Deterioration of spinal sagittal alignment exposes latent cognitive impairment in the general older population: A Japanese cohort survey randomly sampled from a basic resident registry

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Abstract

Background: This study investigated the impact of spinal sagittal alignment on cognitive function in the general older population using a Japanese population cohort constructed from random sampling of the basic resident registry of a rural town.

Methods: Registered citizens of 50 to 89 years old were targeted for this survey. Participants were classified into 8 groups based on age (50's, 60's, 70's, or 80's) and sex (male or female) after random sampling from the resident registry of a cooperating town in 2014. A total of 413 subjects (203 male and 210 female) were enrolled. We analyzed the distribution of cognitive function test scores determined as by Montreal Cognitive Assessment and Mini-Mental State Examination in each age and sex group to assess the impact of radiographic parameters of spinal sagittal alignment on cognitive function tests.

Results: Cognitive function test results tended to decrease with age. Among groups of the same age and sex, cognitive function worsened significantly with poorer spinal alignment. In particular, increases in sagittal vertical axis or global tilt by 1 degree of standard deviation were significantly related to mild cognitive impairment (odds ratio: both 1.4).

Conclusions: Spinal alignment deterioration indicated cognitive function decline in Japanese older people of the same age and sex. Thus, a forward shift in sagittal spinal balance may be regarded as a visible indicator of latent mild cognitive impairment in community-dwelling older people.

Background

The rise in disability rates among older people has become increasingly important because of caregiver costs and associated impairments in quality of life (QOL) [1]. It is widely recognized that spinal sagittal alignment deteriorates with age [2, 3]. A large collapse in alignment hinders standing and walking [4]. Spinal sagittal alignment is strongly correlated to health-related QOL [5] and is an important barometer of health status for seniors. Cognitive function also diminishes with age, with mild cognitive impairment (MCI) being common among older people. MCI may be hard to perceive by the individual and rarely has a critical impact on daily life but is nonetheless a pre-disease condition with a very high probability of progressing to dementia. Several reports have shown that activities of daily living (ADL) and instrumental ADL (IADL) are already adversely affected at the MCI stage [6,7].

Severe spinal imbalance accompanied by a change in spinal alignment is now recognized as adult spinal deformity. In contrast, minor or moderate changes in spinal alignment are often considered a natural process with aging. Although spinal alignment change and cognitive deterioration are individually well known as age-related phenomena, no studies have examined for associations between the two factors.

For the construction of a new population study of Japanese community-dwelling older people, candidates were randomly sampled from the basic resident registry of a cooperating town in an inland rural area to minimize selection bias and obtain a cohort representative of the general population. This

epidemiological study of comprehensive locomotive health in older people was coined “the Obuse study”, bearing the name of the collaborating local government. The present investigation aimed to assess the impact of spinal sagittal alignment on cognitive function in the general older population using the Obuse study cohort.

Methods

Construction of cohort classified by age and sex

The subject group of this study was the Obuse study cohort based on a basic municipal resident registry. The construction procedure of the cohort is described in a previous report [8]. The cohort was composed of approximately 400 residents in their 50's to 80's whose age and gender were uniformly distributed. Table 1 summarizes the baseline characteristics of this group. The Obuse study cohort contained 415 people. A total of 413 participants (203 male and 210 female) were enrolled after the exclusion of 2 cases unable to participate in radiological assessments. The subjects were mainly primary and tertiary industry workers, with relatively few secondary industry workers. The proportion of unemployment increased with age, especially since the general retirement age in Japan is 60-65 years old.

Measurements of spinal alignment

All subjects underwent whole spinal lateral radiography in a standing position (fists on clavicles position) for the measurement of sagittal vertical axis (SVA) and global tilt (GT) as parameters of total spinal alignment as well as cervical SVA (CSVA; the distance between a plumb line from the center of the C2 vertebral body and the posterior superior corner of C7), cervical lordosis (CL; the angle between the C2 inferior endplate and the C7 inferior endplate), thoracic kyphosis (TK), lumbar lordosis (LL), and pelvic tilt (PT) as parameters of local alignment (Figure 1). The averaged value of 2 spine surgeons (M.U. and S.I.) and a trained staff member (R.T. or H.N.) was calculated for each parameter. Inter-rater reliabilities were 0.95 for SVA, 0.71 for GT, 0.96 for CSVA, 0.88 for CL, 0.92 for TK, and 0.89 for PT. The inter-rater reliability for LL was moderate at 0.65. Previously [8], the inter-rater reliability for sacral slope was 0.48 and comparatively lower than those for other spinal parameters. Similarly to LL in this case, variable interpretation of the S1 endplate shape may have decreased reliability among the evaluators.

