Basic Science

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 $23\pm8°$. 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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alteration of cortical hemispheric balance of sensorimotor integration may play an important role in the pathogenesis of IS. © 2013 Elsevier Inc. All rights reserved.

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.

The same surgeon performed all operations. First, rats were placed on a stereotaxic apparatus. A craniotomy was performed over the right hemisphere, removing the portion of skull corresponding to the following stereotaxic coordinates: 2 mm anterior to bregma, 5 mm posterior relative to bregma, 2 mm lateral to the sagittal fissure, and 1 mm lateral to the sagittal crest. In the first group of rats, we lesioned the cerebral cortex 4 mm lateral to the sagittal fissure in a 1-mm wide ribbon from 1 mm anterior to bregma to 4 mm posterior to bregma using bipolar electrocoagulation (ADInstruments, Hastings, United Kingdom). This zone corresponds to the sensory cortex Par 1 [32]. The rat somatosensory cortex is not subdivided into areas homologous to human cortical Brodmann areas 3, 2, and 1. However, one can distinguish a primary (S1) and a secondary (S2) somatosensory area in the parietal cortex. Area S1 can, in turn, be subdivided into three parts: hind leg, front leg, and Par 1. Although there is no dermatomal or precise somatotopic organization, there is a simple two-dimensional map of the body in the rat. This map is inverted, with the representation of the front legs and hind legs medially and the trunk being represented laterally. Par 1 receives inputs from the trunk, tail, and contralateral whiskers [32]. During the procedure, care was taken not to injure the adjacent motor cortex.

Motor-evoked potentials

Motor-evoked potentials (MEPs) were recorded 1 month after surgery. For the MEP recording session, animals were anesthetized with ketamine (0.5 mg/kg), without diazepam or atropine because of their possible effects on neuronal excitability. Next, the rats were placed into the stereotactic apparatus. For the right hemisphere of injured and sham animals, we took advantage of the skull window made in the previous surgery. For the left hemisphere and in control rats, we penetrated the skull with a Steinmann needle. The stimulating electrode was placed over the motor cortex, 4 mm behind bregma and 2 mm lateral to the sagittal fissure. Electromyographic (EMG) activity was recorded using needle electrodes inserted into the triceps surae of the contralateral hind paw.

We determined the motor threshold, defined as the lowest stimulation intensity that induced MEPs of at least 1.5 μV peak-to-peak amplitude in at least five consecutive stimuli. To define the motor threshold, we followed the method of limits with the stimulation intensity being decreased in steps of 0.5 mV. Stimulation was applied with square-wave pulses of 0.15 ms duration. The interval between trials was at least 5 s long to prevent carry-over effects. In all cases, we explored the right hemisphere first, followed by the left hemisphere. The mean duration of recording sessions was 70 min.

Paired-pulse stimulation was used to assess cortico-cortical inhibition and facilitation. The test stimulus (TS) was set at 110% of motor threshold intensity. The conditioning stimulus (CS) was set at 80% of motor threshold intensity. The interstimulus interval (ISI) between TS and CS was randomly varied and included 1, 2, 3, 4, 5, 8, and 10 ms. Trials in which CS elicited a response were discarded. At the beginning of each session, we recorded 10-20 MEPs to TS alone. We then collected blocks of 10 trials with each of two ISI (20 trials in total) and after each block we recorded again 10 MEPs to TS alone to confirm a reliable baseline.

Electromyographic recording was performed with Scope-MacLab (ADInstruments). Data were amplified (100 Hz to 2 kHz band-pass filters) and digitized (5 kHz sampling rate) and stored for offline analysis. Offline, for each MEP, we determined the area under the curve. Area under the curve for MEPs to TS alone and for each of the tested ISIs was averaged offline. Responses to paired stimuli at a given ISI were expressed as a percentage of the average MEP to TS alone for each animal.

Neurologic examination

One month and 3 months after the operation, all rats were neurologically examined by the same individual, who was blind to the treatment groups. We used a neurologic assessment model based on those proposed by Garcia et al. [33], Bederson et al. [34], and Menzies et al. [35] (Table). These methods for assessing neurologic deficit in rats have been validated in studies of experimental cerebral ischemia caused by lesion of the middle cerebral artery.

Radiological examination

Three months after surgery, rats were anesthetized with ketamine, diazepam, and atropine. Posteroanterior radiographs of the spine were performed with rats lying prone decubitus, and lateral radiographs were performed with rats in the right lateral decubitus position. Scoliotic deformities were evaluated by the Cobb method. To avoid interobserver errors, measurements were performed by a single observer who was otherwise not associated with the study, blinded to the treatment groups, and had extensive clinical experience in these type of measurements. Deformities smaller than 10° and those that might be explained by postural factors were not considered scoliosis.

