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Impaired Tactile Acuity in Old Age Is Accompanied by Enlarged Hand Representations in Somatosensory Cortex

Tobias Kalisch[1], Patrick Ragert[1,2], Peter Schwenkreis[2], Hubert R. Dinse[1] and Martin Tegenthoff[2]

[1]Department of Theoretical Biology, Institute for Neuroinformatics, Ruhr-University Bochum, D-44780 Bochum, Germany and [2]Department of Neurology, Ruhr-University Bochum, BG-Kliniken Bergmannsheil, D-44789 Bochum, Germany

The representations of the human hand in primary somatosensory cortex (SI) undergo continuous adaptational plastic processes, which arise from learning, altered use, or injury. The resulting reorganization affects size, extent, and position of the cortical maps, which parallels alterations of tactile behavior indicating a close relationship between map changes and perception. Here we investigate the influence of healthy aging on the cortical hand representation and on age-related changes of tactile performance. Using somatosensory evoked potential mapping in combination with electric source localization, we found that in elderly subjects aged 60–85 years the distance between the dipoles of the index and the little fingers increased indicating an expansion of the representations within SI by approximately 40%. Assessment of tactile spatial 2-point discrimination thresholds in the same subjects showed a strong decline with age. These results indicate that healthy aging strongly affects the homuncular structures of the hand representations within SI. Map expansion typically observed in young and adult subjects during learning is associated with a gain in performance. Whereas learning-related map changes are assumed to result from specific strengthening of synaptic connections, we suggest that the age-related map changes are related to the reduction of intracortical inhibition developing with age.

Keywords: aging, cortical inhibition, somatosensory evoked potentials (SEP), somatotopy, source localization

Introduction

The human aging process has tremendous influences on all stages of sensorimotor processing including reduction of physical activities, changes in peripheral neuronal structures, and changes in cortical functioning. On the other hand, there is also agreement that in elderly, compensatory processes in cortical and subcortical structures play a crucial role for the maintenance and stabilization of performance and behavior (Cabeza et al. 2002; Hutchinson et al. 2002; Ward and Frackowiak 2003). Furthermore, there is evidence that age-related brain changes can be highly regional. Analyzing gray matter density in healthy subjects aging from 7 to 87 years by means of magnetic resonance imaging (MRI) revealed a significant nonlinear decline (Sowell et al. 2003). In another longitudinal study in healthy elderly, measures in the regional brain volumes revealed substantial shrinkage of the caudate, the hippocampus, and the association cortices, with minimal change in the entorhinal and none in the primary visual cortex (Raz et al. 1997).

Given this wide range of age-related changes at many physiological and neuronal levels, it still remains unclear how cortical representations within the somatosensory system are affected by normal, nonpathological aging. Many studies have demonstrated that the cortical hand representation within the primary and secondary SI can be rapidly reorganized by manipulating the amount of use (Recanzone et al. 1992a; Pascual-Leone and Torres 1993; Elbert et al. 1995).

In addition, our labs have shown that map reorganization comparable in magnitude to that found under manipulation of use can be achieved by specifically designed passive tactile stimulation protocols conforming to ideas of Hebbian learning (Godde et al. 2000; Pleger et al. 2001; Dinse et al. 2003; Pleger et al. 2003; Ragert et al. 2004; Dinse et al. 2005; Dinse 2006; Dinse et al. 2006; Kalisch et al. 2007; Kalisch et al. 2008) or centrally by means of transcranial magnetic stimulation (Tegenthoff et al. 2005; Ragert et al. 2008). These studies were of particular interest as they demonstrated a strong relationship between measures of perceptual performance and cortical reorganization implying a close link between behavior and cortical organization (Pleger et al. 2001; Dinse et al. 2003; Dinse et al. 2005; Tegenthoff et al. 2005). Here we extend these studies by addressing the question how age affects tactile perception in parallel to cortical representations. In detail, we focus on the layout of the cortical hand representation within SI in order to explore consequences of normal aging through a combination of psychophysical testing of spatial 2-point discrimination thresholds and noninvasive electric source localization. We here demonstrate that the significant impairment in tactile spatial discrimination performance evolving at high age is accompanied by an expansion of the cortical hand representation. Because cortical map expansion in young subjects is typically associated with skill and performance acquisition, we conclude that map expansion as demonstrated here must represent a specific form of map alteration associated with aging processes, which differs qualitatively from learning-related reorganization occurring in young and adult subjects.

Materials and Methods

Subjects

We investigated 17 right-handed elderly subjects {8 female, range 60–85 years, mean age 68.2 ± 6.8 years (mean ± standard deviation [SD])}. In addition, 19 right-handed young subjects (12 female) with a mean age of 24.5 ± 4.6 years (mean ± SD, range 19–35 years) served as controls. In all subjects, handedness was determined using the "Edinburgh Handedness Inventory" (EHI) (Oldfield 1971). According to this test and self-reports of the subjects, all of them were right-hand dominant (EHI score elderly subjects: 96.47 ± 4.93; EHI score young subjects 98.42 ± 3.75). There were no group-specific differences in EHI scores (t-test, P = 0.187). All subjects gave their written informed consent before participating. The study was approved by the local

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Ethics Committee of the Ruhr-University of Bochum and was performed in accordance with the 1964 Declaration of Helsinki.

All elderly subjects were neurologically healthy as assessed by conventional electroneurography (nerve conduction velocity measurement of the N. medianus) and clinical examination by a neurologist. Individuals with polyneuropathy, peripheral nerve lesion, or other neurological disorders were excluded from the study. Eligibility criteria were lucidity, independence in activities of daily living, absence of motor handicaps like functional impairment because of arthritis, or other causes of joint immobility. Furthermore, medication with central nervous effects in present or reported history was a criterion for exclusion. Additionally, we assessed cognitive abilities using the "Mini Mental State Examination" (Folstein et al. 1975). Only persons scoring 27–30 out of 30 indicative of "no dementia" participated in the study.

Psychophysical Testing

Spatial 2-point discrimination thresholds were assessed on the tip of the index fingers using the method of constant stimuli as described previously (Godde et al. 2000; Pleger et al. 2001; Dinse et al. 2003; Pleger et al. 2003; Dinse et al. 2005; Tegenthoff et al. 2005; Dinse et al. 2006; Kalisch et al. 2007, 2008). We tested 7 pairs of brass needles; in addition 0 distance was tested with a single needle. To overcome problems in the use of 2-point measurements associated with hand-held probes, we used a specifically designed apparatus that allows a standardized and objective form of testing (cf., figures in Dinse et al. 2005, 2006). The apparatus allows a rapid switching between pairs of needles of different separations or the presentation of 1 single needle that are applied to a fixed position on the skin of the fingertips for approximately 1 s. To extract thresholds, we obtain psychometric curves based on many repeated stimulus presentations. According to own unpublished data, acuity thresholds obtained by gratings or by 2-point measurements are highly equivalent (Pearson correlation, $r = 0.716$, $P \leqslant 0.001$, $n = 22$ subjects), although thresholds obtained by gratings are slightly lower in general.

To account for the age-related decline in tactile acuity (Stevens 1992; Woodward 1993; Sathian et al. 1997; Tremblay et al. 2003; Dinse et al. 2005, 2006), we used different needle separations for the 2 age groups: 0.7, 1.0, 1.3, 1.6, 1.9, 2.2, and 2.5 mm for the young group and 1.5, 2.3, 3.1, 3.9, 4.7, 5.6, and 7.0 mm for the elderly group. The diameter of the needles was 0.7 mm, and the diameter of the blunt endings was 200 μm. Application force was about 150–200 mN. Fixation of the test finger prevented subjects from explorative finger movements. As described previously, test–retest reliability using this procedure was 0.90 for young subjects and 0.88 for elderly subjects (Dinse et al. 2006).

