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RESEARCH ARTICLE

Receptive field plasticity of area 17 visual cortical neurons of adult rats

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Abstract In contrast to somatosensory cortex (SI), where the pervasiveness of reorganizational capacities is well-established, plasticity of receptive fields (RFs) of adult primary visual cortex (VI) remains controversial. To investigate RF plasticity in VI of adult rats, we here used intracortical microstimulation (ICMS) to overcome particularities related to stimulus presentation and training procedures which limit comparison across modalities. Our results show that VI RFs can be altered by ICMS; however, changes depended on the pre-ICMS RF size. Initially small RFs expanded after 2 h of ICMS with little signs of recovery within the next hours, while initially large RFs remained unaffected. Inspection of the time course of neuron responses revealed, however, that in large RFs early response components were enhanced, while late response components were reduced resulting in changes of the spatiotemporal RF properties. Although plastic changes in VI showed a substantial heterogeneity, our results indicate a capacity of VI neurons to undergo plastic changes comparable to SI neurons. However, the magnitude and aspects of reversibility appeared to be different suggesting a significant modality-specificity of reorganizational changes of cortical sensory neurons.

Keywords Intracortical microstimulation · Rat · Receptive field · Visual cortex · Plasticity · Spatiotemporal receptive field

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Introduction

The substantial capacities for plastic changes of adult somatosensory cortex following lesion or injury or as a consequence of training, enforced use of a body part or even pure exposure to sensory stimulation are well-acknowledged. However, the nature of plastic reorganizational capacities of visual cortex of adult individuals remains controversial. Although reorganization of adult primary visual cortex after retinal or central lesions appeared well-documented (Calford et al. 2000, 2003, 2005; Chino et al. 1995; Giannikopoulos and Eysel 2006; Gilbert and Wiesel 1992; Kaas et al. 1990; Keck et al. 2008), recent reports challenged this view (Smirnakis et al. 2005; see also Rosa et al. 1995 for discussion of reorganizational capacities). This controversy comes surprising given that many years ago the effect of restricted visual environment was investigated in adult cats showing selective changes of orientation selectivity (Creutzfeldt and Heggelund 1975; Hirsch and Spinelli 1970). Fast and reversible changes of receptive field (RF) size have been reported following masking parts of the visual field (Das and Gilbert 1995; Pettet and Gilbert 1992) or after repetitive pairing protocols (Eysel et al. 1998; McLean and Palmer 1998). For neural changes in the context of perceptual learning see "Discussion". More recently, it was shown in adult mice that repeated passive exposure to a single orientation of grating resulted in a persistent enhancement of evoked response related to that stimulus. This study emphasizes how a strongly driving stimulus can evoke long-term changes after passive stimulation (Frenkel et al. 2006).

To overcome particularities related to stimulus presentation, task constraints, training procedures or to the role of attention which limit direct comparison across sensory modalities, we here used the advantage of intracortical microstimulation (ICMS) to investigate locally the capacities and properties of functional plasticity regardless of effects from

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the sensory periphery and ascending pathways. In this type of induction of plastic processes, changes of synaptic efficacy are induced by delivering repetitive electrical pulse trains via a microelectrode to generate spatially restricted, temporally synchronized discharges (Ronner et al. 1981; Stoney et al. 1968). We and others have extensively utilized this approach to study plastic changes of receptive fields (RFs) and representational maps at cortical and subcortical levels in visual cortex (Godde et al. 2002; Warren and Normann 2005), motor cortex (Gu and Fortier 1996; Nudo et al. 1990), somatosensory cortex (Benali et al. 2008; Dinse et al. 1993, 1997; Recanzone et al. 1992a; Spengler and Dinse 1994) and auditory cortex (Maldonado and Gerstein 1996; Sakai and Suga 2001; Sil'kis and SSh 1995; Talwar and Gerstein 2001; Valentine and Eggermont 2003).

A typical effect of ICMS applied in the hind-paw representation of adult rat primary somatosensory cortex (SI) consisted of a severalfold expansion of receptive field (RF) size due to integration of surrounding skin fields. ICMS-induced reorganization could be detected after 15 min, but much greater effects were observed after 2–3 h of ICMS. Importantly, all changes were reversible within several hours after termination of ICMS (Benali et al. 2008; Dinse et al. 1993, 1997; Spengler and Dinse 1994).

In the present paper we address the question how ICMS applied in visual cortex of adult rats affect visual RFs. To compare RF plasticity between the visual and somatosensory system, we additionally applied ICMS in somatosensory cortex of the same strain of animals. Many studies have shown that RFs have a complex spatiotemporal structure characterized by the built-up and decay of activity over the first tens of seconds after stimulation (DeAngelis et al. 1995; Dinse and Jancke 2001; Eckhorn et al. 1993; Ghazanfar and Nicolelis 2001; Jones and Palmer 1987; Shevelev et al. 1993; Wörgötter and Eysel 2000). In addition to conventional measures of RF size obtained after temporal averaging, we analyzed the time course of RF organization using a response plane mapping technique. Our results show that RFs of neurons recorded in adult rat visual cortex, including their dynamic behavior, can be modified by ICMS. These changes were dependent on the initial RF size. The results indicate a capacity of visual neurons to undergo plastic changes essentially comparable to those described for somatosensory neurons; however, the magnitude and aspects of reversibility appeared to be different from somatosensory cortical neurons.

