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Layer- and Cell-Type-Specific Effects of Neonatal Whisker-Trimming in Adult Rat Barrel Cortex

Soo-Hyun Lee, Peter W. Land, and Daniel J. Simons
Department of Neurobiology, University of Pittsburgh, Pittsburgh, Pennsylvania

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Lee, S-H, Land PW, Simons DJ. Layer- and cell-type-specific effects of neonatal whisker-trimming in adult rat barrel cortex. *J Neurophysiol* 97: 4380–4385, 2007. First published March 28, 2007; doi:10.1152/jn.01217.2006. Tactile deprivation in rats produced by whisker-trimming early in life leads to abnormally robust responses of excitatory neurons in layer 4 of primary somatosensory cortex when the re-grown whiskers are stimulated. Present findings from fast-spike neurons indicate that presumed inhibitory cells fire less robustly under the same conditions. These contrasting effects may reflect altered patterns of thalamocortical input to excitatory versus inhibitory cells and/or changes in the strength of intracortical connections. Despite increased excitability of layer 4, neurons in layer 2/3 respond at control levels even after full whisker re-growth. Layer 4 synapses onto supragranular neurons may be permanently depressed as a result of neonatal sensory deprivation.

INTRODUCTION

Sensory experience influences the development of cortical sensory areas (for review, see Buonomano and Merzenich 1998; Feldman and Brecht 2005; Hensch 2005). In the rodent somatosensory system, neonatal whisker-trimming alters functional organization within cortical layer 4 (L4). Deprivation effects persist even after months of whisker re-growth during adulthood. In trimmed animals, regular-spike units (RSUs), presumed excitatory neurons, display higher spontaneous firing rates, more robust responses to whisker deflection, and weaker inhibitory interactions between neighboring whiskers (Rema et al. 2003; Shoykhet et al. 2005; Simons and Land 1987). These findings may reflect stronger excitation or reduced effectiveness of intracortical inhibition (but see Higley and Contreras 2007 for a different perspective regarding the origins of between-whisker inhibition). A recent in vitro study suggests that early whisker-trimming induces downregulation of intracortical inhibitory transmission (Jiao et al. 2006). To date, however, no in vivo information is available concerning the long-term effect of neonatal deprivation on the response properties of fast-spike units (FSUs), presumed inhibitory neurons.

Responses of layer 2/3 (L2/3) excitatory neurons in cortical columns corresponding to trimmed whiskers are less robust than normal (Allen et al. 2003; Celikel et al. 2004; Diamond et al. 1993; Glazewski and Fox 1996; Glazewski et al. 1998; Rema et al. 2003; Stern et al. 2001; Wallace et al. 2001). These smaller whisker-evoked responses are thought to reflect excitatory L4 to L2/3 synapses that are weaker in strength as a result of developmentally regulated, experience-dependent processes. In these latter studies, however, whiskers were allowed to regrow for a few days only, such that cortical function was assessed while deprivation was ongoing, albeit at a reduced level. Under these conditions, responses in L4 are either smaller than or equivalent in magnitude to those in control animals. With full regrowth, activity in L2/3 may be increased, as in L4. Alternatively, neonatal sensory deprivation may have different effects depending on cortical layer.

Here we use extracellular single-unit recordings of putative excitatory and inhibitory neurons (RSU and FSUs) to examine the receptive field properties of L4 and L2/3 neurons in adult rats the whiskers of which were trimmed for 30 days beginning at the day of birth and then allowed to regrow >30 days, a duration exceeding that required for full regrowth. Compared with normally reared animals, L4 RSUs fire more robustly, whereas FSUs respond less robustly than normal to regrown whiskers. Even though excitatory L4 cells are more responsive, firing rates of L2/3 neurons remain at control response levels. This latter finding is consistent with the hypothesis that L4–L2/3 excitatory synapses are permanently depressed as a result of low activity levels during development. Together, the findings demonstrate that sensory deprivation has different effects in the cortex depending on cell type and laminar location.