All 8 test conditions were presented 8 times in randomized order resulting in 64 tests per session. The subjects, who were not informed about the ratio of needle pairs and single needles (i.e., 7:1), had to decide immediately if they had the sensation of 1 or 2 needles. Subjects were instructed to classify the percept of a single needle or doubtful stimuli as "1" but the distinct percept of 2 stimuli as "2." The summed responses were plotted against the needle distances resulting in a psychometric function, which was fitted by a binary logistic regression (SPSS; SPSS Inc.). Threshold was taken from the fit where 50% correct responses were reached (Fig. 1). All subjects had to attend 2 test sessions to become familiar with the testing procedure before the assessment was started in the third session.

Mapping of Somatosensory Evoked Potentials

In all 36 subjects, somatosensory evoked potentials (SEPs) were recorded after electrical stimulation of the finger d2 (index finger) and d5 (little finger) of each hand. Electrical stimulation was performed using a Digitimer Stimulator DS9A, set to a pulse duration of 0.1 ms and a repetition rate of 3 Hz. Stimulation intensity was adjusted to the 2-fold individual sensation threshold. Electrical pulses were applied by 2 ring electrodes placed on the first and third segment of d2 and in a separate session on the first and third segment of d5 of the right as well as the left hand. Recordings were made using a 32-channel electroencephalogram (EEG) system (Neuroscan, El Paso, TX) from 32 scalp positions evenly distributed over both hemispheres according to the international 10-20 system. Electrode impedance was below 5 kΩ. The Fz electrode was used as a reference. The electrical potentials (band-pass filtered between 1 and 1000 Hz, sampling rate of 5000 Hz) were recorded in epochs from 30 ms before to 100 ms after the stimulus. A total of 1600 stimulus-related epochs were registered for each finger. After each recording, the epochs were digitally filtered (band pass filter: 20–500 Hz, 24 dB/Oct), referenced to a common average, and averaged using the Neuroscan software (Scan 4.1). Further analysis was done using the ASA software (ANT software Enschede, the Netherlands). For source reconstruction of the N20 SEP component, we used the electrode positions of a standard head model provided by ASA. A 3-dimensional (3D) coordinate system was defined for the head model, with the origin (0/0/0) set at the midpoint of the mediolateral axis (y-axis), which joined the center points of the entrance to the acoustic meati of the left and right ear (positive toward the left ear). The posterior–anterior axis (x-axis) was oriented from the origin to the nasion (positive toward the nasion) and the inferior–superior axis (z-axis) was perpendicular to the x-y plane (positive toward the vertex). Electrical source reconstruction for the first negative SEP component (N20) in the hemisphere contralateral to stimulation was performed using a single rotating dipole model as described previously (Pleger et al. 2001; Dinse et al. 2003; Pleger et al. 2003; Schwenkreis et al. 2007). Coordinates of the calculated dipole locations were given relative to the 3D coordinate system. Additionally, maximal dipole strength and goodness of fit (GOF, i.e., inverse residual variance) for the calculated dipole solutions were assessed. A dipole solution was considered as stable if the GOF was >90%. The polar N20 dipole angle difference and the Euclidean distance between the N20 dipole locations after d2 and d5 finger stimulation were used as parameters describing the extension of the cortical hand representation in SI.

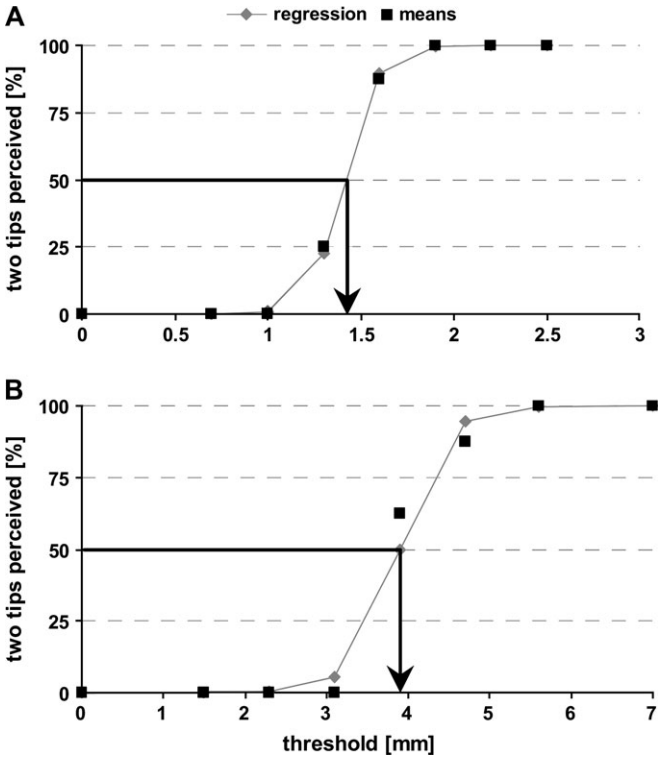

Figure 1. Psychometric functions for 2-point discrimination performance. Examples of 2-point discrimination performance of a young (*A*) and an elderly subject (*B*). Correct responses in percentages (squares) are plotted as a function of needle distances. Based on these results, a logistic regression is calculated (diamonds). The 50% level of correct responses (bold lines) determines the individual 2-point discrimination thresholds (arrows).

Statistical Analysis

Repeated measures analysis of variance (ANOVA) with inner-subject factor SIDE and between-subject factor GROUP was used to calculate side-to-side differences as well as group differences and interactions of

Table 1
Results of SEP mapping in young and elderly subjects

Electrical stimulation	Hand	Finger	*x* coordinate (mm)	*y* coordinate (mm)	*z* coordinate (mm)	Dipole angle (degree)	Dipole-GOF (%)	Dipole-strength (nAm)	N20 latency (ms)	Euclidian distance (d2↔d5) (mm)	Angle difference (degree)
Young subjects (n = 19)	Right	d2	−16.4 ± 1.7	38.1 ± 1.9[a]	44.0 ± 1.5	43.6 ± 2.0[b]	95.9 ± 0.4	9.4 ± 1.1	21.9 ± 0.5[b]	11.0 ± 1.0[ab]	5.3 ± 0.7
		d5	−16.7 ± 2.2[a]	35.6 ± 2.1	47.8 ± 1.5[a]	40.3 ± 2.1	95.0 ± 0.6	8.3 ± 0.8	22.7 ± 0.4[b]		
	Left	d2	−14.2 ± 1.7	−41.2 ± 1.3[a]	42.6 ± 1.2	46.1 ± 1.3[b]	96.1 ± 0.4	10.4 ± 1.0	21.5 ± 0.4[b]	8.4 ± 1.0[ab]	4.7 ± 0.9
		d5	−15.8 ± 1.4[a]	−39.3 ± 1.0	44.2 ± 1.1[a]	44.1 ± 1.2	95.4 ± 0.5	8.0 ± 0.8	21.9 ± 0.3[b]		
Elderly subjects (n = 17)	Right	d2	−22.3 ± 3.1	40.8 ± 1.7[a]	40.5 ± 1.8	49.9 ± 1.9[b]	94.9 ± 0.6	8.5 ± 1.2	25.3 ± 0.6[b]	15.4 ± 1.6[ab]	7.1 ± 1.5
		d5	−25.5 ± 3.4[a]	37.7 ± 1.6	45.5 ± 1.5[a]	44.1 ± 2.3	95.2 ± 0.7	7.2 ± 1.0	24.8 ± 0.6[b]		
	Left	d2	−18.2 ± 3.2	−44.6 ± 1.5[a]	40.0 ± 1.9	50.8 ± 2.2[b]	95.7 ± 0.5	9.1 ± 0.9	24.8 ± 0.6[b]	11.7 ± 1.2[ab]	6.9 ± 1.2
		d5	−18.8 ± 2.6[a]	−39.7 ± 1.1	43.8 ± 1.7[a]	45.6 ± 1.8	95.8 ± 0.6	7.3 ± 0.6	25.0 ± 0.6[b]		