Materials and methods

Animals and preparation

Twenty-three adult male pigmented rats (Dark Agouti; 3–5 months of age) were used for the experiments. Animals were anaesthetized with urethane (1.5 g/kg; i.p.) and held under urethane anesthesia during the entire course of the experiments. Treatment conformed to the National Institution of Health Guide and Care for Use of Laboratory Animals NIH guidelines; all experiments were approved by the German Animal Care and Use Committee. The skull was opened over the right hemisphere, the dura mater was removed and the exposed brain was covered with silicon oil. To prevent eye movements, the contralateral eye was fixated using a wax-coated blackened brass ring attached to the eye. After initial treatment with antibiotic eye-drops (Polyspectran) and atropine sulfate (0.5%), the eyes were rinsed regularly using sterile 0.9% NaCl solution. Body temperature measured rectally was kept at 37.5°C using a feedback-controlled heating pad. In most of the experiments, heart rate was continuously monitored. After the experiments animals were killed under deep anesthesia.

Data acquisition and visual stimulation

Multi-unit activity was recorded extracellularly using glass microelectrodes filled with 3 M NaCl in layer IV of primary visual cortex (area 17). As a rule, electrode penetrations were made about 4 mm lateral and 7.5 mm caudal from bregma corresponding to area 17 (Espinoza and Thomas 1983; Paxinos and Watson 1998; Schober and Winkelmann 1975). Besides that we do not have more information about the absolute position of RF centers in visual field coordinates. Recording depth varied between 550 and 850 µm. Spikes were separated by amplitude discrimination, and the data were stored on a computer hard disk for further analysis. Visual RFs were first located by hand-plotting, and then quantitatively mapped using a response plane technique. 36 square-shaped light stimuli (6 × 6 degrees of visual angle each) were displayed at different locations within a 6 × 6 grid on a 120-Hz computer monitor. Brightness of the stimuli was 3.4 cd/m^2; background illumination was 0.002 cd/m^2. Each stimulus was presented 24 times in a randomized order (duration 25 ms; interstimulus interval 750 ms). The responses to the stimuli at the different positions were summated over the trials to compute post-stimulus time-histograms (PSTHs).

Somatosensory cortex recordings

For an areal and modality comparison, we recorded neurons in the hindpaw representation of somatosensory cortex (SI) after a unilateral craniotomy over the paw representations of primary somatosensory cortex and resection of the dura. The location and the extent of cutaneous RFs on the glabrous skin of the hindpaws were determined by hand-plotting (for details see David-Jürgens et al. 2008). For

quantitative analysis of neuron responses, a mechanical stimulator was used to apply computer controlled tactile stimuli of 8 ms duration at 1 Hz at the RF centers that were summated over 32 trials.

ICMS protocol

To allow comparison with previous ICMS studies, the stimulation parameters were the same as initially introduced by Nudo et al. (1990). ICMS consisted of trains of 13 capacity-coupled current pulses (duration 200 µs, ISI 3 ms, amplitude 6–12 µA, generated by a Master-8 pulse generator) that were delivered at 1 Hz for 2–3 h through the recording glass electrode (Science Products, Germany) at a selected site by means of a WPI stimulus isolation unit (1–2 MΩ, tip diameter approximately 10 μ). It should be noted that in earlier experiments in cat area 18, both glass microelectrodes and quartz glass-coated platinum/tungsten microelectrodes had been used (Godde et al. 2002). RFs were repeatedly measured in intervals of 1 h before and then after ICMS. After termination of ICMS following a pause of several minutes the RF was re-determined. To rule out unspecific effects of the procedure sham experiments were performed in which RFs were repeatedly monitored for several hours without applying stimulation current through the electrode.

Data analysis

For determining RF-size, the response amplitude as integrated from 20 to 180 ms after stimulus onset were calculated for each of the 36 stimulus positions and plotted in a 6 × 6 grid as gray-scale or color-coded plots using custom-written IDL™ software. After linear interpolation, the area where more than 50% of the maximum activity was elicited by visual stimulation was determined for each cell, and used as a measure for RF-size which was expressed as degrees of arc^2. To investigate in how far changes of RF size depend on different activity levels in the center and in the surround of a RF, we additionally analyzed the data using thresholds of 25 and 75% to detect contributions from different regions within the RF.

The temporal structure of visual neuron responses was analyzed by constructing cumulative PSTHs with a temporal resolution of 5 ms (responses of neurons recorded in SI were analyzed using 1-ms bins). The time-resolved development of visual RF-size was studied using the time-slice technique (Dinse et al. 1990), in which RF-size was computed for consecutive 20-ms time steps, thus constructing a spatiotemporal two-dimensional RF-profile. For the type of flashed stimuli used, this approach is equivalent to reverse correlation methods (de Boer and Kuyper 1968). Activity was normalized to maximal activity of a recording site, which allows comparison of activity levels pre versus post. Statistical analysis was performed by Student's paired *t* test.

