

A substantial proportion of subjects with adolescent idiopathic scoliosis display spinal and peripheral proprioceptive deficits

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Aims

Adolescent idiopathic scoliosis (AIS) is considered a multifactorial disease, and proprioceptive deficit (PD) is evident as a potential associated factor. However, existing studies have indicated that only a subgroup of scoliotic adolescents would display PD. The aim of this cross-sectional clinical trial was to investigate the prevalence of, and relationship between, AIS and PD in spinal and peripheral regions.

Methods

A total of 166 participants aged ten to 25 years with AIS were assessed using 3D motion analysis to evaluate their spinal and peripheral proprioceptive abilities. Six proprioceptive tests were used to determine the presence of PD in the trunk, neck, elbow, and knee. PD was characterized by test results that were inferior to the established normative values.

Results

We found that the prevalence of trunk PD was 30.1%, while that of the neck, elbow, and knee was 19.3%, 32.5%, and 32.5%, respectively. We also revealed a correlation between spinal PD and curve magnitudes, suggesting a significant association between trunk PD and the severity of AIS. However, the presence of PD in different body parts was not significantly correlated with one another, indicating that PD may occur in the spine in isolation.

Conclusion

Overall, 50 subjects (30%) with AIS have truncal PD without necessarily the presence of peripheral PD. Moreover, their presence was associated with a larger curve magnitude. Future longitudinal studies are warranted to examine the causal relationship between PD and curve progression in AIS and vice versa.

Take home message

- Prevalence of trunk, neck, elbow, and knee proprioceptive deficit (PD) was 30.1%, 19.3%, 32.5%, and 32.5%, respectively.
- Subjects with trunk PD were found to have more severe Cobb angles of major curve.

- PD is likely to be one of the multifactorial etiologies of adolescent idiopathic scoliosis.

Introduction

Notwithstanding that adolescent idiopathic scoliosis (AIS) has remained a mystery for millennia owing to its uncertain development,^{1,2} it represents the most prevalent

form of spinal deformity that affects millions of the global paediatric population.³ Although most curvatures are not progressive,⁴ scoliotic individuals must live with the curve throughout their lifespan.^{5,6} While genetic factors have been proven to play a crucial role in its initiation,⁷ current evidence suggests that the aetiology of AIS is multifactorial.⁸ Among the various potential causes, neuromuscular abnormality is considered a contributing factor.⁹

Of the neuromuscular factors, proprioception was found to be altered both genetically and clinically in AIS.^{10,11} Given that this particular somatosensation regulates spinal posture and alignment internally,¹² it is almost certain that spinal proprioceptive deficits (PDs) is displayed in patients. Previous studies have identified several genes relevant to proprioception (e.g. *LBX1*, *PIEZO2*, *RUNX3*, *EGR3*, and *ASIC2*) that are mutated in animal models of scoliosis.¹³⁻¹⁶ Likewise, people with AIS also featured poorer proprioceptive senses (e.g. repositioning error and motion detection threshold).¹⁷⁻¹⁹

Nevertheless, further scrutiny of proprioception in scoliosis was challenging in the past. First, there were no standardized spinal and peripheral proprioception assessments for scoliotic subjects. To this end, our team has developed a set of reliable trunk repositioning tests,²⁰ adapted peripheral proprioception tests from previous studies,²¹⁻²³ and used a 3D motion analysis approach to capture proprioception systematically.²⁴ Second, determining a deficiency in proprioception has been difficult due to the absence of established ranges for proprioceptive performance in the general population. To overcome this, we obtained normative values of proprioception from a healthy cohort that matched the subjects in this study in terms of age, sex, and ethnicity.²⁴ Our thorough preparations made it a pivotal moment to explore the relationship between AIS and PD.

Considering the multifactorial inheritance, variable penetrance, and genetic complexity involved in the development of AIS, it is reasonable to expect that only a specific subgroup would exhibit the genetic susceptibility of PD. As such, the present study aimed to evaluate the prevalence of PD in participants with AIS by using our established 3D motion analysis to assess spinal and peripheral proprioceptive abilities and compare them with the predefined cut-off values. We also attempted to investigate the association between the extent of PD and the corresponding severity of spinal curvatures.