All values given as mean ± SEM.
[a]Significant side-to-side difference ($P < 0.05$).
[b]Significant group difference ($P < 0.05$).

both factors for 2-point discrimination thresholds, Euclidian distances, and angle differences (the calculated angles were checked for phase jumps beforehand to assure the appropriate use of ANOVA statistics). The same statistic was conducted for the following parameters: coordinates (x, y, z), angles, GOF, strength, and latency (separately for d2 and d5 dipoles). Because of the discontinuous age distribution in the subject population, linear correlations (Pearson or Spearman) were calculated only within each age group in order to detect possible relations between age, dipole characteristics, and psychophysical performance. All data are presented as mean ± standard error of the mean. P values <0.05 were considered significant. Statistical analysis was performed using SPSS for Windows version 15.0 (SPSS Inc.).

Results

To investigate the relationship between age-related changes of the human hand representations in primary SI and the associated tactile performance, we combined spatial 2-point discrimination testing with electrical source localization of SEPs in SI in young and elderly subjects. For an overview of the N20 dipole coordinates x, y, and z, see Table 1.

Spatial Discrimination Performance

The average 2-point discrimination thresholds of the right index finger were 1.48 ± 0.05 mm in young and 3.39 ± 0.13 mm in elderly subjects (Fig. 2). For the left index finger, average thresholds were 1.46 ± 0.05 mm in young subjects and 3.23 ± 0.18 mm in elderly subjects (Fig. 2). ANOVA revealed a group difference for 2-point discrimination thresholds with significant higher thresholds for elderly subjects ($F_{(1,34)}$ = 168.851, $P \leqslant 0.001$). Within the group of young subjects, we found no correlation between individual thresholds and age (Pearson correlation, $r \leqslant 0.116$, $P \geqslant 0.635$). Within the group of elderly subjects on the other hand, the same analysis revealed at least a trend toward a correlation between individual thresholds and age (Pearson correlation, $r \leqslant 0.439$, $P \geqslant 0.078$).

Age-Related Changes of the Cortical Hand Representation

The size of the Euclidian distances between the N20 dipoles of d2 and d5 was larger in elderly subjects compared with young subjects ($F_{(1,34)}$ = 9.461, P = 0.004) (Fig. 3). For elderly subjects, we found a significant correlation between the individual size of the left-hemispheric Euclidian distance d2–d5 and age (Pearson correlation, r = 0.475, P = 0.004) (Fig. 4), but not for the right-hemispheric Euclidian distance d2–d5 (r = 0.269, P = 0.124) (Fig. 4). We found a significant difference in the size of the cortical hand representation. Euclidian distances between left-hemispheric dipoles were always larger than the distances

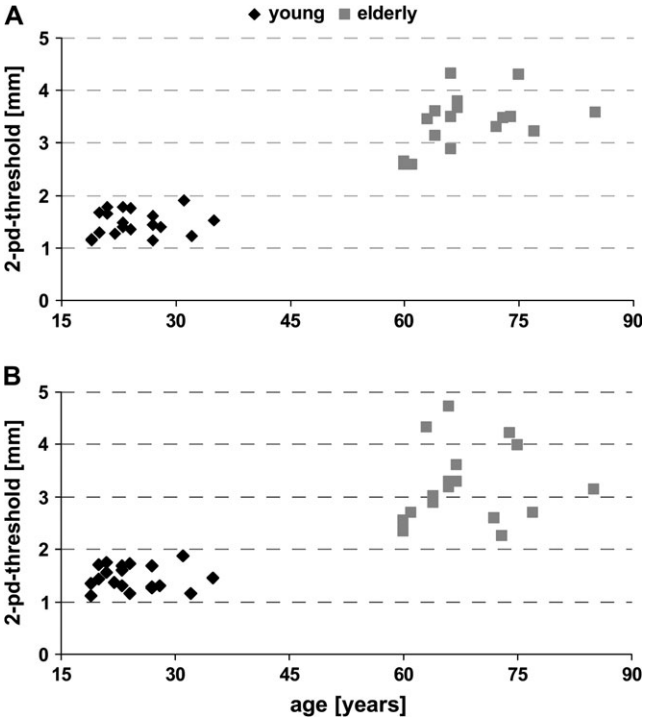

Figure 2. Age-related differences in tactile acuity. Stationary 2-point discrimination thresholds were assessed on the right (*A*) and left (*B*) index fingers. Thresholds of elderly subjects were significantly higher than thresholds of young subjects ($F_{(1,34)}$ = 168.851, $P \leq 0.001$) and showed increased variability.

between right-hemispheric dipoles (repeated measures ANOVA factor SIDE, $F_{(1,34)}$ = 7.461, P = 0.010) (Fig. 3).

In addition, the angle difference between the dipole positions of d2 and d5 relative to the z-axis was calculated, which revealed no significant differences (factors GROUP, SIDE, or interaction of both, $F_{(1,34)} \leqslant 2.623$, $P \geqslant 0.115$). Individual EEG data for a young and an elderly subject are displayed in Figures 5 and 6. Figure 7 displays dipole positions for young and elderly subjects based on group data (Fig. 7).

Age-Related Changes of d2-Dipole Characteristics

Repeated measures ANOVA revealed a significant difference for the angle of the d2 dipoles with larger angles in elderly subjects (factor GROUP, $F_{(1,34)}$ = 5.721, P = 0.022). For the strength of d2 dipoles, we found no significant differences (factors GROUP, SIDE, or interaction of both, $F_{(1,34)} \leqslant 1.514$, $P \geqslant 0.227$).

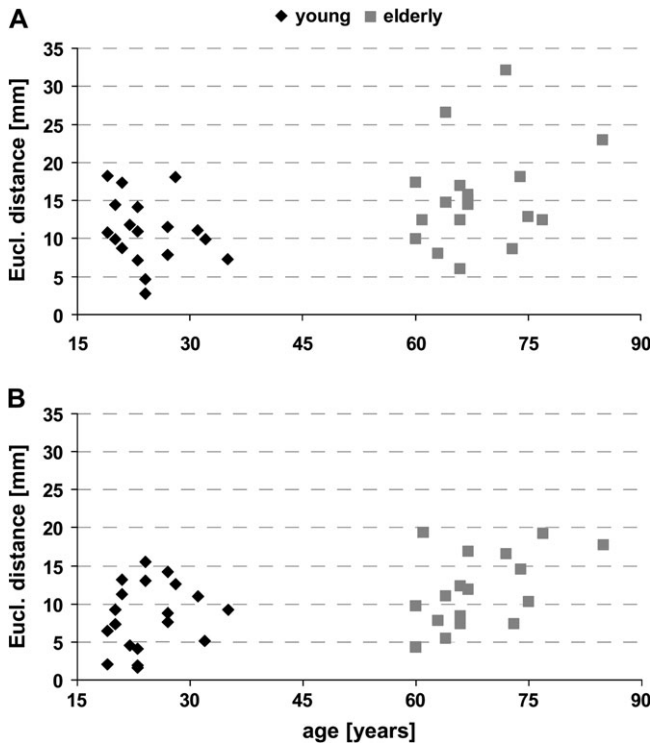

Figure 3. Age-related differences of Euclidian distances. Euclidian distances were calculated between the dipoles of d2 and d5 on the left hemisphere (right hand, *A*) and right hemisphere (left hand, *B*). ANOVA revealed larger distances between right-hemispheric dipoles (factor SIDE, $F_{(1,34)} = 7.461$, $P = 0.010$) and larger distances in elderly subjects (factor GROUP, $F_{(1,34)} = 9.461$, $P = 0.004$).

