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Reorganization of sensory pathways after neonatal hemidecortication in rats

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ABSTRACT

We investigated ascending somatosensory pathways in neonatally hemidecorticated rats. Injection of an anterograde tracer, biotinylated dextran amine (BDA), into the contralesional dorsal root ganglions revealed ipsilateral projections to the dorsal column nuclei (DCN) in hemidecorticated rats as well as in normal rats. Injection of BDA into the DCN on the same side revealed that while most axons projected to the contralateral thalamus, some axons were detected in the ipsilateral thalamus in hemidecorticated rats while such projections were rarely detected in normal rats. The results suggest that aberrant ipsilateral projections of DCN neurons contralateral to the lesion developed after the hemidecortication.

Juvenile brains have a higher capacity to adapt to injury than adult brains. Rats with hemidecortication at the neonatal stage exhibit fairly normal forelimb movements on the side contralateral to the lesion (Barth and Stanfield, 1990; Hicks and D'Amato, 1970, 1975; Takahashi et al., 2009). Such extensive, early brain damage is compensated for by large-scaled reorganization of the corticofugal connections from the undamaged sensorimotor cortex to the ipsilateral motoneurons to restore normal motor function of the forelimb contralateral to the lesion (Barth and Stanfield, 1990; Castro, 1975; Hicks and D'Amato, 1975; Kartje-Tillotson et al., 1986; Leong, 1976; Leong and Lund, 1973; Nah and Leong, 1976a,b; Naus et al., 1985; Rouiller et al., 1991; Takahashi et al., 2009; Umeda et al., 2010; Umeda and Funakoshi, 2013).

Despite a considerable number of studies on the plasticity of the corticofugal pathways, the ascending somatosensory pathways in hemidecorticated rats have been poorly studied. Neonatal hemidecorticated rats exhibit responses to tactile stimulation of the forelimb contralateral to the lesion, although the threshold of sensation in the forelimb on this side is rather high compared to the forelimb on the other side (Schallert and Whishaw, 1984, 1985). The undamaged sensorimotor cortex receives projections only from thalamic neurons on the ipsilateral side, as in normal rats (Sharp and Gonzalez, 1986). Thus, it is still unclear how hemidecorticated rats process tactile and proprioceptive inputs from the periphery contralateral to the lesion.

In this study, we analyzed ascending pathways in the dorsal lemniscal system coursing from the dorsal root ganglion (DRG) neurons to the thalamic nucleus in hemidecorticated rats. Fourteen normal and 14 hemidecorticated Wistar rats were used throughout the experiments. For hemidecortication, the right hemisphere including the sensorimotor cortex of 5 day-old-rats was aspirated as previously described (Takahashi et al., 2009; Umeda and Isa, 2011; Umeda et al., 2010). The pups were then returned to their mother and separated by gender after weaning day. At adulthood (4–7 months old), the rats were used in the following experiments.

First we investigated projections of DRG neurons to the dorsal column nuclei (DCN). After anesthesia with a cocktail of xylazine (10 mg/kg; Bayer Health Care, Monheim, Germany) and ketamine

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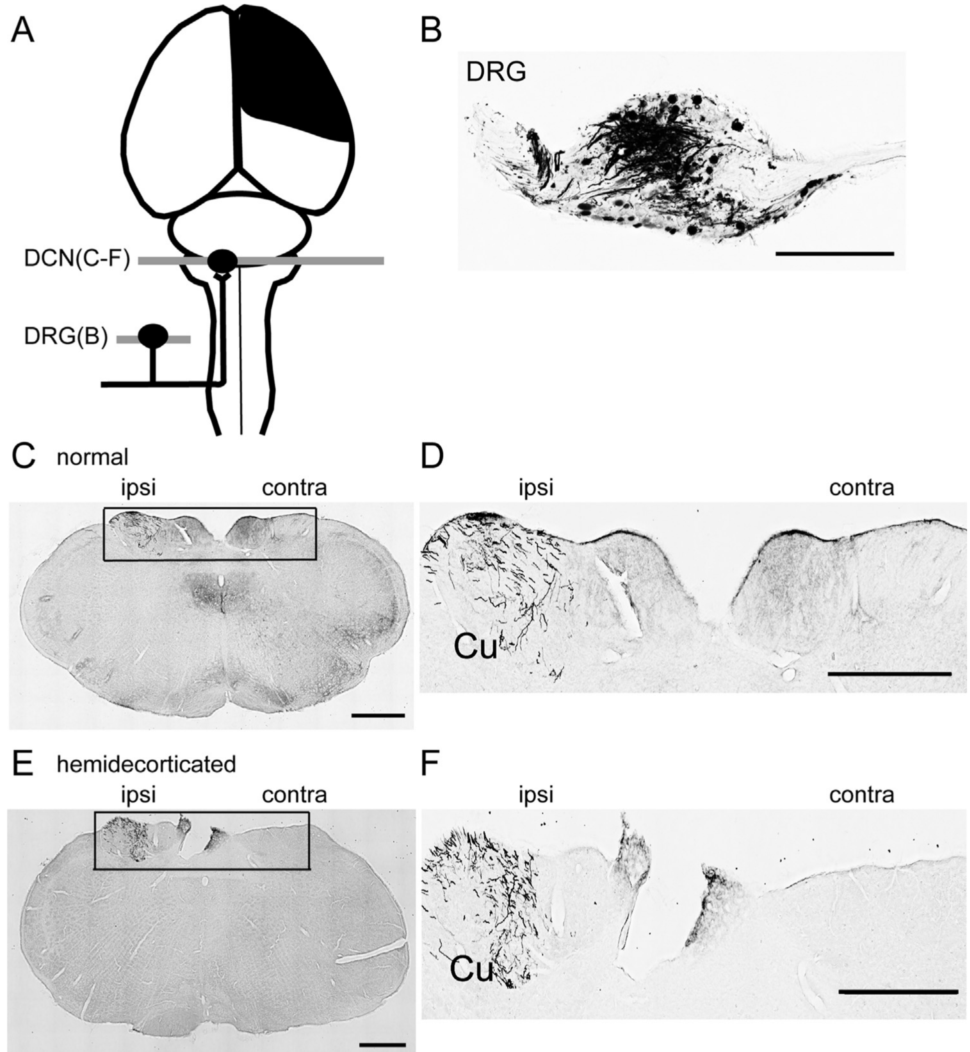