METHODS

Rat pups of both sexes were obtained from two pregnant rats (Sprague-Dawley strain, Harlan, Indianapolis, IN). Pups were randomly assigned either to a normally reared, control group or to an experimental group the whiskers of which were trimmed. All of the large whiskers (rows A-E, arcs 0–6) on the left side of the face were trimmed everyday for 30 days beginning the day of birth (Shoykhet et al. 2005; Simons and Land 1987). The whiskers were allowed to fully regrow for >30 days prior to electrophysiological recording. At the time of recording, the identity of the animal (trimmed vs. control) was unknown to the experimenter. All procedures were approved by the Institutional Animal Care and Use Committee.

Electrophysiological data were collected from 11 control (4 male) and 9 (3 male) trimmed rats according to methods described previously (see Shoykhet et al. 2005). Briefly, animals were anesthetized with 1.5–2.0% halothane during surgical preparation of a small craniotomy over the right barrel cortex. For neuronal recordings, halothane was discontinued, and fentanyl was used to maintain the animal in a lightly sedated state ($\sim$10 $\mu g \cdot kg^{-1} \cdot h^{-1}$ iv). Rats were immobilized with pancuronium bromide, warmed by a heating blanket, and artificially respired. The condition of the rat was monitored throughout the experiment by a computer program that continually assessed electroencephalogram, mean arterial pressure, arterial pulse rate, and the tracheal airway pressure waveform. At the termination of

Address for reprint requests and other correspondence: D. J. Simons, E 1440, Biomedical Science Tower, 200 Lothrop St., University of Pittsburgh, Pittsburgh, PA 15261 (E-mail: cortex+@pitt.edu).

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the recording session, rats were killed with pentobarbital sodium (Nembutal, 100 mg/kg iv) and perfused for cytochrome oxidase (CO) histochemistry (see Simons and Land 1987). The cortical hemisphere was sectioned tangentially, reacted for CO and stained with Nissl. Data are reported only for units recorded within CO-rich barrel centers for L4 or above them for L2/3; units recorded in or superficial to interbarrel septa are not included in the present analyses. L2/3 and L4 correspond to recording depths of 200–700 and 700–950 μm, respectively (Kyriazi et al. 1998).

Cortical extracellular single-unit recordings were obtained using double-barrel glass micropipettes (1 μm tip diameter; 5–10 MΩ impedance at 135 Hz) or similar impedance metal microelectrodes. Deposits of horseradish peroxidase or small lesions were made to mark selected recording sites or electrode tracks (see Simons and Land 1987). Data acquisition involved custom software that parsed and saved spike waveforms for subsequent analyses. Units were classified as RSUs or FSUs on the basis of the shape and duration of spikes (see Bruno and Simons 2002; Simons 1978).

Whisker stimulation and data analysis

A hand-held probe was used to identify the whisker most effective at evoking activity in an isolated cell, i.e., the principal whisker (PW). This and the four immediately adjacent whiskers (AWs) were separately deflected using a piezoelectric stimulator attached to the whisker hair 10 mm from the skin (Simons and Carvell 1989); deflections consisted of 1-mm displacements of 200-ms duration with average onset and offset velocities of ~15 m/s. Whiskers were deflected using ramp-and-hold movements delivered in 10 randomized blocks of eight cardinal directions. Unit responses were compiled into peristimulus time histograms (PSTHs) having 1-ms bin width and quantified as the average number of spikes per stimulus during selected time periods. Responses to stimulus onsets (ON) and offsets (OFF) were computed during a 25-ms period after the beginning of whisker movement away from or back to its resting position. Spontaneous activity of each unit was subtracted from evoked sensory responses where noted. Spontaneous activity was measured during a 100-ms period before stimulus onset. Plateau responses were computed for 100 ms between ON and OFF responses. For direct comparison with ON and OFF responses, spontaneous and plateau responses were normalized to 25 ms. Angular tuning was quantified as the ratio of the response evoked by the maximally effective deflection angle to the average response over all eight angles. Magnitudes of OFF responses relative to ON responses, i.e., OFF-ON ratios, were also examined because previous studies have shown them to be indicative of overall circuit excitability (Kyriazi et al. 1994).