Electromyographic study

At least 2 months after the operation, we performed an EMG study (Chart MacLab, ADInstruments) of the paravertebral muscles in waking animals. We used two needle electrodes inserted through the skin into the paravertebral muscles at the junction of the last thoracic and first lumbar vertebra. The reference electrode was placed subcutaneously at the base of the tail. The spontaneous myoelectric activity of each freely moving rat in its cage was recorded for 1 minute using 100 Hz to 2 kHz band-pass filter settings. Activity was digitized with a sampling rate of 5 kHz and stored for offline analysis. To analyze the results, we identified 5-second periods that were free of artifacts

Table
Scale for neurologic evaluation

Results	Score
1. Spontaneous activity of the rat for 5 min in cage	
No movement	0
Barely moves, not rises up	1
Rises up and moves without reaching three sides of the cage	2
Moves and reaches at least three sides of the cage	3
2. Symmetry in four limbs movement (holding the rat in the air by the tail)	
No movement in one forelimb	0
Minimal movement in one side	1
One side moves and outreaches less than the other	2
Symmetric movement	3
3. Forepaw outstretching (making the rat walk on forelimbs while being held by the tail)	
No movement in one forelimb	0
Slight outstretching on one forelimb	1
Outstretches one forelimb less than the other	2
Symmetry in both forelimbs and walking ability	3
4. Climbing wall of wire cage	
Rat failed to climb	1
Left side is weak	2
Normal climbing	3
5. Lateral resistance, holding the rat by the tail and pushing on the side	
No resistance to displacement toward left	1
Less resistance to displacement toward left	2
Symmetry in resistance to displacement	3
6. Free movement in flat surface	
Turns left, no advance	1
Circular walking to the left	2
Normal gait, straight with turns to both sides, by chance	3
7. Reaction to touch on either side of trunk	
No response on left side	1
Weak response on left side	2
Symmetrical response	3
8. Reaction to vibrissae touch	
No response on left side	1
Weak response on left side	2
Symmetrical response	3

Modified from Garcia et al. [33], Bederson et al. [34], and Menzies et al. [35].

and qualitatively compared the amount of activity and activity pattern across both hemibodies in all animals.

Cerebral histopathology

Animals were sacrificed by decapitation with previous anesthesia 6 months after surgery. Brains were removed and fixated in 10% formalin until histologic examinations were performed. Frontal sections (0.01 mm thickness) were stained with hematoxylin-eosin. The preparations were matched to the stereotactic maps from Paxinos brain atlas [36] and the extent of the lesion defined by manual analysis by an investigator blinded to the rest of the results.

Statistical analysis

The Kolmogorov-Smirnov test was applied to verify the normality of the data samples. We used one-way analysis of
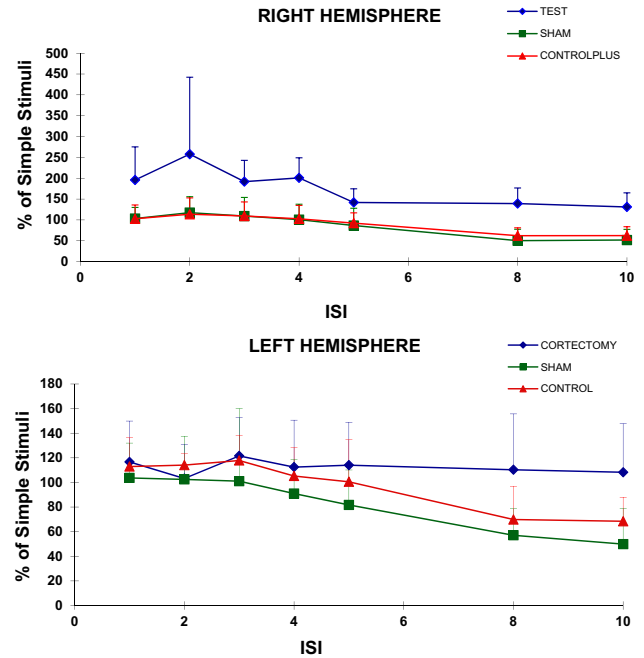

Fig. 1. Values of the paired-pulse evoked potential obtained at the different ISIs. The results are expressed in percentage of those obtained with simple stimuli. ISI, interstimulus interval.

variance followed by the Bonferroni correction to compare the MEPs, motor thresholds, and the Cobb degrees across study groups. Nonparametric Neuroscore data were compared using Kruskal-Wallis test. Significance was set at $p < .05$. SPSS statistical software (IBM Corporation, Armonk, NY, USA) was used for all statistical analysis.