Methods

This manuscript is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.²⁵

Study design

We conducted a clinical investigation in accordance with the guidelines outlined in the Declaration of Helsinki.²⁶ The study protocol received approval from the Institutional Review Board of the University of Hong Kong and Hospital Authority Hong Kong West Cluster (reference: UW 20-525) and was registered on ClinicalTrials.gov (ID no. NCT04682379). Written informed consent was obtained from all participants and their parents. The data collection period was from September 2020 to August 2023. The current dataset was derived from the baseline data of a prospective longitudinal cohort study.

Setting

Participants were instructed to refrain from engaging in moderate or vigorous physical activity for at least 24 hours prior to testing. They were asked to wear a bra top (for females) or no top (for males) and shorts. The testing session consisted of six clinical proprioception tests conducted in a standardized sequence, including three for the trunk and one each for the neck, elbow, and knee. Demonstrations and practices were provided, and they were allowed to perform the movements at their own pace. The tests were repeated if subjects lost balance or opened their eyes during movement or repositioning. All tests were performed in triplicate, with breaks given during a test and between tests. For the trunk proprioception tests,²⁰ participants sat upright in a height-adjustable chair with their feet shoulder-width apart, knees flexed at 90°, arms held across their chest, and eyes looking at a self-perceived horizontal level. They were asked to memorize this sitting posture as the reference position before closing their eyes to perform a series of movements. To conduct the trunk flexion-extension repositioning test, participants were instructed to bend their trunks as far forward as possible, return to an upright position, and repeat the movement. In the trunk lateral-flexion repositioning test, they had to bend to the left, then to the right, and repeat the sequence in reverse. For the trunk axial-rotation repositioning test, participants had to rotate their trunks to the left, then to the right, and repeat the rotation in reverse order. After completing the movements, participants were required to return to their original position. For the neck proprioception tests,²¹ participants memorized their neutral head position as a reference and then rotated their neck to the left or right to the maximum end range once. They then returned the head to its original reference position. In the elbow proprioception tests, participants were required to flex their elbow to a random angle assigned by the examiner as a reference. They then lowered their forearm to a relaxed position with their eyes closed and repositioned it back to the reference point.²² The knee proprioception tests involved sitting in a bar stool chair with back support. Participants were asked to perform movements similar to the elbow test but with knee extension.²³

Participants

To identify potential subjects for the present study, research personnel screened all scoliotic patients consecutively in the scoliosis clinics of the hospital (Duchess of Kent Children's Hospital at Sandy Bay, Hong Kong). Candidates aged between ten and 25 years diagnosed with AIS were invited to participate. Only those who had not undergone any conservative treatments or had failed brace intervention and were awaiting surgical correction were considered eligible for inclusion. We chose these specific criteria to involve subjects for several reasons. Since most candidates were new to the clinic, it allowed us to gather uncontaminated baseline data that was not influenced by prior scoliosis treatments. Further, including those who did not respond to bracing and indicated surgery allows us to include all treatment options for scoliosis. Lastly, we selected this particular age range because older adolescents and young adults typically have more severe curvatures that qualify for surgical intervention. Hence, we could include a range of curvatures, including those that have advanced to a significant degree requiring surgery. Participants were

Table I. Correlation metrics of proprioception in scoliotic subjects.

	TFE	TLF	TAR	NRZ-L	NRZ-R	EFY-L	EFY-R	KEY-L
TLF	0.456*	N/A	N/A	N/A	N/A	N/A	N/A	N/A
TAR	0.548*	0.547*	N/A	N/A	N/A	N/A	N/A	N/A
NRZ-L	0.224*	0.096	0.127	N/A	N/A	N/A	N/A	N/A
NRZ-R	0.186*	0.188*	0.176*	0.622*	N/A	N/A	N/A	N/A
EFY-L	0.053	0.005	0.087	0.218*	0.181*	N/A	N/A	N/A
EFY-R	0.060	0.001	0.088	0.044	0.064	0.311*	N/A	N/A
KEY-L	0.135	0.079	0.142	0.122	0.006	0.142	0.105	N/A
KEY-R	0.225*	0.152	0.194*	0.177*	0.192*	0.164*	0.065	0.422*

*Significant value.