Cognitive function testing

We employed 2 tests to evaluate cognitive function: Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE). As a tool to determine the existence of MCI, the 30-point MoCA provides higher sensitivity and specificity than does the 30-point MMSE, another representative cognitive function evaluation tool [9,10]. Participants with equal to or more than 26 points in MoCA are considered as normal (sensitivity: 94% or more, specificity: 60% or less [11]), with those scoring 25 points or less

having cognitive impairment. Similarly for MMSE, a score equal to or more than 24 points is judged as normal [12,13]. The Japanese version of both questionnaires was used. The cognitive impairment measured in this study was defined solely by screening test (MoCA or MMSE) scores. In order to precisely define cognitive impairment as a disease requiring treatment, further comprehensive examination and exclusion of other conditions would have been required.

Statistical analyses

The mean and standard deviation (SD) of the cognitive function test scores for each age and sex group were calculated along with the prevalence of cognitive impairment. Correlations between age and cognitive function test scores were evaluated by Pearson's correlation coefficient. Calculated cognitive function testing results between genders were assessed using Welch's t-test.

In examinations of the impact of spinal alignment on cognitive function, both factors were considered to be influenced by age and sex. Accordingly, we employed general linear regression models with the value of each cognitive function test score as the response variable, the radiological parameters of spinal alignment as the explanatory variable, and age and sex as the covariate. We used the following formula:

$$E(\text{MoCA or MMSE score}) = \beta 0 + \beta 1 \times (\text{a spinal alignment parameter}) + \beta 2 \times \text{Age} + \beta 3 \times \text{Sex} + \varepsilon$$

E (MoCA or MMSE score) denotes the estimated MoCA or MMSE score value; $\beta 0$, an intercept; $\beta 1$, $\beta 2$, and $\beta 3$, coefficients of explanatory variables; and ε, random error.

The objects of interest estimated from the above formula are $\beta 1$s, indicating the effect points of a spinal alignment parameter on cognitive function tests. We also estimated the impact of a shift of 1 degree of SD of spinal alignment on cognitive hypofunction (i.e., MoCA < 26 points or MMSE < 24 points), as follows:

$$E(\text{cognitive hypofunction}) = \exp[\beta 0 + \beta 1 \times (\text{a spinal alignment parameter}) + \beta 2 \times \text{Age} + \beta 3 \times \text{Sex} + \varepsilon$$

E (cognitive hypofunction) denotes the estimation of whether cognitive hypofunction exists or not.

The objects of interest estimated from the above formula are exp ($\beta 1$)s, indicating the odds ratio of a spinal alignment parameter for cognitive hypofunction.

Statistical analyses were carried out using the statistical package R, version 3.4.3 (available at: http://www.r-project.org). The level of significance was set at $p < 0.05$.

Results

Table 2 summarizes the distributions of each spinal alignment parameter. Since there were some discrepancies in alignment variances between genders, the actual range of a 1 SD shift was different for

males and females in subsequent analyses. Cognitive function test scores tended to decrease with age for both genders (Table 3). Mean MoCA was the normal limit of 26 points in males and females in their 60's, with MCI indicated in subjects in their 70's and 80's. The prevalence rates of MCI in males and females were 28% and 17%, respectively, in their 50's. These increased by decade to more than half of subjects in their 70's and over 80% in their 80's.

Both MoCA and MMSE scores were moderately correlated with age (Table 4). The individual testing methods did not differ significantly between genders (mean score: 25 points for both sexes for MoCA, p = 0.41, and 28 points for both sexes for MMSE, p = 0.75). Figure 2 shows the impact of spinal alignment on cognitive function adjusted by age and sex. A positive shift of 1 SD of SVA, GT, or PT produced a 0.4-0.5 decrease in MoCA score, and a negative LL shift of 1 SD caused a 0.3 decrease. Cervicothoracic alignments (CSVA, CL, and TK) did not significantly affect MoCA results. According to our previous study, SVA, GT, and CSVA (males), CL (females), and PT increased with age, while LL decreased [8]. When interpreting these deviation directions as worsening of alignment, it appeared that diminished global (SVA and GT) and lumbo-pelvic (LL and PT) spinal alignments were indicative of decreased MoCA within the same age and sex. Moreover, greater SVA and GT accompanied higher MCI prevalence rates when adjusted by age and sex. The odds ratio of SVA (+ 1 SD) was 1.4 (95% confidence interval: 1.1-1.9, p = 0.01) and that of GT was also 1.4 (95% confidence interval: 1.1-1.8, p = 0.02) (Figure 3).

Regarding MMSE scores, GT, LL, and PT exhibited similar directions of impact as those of MoCA, with SVA showing no significant relationship. A positive shift of 1 SD of TK produced a 0.2 increase in MMSE score (Figure 2). No significant relationships between the presence of cognitive hypofunction status defined by MMSE scores and spinal sagittal parameter were found (Figure 3).

