Emergence of Radial Nerve Dominance in Median Nerve Cortex After Median Nerve Transection in an Adult Squirrel Monkey

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Schroeder, C. E., S. Seto, and P. E. Garraghty. Emergence of radial nerve dominance in median nerve cortex after median nerve transection in an adult squirrel monkey. J. Neurophysiol. 77: 522–526, 1997. Throughout the glabrous representation in Area 3b, electrical stimulation of the dominant (median or ulnar) input produced robust, short-latency excitation, evident as a net extracellular “sink” in the Lamina 4 current source density (CSD) accompanied by action potentials. Stimulation of the collocated nondominant (radial nerve) input produced a subtle short-latency response in the Lamina 4 CSD unaccompanied by action potentials and followed by a clear excitatory response 12–15 ms later. Laminar response profiles for both inputs have a “feedforward” pattern, with initial activation in Lamina 4, followed by extragranular laminae. Such corepresentation of nondominant radial nerve inputs with the dominant (median or ulnar nerve) inputs in the glabrous hand surface representation provides a likely mechanism for reorganization after median nerve section in adult primates. To investigate this, we conducted repeated recordings using an implanted linear multi-electrode array straddling the cortical laminae at a site in “median nerve cortex” (i.e., at a site with a cutaneous receptive field on the volar surface of D2 and thus with its dominant afferent input conveyed by the median nerve) in an adult squirrel monkey. We characterized the baseline responses to median, radial, and ulnar nerve stimulation. We then cut the median nerve and chronically monitored radial nerve, ulnar nerve and median nerve input with minimal or no change. Using previously described methods (Schroeder et al. 1995), one squirrel monkey (Saimiri sciureus) weighing 0.6 kg was implanted with a plastic cranial pedestal to provide for head restraint and stabilization of the multi-electrode during repeated measurements. To approximate the conditions of micro-electrode mapping experiments, during recording, the monkey was anesthetized with a mixture of xylazine (10 mg/kg) and ketamine (30 mg/kg). Depth of anesthesia was monitored using palpebral and jaw reflexes. Body temperature was kept within normal limits using a water heating blanket.

Laminar CSD and multi-unit activity profiles were obtained by recording with a linear array multicontact electrode, positioned so as to straddle the cortex from the pial surface to the white matter. Tactile stimulation was used to define the cutaneous representation at the recording site and electrical stimulation then was used to quantify the strength, laminar distribution, and temporal pattern of median, ulnar, and radial nerve inputs. Electrical stimulation was provided by 100 μs, constant-current, square-wave pulses applied with bipolar electrodes to the skin of the forearm at points determined to permit isolated stimulation of individual nerves. Stimulation sites and appropriate current levels (2–3 mA) were determined from preliminary studies of nerve stimulation concurrent

METHODS

INTRODUCTION

The glabrous hand surface representation in somatosensory cortical Area 3b of primates appears to be divisible into median and ulnar nerve “territories” based on which peripheral nerve provides the dominant or obvious cutaneous input (Wall et al. 1993). Recently, Garraghty et al. (1994) and Schroeder et al. (1995) suggested that, in addition to its dominant input, the cortex within the glabrous surface representation also receives cryptic or nondominant inputs from the dorsal hand surface, conveyed by the radial nerve. In the latter report, the suggestion was based on the direct observation that in locations dominated by median or ulnar nerve inputs from the glabrous hand surfaces, either cutaneous stimulation of the hand dorsum or electrical stimulation of the radial nerve could produce a “nondominant” pattern of response. Dominant and nondominant responses were characterized by their local postsynaptic potential and action potential patterns, as indexed by laminar profiles of current source density (CSD) and multi-unit activity, sampled using linear array multi-electrodes. Throughout the glabrous representation in Area 3b, electrical stimulation of the dominant (median or ulnar) input produced robust, short-latency excitation, evident as a large current sink accompanied by action potentials in Lamina 4. Stimulation of the collocated nondominant (radial nerve) input produced a subtle short-latency response in the Lamina 4 CSD, unaccompanied by action potentials, and followed by a clear excitatory response 12–15 ms later. Laminar response profiles for both dominant and nondominant inputs had a “feedforward” pattern, with initial activation in Lamina 4, followed by extragranular laminae.