Data were analyzed using Microsoft Excel/visual Basic and Matlab (The MathWorks, Natick, MA). Due to deviations from normality in the distributions of data, statistical significance was evaluated with nonparametric Mann-Whitney *U* test unless otherwise noted. Means ± SD are given throughout text. Results are displayed as means ± SE.

RESULTS

We analyzed 280 units, 143 from control and 137 from trimmed animals. Of the former, 33 RSUs and 44 FSUs were recorded in L4 and 43 RSUs and 23 FSUs in L2/3. In trimmed animals, 45 RSUs and 38 FSUs were sampled in L4, and 37 RSUs and 17 FSUs in L2/3. Reported units were recorded within CO-rich barrel centers for L4 or above them for L2/3.

Effects of neonatal whisker-trimming on RSUs

Consistent with previous studies (Rema et al. 2003; Shoykhet et al. 2005; Simons and Land 1987), whisker-trimming from P1 to P30 significantly increases stimulus-evoked responses and spontaneous activities of RSUs in L4. L4 RSUs in trimmed animals show greater ON, OFF, and plateau responses (Fig. 1*A*, control vs. trimmed, ON: 0.48 ± 0.12 vs. 0.72 ± 0.17 spike/stimulus, $P = 0.0003$; OFF: 0.27 ± 0.12 vs. 0.51 ± 0.19, $P = 0.0001$; plateau: 0.05 ± 0.05 vs. 0.08 ± 0.05, $P = 0.001$). Whisker-trimming also leads to spontaneous activities of L4 RSUs that are approximately twofold greater (0.92 ± 0.72 vs. 2.36 ± 1.86 Hz, $P = 0.002$). To verify that the increased stimulus-evoked responsiveness of L4 RSUs in trimmed animals is not due to higher background firing, we subtracted each unit's spontaneous activity count from its ON and OFF response magnitude. Corrected responses of L4 RSUs were still significantly larger in trimmed than in control animals, the one exception being plateau responses which are normally barely above background levels (data not shown). Increased responsiveness in trimmed animals was disproportionately greater for normally weaker responses, e.g., those