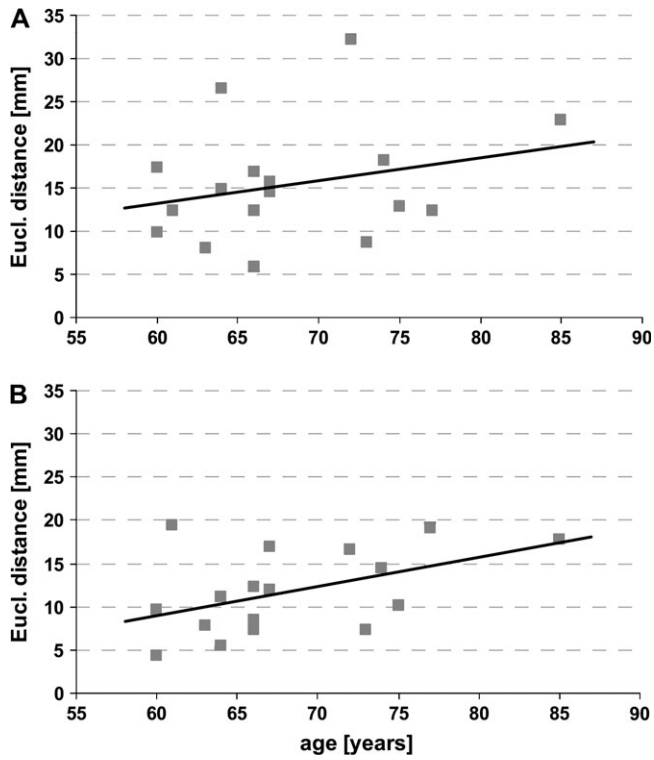

Figure 4. Enlargement of cortical hand representation in old age. The individual size of the left cortical hand representation (right hand, *A*), as estimated by the Euclidian distance between the dipoles of d2 and d5, was significantly correlated with the age of the elderly subjects (Pearson correlation, $r = 0.475$, $P = 0.004$). There was only a trend for the same relation of the right cortical hand representation and the subjects' age (left hand, *B*) ($r = 0.269$, $P = 0.124$).

However, in elderly subjects the latency of the N20 dipole component for d2 was significantly lengthened compared with young subjects ($F_{(1,34)} = 222.515$, $P \leqslant 0.001$). Furthermore, there were no significant differences between the GOF of the d2 dipoles in young and elderly subjects (factors GROUP, SIDE, or interaction of both, $F_{(1,34)} \leqslant 1.565$, $P \geqslant 0.219$).

Age-Related Changes of d5 Dipole Characteristics

For the d5 dipole angles, no significant differences were observed (repeated measures ANOVA factor GROUP, $F_{(1,34)} = 2.789$, $P = 0.104$). The same was true for the strength of d5 dipoles (factors GROUP, SIDE, or interaction of both, $F_{(1,34)} \leqslant 2.653$, $P \geqslant 0.113$). Comparable to the N20 dipole component of d2, in elderly subjects the latency of the N20 dipole component for d5 was significantly lengthened ($F_{(1,34)} = 17.511$, $P \leqslant 0.001$). There were no significant differences for the GOF of the d5 dipoles in young and elderly subjects (factors GROUP, SIDE, or interaction of both, $F_{(1,34)} \leqslant 1.006$, $P \geqslant 0.323$).

Discussion

To obtain insight into age-related differences of the relation between tactile discrimination abilities and cortical representational maps, we combined electric source localization following SEPs mapping with measuring spatial tactile 2-point discrimination thresholds in the same subjects. The psychophysical data confirm a significant deterioration of tactile discrimination performance of the right and left index fingers with increasing age. The behavioral changes were accompanied by changes in the cortical hand representations in SI characterized by an enlargement of the left and right hand representations as indicated by an increase of Euclidian distances between the finger representations of the index and little fingers (Fig. 7).

Age-Related Changes of Human SI

Anatomical and morphological changes that affect the hand and fingers and develop with age are numerous. The density of mechanoreceptors in the skin decreases (Wollard 1936; Bruce 1980), and conduction velocities of peripheral nerves slow down significantly with age (Dorfman and Bosley 1979; Peters 2002). Yet, a causal link between impaired acuity and receptor loss remains controversial as the density of Meissner's corpuscles in the fingers does not match with acuity data (Dillon et al. 2001). Furthermore, fingertip skin conformance was shown to account for some differences in tactile acuity in young subjects, but not for the decline in spatial acuity with aging (Vega-Bermudez and Johnson 2004). Most importantly, despite the accumulation of degenerative processes during aging, recent findings demonstrated that the age-related decline in tactile performance is not inevitable, but subject to restoration by learning and training (Dinse 2006; Dinse et al. 2006; Kalisch et al. 2008) indicative that mechanoreceptor density may play a minor role in determining tactile acuity performance at old age.

In the past, age-related changes of the SI were investigated by means of SEP recordings demonstrating a lengthening of latencies of different somatosensory response components as a function of age (Hume et al. 1982; Strenge and Hedderich 1982; Adler and Nacimiento 1988). More recently, electric or magnetic source localization studies use dipole positions obtained from

