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Normative values of spinal and peripheral proprioception in position sense among healthy adolescents and young adults

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Establishing normative values and understanding how proprioception varies among body parts is crucial. However, the variability across individuals, especially adolescents, makes it difficult to establish norms. This prevents further investigation into classifying patients with abnormal proprioception. Therefore, the primary objective was to address the knowledge gap using three-dimensional motion analysis to capture position sense in adolescents and young adults. The secondary objective was to evaluate the relationship between position sense and age, as well as the interrelationships of position senses across various anatomical sites. Healthy participants aged 10 to 25 years were included. Six position sense tests were implemented on the trunk, neck, elbow, and knee. Data were captured using a three-dimensional motion capture system. The proprioceptive measure was the absolute repositioning error (the difference between the destinated starting position and the corresponding self-reproduced ending position) of each test. A total of 103 participants were recruited. We found that only spinal proprioception was associated with chronological age, whereas peripheral proprioception was not. Subgroup analyses revealed that subjects aged 10 to 13 years had the poorest proprioceptive performance. The normative values of proprioception of various body parts were, trunk flexion-extension test = 25° ± 12°; trunk lateral-flexion test = 23° ± 10°; trunk axial-rotation test = 26° ± 11°; left neck rotation test = 2° ± 1°; right neck rotation test = 3° ± 1°; left elbow flexion test = 5° ± 3°; right elbow flexion test = 5° ± 2°; left knee extension test = 3° ± 2°; right knee extension test = 3° ± 1°. The normative values of proprioception in position sense provided in this study may help identify individuals with proprioceptive deficits and inform targeted interventions to improve proprioception.

Keywords Proprioception, Position sense, Repositioning errors, Absolute errors, Proprioceptive deficits, Normative values, Normative data

Proprioception is a subset of somatosensation that enables sensing the position, movement, and force of body parts[1]. Numerous mechanoreceptors (e.g., muscle spindle and Golgi tendon organ) reside mainly in muscles and tendons that transmit proprioceptive signals to the central nervous system[2]. Despite decades of research, our understanding of proprioception is still limited[3]. There is much to learn about its multiple receptors, underlying mechanisms, neural pathways, and functional significance[4]. Proprioception contributes considerably to motion and postural control[5], and it can be assessed through various methods[6]. These assessments encompass both conscious and unconscious aspects[7], each requiring different evaluation techniques[8]. In this study, we focused on measuring a specific component of proprioception known as position sense. Numerous methods can be employed to evaluate position senses[9], such as passive-to-passive, passive-to-active, active-to-passive, active-to-active, and visual tests. Various outcome measures are used to measure sense or position, including absolute error, constant error, and variable error[10]. This sensation is difficult to measure owing to its prerequisite of isolation from other senses (e.g., tactile) and systems (e.g., vestibular)[11].

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Specifically, the proprioceptive deficit has been linked to various diseases like idiopathic scoliosis[12,13] and cerebral palsy[14]. To identify atypical proprioception in future, reference standards from normal people must first be acquired[15]. Normative values provide a baseline for comparing an individual's proprioceptive abilities to those of the general population, thus healthcare professionals can determine if there is a deviation from the expected range[16]. However, the variability across individuals made it difficult to constitute the norms, especially for adolescents. As the maturing nervous system is thought to play a critical role in proprioception during child development[17], proprioceptive abilities can vary greatly across individuals of different ages[18–20]. This variation makes it hard to establish normative values that represent the range of proprioceptive functions[21].

Numerous studies have examined proprioception in both healthy individuals and clinical populations, typically focusing on a specific body region[22–26]. However, there is a scarcity of research comparing proprioception across multiple regions within the same individuals. Given that proprioception involves the integration of multiple sensory inputs and motor control, measuring it accurately in a systemic manner can be challenging and require specialised equipment. Hence, we sought to examine normal proprioception in multiple body regions using an accurate motion capture technique.

Given the above, we aimed to address the knowledge gaps regarding the normative values of spinal and peripheral proprioception in a group of standardised position sense tests during the developmental stages via a three-dimensional motion analysis. We also aimed to investigate the relationship between position sense and age, and the correlations among position senses across different body parts. Our results may facilitate the identification of young individuals with proprioceptive deficits.