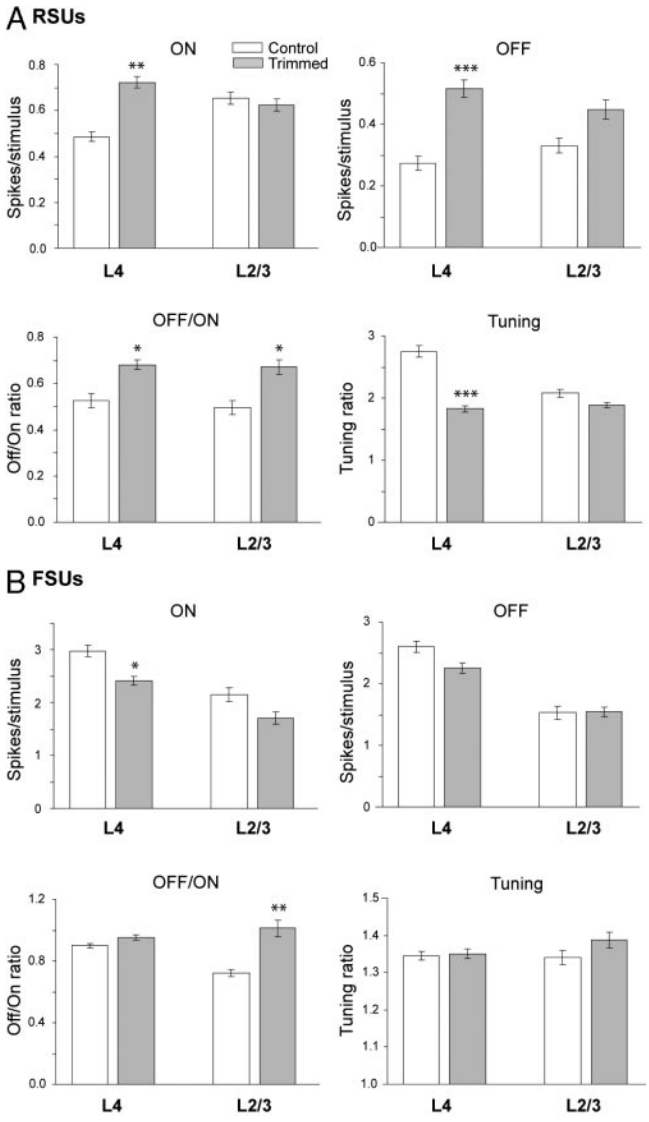

FIG. 1. Effects of whisker trimming on response properties of regular spike units (RSUs, *A*) and fast spike units (FSUs, *B*) in L4 and L2/3. Open bars indicate control animals; gray bars trimmed. Error bars indicate means ± SE. *P*, *<0.05, **<0.005, ***<0.0005.

evoked by whisker deflection offsets versus onsets or by nonpreferred versus preferred angles of whisker deflection. As a result, L4 RSUs from trimmed animals show significantly higher OFF-ON ratios (Fig. 1*A*, control 0.53 ± 0.17, trimmed 0.68 ± 0.14, $P = 0.02$). Similarly, angular tuning of L4 RSUs in trimmed animals is decreased (Fig. 1*A*, tuning ratios; 2.75 ± 0.51 vs. 1.82 ± 0.31, $P = 0.00001$).

In contrast to the effects of deprivation on L4 RSUs, responses of L2/3 RSUs in trimmed animals are comparable in magnitude to those from controls (Fig. 1*A*). ON, plateau, and spontaneous activities in trimmed animals are similar to those from controls (control vs. trimmed: ON, 0.65 ± 0.17 vs. 0.62 ± 0.16 spike/stimulus, $P = 0.27$; plateau, 0.08 ± 0.06 vs. 0.10 ± 0.06, $P = 0.09$; spontaneous, 3.09 ± 2.74 vs. 2.36 ± 1.53 Hz, $P = 0.17$). Again, similar findings obtained when spontaneous firing rates were subtracted from evoked responses. Responses to stimulus offset were slightly increased (0.33 ± 0.15 vs. 0.44 ± 0.19 spike/stimulus, $P = 0.055$) and the increase was even more robust when data were corrected for spontaneous activity. In both cases, increased OFF responses were reflected in a larger OFF-ON ratio for units in trimmed animals (0.67 ± 0.19 vs. 0.49 ± 0.20, respectively, $P = 0.01$). No difference was observed in the angular tuning ratios of L2/3 RSUs in control versus trimmed animals.

Effects of neonatal whisker-trimming on FSUs

Whisker-trimming effects on L4 FSUs are the converse of those on L4 RSUs. L4 FSU ON responses are significantly reduced in trimmed animals despite their elevated spontaneous activities (Fig. 1*B*, ON: 2.98 ± 0.70 vs. 2.42 ± 0.52 spike/stimulus, $P = 0.034$; spontaneous activity: 15.5 ± 5.06 vs. 20.9 ± 7.35 Hz, $P = 0.05$). L4 FSU OFF and plateau responses from trimmed animals are somewhat smaller at trend levels (Fig. 1*B*, OFF: 2.6 ± 0.6 vs. 2.24 ± 0.52 spike/stimulus, $P = 0.063$; plateau: 0.72 ± 0.30 vs. 0.52 ± 0.18, $P = 0.05$). No differences were observed between units in control and trimmed animals for OFF-ON ratios and angular tuning ratios. Note that L4 FSUs in normal animals are normally poorly tuned for deflection angle and also that OFF and ON responses are normally nearly equivalent in size.

As in the case of L2/3 RSUs, ON and OFF response magnitudes and spontaneous activities of L2/3 FSUs are unaffected by whisker-trimming (Fig. 1*B*: control vs. trimmed, ON 2.15 ± 0.63 vs. 1.71 ± 0.43 spike/stimulus, $P = 0.18$; OFF, 1.53 ± 0.48 vs. 1.55 ± 0.30, $P = 0.2$; spontaneous 15.16 ± 7.19 vs. 13.3 ± 4.54 Hz, $P = 0.46$), but plateau responses are somewhat smaller in trimmed animals (0.48 ± 0.20 vs. 0.27 ± 0.12 spike/stimulus, $P = 0.04$). OFF-ON ratios are higher in the latter, largely reflecting slight but not significantly decreased ON and increased OFF responses. Angular tuning of L2/3 RSUs and FSUs is unaffected, with both control and trimmed populations displaying poor tuning relative to L4 RSUs in control animals.