Results

Motor-evoked potentials

There were no differences in motor threshold between animals in the injured, sham, and control groups. Mean motor thresholds were 2.9 (standard deviation [SD], 2.0), 3.2 (SD, 1.7), and 3.1 (SD, 1.8) for the injured, sham, and control groups, respectively. There were also no significant differences in the thresholds of the left and right hemispheres within each group.

Regarding responses to paired-pulse stimulation, there were no differences between the control and the sham groups at any of the explored ISIs. In contrast, cortectomized rats displayed a significant increase in excitability in the right hemisphere as compared with the two control groups ($p < .001$) (Figs. 1 and 2, Top) and a significant right-left hemispheric asymmetry that was not present in the control groups. Indeed, for the left hemisphere, there were no differences between the injured rats and the two control groups at any of the tested ISIs.

Responses to paired-pulse stimulation were divided into a facilitatory phase (ISIs, 1–4 ms) and an inhibitory phase (ISIs, 5–10 ms). There were no interhemispheric
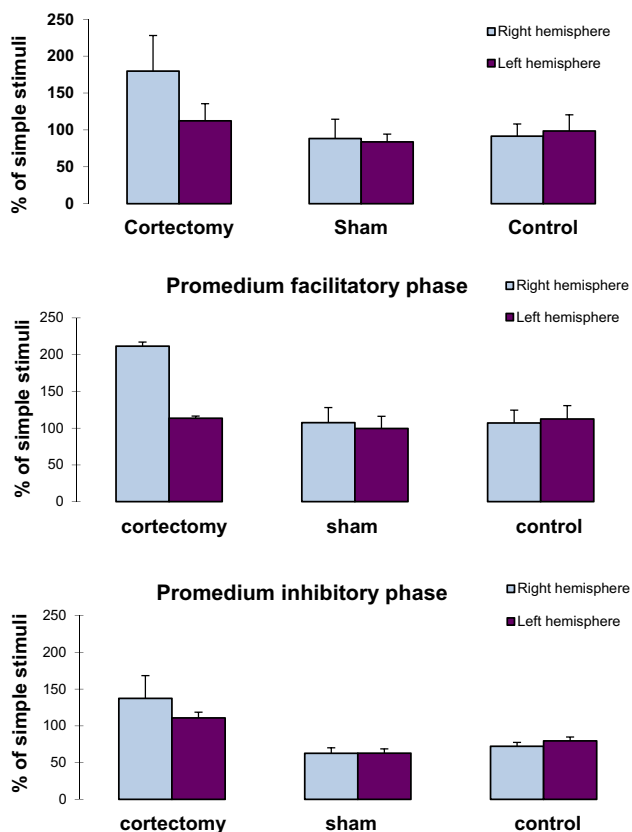
Fig. 2. Average values in the evoked potentials obtained after paired-pulse direct electrical cortical stimulation. (Top) Across all interstimulus intervals (ISIs). (Middle) In the facilitatory phase (ISI, 1–4 ms). (Bottom) In the inhibitory phase (ISI, 5–10 ms). Results are shown in percentage of those obtained with simple stimuli.

asymmetries for either one of these phases in the control or sham groups. However, the facilitatory phase was significantly greater in the right than the left hemisphere in the injured rats and significantly different from either control groups (p<.001) (Fig. 2, Middle).

During the inhibitory phase (ISIs, 5–10 ms), we also observed highly significant differences in the responses of injured rats compared with controls in both the right (p<.001) and left hemispheres (p<.01). In fact, injured rats showed a facilitatory effect, whereas sham and control group animals showed a suppressive effect of CS onto TS responses at ISIs 5 to 10 ms in both hemispheres (Fig. 2, Bottom).