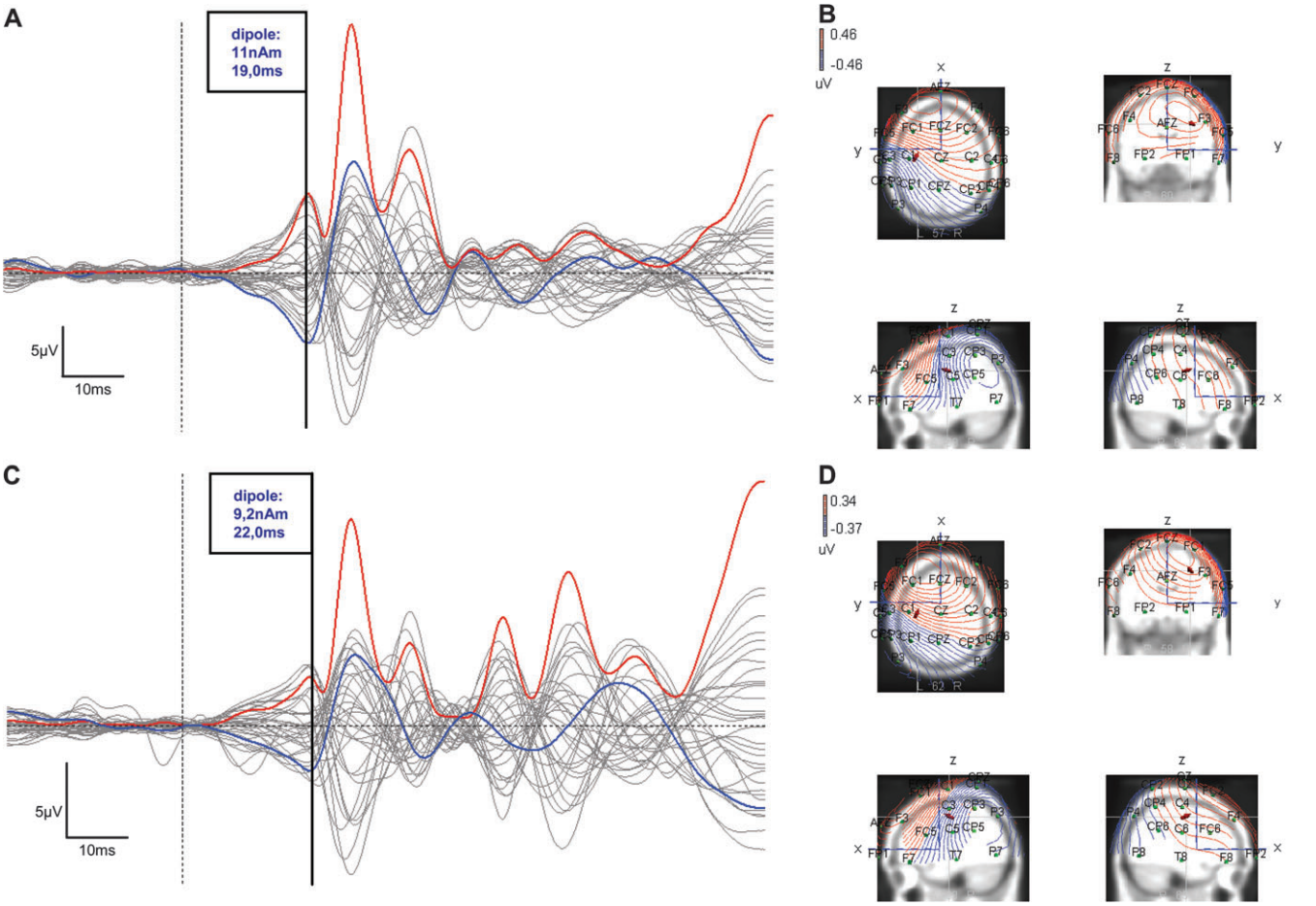

Figure 5. Single-subject EEG data of a young subject. (*A*) Averaged 32 electrode EEG recording (1600 measurements) from −30 to 100 ms relative to electrical stimulation (presented at 0 ms) of the right index finger (dashed line). The global field power (red line) and the source waveform (blue line) were added to the plot. The first maximum of the global field power indicates the timing of the N20 component (solid line). (*B*) Distribution of electrical field lines on the surface of a standard head model, with positive potentials (red lines) and negative potentials (blue lines). The dipole model (red arrow; for specifications see black box in *A*) reconstructs the location and direction of the source of the electrical field recorded on the head surface (*x*-axis: posterior–anterior direction; *y*-axis: mediolateral direction; *z*-axis: inferior–superior direction). Panels *C* and *D* display single-subject data for the same experiment but with stimulation of the right little finger. Electrodes are labeled and arranged according to the 10-20 system.

the N20 component of the SEP and resulting Euclidian distances between them as a marker of the spatial extent and the orderliness of the somatotopy in human SI (Elbert et al. 1995; Sterr et al. 1998); however, little is known about changes of somatosensory representations during normal aging.

N20 dipoles obtained for finger stimulation have been shown to be localized in area 3b of human and monkey primary somatosensory area (Baumgartner et al. 1991; McCarthy et al. 1991; Scherg and Buchner 1993). In contrast, response components later than N20 are most probably due to activation originating in areas 1, 2, 3a, and 4 (Scherg and Buchner 1993), whereas contributions of second somatosensory cortex are believed to develop even later (Hamalainen et al. 1990). We therefore conclude that the age-related changes in dipole localization we describe in this paper most likely characterize human SI.

Overactivation, Compensation, and Recruitment

Age-related reduction in task-induced brain activity is a common observation, but recent neuroimaging studies have also found that elderly subjects may activate certain regions to a greater extent than younger adults (for review, see Persson and Nyberg 2006; Persson et al. 2006). During the execution of motor tasks, decision making, or cognitive tasks, older subjects show an overactivation (Grady 2000; Calautti et al. 2001; Dolcos et al. 2002; Langenecker and Nielson 2003; Morcom et al. 2003; Ward and Frackowiak 2003; Hester et al. 2004). It has been suggested that overactivation may play a compensatory role when cognitive decline is limited, whereas underactivation seems to be the typical pattern when cognitive impairment is in a more progressed state (Persson and Nyberg 2006). According to our data, tactile impairment remained high despite the expansion of cortical maps. We therefore believe that compensation seems to be of minor relevance in the context of our findings.

Map Size Changes as a Predictor of Behavioral Gain

Numerous imaging studies have shown that continuous and long-lasting practice of sensorimotor skills resulted in defined expansions of cortical representations, as described for blind Braille readers and musicians (Pascual-Leone and Torres 1993; Elbert et al. 1995; Pantev et al. 1998; Rauschecker 2001). These studies corroborate earlier animal studies, which demonstrated that training-induced enlargement of cortical maps that is