Materials and methods

This manuscript follows the strengthening the reporting of observational studies in epidemiology (STROBE) statement[27].

Research design

We adopted a prospective, observational, cross-sectional, single-centred clinical study that complied with the Declaration of Helsinki[28]. This study was approved by the institutional review board of The University of Hong Kong and Hospital Authority Hong Kong West Cluster (reference number: UW 20–525) and registered in a publicly accessible database (i.e., ClinicalTrials.gov, identifier: NCT04682379). Participants themselves (for those aged 18 or above) or their parents (for those aged below 18) provided written informed consent before the experiment began. The data collection period was from January 2021 to December 2023.

Setting

The testing sessions took place at the motion analysis laboratory of the Duchess of Kent Children's Hospital in Hong Kong. Study subjects were reminded not to participate in vigorous physical activity before the testing, for example, hiking, jogging, and bicycling. All participants wore a bra top with shorts (for females) or shorts without a top (for males) throughout the testing. The testing session consisted of six position sense tests, including three for the trunk[29], and one each for the neck[30], elbow[31], and knee[32]. The tests for the trunk and neck were designed to return to a neutral position after an active movement, while limb tests were developed to reposition the limb to a predetermined target joint angle. Demonstrations and practices were provided before the data capturing. During the movements, participants could perform at their own pace. The test would be redone when the subject lost balance or opened their eyes during the movement or repositioning. All tests were performed in triplicate. A 30-second and a 1-minute break was given within a test and between tests. Additional rest was allowed as requested by the subjects. Data acquisition for each test commenced just before the initial positioning of the reference and continued until immediately after the repositioning.

Trunk position sense tests[29] Subjects were required to sit upright on a height-adjustable chair with feet at shoulder width, knees flexed at 90 degrees, arms held across the chest, and eyes looked at a self-perceived horizontal level. To begin the test, subjects needed to stay still, maintain, and memorise the sitting posture as a reference position. Next, they were instructed to close their eyes to perform a series of movements until the completion of the test. For the trunk flexion-extension repositioning test, subjects had to bend their trunks forward to the maximum range, return to the upright posture, and repeat the motion once. Regarding the trunk lateral-flexion repositioning test, subjects had to bend to the left, then to the right, return to the upright position, and repeat the motion in reverse order. As for the trunk axial-rotation repositioning test, subjects needed to rotate their trunks to the left, then to the right, return to the upright position, and then repeat the motion once in the opposite sequence. Once the movements were completed, subjects had to return to the reference position and preserve it for three seconds. Position sense data was extracted from the middle 1-second segment of both the starting (reference) and ending (reproduced) positions to minimise movements during the initial and final 1-second periods. The reliability of the trunk tests has been documented in our previous paper[29], revealing intraclass correlation coefficients (ICC) ranging from 0.59 to 0.72.

Neck position sense test[30] A similar setup as the trunk tests was utilised, except arms were rested on the thighs. At first, subjects memorised their neutral head position as a reference and held it for three seconds. Afterwards, they rotated the neck to either left or right to the maximum end range once. Left sided turning was evaluated first (i.e., three repetitions to the left, and then another three repetitions to the right). It ended with backing to the reference position and holding for three seconds. The moderate reliability of the neck tests has been established by prior research, with an ICC value of 0.55[33].

Elbow position sense test[31] The setup was similar to the neck test, with the tested arm placed beside the body at 0 degrees of elbow flexion and the palm facing forward. Each arm was tested individually, starting with the left side. During the test, participants were instructed to keep their upper arms still on the test side. Initially, they flexed their elbow to a random angle (i.e., one each for approximately 45, 90, and 135 degrees, in a random order as determined by visual inspection) assigned by the examiner as a reference and kept it for three seconds. The forearm was then lowered to a relaxed position with eyes closed. In closing, they returned to the reference position and kept it for three seconds. These elbow tests have demonstrated moderate to good reliability, with ICC values ranging from 0.57 to 0.75 reported in the literature[34].