When comparing right and left hemispheres within both groups, there were no asymmetries in the control and sham groups between right and left hemisphere in the inhibitory or facilitatory phases. On the contrary, all rats that underwent right sensory cortectomy showed a clear asymmetry between the hemispheres. The right hemisphere was characterized by a uniformly greater amplitude of evoked potentials for all ISIs, and the interhemispheric difference was larger during the facilitatory phase (p<.001) than during the inhibitory phase (p<.05) (Fig. 2). Fig. 3 shows examples of the responses at 2 and 10 ms in an injured and a sham-operated rat.
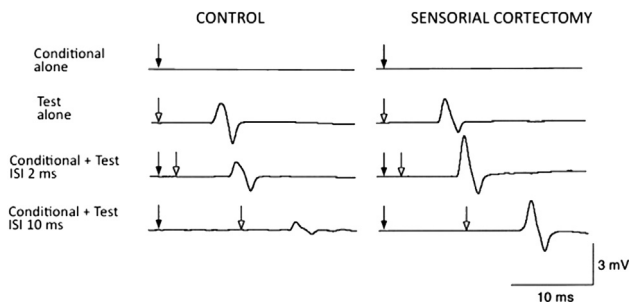

Fig. 3. Motor-evoked potentials after direct electric stimulation on motor cortex. (Left) Sham rat: a conditioning stimulus (black arrow) under the threshold does not elicit electromyographic response. A test stimulus (white arrow) over the threshold provokes a potential. If a conditioning stimulus is applied 2 ms before the test stimulus, a facilitating effect on the potential is produced. When the conditional stimulus is applied 10 ms before the test stimulus, a marked inhibition is produced on the evoked potential. (Right) Rat with sensorial cortectomy: greater facilitation in the evoked responses is observed at both 2 and 10 ms.

Radiological study

We found no scoliosis in control or sham-operated animals. In contrast, 11 animals in the injured group (46%) had scoliotic deformities, with average Cobb angles of 23° (SD, 6) (Fig. 4). Regarding the degree of dorsal kyphosis, there were no differences between animals in the injured group (mean, 46°; SD, 4) and those in either control groups (mean, 53°; SD, 5).

Neurologic evaluation

We detected no behavioral or motor deficits in injured rats compared with control rats, and the three groups of rats exhibited similar scores on all motor and behavioral parameters examined (Table). In addition, we observed no differences in pain sensitivity among the three groups. Some injured rats showed incomplete hypoesthesia on the contralateral side 1 week after surgery, but this deficit improved and returned to control levels within 1 month. Most of the rats with brain injuries had no apparent sensory deficit and were, in fact, indistinguishable from the control and sham-operated rats. There were no significant differences in the neurologic exploration between the groups at 3 months (median values in cortectomized group, 23; control group, 24; sham group, 23; p>.05). None of the rats developed ulcers or skin lesions, which can sometimes result from sensory anesthesia. Animals in all three groups obtained the maximum score of 18 in the motor and behavioral examination.

Electromyographic study

Electromyographic activity was recorded on both sides of the spine musculatures in the awaken animals moving freely in their cages without any constrain. Paravertebral muscle activity patterns showed no evidence of denervation, fibrillation, or spontaneous activity in any of the

Fig. 4. X-ray examination of a rat at 3 months after sensorial cortectomy showing a 25° scoliosis.

Fig. 5. (Top) Histologic slice of a cortectomized rat. Notice the cystic cavity in the cortical area corresponding to the sensorial cortex Par1 (×40, hematoxiline-eosine). (Bottom) Upper view of the entire brain of rat with unilateral sensorial cortectomy in Par1.

groups. Electrical activity was similar on both sides of the spine muscle in all three groups. In addition, there were no significant differences in concavity or convexity between the injured animals that developed scoliosis and those that did not.

Cerebral histopathology

Microscopic examination of brain slices showed cavity areas bounded by a halo of neuronal necrosis. The lesions were confined to Par 1 and did not affect the adjacent motor cortex in any of the animals included in the study (Fig. 5).

Discussion

The main goal of this study was to investigate the impact of lesions to the somatosensory cortex on motor cortical excitability and the growing spine in experimental animals. Consistent with our hypothesis, we found that rats with somatosensory cortectomies affecting the cortical representation of their trunks showed a marked motor cortical hyperexcitability, and 46% of them developed scoliotic deformities.