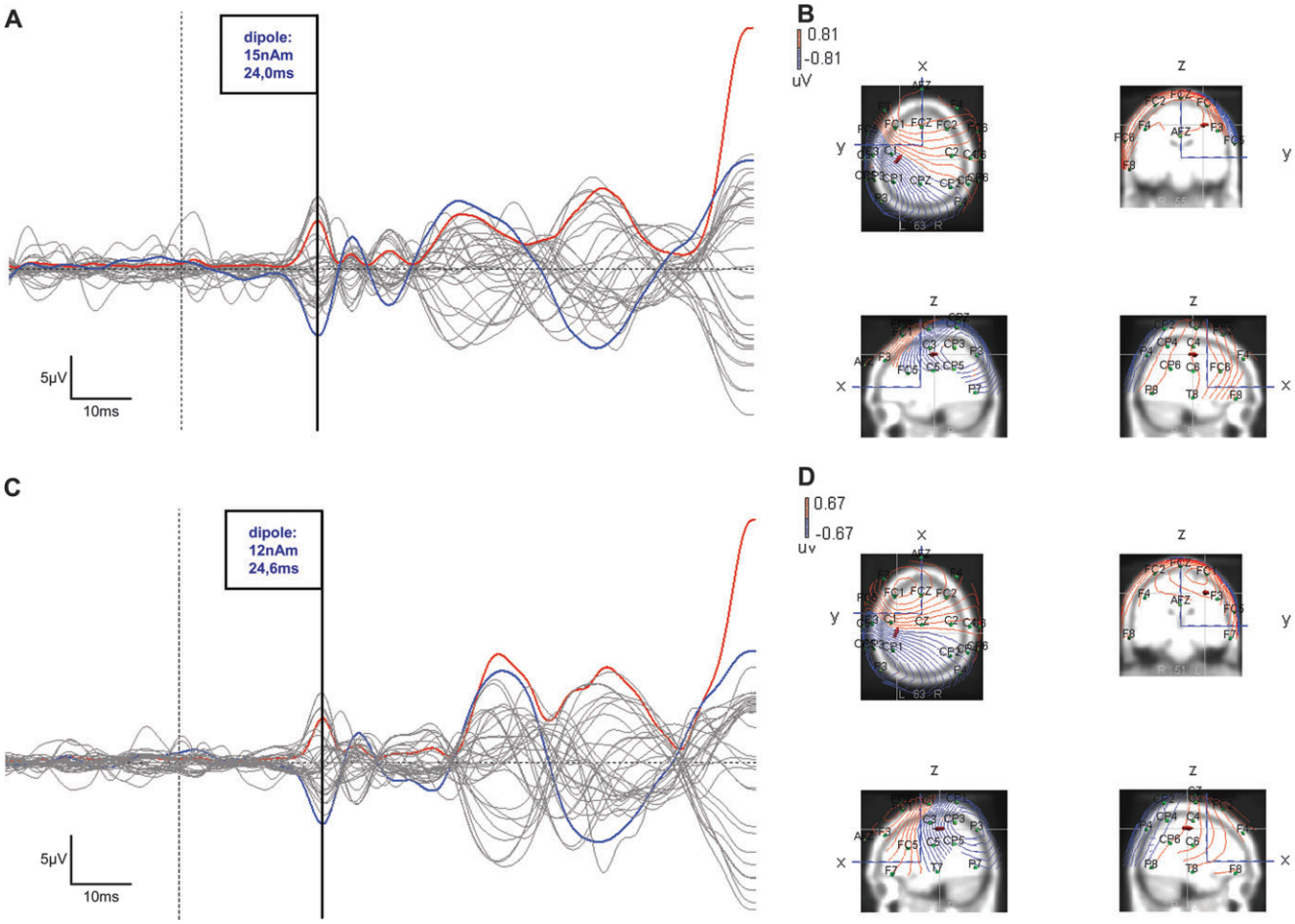

Figure 6. Single-subject EEG data of an elderly subject. (*A*) Averaged 32 electrode EEG recording (1600 measurements) from −30 to 100 ms relative to electrical stimulation (presented at 0 ms) of the right index finger (dashed line). The global field power (red line) and the source waveform (blue line) were added to the plot. The first maximum of the global field power indicates the timing of the N20 component (solid line). (*B*) Distribution of electrical field lines on the surface of a standard head model, with positive potentials (red lines) and negative potentials (blue lines). The dipole model (red arrow; for specifications see black box in *A*) reconstructs the location and direction of the source of the electrical field recorded on the head surface (*x*-axis: posterior–anterior direction; *y*-axis: mediolateral direction; *z*-axis: inferior–superior direction). Panels *C* and *D* display single-subject data for the same experiment but with stimulation of the right little finger. Electrodes are labeled and arranged according to the 10-20 system.

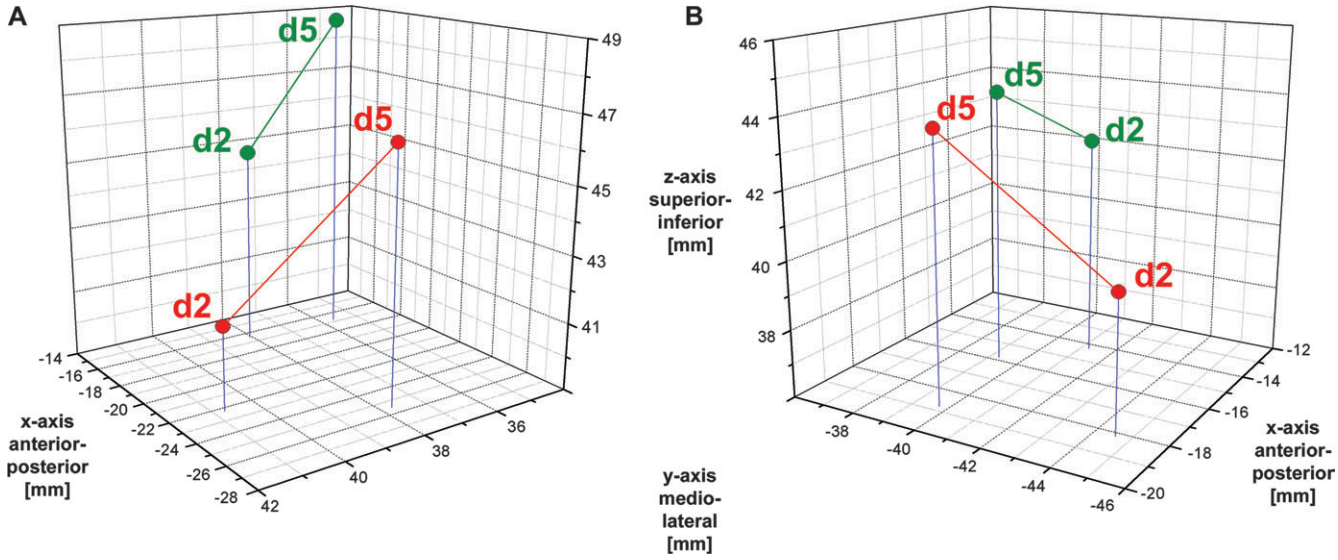

Figure 7. 3D plot of cortical dipole positions and Euclidian distances. The 3-dimensional plots of d2 and d5 coordinates on the left (*A*) and right hemisphere (*B*) shows the Euclidian distances for young subjects (green dots and lines) and elderly subjects (red dots and lines). Besides the significant differences between Euclidian distances of young and elderly subjects ($F_{(1,34)} = 9.461$, $P = 0.004$), we observed a general shift of dipoles toward posterior, inferior, and lateral positions in elderly subjects.

associated with the development of behavioral or perceptual gains (Recanzone et al. 1992b; Recanzone et al. 1993; Dinse and Merzenich 2002). On the other hand, enforced disuse by hand immobilization caused the opposite effect, a shrinkage of cortical hand representations, which was paralleled by a deterioration of discrimination skills (Ragert et al. 2003). Our own work using tactile coactivation to induce perceptual improvement parallel to cortical enlargement based on Hebbian learning principles revealed an even linear relation between the amount of individual perceptual improvement and the amount of individual cortical map expansion (Pleger et al. 2001; Dinse et al. 2003; Pleger et al. 2003). According to recent data, the size of cortical representations predicts performance even under baseline conditions as demonstrated for the visual (Duncan and Boynton 2003), auditory, (Rutkowski and Weinberger 2005) and somatosensory system (Duncan and Boynton 2007).

Accordingly, map size appears to be a reliable predictor of individual performance. However, there are interesting exceptions from that rule implying that the relation between behavior and cortical map dimensions might be more complex (Pascual-Leone et al. 1994; Polley et al. 1999). To unify these seemingly contradictory observations, using a computational mean field approach we have recently shown that map expansion can be paralleled by either a perceptual impairment or an improvement dependent on changes of lateral interaction processes, which are typically not seen in functional magnetic resonance imaging (fMRI) data (Wilimzig et al. 2006).

Reduction of Intracortical Inhibition during Aging

Numerous lines of evidence converge on the observation that during aging intracortical inhibition is reduced. Studies addressing paired-pulse behavior using double-pulse stimulation report that the paired-pulse cortical suppression is significantly smaller in elderly as compared with young adults (Peinemann et al. 2001; Oliviero et al. 2006), which has also been reported for aged rats (David-Jurgens and Dinse 2007). Another study compared the stimulus selectivity of cells in primary visual cortex in young and old macaque monkeys and found evidence for a significant degradation of orientation and direction selectivity in old animals (Schmolesky et al. 2000) consistent with an age-related degeneration of intracortical inhibition. A recent ultrastructural study revealed a significant age-related decline in the numerical density of presumptive inhibitory synapses of the sensorimotor cortex (Poe et al. 2001) demonstrating a deficit in the intrinsic inhibitory circuitry of the aging neocortex. Conceivably, a reduced level of inhibition would allow excitatory processes to spread. It is undisputed that receptive fields (RFs) are kept small through active inhibition (Hicks and Dykes 1983). In a study analyzing RFs and point spread functions in SI of aged rats, an enlargement of RF size and of the size of the cortical point spread function has been described (Spengler et al. 1995; Godde et al. 2002; Dinse et al. 2006) compatible with a general reduction of cortical inhibition.