Knee position sense test[32] This setup was sitting in a bar stool chair with back support, allowing legs to hang freely and arms resting on the back of the chair. Each leg was tested separately, and the left side began first. Throughout the examination, participants were instructed to maintain their thighs stable on the side being tested. The movements mirrored those of the elbow tests but involved knee extension. The examiner randomly assigned the target position for each of the three repetitions (i.e., approximately 113, 135, and 158 degrees). Yet, the knee tests have been recognised as poor reliability, indicated by an ICC value of 0.42[35].

Participants
Healthy individuals aged 10 and 25 were included. Those with known spinal problems, neurologic deficits, psychological disorders, and developmental delays were excluded. All potential subjects were engaged in a recruitment campaign at the local universities. The subject recruitment poster was delivered through bulk electronic mail to students, staff, and alumni. They were also asked to assist in identifying other candidates. A simple telephone interview was performed with the interested parties to screen the eligibility. It was subsequently reviewed through the electronic medical records of the local hospital management system. On the testing date, the absence of scoliosis was screened by the scoliometer on site, and other exclusion criteria were enquired again. The sample size was determined by the maximum number of participants we could recruit through our most extensive efforts over three years.

Measurements
We employed a three-dimensional motion capture system encompassing eight optical cameras (i.e., Nexus 2.15 and MX-T40, Vicon motion systems, United Kingdom) with a sampling rate of 100 Hz. A trained investigator attached 34 retroreflective markers of 9.5 mm diameter on the subject's body by palpating spinous processes or anatomical landmarks (Fig. 1). The spinal markers were placed on the skin proximal to the spinous processes of the 7th cervical vertebra first and then counted inferiorly to the spinous processes to attach the 3rd, 5th, 7th, 9th, 11th thoracic vertebra, 1st, 2nd, 3rd, 4th, 5th lumbar vertebrae, and sacrum. Other markers were placed bilaterally at the front head, lateral one-third shaft of the clavicle, inferior angle of the scapula, costal end of the 12th rib, anterior superior iliac spine, posterior superior iliac spine, shoulder, elbow, thumb side of wrist, knee, and ankle. An occupational therapist experienced with palpation of anatomical references verified the marker placement. Our team has testified to the repeatability of the spinal marker set[29], whereas other markers were adapted from the default setup of the motion analysis.

Variables
Spinal angles in both coronal and sagittal planes were assessed at every thoracic and lumbar marker, by determining the intersection of the measured level marker with its neighbouring proximal and distal markers. The spine's rotational components were calculated from the lower level in comparison to the upper level, which was the sacrum compared to the rib cage, the rib cage compared to the scapula, and the scapula compared to the clavicle. The neck angle was calculated between the line of the middle of the forehead and the 7th cervical vertebra at the start and end. The elbow angle was formulated as the elbow marker with shoulder and wrist markers. The knee angle was computed at the knee marker with anterior superior iliac spine and ankle markers. The outcomes of each test were computed with the average of the three trials. The proprioceptive outcome measures were the total absolute repositioning errors in all anatomical planes between the starting and ending positions of every trunk test, the angle measured in all anatomical planes for the neck test, the differences in angle of all anatomical planes between the starting and ending positions of elbow and knee tests. Demographic data was extracted from the medical records of the hospital system. In particular, age was categorised into four groups for comparative purposes (i.e., aged 10–13, 14–17, 18–21, and 22–25 years). Anthropometric parameters were measured on the same date as the proprioceptive testing.

Bias
We employed several procedures to counteract potential sources of bias. Avoiding high intensity physical activity participation before testing could ensure subjects' natural proprioceptive performance. The dress code of the testing allowed the direct placement of most of the markers onto the skin. Thus, the data could accurately reflect the subject's ability. Another researcher cross-checked every marker placement to avoid human errors. Rest was given as much as possible to prevent fatigue. All tests were done by the subjects themselves without additional tactile and pressure feedback. Three-dimensional analysis provided a complete picture of proprioception without missing any information. The motion capture system minimised the influences of the investigator with a small measurement error.