Together, the findings show that neonatal whisker deprivation differentially affects the responsiveness of RSUs and FSUs in L4 with RSUs displaying increased and FSUs decreased excitability. The apparent increase in excitatory output from the L4 barrel notwithstanding, response magnitudes of L2/3 cells remain largely unchanged. Similar results obtained for layer 4 and 2/3 FSUs when evoked firing rates were corrected for spontaneous activity.

Temporal profiles

We further examined the effects of whisker-trimming by characterizing the time course of whisker-evoked responses. We constructed a peristimulus time histogram (PSTH) for each cell and then computed a mean and variance for each 1-ms bin across the sampled unit population. These millisecond-resolution spike counts (plus SE) of ON responses in control and trimmed animals are shown in population PSTHs in Fig. 2. We compared control and trimmed PSTHs on a millisecond-by-millisecond basis using a nonparametric Mann-Whitney test. Bars at the bottom of the PSTHs indicate statistically significant differences in response magnitudes at each time (1-ms bin) point ($P < 0.05$).

In L4 RSUs, whisker-trimming leads to substantial elevations in response magnitude at the earliest time points, although population response latency remains unchanged. The duration of the response is also increased. To visualize better the temporal dispersion of the spikes independent of response magnitude, we normalized the number of spikes in each 1-ms bin by the total number of spikes occurring within the 25-ms ON response window for each neuron; this equalizes the areas of the control and trimmed PSTHs (Fig. 2, *insets*). Normalized population PSTHs confirm that the earliest component of the response in trimmed animals is relatively larger compared with controls. Similar effects are observed in L2/3 RSUs. In trimmed animals, however, the late component of the response (20–25 ms) is absolutely and relatively smaller. This accounts for the equivalent overall response magnitudes between L2/3 control and trimmed samples. During very early time points, the population response magnitude of L2/3 RSUs in trimmed animals is significantly increased as in L4.

FSUs again display somewhat different effects of whisker-trimming. In L4, the early component of FSU responses is increased only slightly, whereas most of the later time points of the response are smaller—not larger—in trimmed animals. As further illustrated by the normalized PSTHs, spikes in FSUs are more concentrated at early time points and diminished at late time points compared with those in control animals. PSTHs of L2/3 FSUs show a similar effect.

Receptive fields

Whisker-trimming also affects the spatial organization of receptive fields of RSUs and FSUs differently. Figure 3 shows AW/PW ratios obtained by separately deflecting the PW and its caudal AW; AW/PW ratios calculated on the basis of all-angle ON responses averaged for all four AW deflections show qualitatively similar results (data not shown). In agreement with previous studies, the receptive fields of L4 RSUs become spatially broader as a result of whisker-trimming, with the magnitudes of AW responses increasing more than those of the corresponding PWs (0.25 ± 0.07 vs. 0.41 ± 0.12, $P = 0.0009$). AW/PW ratios of L4 FSUs, however, do not differ between control and trimmed animals. Similarly, in L2/3, whisker-trimming is associated with broader receptive fields in RSUs (0.36 ± 0.17 vs. 0.71 ± 0.32, $P = 0.03$) but not in FSUs (0.72 ± 0.34 vs. 0.67 ± 0.36, $P = 0.95$).