The increased cortico-cortical excitability observed in our study is consistent with that reported in other studies exploring cortico-cortical excitability with paired pulses
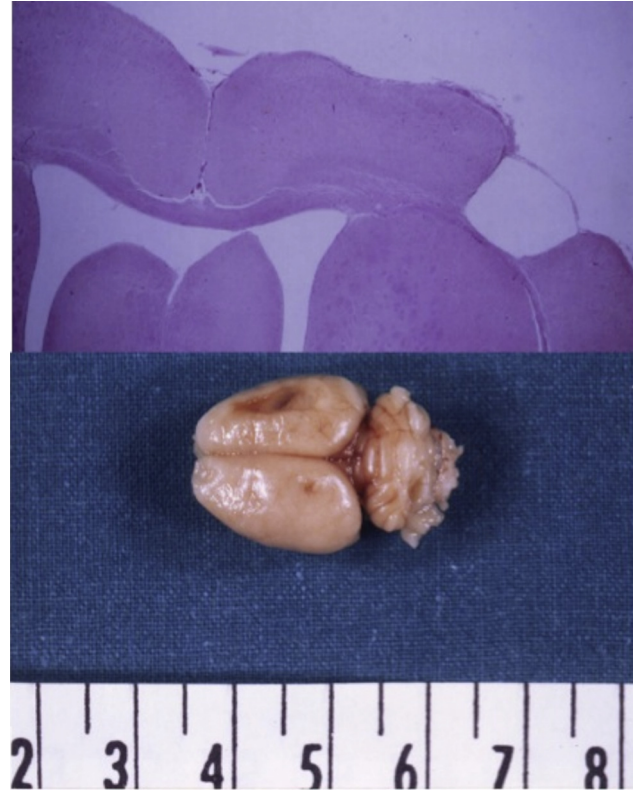
after brain lesions in rats [37–39] and in humans after a lesion of the somatosensory cortex [40]. Changes in cortical excitability in areas distant from the lesion site have been implicated in functional recovery after lesions to the somatosensory cortex [41–43]. In a human study, patients who exhibited functional recovery after stroke were characterized by increased cortical excitability, whereas patients with poor recovery were not [44]. One striking observation in the present study was the lack of neurologic deficits in rats 3 months after sensory cortical lesions. The neurologic model used did not allow us to distinguish between the injury group and the sham-operated group. Surgeries took place when the rats were 3 weeks old, a time at which they still retain a high growth potential. The sensory and motor functional recovery is presumably because of the processes of plasticity that may be linked to the measured shifts in cortico-cortical excitability revealed by paired-pulse stimulation.

These shifts in cortico-cortical excitability could be an epiphenomenon unrelated to the observed scoliosis, but we believe that it may actually be an important pathogenetic mechanism mediating the development of this deformity. First, motor paralysis can produce scoliosis, but we did not observe motor deficits in animal in the injured group and there were no delays in the latency of their MEPs that might suggest pyramidal tract damage. Shifts in were

the only neurophysiological finding that allowed us to distinguish between the different experimental groups after the recovery period. Second, the asymmetrical pattern of cortico-cortical excitability observed after sensory cortectomy is reminiscent of the findings of our prior study in adolescents with IS studied with paired TMS pulses [24]. Third, several studies have produced scoliosis by deafferentation of experimental animals. Although these studies did not examine the presence of shifts in cortico-cortical excitability, there is evidence that interruption of sensory input can cause motor cortical hyperexcitability [45–47]. Finally, in a study in which Parkinsonism was experimentally induced in rats by unilateral injection of 6-hydroxydopamine into the ventral tegmental area, rats developed scoliosis with a convexity toward the side of the lesion and with features similar to those in this study [48]. Although that study did not explore intracortical excitability, patients with Parkinson's disease do show suppression of cortico-cortical inhibition [27]. Interestingly, patients with Parkinson's disease and patients with dystonia (who also show this abnormal intracortical excitability) have a higher prevalence of scoliosis than the normal population, independent of age [29–31]. It is therefore possible that abnormal sensorimotor integration expressed as aberrant intracortical excitability is the common link among all these models and instances of scoliosis.

One limitation of this study lies in the fact that it used four-legged animals. Although motor cortical hyperexcitability is a consistent finding in rats with sensory cortectomy, only approximately half of these rats developed scoliosis. Previous studies have revealed a facilitatory effect of bipedalism in the production of scoliosis in rat neurologic injury models. Tanaka et al. [49] induced motor paralysis in rats by lathyrism and observed the development of scoliosis in 13% of four-legged rats and in 82% of bipedal rats. Pinealectomy, a method to induce scoliosis in experimental animals, has produced scoliosis in bipedal rats but not in quadrupedal rats [50]. In another study in rats with congenital melatonin deficiency, scoliosis was observed in 64% of bipedal rats but in none of the quadrupeds [51]. It is therefore possible that, in our study, being a quadruped acted as a protective factor against the development of the deformity. If so, our results must be considered more remarkable. Despite quadrupedal animals, 46% developed scoliosis in the injured group. We decided not to use bipedal rats because bipedalism is induced by amputating the forelegs. Studies in humans have shown that amputation and peripheral nerve severing alter the excitability of the motor cortex [47,52], and our objective was to specifically evaluate a possible relationship between scoliotic deformity and the asymmetric cortical excitability induced by alteration of cortical sensorimotor integration. Thus, we believed that amputation would act as a confounding factor in our experimental model. It would be interesting for future studies to examine this variable in this model of experimental scoliosis.