Statistical analysis
The same data capture system was used for raw data labelling. Raw data were then processed by a fourth-order low-pass Butterworth filter with a cut-off frequency set at 6 Hz using a customised data analysis programme (MATLAB R2021a, MathWorks, United States). Data were analysed using the SPSS software (version 29.0, IBM, United States) with the p-value < 0.05 set as significant. Descriptive statistics were presented for normative values of proprioception. Pearson's correlation coefficient was performed to assess the relationships between spinal and peripheral proprioception with age. One-way analysis of variance and post hoc tests with the least

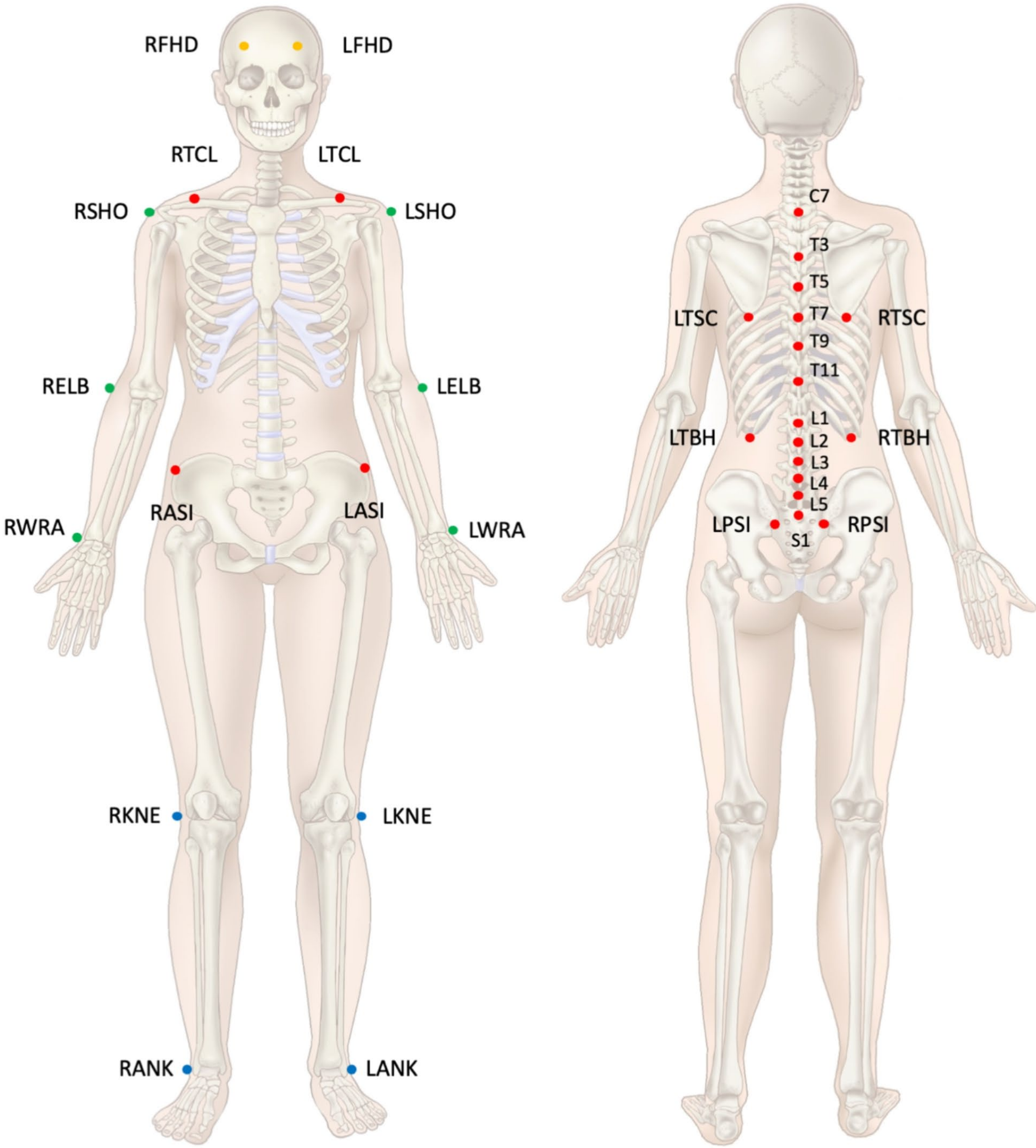

Fig. 1. The marker set of motion analysis.

significant difference were conducted to compare among different age groups, and the corresponding Cohen's d effect size for each subgroup comparison was presented.