EFY-L, elbow flexion test on left side; EFY-R, elbow flexion test on right side; KEY-L, knee extension test on left side; KEY-R, knee extension test on right side; N/A, not applicable; NRZ-L, neck rotation test in left turn; NRZ-R, neck rotation test in right turn; TAR, trunk axial-rotation test; TFE, trunk flexion-extension test; TLF, trunk lateral-flexion test.

ineligible for inclusion if they presented with spinal injury, spinal fracture, spinal tumour, neurological deficits, abnormalities in the brain or spinal cord, developmental delays, or psychological disorders. Electronic medical records were examined to confirm eligibility.

Study size

The required sample size was estimated using the G*Power software v. 3.1 (Heinrich Heine University, Germany). Based on our pilot dataset tested with 19 patients with AIS, the effect size for the difference in major Cobb angle between subjects with and without spinal PD is 0.504, and the allocation ratio between groups was 0.404. Taking into account a two-tailed test, a probability of type I error of 0.05, and a probability of type II error of 0.2, the calculated total sample size was at least 154 participants (including 62 with PD and 92 without PD) for achieving the statistical power (i.e. 80%) and accuracy (i.e. 95%).

Patient characteristics

A total of 166 subjects with AIS were recruited for the study. Of them, 134 (80.7%) were female. Participants had a mean age of 14.9 years (SD 3.0), mean height of 159.5 cm (SD 8.3), mean weight of 48.0 kg (SD 9.8), and mean BMI of 18.8 kg/m² (SD 3.0). The average major Cobb angle was 34.3° (SD 15.8°), with 12.7%, 60.2%, and 27.1% having mild, moderate, and severe curves, respectively.

Measurements

The 3D motion capture system composed of eight optical cameras (Nexus 2.16 and MX-T40; Vicon, UK) with a sampling rate of 100 Hz was used. The subject's body was fitted with 34 retroreflective markers attached by palpation.²⁰ The markers were positioned on the skin proximal to the spinous processes of the seventh cervical vertebra and counted inferiorly to attach the third, fifth, seventh, ninth, and 11th thoracic vertebra; first, second, third, fourth, and fifth lumbar vertebrae; and sacrum. Additional markers were placed on both sides at the front head, lateral one-third shaft of the clavicle, inferior

Table II. Relationship of proprioceptive deficits among body regions.

	Trunk PD	Neck PD	Elbow PD
Neck PD	p = 0.559	N/A	N/A
Elbow PD	p = 0.177	p = 0.132	N/A
Knee PD	p = 0.087	p = 0.863	p = 0.612

N/A, not applicable; PD, proprioceptive deficit.

angle of the scapula, costal end of the 12th rib, anterior superior iliac spine, posterior superior iliac spine, shoulder, elbow, thumb side of the wrist, knee, and ankle.

