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Motor and somatosensory abnormalities are significant etiological factors for adolescent idiopathic scoliosis☆

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ABSTRACT

Objective: In adolescent idiopathic scoliosis (AIS), we explore the role of lateralized motor and somatosensory abnormalities as a possible etiological factor.
Methods: Intraoperative transcranial electrical stimulation was performed in 15 AIS and 14 adult degenerative scoliosis (ADS) patients. Inter-side motor output balance (MOB) by comparing the ratios of right to left motor evoked potentials (MEP) amplitudes, and inter-side motor output excitability (MOE) computed with MEP amplitude, was determined separately for both patients groups.
For somatosensory evoked potentials (SSEP), peak to peak P37 amplitudes from right and left lower limb SSEP and inter-side P37 amplitude ratios were obtained.
Results: Inter-side MOB was significantly asymmetric in AIS patients, contributed mainly by inter-side MOB changes in the upper than the lower limbs. Inter-side MOE comparisons of ipsilateral and contralateral MEP amplitudes were significantly different between AIS and ADS patients. Mean upper limb MEP amplitudes were significantly reduced in AIS patients. Amplitude of the right upper limb MEPs were positively correlated with inter-side MEP ratio. AIS patients show larger mean MEP amplitudes on the same side as the scoliotic curve. Overall, no correlation of Cobb's angle or total levels of scoliosis involvement with inter-side MOB and MOE parameters was found. Inter-side SSEP ratios were significantly higher in AIS patients.
Conclusions: Primary dysfunctional and distributed motor output contributing to abnormalities of inter-side MOB and MOE changes involving the upper limbs is evident in AIS. Simultaneous but independent somatosensory and motor observations seen these patients suggest a central mechanism as an etiological factor.

Scoliosis is a musculoskeletal disorder characterized by a lateral spinal deformity. The biological structures responsible include bones, ligaments and muscles around the spinal column. In the general population, a mild degree of spinal curvature is commonly encountered [1]. However, spinal curvatures of a more severe degree results in considerable morbidity and often require medical intervention.

Several methods of classifying scoliosis are used clinically, based primarily on age, etiology, severity and even location [2]. As the etiology of scoliosis is primarily unknown, particularly in younger age groups, the classification can be broadly divided into congenital scoliosis, adolescent idiopathic scoliosis (AIS) and adult degenerative scoliosis (ADS).

AIS is a common musculoskeletal disorder with unclear etiology and pathogenesis. Current views of AIS as a multifactorial disease with genetic predisposition [3] or local neuromuscular dysfunction [4] have not been universally recognized.

In contrast, adult scoliosis largely comprises ADS, residual AIS, or scoliosis secondary to neuromuscular, traumatic, neoplastic or metabolic diseases [5]. In ADS, local degenerative changes of the spinal column are the primary associations.

Currently, AIS patients with severe progressive spinal deformity are managed with corrective surgery, whereby rods are inserted to reverse the curvature. There is a strong need to elucidate the cause of AIS in order that preventive treatment can be developed and instituted early in the pediatric age group.

☆ YL Lo: conceptualization, analysis, writing article; A Teo: data collection; YE Tan: data collection; S Fook-Chong: data analysis; CM Guo: data collection; WM Yue: data collection; J Chen: data collection; SB Tan: data collection; HWM Lee: data collection: YF Dan: data collection and analysis.

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The idea that AIS develops as a result of a central neurological dysfunction is of recent interest, and is supported by several lines of evidence. Early investigators have demonstrated segmental spinal reflex [6] asymmetries obtained from paraspinal muscle recordings. The focus was also directed at the sensory system, which suggested that AIS patients possess more lateralized brain organization, possibly resulting in asymmetry of neurological functions [1]. The initial concept of an axial motor control problem integrating vestibulopathy, visuaspatial impairment, and cortico-motor maladaptation was proposed as early as 1985 [7]. However, a subsequent study was unable to demonstrate abnormal corticomotorneuronal latencies in children with AIS [8]. From the morphological standpoint, a study involving 40 AIS patients found differences in focal cortical thickness for areas involved in motor and vestibular functions, compared with healthy controls [9]. However, it remains unclear if the changes are primary or secondary as a result of adaptation to the development of scoliosis. A further study by the same group comprising 50 AIS patients also reported larger cerebellar volumes compared to control subjects, and suggested that the differences observed may be related to persistent effort in AIS patients to maintain body balance [10]. Most importantly, whether these observations are primary in nature or the result of adaptation to the scoliotic curvature justify further investigation.

Intraoperative monitoring (IOM) of the motor pathways is a routine procedure for ensuring integrity of corticospinal tracts during scoliosis surgery. In combination with somatosensory evoked potentials (SSEP), motor evoked potentials (MEPs) monitoring is widely utilized in operations with significant risks of spinal cord damage, apart from scoliosis surgery. We have previously demonstrated presence of ipsilateral MEPs during IOM for scoliosis surgery [11]. Ipsilateral MEPs of equivalent or larger amplitudes than contralateral MEPs were readily elicited during IOM of scoliosis surgery. The lack of significant ipsilateral and contralateral MEP latency differences suggests that bilateral motor cortex stimulation has resulted in ipsilateral MEPs, which may have comprised early ipsilaterally-conducted reticulospinal [12], vestibulospinal or propriospinal components, and late transcallosally stimulated corticospinal components [13]. This might also explain the larger amplitudes of ipsilateral MEPs (obtained from ipsilateral stimulation) than contralateral MEPs (derived from contralateral motor cortex stimulation).