Results

In total, 103 healthy participants enrolled. Their characteristics were shown as follows, 64% of females, as well as a mean age, height, weight, and body mass index were 18 ± 5 years (yrs), 162 ± 10 cm, 56 ± 15 kg, and 21 ± 4, respectively.

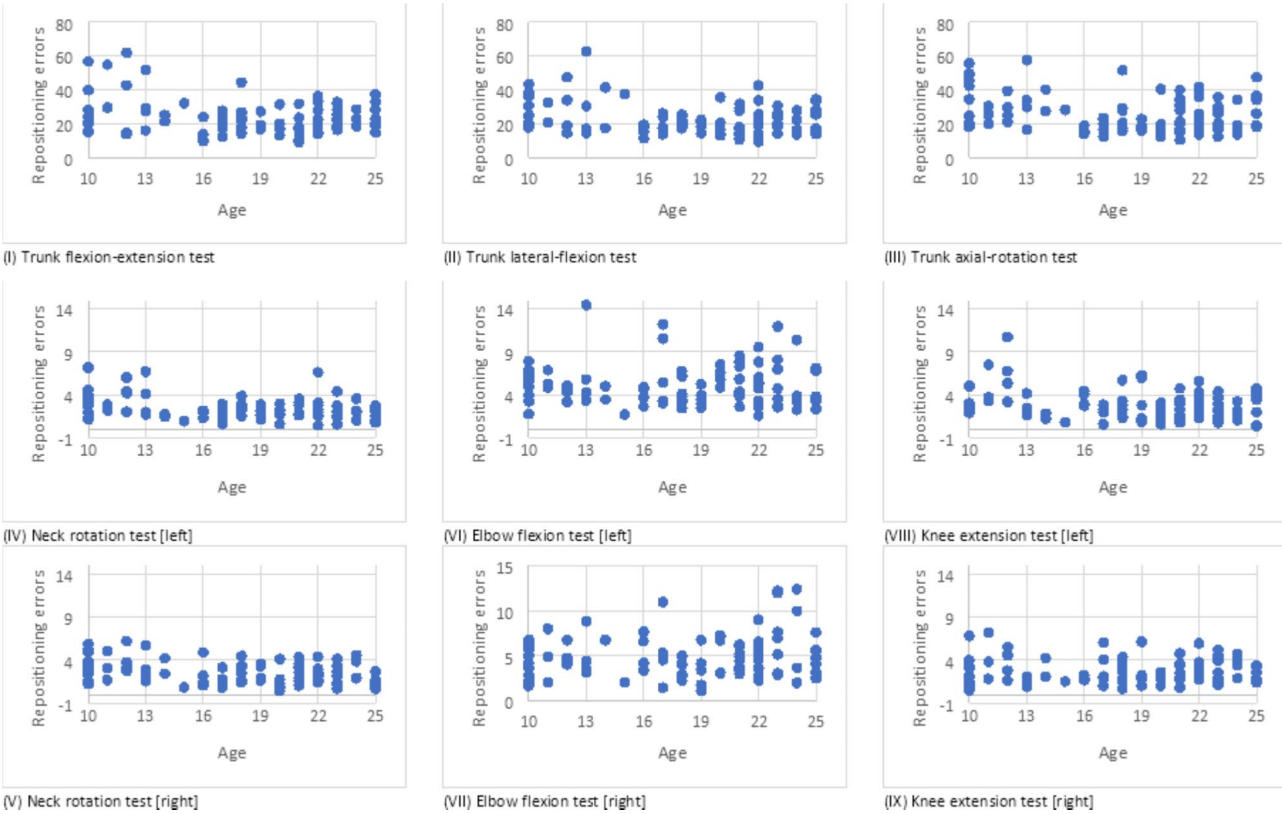

Fig. 2. Scatter plots of absolute repositioning errors in degrees and age in years.