Islands of Cortical Activation—Evidence for Less-Distinctive Representations

A further hint that might shed light on the nature of the age-related map enlargement comes from optical imaging studies of map changes in SI of aged rats. According to these data, the hind limb representation showed a kind of patchy appearance consisting of separated zones of high activity surrounded by regions with little activity, giving rise to separated islands of cortical activity (Godde et al. 2002). A similar finding was observed after local field potential mapping in SI of aged rats (Spengler et al. 1995). Based on computational approaches, it has been discussed that less distinctive cortical representations might emerge as a typical outcome of age-related alterations of neuromodulation, where distinctiveness of cortical maps was assumed to correlate with behavioral measures (Li and Sikstrom 2002).

It is therefore an interesting question to clarify whether age-related changes within the human hand representation show comparable signs of patchyness. As source localization techniques cannot resolve this question, further studies employing fMRI might be able to examine the possibility of the emergence of unresponsive cortical islands as another signature of age-related changes of cortical maps in humans.

Conclusions

We observe that aging processes result in a decline of perceptual abilities, which are paralleled by an expansion of cortical sensory representational maps. In adults, map expansion is typically associated with a gain in perceptual performance. In order to explain this atypical relation between map expansion and behavioral changes, we suggest that the reduction of intracortical inhibition with age, which contributes to larger RF size and greater cortical activation, ultimately leads to the disintegration of cortical maps. In contrast, map expansion based on learning, which results in the development of perceptual skills, is assumed to be the consequence of specific strengthening of synaptic connections, presumably due to Hebbian processes. Combined, our data show that besides changes in cortical functioning arising from lesions, learning, or manipulated use, aging is another relevant factor that affects the humuncular topography and associated behavior. Although the observed phenomenology of map reorganization resembles that found during learning, both forms differ in the underlying mechanisms, which critically determine the direction of perceptual alterations.

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Notes

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Address correspondence to Hubert R. Dinse, Department of Theoretical Biology, Institute for Neuroinformatics, Ruhr-University Bochum, D-44780 Bochum, Germany. Email: hubert.dinse@neuroinformatik.rub.de.

References

Adler G, Nacimiento AC. 1988. Age-dependent changes of short-latency somatosensory evoked potentials in healthy adults. Appl Neurophysiol. 51:55–59.

Baumgartner C, Doppelbauer A, Deecke L, Barth DS, Zeitlhofer J, Lindinger G, Sutherling WW. 1991. Neuromagnetic investigation of somatotopy of human hand somatosensory cortex. Exp Brain Res. 87:641–648.

Bruce MF. 1980. The relation of tactile thresholds to histology in the fingers of elderly people. J Neurol Neurosurg Psychiatry. 43: 730–734.

Cabeza R, Anderson ND, Locantore JK, McIntosh AR. 2002. Aging gracefully: compensatory brain activity in high-performing older adults. Neuroimage. 17:1394–1402.

Calautti C, Serrati C, Baron JC. 2001. Effects of age on brain activation during auditory-cued thumb-to-index opposition: a positron emission tomography study. Stroke. 32:139–146.

David-Jurgens M, Dinse HR. 2007. Age-related effects on cortical excitability as measured with paired pulse technique of neurons recorded in rat somatosensory cortex. In: Society for Neuroscience Abstract, Program No. 402.1/QQ11: Neuroscience Meeting Planner. Society for Neuroscience. Online.

Dillon YK, Haynes J, Henneberg M. 2001. The relationship of the number of Meissner's corpuscles to dermatoglyphic characters and finger size. J Anat. 199:577–584.

Dinse HR. 2006. Cortical reorganization in the aging brain. Prog Brain Res. 157:57–80.

Dinse HR, Kalisch T, Ragert P, Pleger B, Schwenkreis P, Tegenthoff M. 2005. Improving human haptic performance in normal and impaired human populations through unattended activation-based learning. ACM Trans Appl Percept. 2:71–88.

Dinse HR, Kleibel N, Kalisch T, Ragert P, Wilimzig C, Tegenthoff M. 2006. Tactile coactivation resets age-related decline of human tactile discrimination. Ann Neurol. 60:88–94.

Dinse HR, Merzenich MM. 2002. Adaptation of inputs in somatosensory system. Boston: MIT Press.

Dinse HR, Ragert P, Pleger B, Schwenkreis P, Tegenthoff M. 2003. Pharmacological modulation of perceptual learning and associated cortical reorganization. Science. 301:91–94.

Dolcos F, Rice HJ, Cabeza R. 2002. Hemispheric asymmetry and aging: right hemisphere decline or asymmetry reduction. Neurosci Biobehav Rev. 26:819–825.

Dorfman LJ, Bosley TM. 1979. Age-related changes in peripheral and central nerve conduction in man. Neurology. 29:38–44.

Duncan RO, Boynton GM. 2003. Cortical magnification within human primary visual cortex correlates with acuity thresholds. Neuron. 38:659–671.

Duncan RO, Boynton GM. 2007. Tactile hyperacuity thresholds correlate with finger maps in primary somatosensory cortex (S1). Cereb Cortex. 17:2878–2891.

Elbert T, Pantev C, Wienbruch C, Rockstroh B, Taub E. 1995. Increased cortical representation of the fingers of the left hand in string players. Science. 270:305–307.

Folstein MF, Folstein SE, McHugh PR. 1975. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 12:189–198.

Godde B, Berkefeld T, David-Jurgens M, Dinse HR. 2002. Age-related changes in primary somatosensory cortex of rats: evidence for parallel degenerative and plastic-adaptive processes. Neurosci Biobehav Rev. 26:743–752.

Godde B, Stauffenberg B, Spengler F, Dinse HR. 2000. Tactile coactivation-induced changes in spatial discrimination performance. J Neurosci. 20:1597–1604.

Grady CL. 2000. Functional brain imaging and age-related changes in cognition. Biol Psychol. 54:259–281.

Hamalainen H, Kekoni J, Sams M, Reinikainen K, Naatanen R. 1990. Human somatosensory evoked potentials to mechanical pulses and vibration: contributions of SI and SII somatosensory cortices to P50 and P100 components. Electroencephalogr Clin Neurophysiol. 75:13–21.

Hester R, Fassbender C, Garavan H. 2004. Individual differences in error processing: a review and reanalysis of three event-related fMRI studies using the GO/NOGO task. Cereb Cortex. 14:986–994.

Hicks TP, Dykes RW. 1983. Receptive field size for certain neurons in primary somatosensory cortex is determined by GABA-mediated intracortical inhibition. Brain Res. 274:160–164.

Hume AL, Cant BR, Shaw NA, Cowan JC. 1982. Central somatosensory conduction time from 10 to 79 years. Electroencephalogr Clin Neurophysiol. 54:49–54.

Hutchinson S, Kobayashi M, Horkan CM, Pascual-Leone A, Alexander MP, Schlaug G. 2002. Age-related differences in movement representation. Neuroimage. 17:1720–1728.

Kalisch T, Martin T, Dinse H. Forthcoming 2008. Improvement of sensorimotor functions in old age by passive stimulation. Clin Interv Aging.

Kalisch T, Tegenthoff M, Dinse HR. 2007. Differential effects of synchronous and asynchronous multifinger coactivation on human tactile performance. BMC Neurosci. 8:1471–2202.

Langenecker SA, Nielson KA. 2003. Frontal recruitment during response inhibition in older adults replicated with fMRI. NeuroImage. 20:1384–1392.