Results

We measured receptive fields (RFs) using the response plane technique. Average RF-size as defined as the area in which stimulation elicited more than 50% of the maximum activity was 303.2 ± 29.8 (SEM) degrees of arc^2 (n = 35), which is in the normal range of rat RF size as described earlier for albino rats (Burne et al. 1984; Girman et al. 1999; Shaw et al. 1975). Out of these, 27 cells were studied before and after application of the ICMS protocol. Eight cells were used as controls and were tested under sham stimulation conditions. For areal and modality comparison, in three additional animals (Dark Agouti), the identical ICMS protocol was applied in somatosensory cortex. In addition, we used unpublished data of seven ICMS experiments performed in the somatosensory cortex of adult male Sprague–Dawley rats. Results from both strains revealed equivalent results.

Effects of ICMS on RF size of neurons recorded in visual cortex

As a first step, we analyzed the size of all RFs tested before and after ICMS by temporally averaging neural responses between 20 and 180 ms after stimulus onset. After ICMS we observed a moderate increase of RF size. On average, visual RFs enlarged by 15.3% (pre 278.6 ± 31.6 degrees of arc^2; post 321.2 ± 37.4 degrees of arc^2; n = 27; P = 0.035; Fig. 1a). To get insight into possible constraints controlling visual RF plasticity, we analyzed how the ICMS-induced changes depended of the pre-ICMS RF size (Fig. 1b). The largest changes were observed for initially small RFs, which were predominantly enlarged, although a considerable portion was not affected by ICMS. In contrast, an about equal proportion of large RFs showed either a small enlargement or no effects or even a reduction in size.

To further quantify this behavior, we subdivided the recorded set of RFs based on the above described analysis into small (<250°) and large RFs (>250°). This analysis corroborated a substantial increase in size for small but not for large RFs. Figure 2 illustrates examples of a small (Fig. 1a) and a large RF (Fig. 1b) as contour plots of temporally averaged neural response recorded before and after termination of 2 h of ICMS. On average, for small RFs (<250) we found pre-ICMS 161.8 ± 11.1 degrees of arc^2 and post-ICMS 238.6 ± 26.9 degrees of arc^2 (n = 16; P < 0.0005). In contrast, large RFs showed a non-significant increase from 411.1 ± 25.9 degrees of arc^2 to

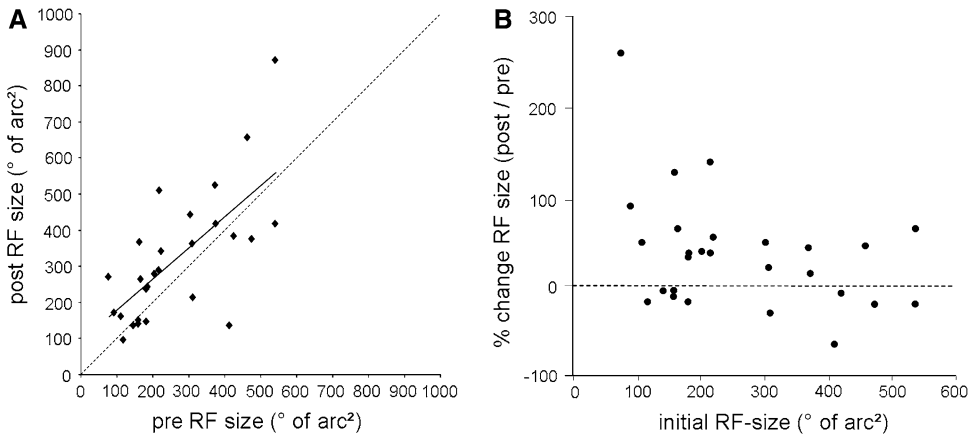

Fig. 1 **a** *Scatter-plot* of pre- and post-RF size with regression line ($R^2 = 0.475$) for all recorded RFs. ICMS resulted in a significant expansion of RF size ($P < 0.05$). **b** Baseline-dependence of RF-size changes. *Scatter-plot* of percentage of change of RF-size after ICMS (post/pre) as a function of initial pre-ICMS RF-size

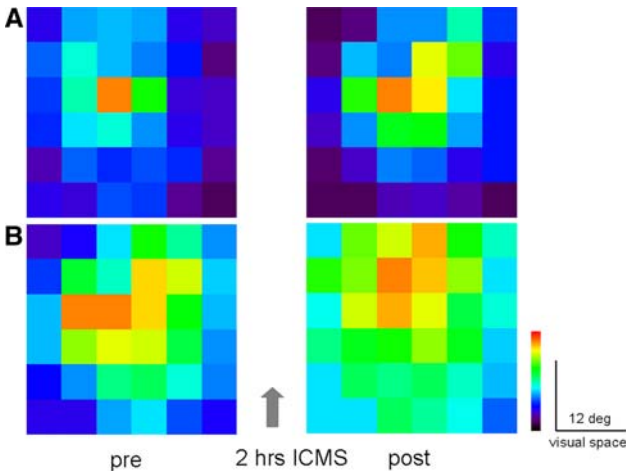

Fig. 2 Examples of visual receptive fields recorded in area 17 before and after ICMS. Shown are response planes as *contour plots* for a RF smaller (**a**) and larger than 250° of arc^2 (**b**) recorded before (pre) and after termination of 2 h of ICMS (post). *Contour plots* were obtained after temporally averaging neural responses between 20 and 180 ms after stimulus onset. *Color code* indicates normalized activity levels with *blue* indicating low and *red* high activity. The 6 × 6 grid of *square-shaped* light stimuli covered a total of 36 × 36 degrees of visual angle

