other differences in experimental parameters between the two studies; the digits examined (D1 and D5 vs. D1, D2 and D5), the stimulus method used (tactile vs. electric), the stimulus frequency (0.5 Hz vs. 2.0 Hz), the sampling frequency (500 Hz vs. 10 kHz), the averaging number (1000 vs. 2000) and the SEF components analyzed (M50 vs. N20m and P30m). Thus, the discrepancies may stem in part from these methodological and/or analytical differences in the experiments.

First, index finger (D2) plays an important role among the fingering digits and thus the cortex receiving inputs from this finger may be susceptible to use-dependent reorganization. In support of this conjecture, it was found that the dipole locations of D2 estimated from N20m and P30m was shifted anteriorly and the D2-D5 distance was increased in the left hand of string players.

Second, electrical stimulation of the finger bypasses mechanoreceptors and directly elicits action potentials from the digital nerve. Therefore, there is no specificity in the recruited fiber types whether it is stimulated across the finger pad or the joint. The electrical stimulation of digits at the intensity employed in the present study elicits very brief superficial tactile sensation. This sensation is apparently different from other sensations such as deep, temperature or pain sensations. Because of inherent brevity of the stimulus duration (0.2 ms), electrical stimulation is perceived as somewhat artificial. However, the superficial nature of skin sensation is similar between the tactile and electrical stimuli (see Iguchi et al., 2002). Mechanical stimulation of the fingertip elicits the densely innervated low threshold rapid adapting and slowly adapting type I receptors and also the pacinian receptors (Johansson and Vallbo, 1979; Mizobuchi et al., 2000), while electrical stimulation activates the afferent fibers from all of them and also the joint afferents. The 3 classes of cutaneous afferents project to area 3b and the joint afferents to area 3a (Kaas et al., 2002; Recanzone et al., 1992a). Although the two types of stimuli elicit different numbers of peripheral nerve action potentials (single for electric vs. multiple for tactile), the waveforms of somatosensory evoked potentials (SEPs) are very similar, provided that the rise-time of the mechanical stimuli is fast enough (<1 ms) (Hashimoto, 1999; Hashimoto et al., 1989, 1990, 1991a,b). If it is accepted that N20m and P30m SEF components reflect activity of pyramidal cells in area 3b, then the responsivity of this pyramidal cell population may not be the same with but very similar to that elicited by mechanical stimulation. Thus, the electrical stimulation can simulate real-life sensory experiences to a certain degree. There are a number of published data suggesting close correspondences in the localizations of digits in area 3b along the central sulcus between electrical and mechanical stimulation, although the direct comparison has not been made (Suk et al., 1991; Ohtomo et al., 1996; Pizzella et al., 1999; Iguchi et al., 2001, 2002). This colocalization is more likely than to consider that the digits are represented in distinct areas in 3b for electrical and mechanical stimulation. It should be remembered that, within area 3b, fingertips are represented deep in the central sulcus near the area 3a and the middle and proximal part of the fingers in progressively shallower part toward the area 1 border in the animal studies (Nelson et al., 1980; Recanzone et al., 1992a). However, these segregated representations are less clear in humans (Hashimoto et al., 1999a,b).

Third, in order to obtain robust and reproducible SEF responses to mechanical stimulation, a stimulation frequency of 0.5 Hz or less is optimal (Elbert et al., 1995; Hashimoto et al., 1988; Hashimoto, 1999). This limitation is imposed mainly by mechanical properties of the glabrous skin (Goodwin et al., 1989; Hashimoto, 1999). On the other hand, electrical stimulation elicits robust and reproducible SEF responses at 4 Hz or less as far as N20m and P30m are concerned (Hashimoto et al., 1996, 1999a,b,c,d, 2000, 2001; Klostermann et al., 1999; Kimura and Hashimoto, 2001). Therefore, early cortical responses such as N20m and P30m are little affected at a stimulus frequency of 2 Hz. Thus the stimulus frequencies for the two studies are appropriate. The rhythm of the music normally played by string players is much faster than 0.5 Hz and may be closer to 2 Hz. However, we have not examined specifically stimulus frequency-dependent SEF changes in string players. To our knowledge, no observations of resonant frequency characteristics of string players appear in the literature. Thus the issue of stimulus frequency is open for future studies.

Fourth, the effects of sampling rate and number of trials for averaging on M50 and N20m or P30m may not be identical: the sampling rate of 500 Hz and 1000 trials seem appropriate for M50 but are insufficient for N20m and P30m. Thus we used the sampling rate of 10 kHz and the trial number of 2000. Therefore, the recording parameters for the two studies are also appropriate.