Variables

Raw motion data were processed by a fourth-order low-pass Butterworth filter with a cut-off frequency of 6 Hz. We assessed the spinal angles in coronal and sagittal planes at every thoracic and lumbar marker by determining the intersection of the measured level marker with its neighboring proximal and distal markers, and the rotational component was calculated from the lower level in comparison to the upper level of the trunk local regions. The neck angle was determined between the lines of the middle of the forehead and the seventh cervical vertebra at the beginning and end of the test. For the elbow angle, we used the elbow marker in conjunction with the shoulder and wrist markers. Regarding the knee angle, we calculated it using markers placed at the anterior superior iliac spine, knee, and ankle. We took the average of three trials for each test outcome. The proprioceptive outcome measures were the total absolute repositioning errors in all anatomical planes between the starting and ending positions (for trunk proprioception test), the angle measured in all anatomical planes (for neck proprioception test), and the differences in angle of all anatomical planes between the starting and ending positions (for elbow and knee proprioception tests). In light of the primary objective, we operationally defined the trunk PD as having a poorer test result in any of the three trunk tests with reference to the normative values.²⁴ The details of the data generated from the non-AIS cohort have been published elsewhere.²⁴ The neck, elbow, and knee PD were defined as having an inferior test result on either the left or right side compared to the norms from our healthy participants.²⁴ Using our previous findings on healthy controls, the mean test score plus a SD was the cut-off value for having PD in each proprioception test.²⁴ Specifically, the Cobb angles of the major curve, proximal thoracic curve, main thoracic curve, thoracolumbar or lumbar curve, and the convexity of the major curve were measured. The degree of curve severity was classified as mild, moderate, and severe if it ranged from 10° to 19°, between 20° and 39°, and over 40°, respectively.

Statistical analysis

SPSS software v. 29.0 (IBM, USA) was employed to analyze the data with a significance level of 0.05. Descriptive statistics were used to present the distribution of PD in different body parts. Independent-samples *t*-test and proportions test compared proprioceptive performance and potential associated demographic and radiological factors

in participants with and without PD. Pearson's correlation coefficient and chi-squared test examined the associations between proprioceptive abilities and PD between spinal and peripheral regions.

Results

Within our cohort, trunk PD had a prevalence of 30.1%, while neck PD had a rate of 19.3%. PD in the elbow was present in 32.5% of cases, and it was also observed in 32.5% of cases in the knee. The distribution of PD in our participants is shown in Figure 1. Specifically, 42.8% of study subjects had PD in one region, while 19.3%, 7.8%, and 2.4% had PD in two, three, and all four regions, respectively.

Additionally, subjects with trunk PD had larger repositioning errors in the trunk flexion-extension test (mean difference (MD) 13.1°, $p < 0.001$), trunk lateral-flexion test (MD 14.2°, $p < 0.001$), and trunk axial-rotation test (MD 14.3°, $p < 0.001$) than their counterparts. Subjects with neck PD have also shown greater repositioning errors in the left turn (MD 2.3°, $p < 0.001$) and right turn (MD 1.7°, $p < 0.001$) of the neck rotation test compared to those without deficits. Likewise, participants with elbow PD presented larger repositioning errors on the left hand (MD 3.4°, $p < 0.001$) and right hand (MD 4.1°, $p < 0.001$) of the elbow flexion test compared to other subjects. Individuals with knee PD possessed greater repositioning errors on the left leg (MD 2.3°, $p < 0.001$) and right leg (MD 2.7°, $p < 0.001$) of the knee extension test. The comparisons of proprioceptive test outcomes between subjects with and without PD are illustrated in Figure 2.

Interestingly, the proprioceptive ability of a given region was not correlated with any other region. The correlation metrics are visible in Table I. Relationships among PD were also not significantly associated. The chi-squared test results are presented in Table II.

Considering the associated demographic factors for PD, subjects with trunk PD were characterized by younger age (MD 1.2 years, $p = 0.021$), shorter height (MD 4.1 cm, $p = 0.003$), and more females (with PD 90.0%; without PD 76.7%; $p = 0.047$). Subjects with neck PD were also less immature in age (MD 1.3 years, $p = 0.009$). However, no demographic factors were significantly related to elbow or knee PD.

To address the association between AIS and PD, subjects with trunk PD were found to have more severe Cobb angles of the major curve (MD 4.6°, $p = 0.041$) and the thoracolumbar or lumbar curve (MD 6.8°, $p = 0.003$). It indicated that there was an association between trunk PD and major curve magnitude, and the curves seemed more common in the lower back area. Subjects with knee PD had a smaller main thoracic Cobb angle (MD 7.0°, $p = 0.026$). Further, subjects with elbow PD had more right sided major curves (with PD 68.5%; without PD 50.9%; $p = 0.032$).