	Group 1: 10–13 yrs (*n* = 23)	Group 2: 14–17 yrs (*n* = 19)	Group 3: 18–21 yrs (*n* = 30)	Group 4: 22–25 yrs (*n* = 31)	G1 vs. G2	G1 vs. G3	G1 vs. G4	G2 vs. G3	G2 vs. G4	G3 vs. G4
TFE	32.5 ± 15.2	24.9 ± 14.8	19.6 ± 7.3	24.3 ± 6.6	d = 0.506*	d = 1.153*	d = 0.750*	d = 0.502	d = 0.059	d = 0.674
TLF	29.5 ± 13.4	23.0 ± 8.5	19.5 ± 5.8	22.5 ± 7.6	d = 0.556*	d = 1.015*	d = 0.666*	d = 0.498	d = 0.068	d = 0.426
TAR	33.4 ± 12.7	24.1 ± 11.2	22.5 ± 9.1	26.4 ± 9.2	d = 0.760*	d = 1.006*	d = 0.642*	d = 0.166	d = 0.225	d = 0.424
NRZ-L	3.3 ± 1.6	2.0 ± 0.9	2.1 ± 0.7	2.1 ± 1.2	d = 0.880*	d = 0.879*	d = 0.765*	d = 0.178	d = 0.117	d = 0.014
NRZ-R	3.4 ± 1.5	2.3 ± 1.2	2.3 ± 1.1	2.2 ± 1.0	d = 0.747*	d = 0.846*	d = 0.994*	d = 0.029	d = 0.158	d = 0.134
EFY-L	5.8 ± 3.3	5.7 ± 3.5	5.0 ± 1.8	5.2 ± 3.1	d = 0.022	d = 0.319	d = 0.170	d = 0.291	d = 0.145	d = 0.102
EFY-R	4.4 ± 2.0	5.4 ± 2.6	4.0 ± 1.6	5.5 ± 2.9	d = 0.505	d = 0.148	d = 0.452	d = 0.695	d = 0.012	d = 0.598*
KEY-L	4.0 ± 2.6	2.3 ± 1.0	2.5 ± 1.4	2.7 ± 1.3	d = 0.767*	d = 0.703*	d = 0.621*	d = 0.131	d = 0.313	d = 0.151
KEY-R	2.7 ± 1.8	2.5 ± 1.3	2.3 ± 1.3	2.9 ± 1.2	d = 0.072	d = 0.201	d = 0.168	d = 0.148	d = 0.296	d = 0.445

Table 1. Proprioceptive performance in position sense among different age groups. Note. yrs = years; G1 = group 1; G2 = group 2; G3 = group 3; G4 = group 4; TFE = trunk flexion-extension test; TLF = trunk lateral-flexion test; TAR = trunk axial-rotation test; NRZ-L = neck rotation test in left turn; NRZ-R = neck rotation test in right turn; 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; d = Cohen's d effect size; * as significant.

While spinal position sense was associated with age (trunk flexion-extension test: r=-.273, $p = .009$; trunk lateral-flexion test: r=-.276, $p = .009$; trunk axial-rotation test: r=-.238, $p = .023$; neck rotation test in left turn: r=-.306, $p = .003$; neck rotation test in right turn r=-.355, $p < .001$), peripheral position sense revealed neither strong association nor statistical significance. Correlation analyses are illustrated in Fig. 2.

Pairwise comparisons showed that only the youngest subjects had poorer spinal and lower limb position senses than other age groups (Table 1). There were significant differences in trunk flexion-extension, trunk lateral-flexion, trunk axial-rotation, neck rotation, and knee extension tests between the group of 10 to 13 years and the other age groups.

Regarding the relationships between spinal and peripheral position senses (Table 2), the trunk tests showed correlations with the neck tests. The trunk flexion-extension test was linked to the knee test on the left side.