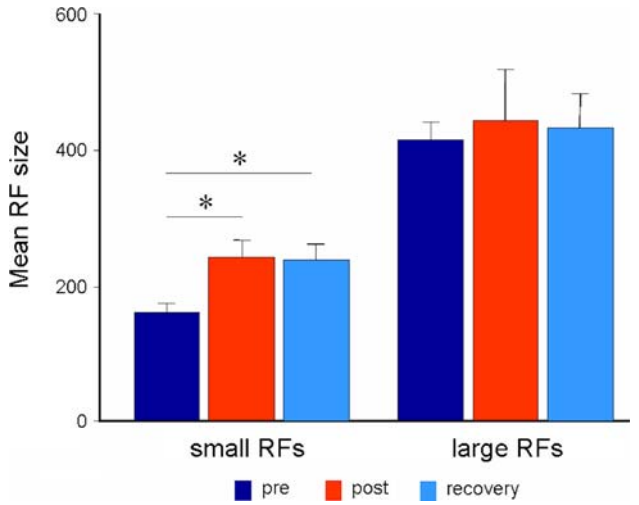

Fig. 3 Mean RF-sizes in degrees of arc^2 (±SEM) pre and post-ICMS for RFs smaller ($n = 16$) and larger than 250° of arc^2 ($n = 11$). A significant expansion of RF size occurred only for initially small RFs (*$P < 0.0005$). In addition, RF sizes are shown for the observation period 3–6 h after termination of ICMS, which, for small RFs, revealed no indication of recovery to baseline ($n = 12$; pre vs. recovery $P < 0.001$; post vs. recovery $P > 0.1$)

437.1 ± 60.1 degrees of arc^2 after ICMS ($n = 11$, $P > 0.1$), see also Fig. 3. Accordingly, small RFs increased by 52.7 ± 17.9%, whereas large RFs changed only by 6.3 ± 12.0% ($P < 0.05$). These data suggest that ICMS had no uniform effect on RF size, but the magnitude of changes appeared to be largely determined by the pre-ICMS size. Assuming that the size of RFs is controlled by mechanisms such as inhibitory surrounds and subthreshold contributions, the results suggest a differential sensitivity of RF organization to plastic changes.

Results of sham stimulation control experiments

In the sham-stimulation control experiments no changes in RF-size were found post-sham-ICMS (pre 404.8 ± 67.6 degrees of arc^2; post 400.6 ± 67.1 degrees of arc^2; $n = 8$). Seven of these neurons had large RFs according to the criterion used above. For the remaining neuron with a small RF no changes were found as well (pre-sham-ICMS 163.3, post-sham-ICMS 164.6 degrees of arc^2).

Effects on the temporal structure of visual neuron responses

In order to examine how the temporal response profile of area 17 neurons was affected by ICMS, we analyzed the time structure of neuron responses following visual stimulation before and after ICMS by constructing cumulative PSTHs, which illustrate the population activity of all cells tested. To account for differential effects of RF size as demonstrated above, we separately analyzed small and large RFs (Fig. 4). This analysis revealed that the time structure of the responses of cells with small RFs remained largely

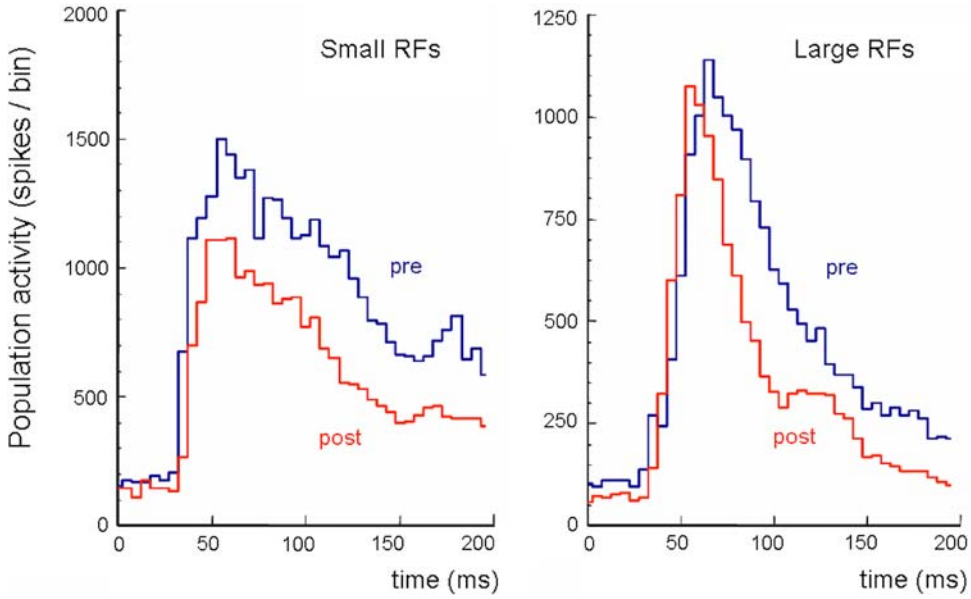

Fig. 4 Cumulative PSTHs showing population activity following visual stimulation of the RFs obtained after pooling all neuron responses separately for all RFs smaller ($n = 16$; *left*) and larger than 250° of arc^2 ($n = 11$; *right*). Time course of population activity before (*blue*), and after ICMS (*red*)

unaffected by ICMS, although the overall responsiveness was slightly reduced. In contrast, in cells with large RFs the magnitude of the peak response was not affected by ICMS; however, the latency of responses was shortened and the late response components were suppressed resulting in an overall shortening of the response duration.