Discussion

This is the first study to systematically scrutinize the prevalence of spinal (trunk and neck) and peripheral (elbow and knee) PD in participants with AIS. Using our established proprioception assessments and clinical diagnosis of PD, we found that 19% to 32% of individuals showed PD in the trunk, neck, elbow, and knee. More importantly, the current results revealed a significant correlation between spinal PD and the

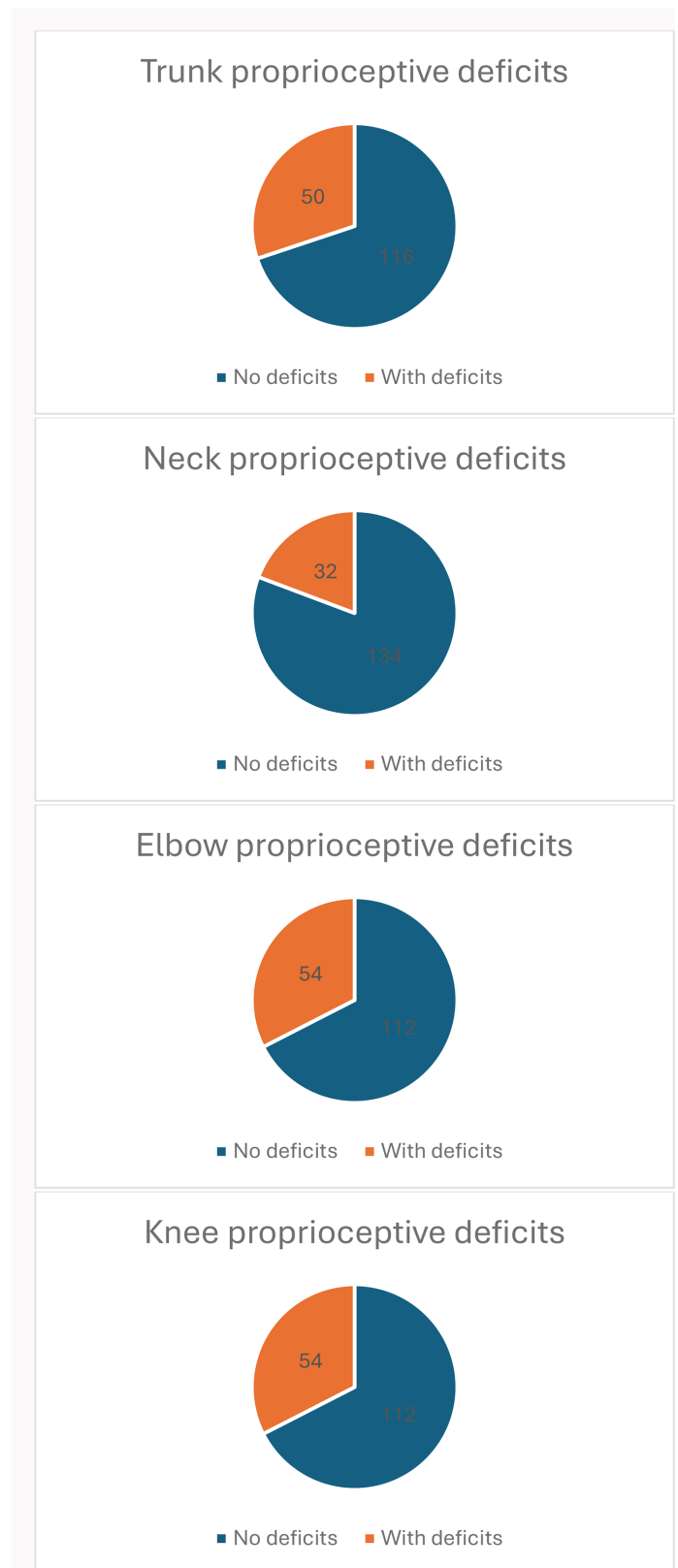


Fig. 1 Distribution of proprioceptive deficits in different regions.

magnitude of the curve. This implies that PD could be related to the progression of the curve in AIS.

