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Research Report

In vivo magnetic resonance imaging at 11.7 Tesla visualized the effects of neonatal transection of infraorbital nerve upon primary and secondary trigeminal pathways in rats

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ABSTRACT

Using 11.7 T ultra high-field T2-weighted MRI, the present study aimed to investigate pathological changes of primary and secondary trigeminal pathways following neonatal transection of infraorbital nerve in rats. The trigeminal pathways consist of spinal

Abbreviations: 5Gn, trigeminal ganglion; 7n, facial nerve; Cbc, cerebellar cortex; cbm, cerebellar medulla; CSF, cerebrospinal fluid; eml, external medullary lamina; Gd-DTPA, Gadolinium diethylenetriamine penta-acetic acid; ic, internal capsule; ml, medial lemniscus; ION, infraorbital nerve; P0, postnatal day 0; P10, postnatal day 10; Pr5, trigeminal principal sensory nucleus; py, pyramidal tract; Rt, thalamic reticular nucleus; sp5t, spinal trigeminal tract; SPFPC, subparafascicular thalamic nucleus, parvicellular part; str, superior thalamic radiation; T1, longitudinal relaxation time; T2, transverse relaxation time; TE, echo time; TR, repetition time; V1, ophthalmic nerve; V2, maxillary nerve; V3, mandibular nerve; VP, ventral posterior nucleus of thalamus; VPL, ventral posterolateral nucleus of thalamus; VPM, ventral posteromedial nucleus of thalamus

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trigeminal tract, trigeminal sensory nuclear complex, medial lemniscus, ventromedial portion of external medullary lamina and ventral posterior nucleus of thalamus. By selecting optimum parameters of MRI such as repetition time, echo time, and slice orientation, this study visualized the trigeminal pathways in rats without any contrast agents. Pathological changes due to the nerve transection were found at 8 weeks of age as a marked reduction of the areas of the trigeminal pathways connecting from the injured nerve. In addition, T2-weighted MR images of the trigeminal nerve trunk and the spinal trigeminal tract suggest a communication of CSF through the trigeminal nerve between the inside and outside of the brain stem. These results support the utility of ultra high-field MRI system for noninvasive assessment of effects of trigeminal nerve injury upon the trigeminal pathways.

1. Introduction

In recent years, a remarkable progress of MRI techniques has made possible to visualize fine morphology of nervous system at the sub-millimeter scale (Jahnke et al., 2007; Wu et al., 2010). Those studies revealed that the trigeminal nerve consists of three components in rats (Does and Gore, 2002), nerve tracts of the sciatic nerve were visualized with a contrast agent in rats (Chen et al., 2011) and the volume of dorsal root ganglia decreased after peripheral nerve injury (West et al., 2007). MRI has also several limitations even at present. MR images are constructed from different tissue variables like proton density and relaxation times (longitudinal relaxation time (T1) and transverse relaxation time (T2)) for protons. Since the differences in T1 and T2 between the white and gray matters are small, MR image contrast is poor and therefore the contrast agents have been often necessary in the MRI studies of brain (Inui-Yamamoto et al., 2010; Eschenko et al., 2012). As a result, the nervous tissue can be classified into only three groups, white matter, gray matter and cerebrospinal fluid (CSF) using ordinary MR images. It means that MRI is difficult to definitely discriminate such important structures as cortical layers and thalamus nuclei. In spite of those difficulties, it is expected that an optimum selection of MRI parameters such as repetition time (TR), echo time (TE) and slice orientation enhances the image contrast and discriminates neighboring tissues of nervous system without contrast agents. The purpose of the present study is to show the possibility written above and further to examine pathological changes of the primary and secondary trigeminal pathways following neonatal transection of infraorbital nerve (ION), one of the branches of maxillary division of the trigeminal nerve, using an 11.7 T ultra high-field MRI system.

To visualize the pathways connecting from the trigeminal nerve to the central nervous system, it is necessary to discriminate between external medullary lamina (eml) and internal capsule (ic) both of which are white matter. There is a thin (<0.4 mm) layer of gray matter called thalamic reticular nucleus (Rt) between them (Paxinos and Watson, 2004). Since Rt receives input from thalamocortical and corticothalamic projections (Carman et al., 1964; Jones, 1975; Pinault et al., 1995a, 1995b; Parent and Carpenter, 1996; Alexander and Godwin, 2006; Zikopoulos and Barbas, 2006), then Rt has nerve fibers as many as the white matter like eml and ic has, which reduces the MR signal contrast among eml, Rt and ic. Considering this fact as well as thinness of Rt, it is supposed difficult for MRI to discriminate eml from ic. However the spatial resolution of MRI increases with the static magnetic field strength (Magee et al., 2003), therefore 11.7 T is expected sufficient for discriminating among eml, ic and Rt. Another difficulty in visualizing the trigeminal pathway is to distinguish ventral posteromedial thalamic nucleus (VPM) and trigeminal principal sensory nucleus (Pr5) from the surrounding tissue, because they are all gray matters. Actually, there have been no studies to visualize them using MRI without any contrast agents. However, sensory neurons in VPM and Pr5 are in barrel-like arrangements (Ma, 1991; Land et al., 1995) with a hollow center of lesser cell density surrounded by a circle of higher cell density. Since the hollows are filled with fibers, there should be a certain difference in T2 between VPM/Pr5 and the surrounding tissue. Further in the present study, T2-weighted MRI was employed to observe pathological changes of cerebral tissues following ION transection, since it is suitable to visualize pathological changes of living tissues (McRobbie et al., 2003; Payne et al., 2011).

A number of anatomical studies have provided the evidences that the effects of peripheral nerve injury on the somatosensory system essentially depend on the time of suffering from injury. In the sensory system during development, several studies have suggested that an intact afferent input is crucial for survival of central sensory neurons (Levi-Montalcini, 1949; Cook et al., 1951; Matthews and Powell, 1962; Powell and Erulkar, 1962; Kupfer and Palmer, 1964; Waite, 1984; Born and Rubel, 1985; Finlay et al., 1986). In the neonatal period, the peripheral nerve injury induces apoptosis in the contralateral thalamus (Baldi et al., 2000). In the adult on the other hand, the peripheral nerve injury induces relatively minor morphological changes in the dorsal root ganglion (Sugimoto and Gobel, 1982). Thus in the nervous system, a critical period with high plasticity is considered to exist early in life. Several studies estimate the critical period of central nervous system within 7 days of age in rats (Belford and Killackey, 1980; Baldi et al., 2000; Harris et al., 2008). The present study investigated the effects of ION transection in rats at postnatal day 0 (P0).