Li SC, Sikstrom S. 2002. Integrative neurocomputational perspectives on cognitive aging, neuromodulation, and representation. Neurosci Biobehav Rev. 26:795–808.

McCarthy G, Wood CC, Allison T. 1991. Cortical somatosensory evoked potentials. I. Recordings in the monkey Macaca fascicularis. J Neurophysiol. 66:53–63.

Morcom AM, Good CD, Frackowiak RS, Rugg MD. 2003. Age effects on the neural correlates of successful memory encoding. Brain. 126:213–229.

Oldfield RC. 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia. 9:97–113.

Oliviero A, Profice P, Tonali PA, Pilato F, Saturno E, Dileone M, Ranieri F, Di Lazzaro V. 2006. Effects of aging on motor cortex excitability. Neurosci Res. 55:74–77.

Pantev C, Oostenveld R, Engelien A, Ross B, Roberts L, Hoke M. 1998. Increased auditory cortical representation in musicians. Nature. 392:811–814.

Pascual-Leone A, Grafman J, Hallett M. 1994. Modulation of cortical motor output maps during development of implicit and explicit knowledge. Science. 263:1287–1289.

Pascual-Leone A, Torres F. 1993. Plasticity of the sensorimotor cortex representation of the reading finger in Braille readers. Brain. 116(Pt 1):39–52.

Peinemann A, Lehner C, Conrad B, Siebner HR. 2001. Age-related decrease in paired-pulse intracortical inhibition in the human primary motor cortex. Neurosci Lett. 313:33–36.

Persson J, Nyberg L. 2006. Altered brain activity in healthy seniors: what does it mean? Prog Brain Res. 157:45–56.

Persson J, Nyberg L, Lind J, Larsson A, Nilsson LG, Ingvar M, Buckner RL. 2006. Structure-function correlates of cognitive decline in aging. Cereb Cortex. 16:907–915.

Peters A. 2002. The effects of normal aging on myelin and nerve fibers: a review. J Neurocytol. 31:581–593.

Pleger B, Dinse HR, Ragert P, Schwenkreis P, Malin JP, Tegenthoff M. 2001. Shifts in cortical representations predict human discrimination improvement. Proc Natl Acad Sci USA. 98: 12255–12260.

Pleger B, Foerster AF, Ragert P, Dinse HR, Schwenkreis P, Malin JP, Nicolas V, Tegenthoff M. 2003. Functional imaging of perceptual learning in human primary and secondary somatosensory cortex. Neuron. 40:643–653.

Poe BH, Linville C, Brunso-Bechtold J. 2001. Age-related decline of presumptive inhibitory synapses in the sensorimotor cortex as revealed by the physical disector. J Comp Neurol. 439:65–72.

Polley DB, Chen-Bee CH, Frostig RD. 1999. Two directions of plasticity in the sensory-deprived adult cortex. Neuron. 24:623–637.

Ragert P, Franzkowiak S, Schwenkreis P, Tegenthoff M, Dinse HR. 2008. Improvement of tactile perception and enhancement of cortical excitability through intermittent theta burst rTMS over human primary somatosensory cortex. Exp Brain Res. 184:1–11.

Ragert P, Pleger B, Völker B, Maier C, Schwenkreis P, Tegenthoff M, Dinse H. 2003. Impaired tactile performance in patients with hand immobilisation. Soc Neurosci Abstr. 29:37913.

Ragert P, Schmidt A, Altenmuller E, Dinse HR. 2004. Superior tactile performance and learning in professional pianists: evidence for meta-plasticity in musicians. Eur J Neurosci. 19:473–478.

Rauschecker JP. 2001. Cortical plasticity and music. Ann NY Acad Sci. 930:330–336.

Raz N, Gunning FM, Head D, Dupuis JH, McQuain J, Briggs SD, Loken WJ, Thornton AE, Acker JD. 1997. Selective aging of the human cerebral cortex observed in vivo: differential vulnerability of the prefrontal gray matter. Cereb Cortex. 7:268–282.

Recanzone GH, Jenkins WM, Grajski KA, Dinse HR. 1992a. Topographic reorganization of the hand representation in cortical area 3b owl monkeys trained in a frequency-discrimination task. J Neurophysiol. 67:1031–1056.
Recanzone GH, Merzenich MM, Jenkins WM, Grajski KA, Dinse HR. 1992b. Topographic reorganization of the hand representation in cortical area 3b owl monkeys trained in a frequency-discrimination task. J Neurophysiol. 67:1031–1056.
Recanzone GH, Schreiner CE, Merzenich MM. 1993. Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. J Neurosci. 13:87–103.
Rutkowski RG, Weinberger NM. 2005. Encoding of learned importance of sound by magnitude of representational area in primary auditory cortex. Proc Natl Acad Sci USA. 102:13664–13669.
Sathian K, Zangaladze A, Green J, Vitek JL, DeLong MR. 1997. Tactile spatial acuity and roughness discrimination: impairments due to aging and Parkinson's disease. Neurology. 49:168–177.
Scherg M, Buchner H. 1993. Somatosensory evoked potentials and magnetic fields: separation of multiple source activities. Physiol Meas. 14(Suppl 4A):A35–A39.
Schmolesky MT, Wang Y, Pu M, Leventhal AG. 2000. Degradation of stimulus selectivity of visual cortical cells in senescent rhesus monkeys. Nat Neurosci. 384–390.
Schwenkreis P, El Tom S, Ragert P, Pleger B, Tegenthoff M, Dinse HR. 2007. Assessment of sensorimotor cortical representation asymmetries and motor skills in violin players. Eur J Neurosci. 26:3291–3302.
Sowell ER, Peterson BS, Thompson PM, Welcome SE, Henkenius AL, Toga AW. 2003. Mapping cortical change across the human life span. Nat Neurosci. 6:309–315.
Spengler F, Godde B, Dinse HR. 1995. Effects of ageing on topographic organization of somatosensory cortex. Neuroreport. 6: 469–473.
Sterr A, Muller MM, Elbert T, Rockstroh B, Pantev C, Taub E. 1998. Changed perceptions in Braille readers. Nature. 391:134–135.
Stevens JC. 1992. Aging and spatial acuity of touch. J Gerontol. 47:P35–P40.
Strenge H, Hedderich J. 1982. Age-dependent changes in central somatosensory conduction time. Eur Neurol. 21:270–276.
Tegenthoff M, Ragert P, Pleger B, Schwenkreis P, Forster AF, Nicolas V, Dinse HR. 2005. Improvement of tactile discrimination performance and enlargement of cortical somatosensory maps after 5 Hz rTMS. PLoS Biol. 3:e362.
Tremblay F, Wong K, Sanderson R, Cote L. 2003. Tactile spatial acuity in elderly persons: assessment with grating domes and relationship with manual dexterity. Somatosens Mot Res. 20:127–132.
Vega-Bermudez F, Johnson KO. 2004. Fingertip skin conformance accounts, in part, for differences in tactile spatial acuity in young subjects, but not for the decline in spatial acuity with aging. Percept Psychophys. 66:60–67.
Ward NS, Frackowiak RS. 2003. Age-related changes in the neural correlates of motor performance. Brain. 126:873–888.
Wilimzig C, Jancke D, Dinse HR. 2006. Spatial discrimination and its learning-induced alterations depend on changes of inhibitory cortical interactions. Soc Neurosci Abstr. 5326, P2.
Wollard HH. 1936. Intraepidermal nerve endings. J Anat. 71:55–62.
Woodward KL. 1993. The relationship between skin compliance, age, gender, and tactile discriminative thresholds in humans. Somatosens Mot Res. 10:63–67.