Fifth, M50 and N20m are the first major cortical responses after tactile and electrical stimulation, respectively. Although the two components are not exactly homologous, because the dipole orientation is opposite in direction (posterior for M50 and anterior for N20m), M50 and N20m are both generated in area 3b (Allison et al., 1989; Elbert et al., 1995; Hashimoto et al., 1996, 1998, 1999a,b,c,d, 2000, 2001; Iguchi et al., 2001). Given the reported enlarged map estimated from M50 and thus the increased number of pyramidal cells responding to the left digits in area 3b in the string players, these plastic changes, if present, might be reflected in the dipole locations and strengths, and in the Euclidean distances estimated from N20m in the present study. This was not the case for the N20m dipole strengths and Euclidean distances. However, we found an anterior shift of D1 and D2 ECDs in string players instead of the medial shift in the previous study.

It is probably more appropriate to compare the mechanical M50 with electric P30m, because the dipole orientation of the two components is very similar. Our results showed that there were no significant differences in the dipole parameters between the left and right digits in string players or between the left digits of string players and controls. The only observable differences were in the dipole location for the anterior-posterior direction and in the D2-D5 distance between the left digits of string players and controls.

4.2. Anterior shift of D1 and D2 representations and longer D2-D5 cortical distances in the left hand of string players

The attainable spatial resolution of MEG measurements can be estimated from the signal-to-noise ratio of the magnetic recordings (Hari et al., 1988; Hashimoto et al., 1996, 2000; Kimura and Hashimoto, 2001). Spatial resolution of the present MEG measurements allows us to resolve the dipole locations with a distance of about 1 mm (see Hashimoto et al., 1996, 2000; Kimura and Hashimoto, 2001). Thus, the medial shifts of D1 (5 mm) and D5 (7 mm) for the left hand of string players documented in the previous study are well within the resolving capacity of our measurements. However, no such shifts were observed for D1, D2 and D5 of the left hand in string players in this study. On the other hand, the anterior shift was observed in D2 estimated from N20m and P30m ECDs and in D1 from N20m ECDs.

In a microelectrode mapping study of monkey area 3b, the reorganization was found after behaviorally controlled tactile stimulation was delivered on the distal phalanges of one or two fingers (D2, D3 and D4). First, the stimulated skin surfaces were represented over expanded cortical areas at the expense of more proximal surfaces within the same digit and of the adjacent digits (Jenkins et al., 1990). Second, the rostral border of area 3b shifted rostralward, manifesting an expansion of cutaneous area 3b fingertip representation into cortical field 3a. Third, significant lateralward translocations of the borders between the representations of the hand and face were recorded in all the trained monkeys. Thus, the expansion of cortical representations in the anterior-posterior direction is toward deeply situated area 3a and at the same time toward the border of areas 3b and 1. In this situation, the center of gravity of an activated area represented by a dipole location in MEG measurements may stay at a similar location, and only the dipole strength is increased. Therefore, the preferential direction of movements in the ECDs for trained digits should be lateralward into the face area within area 3b along the central sulcus. The representational shifts in the human experiments (Elbert et al., 1995) were medialward and opposite in direction and are very hard to reconcile with the physiological mapping study in monkeys (Jenkins et al., 1990). It appears difficult to explain the discrepancy between the animal and human studies in the direction of cortical enlargement by the different tasks involved. It is more natural to consider that the thumb representation will expand laterally to face area or at least stay at the pre-training original position, and that the little finger representation shifts medially to arm area in string players, because the mutual competition is less keen between the two adjacent areas (D1-face and D5-arm), respectively. Thus the medial expansion of little finger area is plausible but that of thumb may be less so. Our failure of observing such systematic shifts in the finger representations of string players suggests that the expansion toward medial direction along the central sulcus is small, if any, and probably beyond the detection capacity of the present MEG measurements.

In the somatosensory hand area in humans, the central sulcus takes a curved course resembling the inverted letter Ω (Ohtomo et al., 1996; Yousry et al., 1997; Pizzella et al., 1999). Therefore, our finding of the anterior shift of D1 and D2 in string players suggests two possibilities. First, the cortical activation after D1 and D2 stimulation in string players can be seen as an extended sheet of dipoles and the ECD model gives us an estimate of the center of gravity of this activity. Given that the lateral part of the inverted Ω receives projection from D1 and D2, the center of gravity of this activation can well be in the precentral wall (area 4) instead of in the postcentral wall (area 3b) (Huttunen, 1997). This may not be the case, however, because the dipole strengths for D1 and D2 in string players were not larger than those in controls. Second, it is more likely that the representations of D1 and D2 shift anteriorly along the lateral part of the inverted Ω. The anterior D2 shift may contribute to the longer D2-D5 distance in the string players. This interpretation seems to be supported by the animal study (Jenkins et al., 1990), but further studies are needed to establish the direction of representational expansion.