In our study, we observed no differences in the spontaneous myoelectric activity in the paravertebral muscles of rats that had developed scoliosis, although the cortical hyperexcitability was constant in all cases with sensory cortectomy. The lack of asymmetries in injured rats and the absence of differences with the controls suggest that the deformity is not caused by lesions of the motor pathway. Increased intracortical excitability did not translate into an alteration of the resting EMG activity in the paravertebral muscles in the rats undergoing cortectomies. Subtle findings might have been obtained using quantitative EMG analysis approaches. However, patients with idiopathic dystonia, who also show a similar intracortical hyperexcitability, exhibit normal EMG recordings of muscles at rest outside the episodes of muscle spasms [53]. Some studies in patients with IS have shown a normal EMG of the paraspinal muscles [54–58]. However, other studies have found EMG differences in patients with IS compared with healthy controls. One interpretation of these findings is that the EMG results are because of anomalous motor balance involved in the pathogenesis of the deformity [59,60]. Other authors interpret the EMG anomalies differently, considering them to be secondary to the deformity. Indeed, similar EMG findings have been observed in patients with congenital and IS [57], and differences in myoelectric activity increase as the curvature increases [54,56]. In our model, the mean Cobb angle of deformity was 23°, which might not be sufficient to cause adaptive myoelectric changes. In any case, the absence of abnormalities or side-to-side differences in paravertebral EMG activity in our cortectomized animals suggests that the cortical hyperexcitability observed in rats with sensory cortectomy can cause deformities through poor motor control rather than through sustained muscle tone alterations such as spasticity.

In conclusion, our findings support the hypothesis that the etiology of IS is linked to poor sensorimotor integration and increased motor cortico-cortical excitability. It is noteworthy that a striking asymmetry in motor excitability between both hemispheres was observed in this study, similar to the asymmetric hyperexcitability previously found in patients with IS. It is possible that dysfunctional intracortical facilitatory and inhibitory circuits in IS result in inadequate muscular output by acting asymmetrically. The effects of this asymmetric motor cortical hyperexcitability on a growing spine may contribute to the development of scoliosis.

References

[1] Adler N, Bleck EE, Rinsky IA, Young W. Balance reactions and eye hand coordination in idiopathic scoliosis. J Orthop Res 1986;4: 102–7.

[2] Byl NN, Gray JM. Complex balance reactions in different sensory conditions: adolescents with and without idiopathic scoliosis. J Orthop Res 1993;11:215–27.

[3] Herman R, Mixon J, Fisher A, et al. Idiopathic scoliosis and the central nervous system: a motor control problem. Spine 1985;10:1–14.

[4] Sahlstrand T, Örtengren R, Nachemson A. Postural equilibrium in adolescent idiopathic scoliosis. Acta Orthop Scand 1978;49: 354–65.

[5] Nault ML, Allard P, Hinse S, et al. Relations between standing stability and body posture parameters in adolescent idiopathic scoliosis. Spine 2002;27:1911–7.

[6] Lao MLM, Chow DHK, Guo X, et al. Impaired dynamic balance in adolescent with idiopathic scoliosis and abnormal somatosensory evoked potential. J Pediatr Orthop 2008;28:846–9.

[7] Beaulieu M, Toulotte C, Gatto L, et al. Postural imbalance in nontreated adolescent idiopathic scoliosis at different periods of progression. Eur Spine J 2009;18:38–44.

[8] Cook SD, Harding AF, Burke SW, et al. Upper extremity proprioception in idiopathic scoliosis. Clin Orthop Relat Res 1986;213: 118–24.

[9] Keessen K, Crowe A, Hearn M. Proprioceptive accuracy in idiopathic scoliosis. Spine 1992;17:149–55.

[10] Barrack RL, Wyatt MP, Whitecloud TS, et al. Vibratory hypersensitivity in idiopathic scoliosis. J Pediatr Orthop 1988;8:389–95.

[11] McInnes E, Hill DL, Raso VJ, et al. Vibratory response in adolescents who have idiopathic scoliosis. J Bone Joint Surg Am 1991;73A:1208–12.

[12] Pincott JR, Taffs LF. Experimental scoliosis in primates: a neurological cause. J Bone Joint Surg Br 1982;64-B:503–7.