We observed that PD did not have a systemic effect on individuals with AIS. Since spinal PD and AIS share the same location of origin, it is conceivable that spinal proprioception may directly impact the spinal curves. Conversely, we inferred

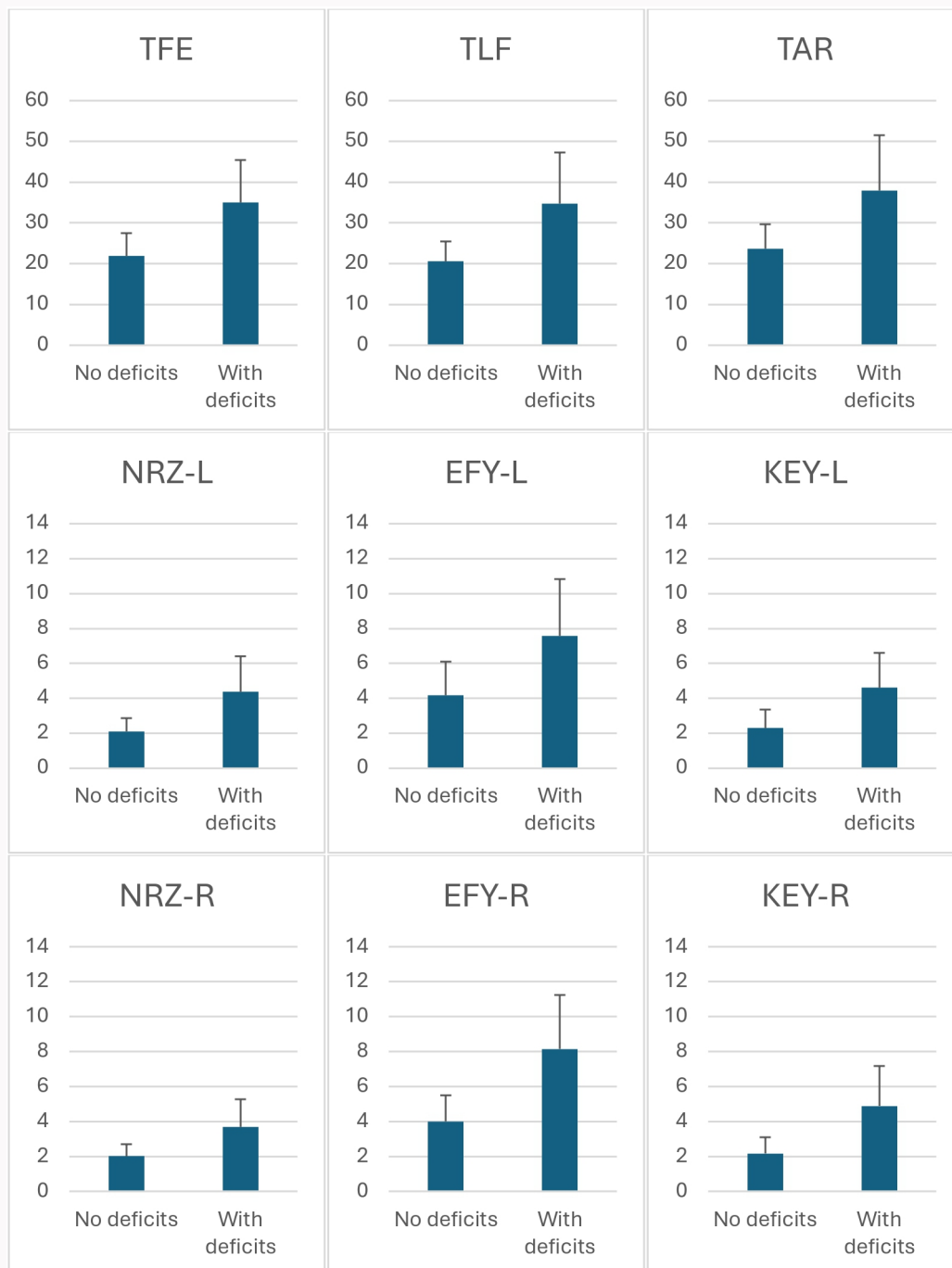


Fig. 2

Differences in repositioning errors between groups. EFY-L, elbow flexion test in left side; EFY-R, elbow flexion test in right side; KEY-L, knee extension test in left side; KEY-R, knee extension test in right side; TAR, trunk axial rotation test; TFE, trunk flexion-extension test; TLF, trunk lateral-flexion test; NRZ-L, neck rotation test in left turn; NRZ-R, neck rotation test in right turn.

that peripheral PD may be a compensatory effect secondary to the biomechanical changes resulting from scoliosis as a presentation of abnormal gait.²⁷ Peripheral proprioception could also be influenced by other underlying factors in the central nervous system that may also cause scoliosis, such as abnormal brain oscillatory activity,²⁸ or defects in cerebrospinal fluid flow.²⁹ Hence, using peripheral PD to evaluate the presence or prognosis of AIS may be inappropriate.

Our results demonstrated that only a sub-group of AIS was susceptible to spinal PD, which may be due to genetic variation. It aligns perfectly with prior literature on the

relationship between scoliosis and proprioception.³⁰ In other words, this explains why AIS is called a multifactorial disease. This spinal condition is thought to result from the interaction of genetic and environmental factors.³¹ While genetics and heredity may act as a main character in the development of scoliosis, identifying the exact gene responsible is unlikely to happen.³² Hence, the formation of AIS is probably influenced by a variety of factors together. Combining all the results makes it obvious that spinal PD could be an underlying cause of AIS, and impaired proprioception in the spine would be

a clinical manifestation. This would make spinal PD the first known phenotype of AIS.

Regarding the associated demographic factors, it was observed that individuals with spinal PD exhibited immaturity of growth. Although our previous findings revealed a negatively correlated age effect on spinal proprioception in the healthy population,²⁴ this phenomenon was not applied in our subjects with AIS. There were no significant correlations between proprioception and age in our cohort. It may suggest that this unique subgroup of AIS developed its curvature at a younger age. While most of the curves progress during growth spurts,³³ there are some cases where curve deterioration occurs before puberty. Collectively, it may hint that this AIS phenotype is characterized by an early onset of spinal curves.