	TFE	TLF	TAR	NRZ-L	NRZ-*R*	EFY-L	EFY-*R*	KEY-L
TLF	0.690*							
TAR	0.653*	0.729*						
NRZ-L	0.278*	0.313*	0.349*					
NRZ-R	0.285*	0.349*	0.299*	0.515*				
EFY-L	0.113	0.158	0.146	0.042	0.166			
EFY-R	0.094	0.134	0.126	0.044	0.024	0.420*		
KEY-L	0.202*	0.158	0.114	0.085	0.232*	0.216*	0.017	
KEY-R	0.005	0.062	0.015	0.043	0.169	0.116	0.105	0.324*

Table 2. Correlation metrics of spinal and peripheral position sense. Note. TFE = trunk flexion-extension test; TLF = trunk lateral-flexion test; TAR = trunk axial-rotation test; NRZ-L = neck rotation test in left turn; NRZ-R = neck rotation test in right turn; 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; * as significant.

	Mean	Standard deviation	Cut-off 1	Cut-off 2
Trunk flexion-extension test	24.8	11.6	36.3	47.9
Trunk lateral-flexion test	23.1	9.5	32.7	42.2
Trunk axial-rotation test	26.3	11.0	37.3	48.3
Neck rotation test in left turn	2.4	1.3	3.7	4.9
Neck rotation test in right turn	2.6	1.3	3.8	5.1
Elbow flexion test in left side	5.4	2.9	8.3	11.3
Elbow flexion test in right side	4.8	2.4	7.2	9.6
Knee extension test in left side	2.9	1.8	4.7	6.5
Knee extension test in right side	2.7	1.4	4.1	5.5

Table 3. Normative values of position sense in adolescents and young adults. Note. Cut-off value 1 as mean plus standard deviation; Cut-off value 2 as mean plus two times standard deviation.

Additionally, the neck test in the right turn was correlated with the knee test on the left side, and the elbow test on the left side was associated with the knee test on the left side. The remaining tests did not appear to have significant relations with one another. That said, all tests in the same tested regions were intercorrelated.

Lastly, the normative values of proprioception in position sense were presented as shown below (i.e., trunk flexion-extension test = 24.8° ± 11.6°; trunk lateral-flexion test = 23.2° ± 9.5°; trunk axial-rotation test = 26.3° ± 11.0°; neck rotation test in left turn = 2.4° ± 1.3°; neck rotation test in right turn = 2.6° ± 1.3°; elbow flexion test in left side = 5.4° ± 2.9°; elbow flexion test in right side = 4.8° ± 2.4°; knee extension test in left side = 2.9° ± 1.8°; knee extension test in right side = 2.7° ± 1.4°). Cut-off values for abnormal position sense are also recommended in Table 3.

Discussion

Our present study determined the normative values of spinal and peripheral proprioception utilizing position sense in typically developed adolescents and young adults. We found that only the spinal rather than peripheral position sense was associated with chronological age, particularly participants aged 10 to 13 featuring the highest absolute repositioning errors. Nevertheless, numerous uncertainties persist in existing knowledge, like the underlying mechanisms of its development.

Upon close examination of the literature, it is evident that our current data closely aligns with previous findings for normative values, particularly for the neck[36], elbow[37], and knee regions[22]. However, comparing our proposed measurement of trunk position sense, an integrated absolute error across all anatomical planes, with prior studies is challenging[38,39]. Some scholars may contend that the variability in our trunk position sense assessments is relatively pronounced. This is primarily due to our implementation of an extensive marker set encompassing the trunk, which allows for a comprehensive representation of the cumulative effects across the thoracic and lumbar spinal regions. We deliberately refrain from utilizing simpler truncal measures, such as relying on the C7 and sacrum markers, as this would substantially compromise the fidelity of the metrics we aim to obtain. Given the complexity of the spinal structure comprising numerous vertebrae, excluding the intervertebral segments did not align with our objectives. Furthermore, by employing a metric that aggregates deviations from captured postures, we can discern that the differences manifest in both the thoracic and lumbar spine, leading to elevated values in certain individuals.

The proprioceptive deficit has been linked to several neuromuscular disorders, such as idiopathic scoliosis[12,13]. Future investigations may reference the provided norms of position sense (i.e., cut-off values of mean plus one or two standard deviation) to determine whether a candidate has abnormal proprioception. However, it is essential to exercise caution when interpreting the provided normative values, as their relevance is limited to tests performed under the same setup as in this study.