[13] Barrios C, Tunon MT, De Salis JA, et al. Scoliosis induced by medullary damage: an experimental study in rabbits. Spine 1987;12: 433–9.

[14] Pincott JR, Davies JS, Taffs LF. Scoliosis caused by dorsal spinal nerve roots. J Bone Joint Surg Br 1984;66B:27–9.

[15] Suk SI, Song HS, Lee CK. Scoliosis induced by anterior and posterior rhizotomy. Spine 1988;14:692–7.

[16] Barrios C, Arrotegui JI. Experimental kyphoscoliosis induced in rats by selective brain stem damage. Int Orthop 1992;16:146–51.

[17] Hallet M. The neurophysiology of dystonia. Arch Neurol 1998;55: 601–3.

[18] Tinazzi M, Rosso T, Fiaschi A. Role of the somatosensory system in primary dystonia. Mov Disord 2003;18:605–22.

[19] Brinker MR, Willis JK, Cook SD, et al. Neurologic testing with somatosensory evoked potentials in idiopathic scoliosis. Spine 1992;17:277–9.

[20] Maguire J, Madigan R, Wallace S, et al. Intraoperative long latency reflex activity in idiopathic scoliosis demonstrate abnormal central processing. A possible cause of idiopathic scoliosis. Spine 1993;18:1621–6.

[21] Machida M, Dubousset J, Imamura Y, et al. Pathogenesis of idiopathic scoliosis: SEPs in chicken with experimentally induced scoliosis and in patients with idiopathic scoliosis. J Pediatr Orthop 1994;14:329–35.

[22] Domenech J, Garcia-Martí G, Martí-Bonmatí L, et al. Abnormal activation of the motor cortical network in idiopathic scoliosis demonstrated by functional MRI Eur Spine J 2011;20: 1069–78.

[23] Goldberg CJ, Dowling FE, Fogarty EE, Moore DP. Adolescent idiopathic scoliosis and cerebral asymmetry. An examination of a nonspinal perceptual system. Spine 1995;20:1685–91.

[24] Doménech J, Tormos JM, Barrios C, Pascual-Leone A. Motor cortical hyperexcitability in idiopathic scoliosis: could focal dystonia be a subclinical etiological factor? Eur Spine J 2010;19: 223–30.

[25] Ridding MC, Sheean G, Rothwell JC, et al. Changes in the balance between motor cortical excitation and inhibition in focal task specific dystonia. J Neurol Neurosurg Psychiatry 1995;59:493–8.

[26] Ikoma K, Samii A, Mercuri B, et al. Abnormal cortical motor excitability in dystonia. Neurology 1996;46:1371–6.

[27] Ridding MC, Inzelberg R, Rothwell JC. Changes in excitability of motor cortical circuitry in patients with Parkinson disease. Ann Neurol 1995;37:181–8.

[28] Grimes JD, Hassan MN, Trent G, et al. Clinical and radiographic features of scoliosis in Parkinson disease. Adv Neurol 1986;45: 353–5.

[29] Jankovic J, Leder S, Warner D, et al. Cervical dystonia: clinical findings and associated movement disorders. Neurology 1991;41: 1088–91.

[30] Defazio G, Abbruzzese G, Girlanda P, et al. Primary cervical dystonia and scoliosis: a multicenter case-control study. Neurology 2003;60:1012–5.

[31] Baik JS, Kim JS, Park HP, et al. Scoliosis in patients with Parkinson's disease. J Clin Neurol 2009;5:91–4.

[32] Zilles K, Wree A. Cortex: areal and laminar structures. In: Paxinos G, ed. The rat nervous system. Sydney, Australia: Academic Press, 1985.

[33] Garcia JH, Wagner S, Liu KF, Hu XJ. Neurological deficit and extend of neuronal necrosis attributable to middle cerebral artery occlusion in rats. Statistical validation. Stroke 1995;26:627–35.

[34] Bederson JB, Pitts LH, Tsuji M, et al. Rat middle cerebral artery occlusion: evaluation of the model and development of a neurologic examination. Stroke 1986;17:472–6.

[35] Menzies SA, Hoff JA, Betz AL. Middle cerebral artery occlusion in rats: a neurological and pathological evaluation of a reproducible model. Neurosurgery 1992;31:100–7.

[36] Paxinos G. The rat brain in stereotaxic coordinates. Sydney, Australia: Academic Press, 1982.

[37] Neumann-Haefelin T, Witte OW. Periinfarct and remote excitability changes after transient middle cerebral artery occlusion. J Cereb Blood Flow Metab 2000;20:45–52.