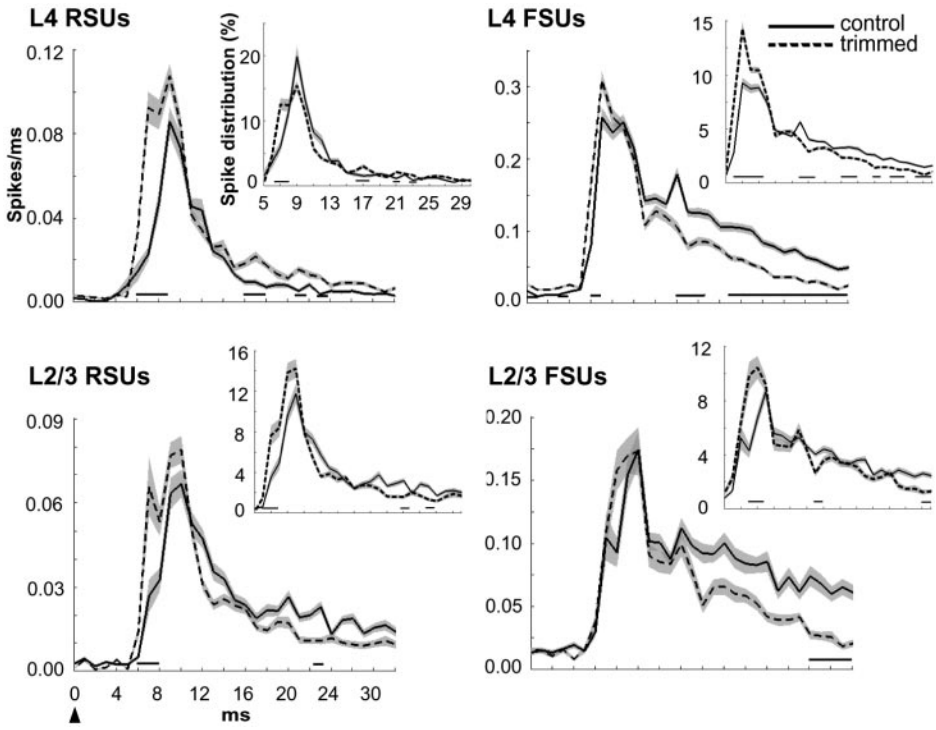

FIG. 2. Effects of whisker-trimming on temporal profiles of ON responses. Solid and dashed lines show population peristimulus time histograms (PSTHs) from control and trimmed animals, respectively. Gray shading represents SE (1-ms bin size). Bars just above the *x* axis indicate statistically significant differences ($P < 0.05$) in response magnitudes of control and trimmed at each millisecond. *Insets*: normalized population PSTHs. The number of spikes in each 1-ms bin is normalized by the total number of spikes occurring the 25-ms ON response window for each neuron. 0 ms = deflection onset.

The data in Fig. 3 are consistent with previous findings that the receptive fields of L4 RSUs are more spatially focused than those of FSUs (Bruno and Simons 2002; Kyriazi et al. 1998). Also, receptive fields of L2/3 RSUs are larger than those in L4 (Armstrong-James and Fox 1987; Simons 1978). Present findings show additionally in control animals that FSU receptive fields are broader in L2/3 than in L4. In general, these laminar- and cell-type-specific effects are qualitatively maintained in whisker-trimmed animals, the major difference being that RSU receptive fields broaden and thus become more similar to those of FSUs.

DISCUSSION

The present findings demonstrate that neonatal whisker-trimming followed by complete whisker regrowth leads to layer- and cell-type-specific effects within barrel-related columns of primary somatosensory cortex. Consistent with previous reports (Shoykhet et al. 2005; Simons and Land 1987), RSUs (presumed excitatory cells) in deprived L4 barrels display abnormally high levels of spontaneous and stimulus-evoked activities. Also RSU firing is increased during the earliest few milliseconds of the ON response. Such early increases are not observed during GABA antagonism (Kyriazi et al. 1998), suggesting a role for increased activation by thalamocortical synapses (Simons and Land 1987 and see following text). By contrast, FSUs (presumed inhibitory neurons) respond less vigorously to whisker stimuli although their spontaneous activities are somewhat elevated relative to control values. Corresponding firing increases were not observed in supragranular neurons, many of which presumably receive direct L4 excitatory outputs (Feldmeyer et al. 2002; Lubke et al. 2003; Silver et al. 2003). Firing rates of L2/3 RSUs and FSUs in trimmed animals are similar to control levels. As in L4, however, neonatal whisker-trimming leads to less spatially focused receptive fields in L2/3 RSUs, reflecting a disproportionate increase in the strength of responses evoked by neighboring versus the columnar whisker. A similar disproportionate change in weak versus robust responses are produced by microiontophoretic application of GABA antagonists onto barrel cortex neurons, and this is accompanied by decreases in receptive field focus (Kyriazi et al. 1996a,b). Larger adjacent whisker could also reflect stronger activation of RSUs by multiwhisker thalamic inputs (see following text).