The normal corepresentation of nondominant dorsal hand (radial) inputs with the dominant (median or ulnar) inputs in the glabrous hand surface representation would seem to provide a clear vehicle for the biased patterns of reorganization found after peripheral nerve section (Garraghty and Muja 1996; Garraghty et al. 1994; Merzenich et al. 1983a,b). The present experiment tested the prediction that in median nerve cortex, after removal of the dominant input, the nondominant, radial nerve input would acquire the physiologic characteristics of the dominant input.
with recording of electromyographic responses from appropriate
distal musculature (see also Schroeder et al. 1995). For median
nerve, the optimal stimulation point was found to be at the ventral
forearm, 1–2 cm proximal to the wrist, whereas that for the radial
nerve was at the mid-dorsal forearm. Current settings were adjusted
to produce isolated suprathreshold activation of the appropriate
distal musculature. With this level of stimulation, it is safest to
assumed that no type of fiber within the target nerve was excluded
from stimulation. This could pose a problem for the present study
if the “nondominant” radial nerve response in median nerve cortex
was actually a long-latency response to cutaneous input, stemming
from the shock evoked hand twitch and conveyed by the median
nerve. However, there was a built-in control for this possibility in
that the “nondominant” radial nerve response observed at baseline
was unchanged in the acute phase of recording after the median
nerve was cut and the route of cutaneous inputs in question was
removed.

After mapping penetrations, the multi-electrode was perma-
nently affixed at a site in Area 3b, having a cutaneous represen-
tation on the proximal volar surface of D2 and displaying a “median
erve dominant” electrical stimulation profile. Baseline median,
radial, and ulnar nerve responses were measured before the median
nerve was cut and ligated in the mid-forearm (see Garraghty and
Muja 1996). Recordings were taken immediately after nerve sec-
tion and then, beginning on the fifth postoperative day, three times
weekly for 4 wk. The monkey then was killed and the brain was
removed for histologic analysis.

RESULTS

Figure 1, A and B, displays laminar CSD and multi-unit
activity profiles produced by electrical stimulation of the
median and radial nerves, recorded with the multi-electrode
array implanted in the median nerve representation in Area
3b. The collocated median and radial nerve profiles conform
precisely to earlier descriptions (Schroeder et al. 1995). In
this site, median nerve stimulation produced the largest
short-latency activity and a “classic” sensory cortical lam-
nar activation sequence (Fig. 1A). Initial response in Lam-
ina 4 (arrow) is indicated by a current sink with a concomi-
tant increase in multi-unit activity (MUA) and this is fol-
lowed by similar excitatory response configurations in the
extragranular laminae. The largest excitatory response is
centered in Lamina 3. Throughout the laminae, large current
sinks and MUA increases (indicative of net depolarization
of local neurons) are followed by current sources with MUA
reductions (indicative of hyperpolarization). In the radial
nerve response profile (Fig. 1B), the initial short-latency
response in the middle laminae is subtle; there is a small
transmembrane current flow component without a discern-
able MUA correlate. The laminar sequence and distribu-
tion of activity are similar to those of the median nerve
profile, but the clear excitatory response, signaled by trans-
membrane current flow and associated MUA activity, begins
12–15 ms later. Ulnar nerve stimulation produces a very
poor response in this site (not shown). In sum, the median
nerve provides the dominant input to this site, as indicated by
the robust, short-latency activity; the radial nerve provides
a substantial, but nondominant, input; and the ulnar nerve
provides little or no input.

Median nerve section induced a progressive change in the
radial nerve profile. Figure 1, C and D, display the radial
nerve-evoked profile at 7 and 21 days after median nerve
section. The notable change from the presection profile is
that the +7 day profile displays clear short-latency excita-
tion, beginning with the initial response in Lamina 4 and
continuing with the subsequent responses in supra- and infra-
granular sites. At +21 days, the pattern of change clearly
has progressed, in that response amplitudes, as indexed by
both CSD and multi-unit activity, have increased. Despite
these changes, the basic feedforward laminar activation se-
quency is maintained; there is initial response in Lamina 4,
followed by activation of the extragranular laminae.