Fig. 1. BDA labeling in normal and hemidecorticated rats following BDA injection into the left DRGs. (A) Schematic drawing illustrating location of sections through the DRGs and the dorsal column nuclei. (B) A photomicrograph of the BDA-injection site in the DRG. (C) A photomicrograph of labeled axons in the ipsilateral DCN of a normal rat. Moderate labeling on the contralateral side is an artifact made during DAB staining. (D) A high-magnification view of the boxed region in (C). (E) A photomicrograph of labeled axons in the ipsilateral DCN of a hemidecorticated rat. (F) A high-magnification view of the boxed region in (E). Scale bars = 500 μm.

(60 mg/kg; Daiichi sankyo, Tokyo, Japan), pressure injections of 0.5 μl of 0.5% biotinylated dextran amine (BDA; MW 10,000; Molecular probes, Eugene, OR, USA) were made into the left DRGs at the C6 and C7 levels (5 normal rats and 5 hemidecorticated rats; Fig. 1B). Two weeks after injection, transverse sections (50 μm) were taken from the DRGs, the spinal cord, and the brain stem of rats that were transcardially perfused with 4% paraformaldehyde (Fig. 1A). Every fourth section was processed for the nickel-enhanced DAB reaction protocol (Takahashi et al., 2009) and some sections were counterstained with cresyl violet. The stained slices were observed under a fluorescent microscope BZ-8000 (KEYENCE, Osaka, Japan).

In both normal (Fig. 1C and D) and hemidecorticated (Fig. 1E and F) rats, labeled fibers traveled only in the dorsal funiculus ipsilateral to the injection, and terminated in the ipsilateral DCN. No labeled fibers were detected in the contralateral DCN in either group of rats. This suggests that DRG neurons made connections with neurons in the DCN on the ipsilateral side in hemidecorticated rats as well as in normal rats.

Next, we investigated projections of neurons in the DCN. BDA was delivered iontophoretically (DC current, 4.0 μA, 5 s on and 10 s off for 10 min) to the left DCN of 9 normal rats and 9 hemidecorticated rats (0.5 mm rostral, 1.5 mm lateral to the obex, 0.4–0.5 mm deep from the surface, according to the rat brain atlas (Paxinos et al., 1985)). Two weeks after injection, coronal sections (50 μm) were taken from the brain stem covering the medulla, the pons, and the thalamus (Fig. 2A). The sections were processed and observed as in the labeling of DRG neurons.

BDA labeling was densely distributed around the injection site in the cuneate nucleus as seen in Fig. 2B. Labeled fibers from the cuneate nucleus traveled toward the ventral part of the medulla (Fig. 2C) and crossed the midline in both normal and hemidecorticated rats. In normal rats, varicose fibers and terminal-like structures along the labeled fibers were observed extensively in two thalamic nuclei, the ventro-posterior lateral nucleus (VPL) and the posterior nucleus on the contralateral side via the medial lemniscus (Fig. 2D and E). In hemidecorticated rats, many labeled varicose fibers and terminal-like structures were observed in the contralateral VPL and posterior nucleus (Fig. 2F and G). Furthermore, some labeled fibers and varicosities were also detected in the ipsilateral VPL (Fig. 2F–H). In many of the hemidecorticated rats, recrossing fibers to the ipsilateral thalamic nucleus were found at the same rostro-caudal level as the thalamus (Fig. 2I and J). This observation supports an increased number of ipsilateral projections in hemidecorticated rats.