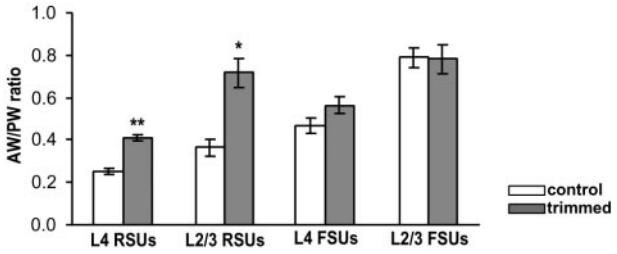

FIG. 3. Effects of whisker-trimming on receptive field focus. Adjacent: principal whisker (AW:PW) is the ratio of the ON response of the immediately caudal AW to that of each neuron's PW.

Neonatal whisker-trimming and regrowth, as employed here, leads to impairment in the ability of animals to perform some types of whisker-based tactile discriminations (Carvell and Simons 1996). Our finding of normal firing rates of L2/3 neurons is thus unexpected inasmuch as supragranular laminae constitute a major output of the barrel-related cortical column. Behavioral effects are, however, task dependent. Deprived animals are unimpaired on tasks that can normally be performed with only a single whisker but are severely deficient on discriminations that normally require the presence of two or more neighboring whiskers and hence spatiotemporal integration of their inputs. The latter deficits may reflect findings that whisker-trimming leads to abnormal response timing and larger receptive fields in L4 and 2/3 RSUs and, at least in L4,

weaker suppressive influences of neighboring whiskers (Shoykhet et al. 2005), which are likely reflected in L2/3 as well.

Increased responsiveness of L4 RSUs, together with decreased responsiveness of FSUs, renders L4 circuitry abnormally excitable in sensory deprived animals. Previous studies with whisker-trimming paradigms similar to that used here also report increased spontaneous and evoked responses of L4 RSUs (Rema et al. 2003; Shoykhet et al. 2005; Simons and Land 1987). Increased neuronal excitability has been observed also after visual or auditory deprivation (Kotak et al. 2005; Maffei et al. 2004). L4 FSUs, on the other hand, are significantly less responsive to stimulation of regrown whiskers despite the elevated activities of nearby excitatory neurons that likely synapse on them. Less-active FSUs could lead to abnormally high firing rates of RSUs. Increased RSU excitability may be due to a number of other factors as well, including altered intrinsic properties, stronger connections among excitatory barrel neurons and/or abnormal patterns of thalamocortical synaptic input (see following text). Neonatal whisker-trimming in mice has been reported to result in decreased numbers of TC synapses onto barrel neurons and reductions in the number of presumed inhibitory synapses (Sadaka et al. 2003), altered spike thresholds (Barth et al. 2004), downregulation of GABA receptors (Fuchs and Salazar 1998), and reduced inhibitory synaptic transmission in L4 (Jiao et al. 2006). Other studies in rats also report reductions in the number of inhibitory synapses (Micheva and Beaulieu 1995a,b, 1996). In conjunction with the findings of Sadaka et al., results suggest a decrease in the ratio of inhibitory to excitatory synapses of nonthalamic origin. All of these studies were, however, conducted without prior whisker re-growth and may thus reflect on-going effects of deprivation that might not be applicable to our experimental paradigm.