4.3. Effects of training versus deafferentation on cortical reorganizations

The present findings stand in sharp contrast with the robust and extensive reorganization of adult brain after peripheral denervation (see for review Buonomano and Merzenich, 1998; Jones, 2000; Florence, 2002; Kaas, 2002). Conceptually, a similar robust reorganization is anticipated by behavioral training or sensory experience, because the increase or decrease of sensory inputs is a continuum, resulting in either the representational expansion or shrinkage. However, the effects of the training and of the deafferentation on cortical reorganizations are not symmetrical in strength. With an absolute absence of competition, a large-scale reorganization in the range of 10–15 mm is produced in monkeys (Pons et al., 1991) and humans (Elbert et al., 1994) after extensive denervation such as dorsal root sections or limb amputation. Conversely, with strong mutual competition among the fingering digits on one hand and between the training (fingertips) and adjacent non-training (proximal part of fingers and palm) skin sites, the scale of reorganization should be much smaller as compared with the denervation-induced reorganizations. This interpretation is supported by invariant dipole strengths among the corresponding digits of string players and controls.

4.4. Increased number of HFOs reflects enhanced activity of fast-spiking inhibitory interneurons in area 3b

In addition to the findings derived from N20m and P30m, the number of HFO peaks was increased for the left D5 in string players. Although it failed to reach significance by a margin, the number of HFO peaks was also increased for the left D1 in string players. This suggests enhanced activity of fast-spiking inhibitory interneurons, facilitating coherent responses in the population of target pyramidal cells in area 3b (Hashimoto et al., 1996, 1999d; Jones et al., 2000; Ozaki et al., 2001; Tanosaki et al., 2001, 2002; see also Curio, 2000; Hashimoto, 2000, 2003 for review). Because real-life sensory stimuli such as tactile stimulation have inherent temporal jitters in a series of stimuli and are not sharp enough to elicit coherent action potentials in the peripheral nerve fibers, it is extremely difficult to record noninvasively the average population response of HFOs from outside the head. However, it is possible to record HFOs in the form of local field potentials, unit extracellular activities or intracellular potentials from the SI in animals for natural stimulation (Jones et al., 2000; Swadlow et al., 1998).

It has been demonstrated recently that, by repetitive whisker stimulation, a use-dependent increase in the density of dendritic spines occurs in both excitatory and inhibitory synapses in the adult mouse barrel cortex. Furthermore, it was shown that although the increase in the density of spines and excitatory synapses is transient, the increase in spinous inhibitory synapses is long lasting (Knott et al., 2002; see also Keller, 2002 for review). Such dramatic and long-lasting changes in the inhibitory synapses may be the morphological basis of enhanced HFOs in string players.

For control subjects, the D1 and D2 have specific functions for precision grasping (see Tanosaki et al., 2001) and D5 has less importance in daily activities. In contrast, D5 has the functional importance equal to D2 and is probably more than D1 in string players. Thus the effects of musical training on cortical plasticity might be the largest for D2 and D5. The present findings are in line with the monkey experiments on a temporally based tactile discrimination task that stimulation of the trained skin sites resulted in temporally sharper and shorter latency responses in area 3b (Recanzone et al., 1992c). The sharpening of response in cortical area 3b pyramidal neurons or the decreased variance in the representation of each stimulus cycle can account for behaviorally measured frequency discrimination performance in monkeys.

In string players, the processing of not only spatial but also temporal features of the sensory stimulus on the fingertips is equally crucial in sensorimotor coordination for playing the instruments. Furthermore it was found that HFOs of both the trained and non-trained hands of string players were larger in number than those of controls. It is tempting to speculate that music practice produces cortical plasticity not only for the fingering digits but also for the non-fingering digits, because both hands work together with a fine temporal synchrony. However, it should be remembered that an enormous difference in sensory training/stimulation is probably much more significant than the synchrony effect. In monkeys, 3b maps from the hemisphere ipsilateral to the trained digit were not altered by the training

(Recanzone et al., 1992c). However, we have no experimental data to suggest that the synchrony affects HFOs.

4.5. Conclusions

Taken together, the training-dependent reorganization of somatosensory cortex in string players is manifest not only in the enlarged cortical representation but also in the enhanced HFOs presumably representing activity of the fast-spiking interneurons. This altered activity of fast-spiking inhibitory interneurons, however, does not have the power strong enough to influence explicitly the downstream pyramidal neurons in area 3b as evidenced by invariant amplitude of N20m and P30m. This being said, it is possible that the trend for shorter latencies for left digits of the string players reflects the effects of enhanced activity of fast-spiking inhibitory interneurons in area 3b, in addition to the enhanced synaptic transmission in the ascending somatosensory system.

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