Theoretically, the central nervous system matures in adulthood[40]. We expect that its allied sensory systems follow the same trend. However, the current results showed that only spinal position sense was shown to be negatively associated with the age effect. It may suggest that spinal proprioception still develops during adolescence and young adulthood[38], whereas peripheral proprioception may have matured before puberty. This hypothesis is partially supported by the literature, where forearm and wrist proprioception were not much different across childhood[23,41]. Another study on knee proprioception also exhibited outcomes comparable to those of our present study[22].

Interestingly, we found that spinal and peripheral position senses were not associated. Despite several pairs of tests showing statistical relations, all of them revealed very weak associations and could potentially be attributed to random effects. It may indicate that the position sense of different regions matures independently, which means each region has its unique proprioceptive ability without being much affected by other regions[42]. Another possible explanation is that proprioception is easily affected by external factors, for instance, various sports participation and different types of leisure activities[43]. Further, it may be attributed to the fact that the number of proprioceptors in muscles and tendons varies in different regions[44]. The underlying mechanism is yet to be known.

Sense of position can be measured using to-neutral tests or to-target tests. In this study, we used to-neutral tests for the spine and to-target for the limbs. Spinal position sense tests are to-neutral tests and peripheral position sense tests are to-target tests due to the distinct functions and roles of the axial and appendicular skeletons. The axial skeleton, consisting of the trunk and neck, primarily focuses on returning to a neutral position after movements[45,46]. In contrast, the appendicular skeleton, comprising the limbs, is premeditated for a wide range of precise movements[47]. This distinction explains why trunk and neck position sense tests emphasise returning to a neutral position, while limb tests evaluate the ability to move toward a specific target.

We observed that conducting the optimal number of repetitions (i.e., six repetitions) might not be feasible due to time constraints. Since each participant required 27 trials to complete all tests, the whole testing session already lasted approximately an hour, including setup time. Providing children typically have difficulty maintaining concentration for extended periods, we decided to limit the tests to three repetitions each to keep the sessions short. This could minimise the potential impact on test results due to reduced concentration or fatigue, particularly for tests near the end of the session.

Future studies should validate our results on the age effect of spinal proprioception. Since we only assessed growth based on chronological age, it might not truly reflect one's developmental milestones. Alternative measures should be exploited (e.g., skeletal maturity using bone age)[48]. Along with the growth evaluation, other parameters should be explored to see whether age is an independently associated factor. Given that the present study had a cross-sectional design, further longitudinal studies are warranted to clarify whether growth affects the development of proprioception in each region. Moreover, the development of peripheral proprioception in the shoulder, wrist, hip, and ankle should be investigated. Because proprioception involves more than just position sense alone, it would be meaningful to see whether reposition performance is related to motion/movement detection. Given the limited availability of pragmatic proprioception tests in a busy clinical setting, there is a need for novel diagnostic tests of proprioception that are more feasible, affordable, and swift.

Several limitations were noted in the present study. Subject recruitment was considerably influenced by the global pandemic, resulting in a relatively small sample size. Of the study subjects, some medical information may still be lacking to confirm their health status since people may have never seen in public hospitals. One identified limitation pertains to the utilisation of only three repetitions for each test. It is advisable to augment the repetitions to 6 as a means to address concerns related to reliability. Besides, confounders were not fully controlled for proprioception, for instance, physical activity participation, type of leisure activity, and sedentary behaviours. The reliability of the current position sense tests was compared with existing literature. While the tests for the neck and elbow were found to be comparable, the knee test was deemed unsatisfactory. This discrepancy may be attributed to differences in testing procedures.

Conclusion

We provided the normative values of spinal and peripheral proprioception using position sense in healthy adolescents and young adults. Our results suggested that only spinal but not peripheral proprioception improved with age. Future studies should validate the results with a larger sample size and longitudinal follow-ups.

Data availability

Raw data supporting the study findings are available from the corresponding author upon request.

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KL, KK, JC, KP, AW, DC, and KC contributed to the conception of the work, the acquisition, analysis, and interpretation of data for the work, drafting the work, and revising it critically for important intellectual content, final approval of the version to be submitted, as well as agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Declarations

Competing interests
The authors declare no competing interests.

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