Spatiotemporal dynamics of visual receptive fields

To evaluate how the described changes in the temporal structure of the neuron responses in area 17 affect the spatiotemporal development of RFs, we analyzed their dynamics in a time resolved manner. Figure 5 shows an example of the ICMS-induced changes of the dynamic structure for a neuron with a large RF plotted in 20-ms time steps pre- and post-ICMS; time interval between recordings of time-resolved contour plots was 1 h. After 2 h of ICMS, the temporal development of the activity within the RF was altered: The RF builds up and decayed faster than pre-ICMS. In terms of RF dimensions, the size of the RF during the early response episode (40–60 ms) was enlarged but markedly reduced during the late episodes (>80 ms). We found no recovery of this effect within the period of 3–6-h post-ICMS for neurons of rat visual cortex. Analysis of neurons with small RFs revealed no changes of the temporal structure which is consistent with the unchanged population activity post-ICMS shown above (Fig. 4).

To analyze the ICMS-effects on the spatiotemporal structure in more detail, we calculated the time resolved RF-size pre- and post-ICMS for the group of neurons with small and large RFs and for the sample of neurons that underwent sham-stimulation. As illustrated in Fig. 6a, for neurons with small RFs no significant effects of ICMS on the time resolved RF-size were found. In contrast, for neurons with large RFs we found that during the early response episodes 40–60 ms after stimulus onset, the averaged RF-size was enlarged by 221% ($P < 0.005$, $n = 11$; Fig. 6b). No changes were found for the next time step 60–80 ms ($P > 0.5$). However, during the late response episodes 80–100 and 100–120 ms after stimulation, we found a significant reduction of RF size by 52 and 85%, respectively ($P < 0.001$). For the group of sham-stimulated neurons, no significant changes were observed (Fig. 6c).

To determine the extent of changes of RF portions characterized by different activity levels, we reanalyzed the data by thresholding the evoked activity at 25, 50 and 75% of maximal activity. While 25% thresholded areas show effects from peripheral, low activity portions of the RF, 75% thresholded areas largely capture the effects coming from central RF domains. Our analysis revealed that the ICMS-induced changes are essentially carried by all RF portions (Fig. 7 for large RFs). However, the strong suppression of responses apparent during the late response episodes appears particularly due to shrinkage of peripheral, low-activity RF domains.

Recovery of ICMS-induced effects

We assessed RF size up to 3–6 h after termination of ICMS to obtain information about the stability and duration of ICMS-induced effects in rat visual cortex. We observed no recovery from the effects within our observation period (Figs. 3, 5). On average, during the recovery period, the size of small RFs was 234.8 ± 23.35 degrees of arc^2 ($n = 12$; pre vs. recovery $P < 0.001$; post vs. recovery $P > 0.1$), while the size of large RFs was 425.3 ± 44.5

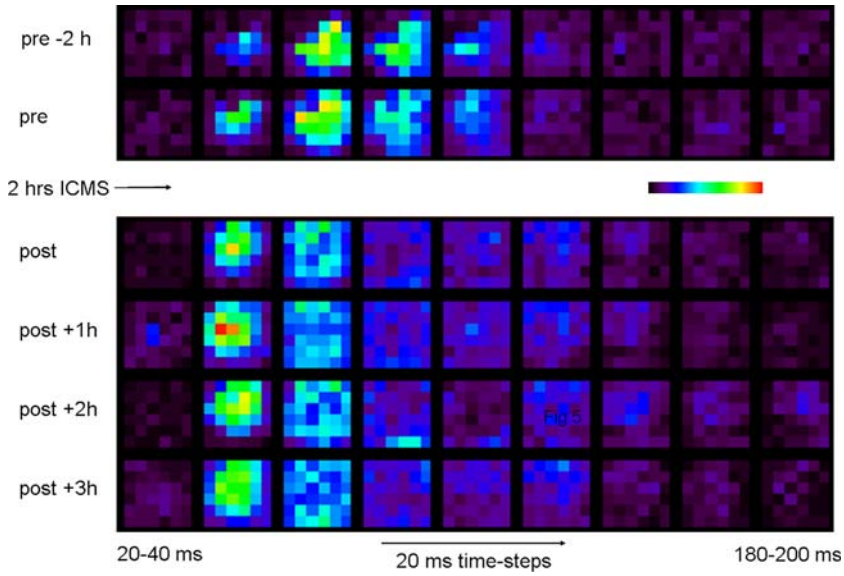

Fig. 5 Example of the temporal development of a large visual RF pre- and post-ICMS. Shown are *contour plots* of the response planes for successive 20-ms time steps covering 20–200 ms after stimulus onset. Each *row* represents the measurement of response planes during one trial. Shown are two trials before ICMS separated by 2 h to illustrate stability of activation. The next four *rows* show measurements after ICMS separated by 1 h, starting immediately after termination of ICMS. ICMS-induced changes are present after 3 h indicating little reversibility of the effects within the observation period. *Color code* indicates normalized activity levels with *blue* indicating low and *red* high activity. The 6 × 6 grid of *square-shaped* light stimuli covered a total of 36 × 36 degrees of visual angle