Firing rates of L2/3 neurons remain within their normal range in spite of increased excitability of L4 barrel circuitry. Many studies have reported decreased responses in L2/3 neurons in barrel-related columns corresponding to deprived whiskers (Allen et al. 2003; Celikel et al. 2004; Diamond et al. 1994; Glazewski and Fox 1996; Glazewski et al. 1998; Rema et al. 2003; Stern et al. 2001; Wallace et al. 2001). These effects are thought to reflect synaptic depression at excitatory L4 to L2/3 synapses (see also Bender et al. 2006). A common feature of all of these studies is that cortical function is assessed before the trimmed whiskers are fully regrown (see Shoykhet et al. 2005). In addition, some whiskers were removed while others remained intact. Such partial deprivation may allow stronger competitive interaction between spared versus deprived barrel columns. The current findings using an all-whisker deprivation paradigm and those from a related recent study (Shoykhet et al. 2005), however, are qualitatively similar to results obtained in deprived barrels situated adjacent to nondeprived barrels (Simons and Land 1987). Present results therefore suggest that, after whisker regrowth, synaptic weakening established during deprivation may persist, countervailing the effects of increased activity of excitatory L4 neurons. Control-level responsiveness of L2/3 neurons may additionally reflect changes in the L2/3 local circuitry itself. In this regard, L2/3 RSUs from trimmed animals display substantial reductions in the magnitudes of their late response components. Total response magnitude remains at control levels, however, because the quickest whisker-evoked responses are increased in size, similar to effects observed in L4 RSUs.

A decrease in the ratio of symmetric (inhibitory) to asymmetric (excitatory) synapses of cortical origin (see preceding text) could readily account for increased excitability of RSUs but not the decreased responsiveness of FSUs. In addition to loss of inhibitory synapses, Sadaka et al. report equivalent decreases in the numbers of thalamocortical synapses onto both spiny (excitatory) and smooth (inhibitory) cells. Assuming that such reductions in thalamocortical synaptic density occur in our paradigm of whisker re-growth, how could fewer (excitatory) thalamocortical synapses onto excitatory and inhibitory barrel cells lead to both a greater responsiveness of RSUs and a decrease in responsiveness of FSUs? In barrels, responses of RSUs are tightly regulated by strong feedforward inhibition (Alonso and Swadlow 2005; Bruno and Simons 2002; Pinto et al. 2000, 2003; Wilent and Contreras 2004). Normally, the most strongly responsive thalamocortical (TC) neurons contact FSUs only and not RSUs (Bruno and Simons 2002), perhaps reflecting a developmentally regulated spike-timing-dependent process whereby the most active TCUs can maintain synapses only on (highly responsive) FSUs that have a high probability of firing in response to an incoming TC spike. Such spike-timing-dependent plasticity mechanisms were first described for excitatory synapses onto excitatory neurons (see Bi and Poo 1998), and similar effects may exist also at excitatory to inhibitory neuron connections (Lamsa et al. 2005). As suggested by Bruno and Simons, the bias of strongly active TCUs contacting FSUs could be diminished by whisker-trimming. During deprivation wherein thalamocortical activity levels are presumably reduced (Durham and Woolsey 1978; Kelly et al. 1999), RSUs, the intrinsically low firing rates of which are normally poorly matched to those of the most highly active TC cells, would now be successfully contacted by them; such contacts would be maintained when whiskers are allowed regrow later in life. Alternatively, synapses from highly active TCUs, which normally might be made on RSUs and subsequently eliminated through activity-dependent mechanisms, could remain with whisker trimming. This would require a mechanism wherein preexisting TCU-RSU synapses are normally removed as a result of temporally uncorrelated pre- and postsynaptic activities. For either case, a testable prediction is that neonatal whisker trimming and regrowth will result in the most highly responsive TCUs contacting RSUs and FSUs with more similar probabilities.

A redistribution of TC cell-specific synapses on excitatory barrel neurons would, on deflection of regrown whiskers, render RSU responses in trimmed animals more similar to those of FSUs in normal animals. RSUs would fire more robustly and increased spiking would occur early in the response. These effects might be observed even if the total numbers of thalamocortical synapses onto excitatory barrel neurons are reduced. Similarly, FSUs may respond less vigorously due to fewer TC synapses on them. Coupled with a diminution in local inhibition, changes in thalamocortical connectivity could lead to a net increase in barrel circuit excitability.

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