To summarize the time course of the change in the radial
nerve-evoked response, Fig. 2 (left) presents radial nerve-
evoked responses at baseline (precut) along with those sam-
ped acutely and at intervals after median nerve section. The
data format is a condensed representation of the CSD profile,
the average rectified current flow (AVREC) waveform, which
is derived by full-wave rectifying each CSD wave-
form and averaging them together (Schroeder et al. 1995).
Because the AVREC is derived from the CSD, it has a more
direct relationship to postsynaptic potentials, than to action
potentials. Thus response features noted in the AVREC
waveform may be manifested poorly or absent in concomi-
tant MUA patterns (for detailed discussion of this point, see
Schroeder et al. 1995). On the right are median nerve stump
and ulnar nerve-evoked waveforms at selected time points
(i.e., at precut baseline and at 5 and 28 days postmedian
nerve section).

In the baseline and acute postcut recordings, the prominent
initial response to radial nerve stimulation begins at ~30
ms poststimulus. It is preceded by an epoch of smaller re-
sponse that begins at 7–10 ms poststimulus (described
above) and is often not evident in the AVREC waveform.
The obvious change in the radial nerve AVREC waveform
after median nerve transection is a decrease in the latency
and increase in the amplitude of the prominent excitatory
response. No change was observed on the day of the median
nerve section, but a decrease in the excitatory response la-
tency was apparent in the first postcut recording on day 5.
Thereafter, there was a progressive amplitude increase that
appeared to asymptote by 21 days postcut. The median and
ulnar nerve responses in this site appeared largely unchanged
throughout the postcut period.

DISCUSSION

The main finding of the present study is that in median
nerve cortex, after removal of the “dominant,” median
nerve input, the pre-existing, “nondominant,” radial nerve
response undergoes progressive increase in amplitude and
decrease in latency, eventually assuming the physiologic
characteristics of the dominant input. The time course of
reorganization, as studied in one subject here, parallels that
outlined by micro-electrode mapping of several subjects in
the experiments of Merzenich et al. (1983b). This time
course is consistent with a use-dependent “Hebbian-like”
potentiation of inputs, such as that implicated by the finding
that similar reorganization is prevented by N-methyl-D-
aspartate (NMDA)-receptor blockade (Garraghty and Muja
1996). Also consistent with earlier work (Garraghty and
Fig. 1. A: laminar CSD and multi-unit activity (MUA) profiles elicited by electrical stimulation of the median nerve. Profiles were obtained using a linear array, multi-contact electrode, fixed in a position covering sites extending from approximately Lamina 2/3 border down into white matter. Position of Lamina 4 is indicated by arrow (left). A functional indicator of ventral (white matter) border of cortex is a rapid drop in current source density (CSD) amplitude, often accompanied by high-amplitude MUA (see Schroeder et al. 1995); this is most evident in D. B: a laminar activity profile evoked by radial nerve stimulation in the same site. C and D: radial nerve-evoked activity profiles sampled at +7 and +21 days post median nerve section.

Muja 1996; Merzenich et al. 1983a, b), we find little evidence of an expansion of ulnar nerve representation in the deprived cortex. The overall pattern of results supports the view (Garraghty and Kaas 1991; Garraghty et al. 1994; Schroeder et al. 1995) that pre-existing anatomic circuitry can account for the more protracted, as well as the immediate, phase of reorganization (see e.g., Cusick et al. 1990) that follows nerve injury.
It is noteworthy that the radial nerve response, in its baseline (precut) form and throughout reorganization, maintains a characteristic "feedforward" laminar activation profile, with an initial response in Lamina 4, and subsequent responses in the extragranular laminae (see also Schroeder et al. 1995). This observation is inconsistent with the notion that adult plasticity, in contrast to developmental plasticity, uses "associative" (feedback and lateral) circuits rather than feedforward circuits (Singer 1995).

Our results provide an additional extension of previous work by demonstrating that the injured median nerve retains its access to cortex after reorganization. This is important because it indicates that the reorganization that follows peripheral nerve transection is not enabled by any substantial reduction in the central connections of dorsal root ganglion neurons whose peripheral processes comprise the median nerve. Thus the elimination of "normal" patterns of peripheral sensory activation by cutting the median nerve is sufficient to permit the emergence of the underlying radial nerve inputs to "median nerve cortex." The elimination of the afferents themselves is not necessary.

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REFERENCES