These findings are corroborated by others. Rothwell et al. [14] electrically stimulated the motor cortex in neurologically normal scoliosis patients and made epidural electrode recordings. They concluded that at threshold, corticospinal neurons are stimulated at the motor cortex level. With higher intensities, however, stimulation of more caudal elements at the pyramidal decussation level can be achieved. A previous study by Szelenyi et al. [15] had postulated that stimulating of deep white matter motor tracts may be effected by simultaneous recording of ipsilateral and contralateral MEPs with higher stimulation intensity. This is consistent with our technique of using the cross scalp stimulation position [16].

Hence, during IOM, we have the unique opportunity to obtain suprathreshold stimulation of the motor cortex and more caudal structures. Ipsilateral and contralateral responses obtained bilaterally can provide information pertaining to the lateralization of excitability and balance of motor outputs. In this study, we compare patients with AIS and ADS for the first time, in order that questions pertaining to the role of descending motor pathways in the pathogenesis of AIS can be addressed.

Similarly, AIS clinical studies have reported separately the occurrence of subclinical abnormalities in somatosensory evoked potential (SSEP) recordings [17], and have related findings to the occurrence of gait or balance control dysfunction [18–20]. To this end, we also explore if concurrent somatosensory abnormalities play a contributory role in the development of AIS.

1. Methods

1.1. Patients

We studied 29 right-handed scoliosis patients in total, comprising 15 AIS (mean age: 17.3, range: 11 to 27, 2 men, 10 with right curvature) and 14 ADS (mean age: 61.4, range: 45 to 81, 2 men, 9 with right curvature). The study protocols were previously approved by the institutional ethical committee. The patients were evaluated and examined to ensure that they were neurologically normal. Underlying medical conditions, including neuromuscular disorders, diabetes, renal diseases and stroke were excluded. All AIS patients were referred for surgical correction of spinal deformity. The ADS patients all had significant degenerative changes, including disk disease, exit foraminal stenosis and extensive osteophytosis. Three patients had concomitant spondylolisthesis. These changes were observed both radiologically and intraoperatively. None had any motor weakness, but 2 patients reported hyperesthesia over bilateral knee regions and 4 patients showed mildly diminished ankle reflexes bilaterally.

1.2. Transcranial electrical stimulation (TES)

Intraoperative TES was performed with a Nicolet Endeavor CR (Nicolet Corp, Middleton, USA) IOM system. Stimulating electrodes consisted of 9 mm gold-plated disk electrodes at C3C4 (International 10–20 system) affixed with collodion. C3 was designated the active stimulating electrode position for left cortical stimulation, while C4 was for right cortical stimulation correspondingly. This is termed cross scalp stimulating position and is utilized for all patients. TES trains delivered by the active stimulating electrode consisted of 5 pulses of duration 0.5 ms at a frequency of 250 Hz, up to a maximum intensity of 400 V. TES stimulation output was increased sequentially until a morphologically reproducible MEP with the largest amplitude was elicited. The intensity was then increased and fixed at 10% above this threshold intensity to obtain a supramaximal MEP response (termed maximum MEP response). MEP recordings were obtained with 13 mm disposable subdermal needles (Technomed Europe, Beek, Netherlands) bilaterally. Amplifier filter settings were set at 10 Hz and 2 kHz. Input impedance of stimulating and recording electrodes was maintained below 5 kOhm.

1.3. Anesthesia

The patients underwent total intravenous anesthesia (TIVA), maintained with propofol infusion. For induction of anesthesia, sodium thiopentone at 4 mg/kg and fentanyl at 2 mcg/kg was administered. A dose of 0.8 mg/kg of intravenous atracurium was used to facilitate endotracheal intubation. No further doses of neuromuscular blocking agents were used subsequently. TIVA was maintained using the regimen of 10 mg/kg of propofol for the first 10 min, 8 mg/kg for the next 10 min and 5 mg/kg for the subsequent length of operation. For ventilation, 50% air in oxygen was administered. Morphine was titrated as required for pain relief. Electrocardiography, pulse oximetry, capnography and direct radial artery pressures were monitored continuously. All patients were kept normothermic with a warming blanket. Normotensive anesthesia was maintained throughout the operation.

After approximately 45 min post-induction, a train of 4-twitch assessment was performed using a portable nerve stimulator (Fischer Paykel NS242, United Kingdom) on the median nerve over the wrist. TES was commenced only when the amplitude of the fourth twitch from the abductor pollicis muscle was visibly similar in amplitude to the first, suggesting that the effects of neuromuscular blocking agents have subsided. An interval of 1 to 2 min was allowed between each train of TES.