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Somatosensory cortectomy induces motor cortical hyperexcitability and scoliosis: an experimental study in developing rats

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Abstract

BACKGROUND CONTEXT: Dysfunctions in sensorimotor integration, reminiscent to those described in idiopathic dystonia, have been found in idiopathic scoliosis (IS) and might be involved in its pathogenesis. Studying the effects of experimental disruption of sensory cortex may shed further insight into the etiopathology of IS.

PURPOSE: To evaluate whether disruption of central sensorimotor integration through partial ablation of the somatosensory cortex leads to scoliosis in developing rats and to describe the effects of such an intervention on motor cortico-cortical inhibition and facilitation.

METHODS: Fifty Wistar rats aged 3 weeks were used in the study. Twenty-four rats underwent craniotomy and electrocoagulation of the sensory cortex (PAR1) in the right hemisphere. A second group of 16 rats underwent a sham operation with craniotomy but no electrocoagulation. A third group of 10 rats was used as intact controls. Four weeks after surgery, motor cortical excitability was assessed with paired-pulse electrical cortical stimulation. Neurologic and behavioral examinations were completed serially, and 10 weeks after surgery, X-ray examinations were performed in anesthetized rats to assess spinal curvature. Electromyographic recordings of paravertebral muscle activity were performed in waking rats. At the end of the study, rats were sacrificed, and histologic examinations of brain tissue were performed to confirm the extent of the lesion. A grant from a Government Health Research Fund without salaries assignment financed the study.

RESULTS: Almost half of the animals with somatosensory cortectomy (46%) developed scoliosis, with an average Cobb angle of $23\pm8^{\circ}$. None of the animals in the sham or control groups developed scoliosis. Despite cortical lesions, no motor or behavioral deficits were apparent in the experimental group, and cortectomized rats were neurologically indistinguishable from sham or control animals, except for the presence of scoliosis. Cortico-cortical inhibition was significantly reduced in the hemisphere of scoliotic concavity in the cortectomized group but was normal in the other groups.

CONCLUSIONS: These findings indicate that altered sensorimotor integration may cause scoliosis without noticeable motor impairment. Reduced cortico-cortical inhibition was observed in cortectomized rats. This finding is consistent with results in adolescents with IS and suggests that

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The disclosure key can be found on the Table of Contents and at www.TheSpineJournalOnline.com.

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alteration of cortical hemispheric balance of sensorimotor integration may play an important role in the pathogenesis of IS.

Keywords: Idiopathic scoliosis; Cerebral cortex; Experimental scoliosis; Etiology; Cortico-cortical inhibition

Introduction

In recent decades, research on the etiology of idiopathic scoliosis (IS) has intensified. Some authors have suggested that a subclinical alteration of the central nervous system may be involved in the pathogenesis of IS. Several clinical studies have identified abnormalities in proprioception and balance in patients with IS compared with healthy controls. For example, IS patients exhibit alterations in postural balance control [1–7], asymmetries in the positional discrimination of large joints [8,9], and altered sensitivity to vibrations [10,11]. Animal models of scoliosis can be induced experimentally by selectively injuring neural structures involved in sensory input at the spinal level, such as the posterior horns and Clarke's column [12], the posterior columns [13], and the posterior roots [14,15]. In addition, injuring the brainstem nuclei related to postural balance can also induce scoliosis [16].

Lateral and rotational movements and the stability of the axial skeleton are regulated by a mechanism involving postural reflexes that are modulated by proprioceptive afferents. Defective sensory input or anomalous sensorimotor processing might result in impaired postural tone, leading to spinal deformities. Alterations in the integration of sensory input have been involved in the pathogenesis of dystonia [17,18]. Thus, IS might represent a skeletal manifestation secondary to unbalanced, unilateral axial dystonia caused by abnormal sensorimotor integration.

Some authors suggest that the somatosensory abnormalities found in patients with IS result from cortical processing abnormalities rather than conduction abnormalities [3,19–22]. The deficits in perception and learning, and the changes in the organization of cognitive processing often observed in IS, reinforce the idea that cortical dysfunction could be associated with IS [23]. Previous studies examining somatosensory-evoked potentials in IS patients have revealed a selective delay in the N37-evoked potential arising in the cerebral cortex [21]. These results suggest that IS could result from the dysfunctional cortical processing of proprioceptive afferents rather than alterations in afferent pathways themselves.

Recent studies using transcranial magnetic stimulation with paired pulses have found that adolescents with IS exhibit abnormal cortical motor hyperexcitability similar to that observed in dystonic patients [24]. These findings could explain the sustained muscle contractions and the lack of selectivity of stimulated muscles [25], which could lead to scoliotic deformity in the growing spine. Patients with movement disorders, such as focal and generalized idiopathic dystonia and Parkinson's disease, show an abnormal level of cortico-cortical inhibition [25–27]. In these patients, the incidence of scoliosis is between 39% and 90% [28–31]. Similar to IS patients, patients with idiopathic dystonia show alterations in the central integration of sensory inputs, and these alterations have been proposed as etiopathogenic factors in this movement disorder [17]. It is therefore possible that the deregulation of facilitatory and inhibitory intracortical motor circuits is caused by poor sensory integration at the cortical level and that this abnormal motor cortical hyperexcitability is relevant to the development of scoliotic deformities.

The aim of the present study was to test the hypothesis that unilateral damage to the somatosensory cortex would lead to scoliosis in developing rats and that this skeletal deformity would be associated with changes in cortico-cortical motor excitability reminiscent of those found in dystonia. To the best of our knowledge, the effects of the disruption of cortical sensory input in an experimental model of the growing spine have not been evaluated. The demonstration that an experimental animal model of scoliosis can be induced by altering the modulation of motor cortical signals using sensory cortectomy would support the hypothesis that IS, like dystonic-type disorders, can be caused by defective central sensory integration.

Materials and methods

Fifty Wistar rats (3 weeks old; weight, 95–125 g) were used for this study. The rats were randomized by flipping a coin into cortectomy group (n, 24) and control group (n, 26) before each surgical session. The 26 rats allocated in the control group were randomized again, also by flipping a coin, into sham operation (n, 16) and intact control (n, 10). The rats in the cortectomy group (n=24) underwent a right hemispheric lesions of the sensory cortex. This group was larger to account for possible differences in the eventual extent of the cortectomy and possible variability in neurologic consequences and overall morbidity. To control for the effects of the surgical intervention itself, animals in a second group (sham group, n=16) were subjected to a craniotomy, but no cortectomy was conducted. The third group of 10 healthy animals served as a no-intervention control (control group). The study was approved by the local research committee and followed the animal testing recommendations of the WMA Hong Kong Agreement of 1989. A grant from a Government Health Research Fund without salaries assignment financed the study.

Animals assigned to the injured and sham groups were anesthetized with ketamine (0.5 mg/kg), diazepam (0.4 mg/kg), and atropine (0.1 mg/kg), administered intraperitoneally.