Most importantly, the association between AIS and trunk PD was expressed in terms of curve magnitude. We found that only individuals with trunk PD showed larger Cobb angles. Specifically, our ad-hoc analysis exhibited that those with trunk PD had more severe curves with an odds ratio of 2.188 (95% CI 1.003 to 4.771, $p = 0.046$). These have implied that proprioception may be related to the progression of the curves. Since impaired proprioception can result in a loss of spinal alignment,³⁴ it is possible that scoliotic adolescents with trunk PD may experience more rapid curve progression compared to those with normal proprioception. To investigate this relationship further, it is vital to conduct a prospective longitudinal study targeting the determination of trunk PD on curve progression in a representative cohort of patients.

It is important to consider certain limitations when interpreting the results of the present study. Our participants were only recruited from one of the two scoliosis clinics in Hong Kong, which might not represent the entire local population with AIS. Since this study used a cross-sectional design, a prospective longitudinal study would be able to reveal the effects of proprioception on the progression of scoliosis over time.

In conclusion, the prevalence of PD within our cohort varied across different body regions, and the presence of PD in one region was unrelated to PD in other regions. Demographic factors associated with spinal PD were related to growth markers. Subjects with trunk PD had more severe Cobb angles for their major curves. These findings suggested that PD were common in scoliotic adolescents, but only those with spinal PD were more likely to have severe curves. Further studies are warranted to determine the causal relationship between PD and curve progression.

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A. Y. L. Wong: Methodology, Supervision, Writing – original draft, Writing – review & editing.

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K. M. C. Cheung: Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

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Data sharing

The data that support the findings for this study are available to other researchers from the corresponding author upon reasonable request.

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