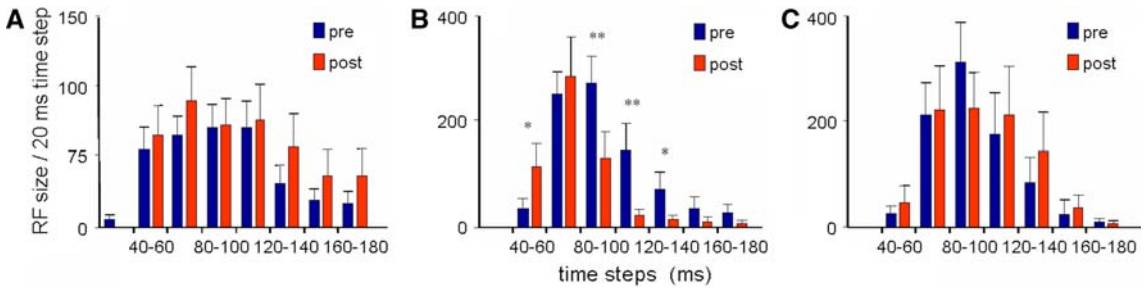

Fig. 6 Quantitative analysis of the mean time course of RF-sizes in degrees of arc^2 (±SEM) pre (*blue*) and post (*red*) ICMS for small RFs ($n = 16$; **a**), large RFs ($n = 11$; **b**), and for RFs before and after sham-ICMS ($n = 8$; **c**). *Abscissa* gives time from 40–60 to 160–180 ms in steps of 20 ms. *Asterisks* indicate significant differences between pre- and post-ICMS (*$P < 0.005$, **$P < 0.001$)

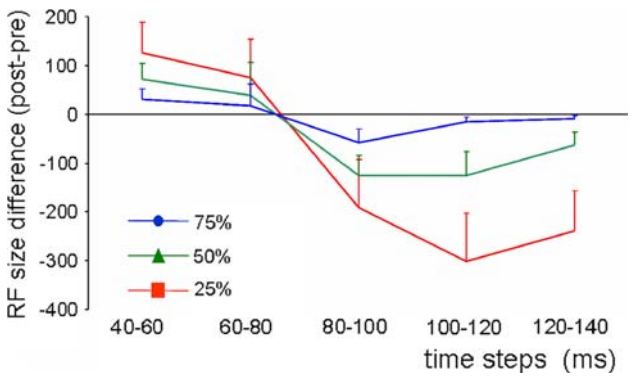

Fig. 7 Quantitative analysis of the time course of averaged differences of RF-sizes (post–pre) for all large RFs ($n = 11$). *Abscissa* gives time from 40–60 to 120–140 ms in steps of 20 ms. Shown are three conditions of thresholding activity at 75% (*blue*), 50% (*green*) and 25% (*red*)

degrees of arc^2 ($n = 7$, pre vs. recovery $P > 0.1$; post vs. recovery $P > 0.1$).

Effects of ICMS on RF size of neurons recorded in somatosensory cortex (SI)

To confirm the capability of ICMS to induce substantial reorganizational changes of RFs of rat primary somatosensory (SI) cortex, we applied the identical stimulation protocol in the same strain of rats of the same age in the hindpaw representation of SI cortex (Fig. 8). 2 h of ICMS lead to a severalfold increase in the size of the cutaneous RFs as determined by hand-plotting. About 4 h after termination of ICMS, there was a clear trend for RF-size to return to control values confirming the reversibility of the effect as described earlier (Benali et al. 2008; Dinse et al. 1997;