[38] Buckremer-Ratzmann I, Witte OW. Extended brain disinhibition following small photothrombotic lesions in rat frontal cortex. Neuroreport 1997;8:519–22.

[39] Schiene K, Bruehl C, Zilles K, et al. Neuronal hyperexcitability and reduction of GABAA-receptor expression in the surround of cerebral photothrombosis. J Cereb Blood Flow Metab 1996;16: 906–14.

[40] Liepert J, Restemeyer C, Kucinski T, et al. Motor strokes: the lesion location determines motor excitability changes. Stroke 2005;36: 2648–53.

[41] Nudo RJ. Recovery after damage to motor cortical areas. Curr Opin Neurobiol 1999;9:740–7.

[42] Witte OW. Lesion induced plasticity as a potential mechanism for recovery and rehabilitative training. Curr Opin Neurol 1998;11: 655–62.

[43] Swayne OBC, Rothwell JC, Ward NS, Greenwood RJ. Stages of motor output reorganization after hemispheric stroke suggested by longitudinal studies of cortical physiology. Cereb Cortex 2008;18: 1909–22.

[44] Bütefisch CM, Netz J, Wesling M, et al. Remote changes in cortical excitability alter stroke. Brain 2003;126:470–81.

[45] Ziemann U, Corwell B, Cohen LG. Modulation of plasticity in human motor cortex after forearm ischemic nerve block. J Neurosci 1998;18:1115–23.

[46] Brasil-Neto JP, Valls-Solé J, Pascual-Leone A, et al. Rapid modulation of human cortical motor outputs following ischaemic nerve block. Brain 1993;116:511–25.

[47] Sailer A, Molnar GF, Cunic DI, Chen R. Effects of peripheral sensory input on cortical inhibition in humans. J Physiol 2002;544: 617–29.

[48] Herrera-Marschitz M, Utsumi H, Ungerstedt U. Scoliosis in rats with experimentally induced hemiparkinsonism: dependence upon striatal dopamine denervation. J Neurol Neurosurg Psychiatry 1990;53:39–43.

[49] Tanaka H, Kimura Y, Ujino Y. The experimental study of scoliosis in bipedal rat in lathyrism. Arch Orthop Trauma Surg 1982;101: 1–27.

[50] Machida M, Murai I, Miyashita Y, et al. Pathogenesis of idiopathic scoliosis. Experimental study in rats. Spine 1999;24:1985–9.

[51] Oyama J, Murai I, Kanazawa K, Machida M. Bipedal ambulation induces experimental scoliosis in C57BL/6J mice with reduced plasma and pineal melatonin levels. J Pineal Res 2006;40: 219–24.

[52] Schwenkreis P, Witscher K, Janssen F, et al. Changes of cortical excitability in patients with upper limb amputation. Neurosci Lett 2000;293:143–6.

[53] Ostergaard L, Fuglsang-Frederiksen A, Sjö O, et al. Quantitative EMG in cervical dystonia. Electromyogr Clin Neurophysiol 1996;36:179–85.

[54] Reuber M, Schultz A, McNeill T, Spencer D. Trunk muscle myoelectric activities in idiopathic scoliosis. Spine 1983;8: 447–56.

[55] Mahaudens P, Banse X, Mousny M, Detrembleur C. Gait in adolescent idiopathic scoliosis: kinematics and electromyographic analysis. Eur Spine J 2009;18:512–21.

[56] Zetterberg C, Bjork R, Ortengren R, Andersson GB. Electromyography of the paravertebral muscles in idiopathic scoliosis. Measurements of amplitude and spectral changes under load. Acta Orthop Scand 1984;55:304–9.

[57] Guth V, Abbink F. Comparative electromyography and kinesiology studies of congenital and idiopathic scoliosis [in German]. Z Orthop Ihre Grenzgeb 1980;118:165–72.

[58] Gaudreault N, Arsenault AB, Larivière C, et al. Assessment of the paraspinal muscles of subjects presenting an idiopathic scoliosis: an EMG pilot study. BMC Musculoskelet Disord 2005;10:6–14.

[59] Avikainen VJ, Rezasoltani A, Kauhanen HA. Asymmetry of paraspinal EMG-time characteristics in idiopathic scoliosis. J Spinal Disord 1999;12:61–7.

[60] Cheung J, Halbertsma JP, Veldhuizen AG, et al. A preliminary study on electromyographic analysis of the paraspinal musculature in idiopathic scoliosis. Eur Spine J 2005;14:130–7.