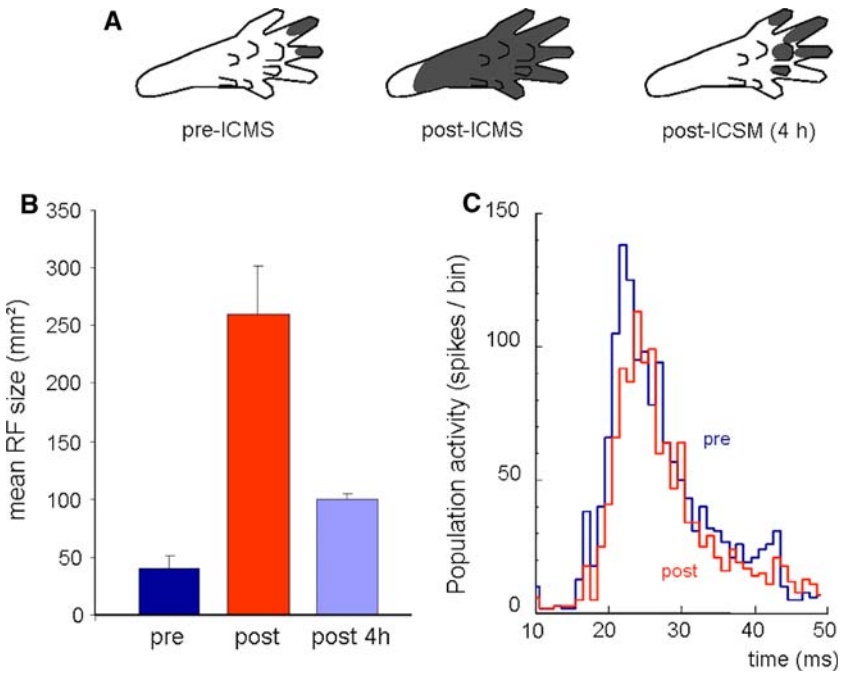

Fig. 8 ICMS in somatosensory cortex. **a** Example of a cutaneous RF (*black*) on a figurine of the hindpaw as determined by hand-plotting recorded in somatosensory cortex before (pre-ICMS), immediately after (post-ICMS), and 4 h after termination of ICMS (post-ICMS 4 h). **b** Average RF size in mm^2 skin surface (±SEM) for pre-ICMS (*dark blue*), post-ICMS (*red*), and 4 h after termination of ICMS (*light blue*). **c** Cumulative PSTH showing population activity following tactile stimulation to the RFs obtained after pooling all neuron responses. Time course of population activity before (*blue*) and after ICMS (*red*)

Spengler and Dinse 1994). Averaged RF size on the hindpaw increased from pre-ICMS 39.9 ± 11.1 mm^2 to 260.3 ± 40.7 mm^2 after ICMS and recovered to 99.9 ± 4.6 mm^2 4 h after termination of ICMS.

We also analyzed the time structure of responses in SI, using the neurons' responses to computer controlled tactile stimuli (Fig. 8c). In general, responses recorded in SI were characterized by shorter latencies and shorter durations making them more transient than the responses recorded in area 17. In contrast to the findings described for area 17, after ICMS changes in the time structure of SI neurons were observed neither for latency nor for the duration of the responses.

Discussion

We used intracortical microstimulation (ICMS) to study the plastic capacities of neurons recorded in layer IV of adult rat area 17. Generally, ICMS-effects depended on the RF-size assessed pre-ICMS. For initially small RFs, 1–2 h of ICMS leads to an expansion, while initially large RFs remained unaffected. However, inspection of the time course of the responses revealed that for large RFs early response components were enhanced, while late response components were reduced. These changes of the temporal structure were reflected in changes of the spatiotemporal properties of RFs.

ICMS has been frequently used in the somatosensory, auditory and visual system as a tool to induce plastic changes of RFs and cortical representational maps. In the visual cortex of adult cats, a few hours of intracortical microstimulation (ICMS) have been shown to result in an enlargement of the cortical representational zone at the ICMS site and an extensive restructuring of the layout of orientation preference maps up to several millimeters away, paralleled by dramatic changes of pinwheel numbers and locations (Godde et al. 2002). Another study examined the nature and extent of reorganization induced by repetitive electrical stimulation in V1 of adult cats, which found that RF size can be increased. However, the effects were reported to be small in magnitude (Warren and Normann 2005).

The ICMS protocol differs from conventional methods of low- or high-frequency stimulation to induce synaptic plasticity such as long-term potentiation (LTP) or long-term depression (LTD). When used in a slice preparation of adult rat somatosensory cortex, it was reported that ICMS close to the stimulation site evoked a depression of local field potentials implying a distinct form of synaptic depression of excitatory mechanisms (Heusler et al. 2000).

It had been suggested earlier that mechanism that can account for ICMS-induced changes found in SI results are those entailing either sprouting of axons and/or dendrites and the creation and elimination of synapses, or a mechanism of strengthening and weakening of existing synapses (Recanzone et al. 1992a). While the observation period of several hours may be too short for promoting axon sprouting, growth of synapses has been reported to occur following application of LTP-protocols within a short period of time (Engert and Bonhoeffer 1999, but has so far not been linked to ICMS effects.

Evidence for changes of synaptic transmission comes from a study, where ICMS application has been combined with immunohistochemical methods in the same individual animals to investigate how plasticity of cortical maps in rat somatosensory cortex is linked to changes in the spatial distribution of inhibitory and excitatory neurotransmitters (Benali et al. 2008). These data revealed a differential spatiotemporal pattern of upregulation and downregulation of specific factors for the glutamatergic and the GABAergic system, which developed in parallel to changes of RF size in SI. Close to the stimulating electrode a reduction of the calcium-binding protein parvalbumin was observed in inhibitory neurons as well as a low expression of the activity marker c-Fos. In contrast, reorganization in the hindpaw representation and in the adjacent SI cortical areas was accompanied by a major increase of the excitatory transmitter glutamate and c-Fos. Interestingly, RF size increased in both zones indicating that different mechanisms might yield the same net effects observed at a level of RFs. At present, it remains elusive whether similar results hold for visual cortex.

Our data confirm substantial plastic capacities of adult visual cortical neurons, although RF size was affected for only a subset of the neurons with smaller initial RFs. On the other hand, reorganizational changes induced by an identical ICMS protocol applied in the same animal in SI also revealed differences. For example, while only a subpopulation of initially small visual cortical RFs increased in size by approximately 50%, RFs recorded in somatosensory cortex increased by more than 100% independent of their initial size. On the other hand, for visual cortical neurons with large RFs, the time-structure of neuron responses to visual stimulation was changed, an observation, which could not be made for plastic changes in SI. Another difference was that the RF changes in area 17 neurons were not reversible within the observation period of 3–6 h after ICMS-termination. This finding is in agreement with the data reported obtained in VI of adult cats, were in most cases ICMS-induced changes of orientation preference maps did not fully recover even up to 18 h after termination of ICMS (Godde et al. 2002). In contrast, RF enlargement of neurons recorded in somatosensory cortex typically recovers to baseline within a few hours (Dinse et al. 1993, 1997; Spengler and Dinse 1994). Combined, these observations point to the existence of area or modality-specificities of plastic changes (cf. Dinse and Böhmer 2002; Seitz and Dinse 2007). It should be noted that the comparison between VI and SI plasticity is largely based upon the striking similarities of RF organization found in visual, auditory and somatosensory areas with respect to the spatiotemporal distribution of excitation and inhibition (Dinse and Schreiner 2002). However, a quantitative comparison allowing for statistical evaluation is hindered by limitations to infer equivalences in stimulation energies.

Activity-dependent synaptic plasticity had been compared in vivo in two cortical areas of the adult monkey visual system. While discontinuous high-frequency electrical stimulation of intrinsic horizontal connections in the inferotemporal cortex caused long-term potentiation of extracellular field potentials, the identical stimulation protocol evoked long-term depression in V1 (Murayama et al. 1997). Another study compared the effects of long-term potentiation of population spikes after tetanic white matter stimulation in auditory cortex (AI) and V1 and found that the amplitude of LTP in AI was twice that in VI, while no differences were found for low frequency stimulation (Kudoh and Shibuki 1997). Using receptor autoradiography significant differences in the lamina and area-specific distributions of various transmitter receptors were described (Scheperjans et al. 2005; Zilles et al. 2004). Using in situ hybridization different levels of expression of GAP-43 mRNA were found for integrative areas of the neocortex and for cortical areas involved in the initial processing of sensory information (Neve et al. 1988).

Further evidence for significant differences between visual and somatosensory plasticity comes from the field of perceptual learning. Although there is abundant evidence that training and practice lead to improvement of visual performance (Crist et al. 1997; Fahle and Morgan 1996; Fahle and Poggio 2002; Ito et al. 1998; Karni and Sagi 1991; Watanabe et al. 2001), the nature of how this improvement is coded cortically remains controversial. In the tactile domain, skill acquisition has been shown to be associated with map expansion in those cortical representations that received stimuli during perceptual learning. Importantly, there was a linear correlation between the individual amount of perceptual improvement induced by the training and the individual amount of cortical map expansion (Recanzone et al. 1992b). Similarly, imaging studies have provided evidence that extensive use and practice result in expansion of cortical representations in blind Braille readers (Pascual-Leone and Torres 1993) or string players (Elbert et al. 1995), which both are characterized by higher perceptual skills.

In the visual domain, subjects showed a marked improvement of orientation discrimination over days, which was highly specific for position and orientation suggesting a critical role of early visual areas (Schoups et al. 1995). Similar to the studies performed in SI, one could expect that there would be a recruitment of cells toward the trained orientation, which was, however, not the case. Instead, findings from firing behavior recorded in VI from monkeys trained in an orientation discrimination task revealed that the population of trained neurons, those that preferred the trained orientation, exhibited a lower firing rate than the neurons preferring other orientations (Schoups et al. 2001). To examine how neuronal response properties

in the early visual system may change with practice, monkeys were trained in another study for more than 6 months in an orientation discrimination task. During training the monkeys' performance gradually improved; however, in most respects RF properties in the representations of the trained and untrained regions were indistinguishable (Ghose et al. 2002). According to more recent studies, during the first few weeks of visual texture discrimination training, both brain activation in a V1 subregion corresponding to the trained visual field quadrant and task performance increased. However, several weeks later, while performance level was maintained, brain activation decreased to the level observed before training suggesting that V1 in adults is causally related to acquisition of visual skills (Yotsumoto et al. 2008).

To conclude, our results show that a subset of RFs recorded in adult visual cortex can undergo significant changes; however, there is also evidence that ICMS-induced plastic changes differ in many aspects from those evoked in SI cortex. Conceivably, there are differences in cellular, pharmacological and histochemical properties between sensory cortical areas that might reflect modality-specific adaptations of processing stimuli in different modalities, which might modulate and constrain plastic capacities. As a further possibility, we suggest that although VI and SI are regarded primary cortical areas, the type of preprocessing occurring subcortically and at the level of the retina renders VI and SI areas dissimilar in terms of their position within a hierarchy of bottom–up and top–down processing, thereby affecting the readiness and susceptibility for plastic reorganization.

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