Discussion

In the present cohort study of over 400 subjects randomly selected from a rural Japanese town registry, a deterioration of spinal sagittal alignment was seen to indicate cognitive decline. Both parameters decreased with age. When grouped by age and sex, worsened spinal alignment coexisted with decreased cognitive function. Notably, a 1 SD increase in SVA or GT was significantly associated with the presence of MCI after adjustment for age and sex (odds ratio: both 1.4).

Also termed pre-dementia, MCI is common in older people and its frequency is rising in aged and super-aged societies [14]. MCI includes problems with memory, language, thinking, and judgment but does not comprise dementia; thus, some cases of MCI do not deteriorate further. In individuals over the age of 70 years, 14% have sufficient cognitive impairment to warrant a diagnosis of dementia [15]. Gait slowing is common among patients with this condition [16-18]. In the Obuse study cohort, the prevalence rate of MCI reached more than half among participants in their 70's and over 80% among those in their 80's.

Adult spinal deformity (ASD) and frailty are closely and interactively related [19]. Patients with ASD cannot exercise muscular strength sufficiently and often exhibit symptoms of intermittent claudication due to back pain [20]. Pressure on the abdomen may also cause losses of appetite and weight and

contribute to frailty. Frailty is a pre-disease condition comprehensively summarizing the symptoms accompanying aging and includes the concept of a decline in social activity due to mental and physical changes. Frailty is reversible, but in severe cases, the patient's ASD may deteriorate permanently.

On the other hand, spinal alignment changes less severe than those in ASD are not included in frailty. These alterations tend to be regarded as a natural consequence of age. However, MCI with spinal alignment changes is a factor contributing to frailty through mental and social decline. Although it remains difficult to prove a direct causal relationship between postural changes and MCI, our results demonstrate that spinal alignment change and MCI are correlated phenomena occurring simultaneously with age. Thus, when visible appearance changes in posture occur, appropriate diagnostic measures are warranted in consideration of the possibility of cognitive impairment to help prevent frailty, dementia, and bedridden status.

The limitations of the current investigation include a cross-sectional design and possibility of selection bias. Further longitudinal studies are being planned to investigate the causal relationship between spinal alignment and cognitive function over time. As this was a non-compulsory survey, the proportion of randomly sampled people who ultimately participated in the survey was less than half, implying incomplete selection bias elimination. Nevertheless, the Obuse study cohort very closely resembled the average Japanese population due to its distinctive survey design. In order to maintain ADL, IADL, and QOL in older people, it will be necessary to monitor for signs of impending cognitive impairment that may lead to frailty and dementia. Our results showed that anteriorization of spinal balance existed at the onset of cognitive impairment. Thus, greater attention is warranted to changes in posture among community-dwelling older people.

Conclusions

Our investigation of the impact of spinal sagittal alignment on cognitive function in an older Japanese population based on a resident registry demonstrated that spinal alignment deterioration indicated cognitive function decline among patients of the same age and sex. The anteriorization of spinal balance may therefore represent a visible indicator of MCI in older people.

Abbreviations

QOL: Quality of Life

MCI: Mild Cognitive Impairment

ADL: Activities of Daily Living

IADL: Instrumental ADL

SVA: Sagittal Vertical Axis

GT: Global Tilt

CSVA: Cervical SVA

TK: Thoracic Kyphosis

LL: Lumbar Lordosis

PT: Pelvic Tilt

MoCA: Montreal Cognitive Assessment

MMSE: Mini-Mental State Examination

SD: Standard Deviation

ASD: Adult Spinal Deformity

Declarations

Ethics approval and consent to participate

This study was approved by the investigational review board of our hospital (approval number: 2792). Written consent was obtained from all participants. All research was conducted in accordance with the STROBE guidelines for observational research.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Availability of data and material

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Contributions

SI and JT designed the study and wrote the manuscript. HN, SI performed the data analysis and wrote the manuscript. MU, RT, NS and AS provided clinical experience and wrote the manuscript. HK and JT supervised the whole study. All authors read and approved the final manuscript.

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Tables

Table 1. Baseline characteristics of the study cohort.

Sex	Age	N	Height (cm)	Weight (kg)	BMI (kg/m^2)	Job (Pri; Sec; Ter; None)
Male	50's	50	171.8 (6.0)	67.1 (9.1)	22.7 (2.9)	3; 7; 40; 0
	60's	53	166.7 (4.7)	66.9 (7.7)	24.1 (2.7)	18; 5; 19; 11
	70's	55	163.2 (5.0)	60.0 (10.3)	22.5 (3.4)	22; 2; 8; 23
	80's	45	160.1 (5.7)	57.5 (8.5)	22.4 (2.8)	19; 0; 3; 23
	All	203	165.6 (6.8)	63.0 (9.8)	22.9 (3.0)	62; 14; 70; 57
Female	50's	47	158.1 (4.9)	55.4 (9.0)	22.2 (3.8)	5; 4; 29; 9
	60's	61	152.8 (5.4)	52.2 (7.6)	22.3 (2.8)	21; 4; 17; 19
	70's	54	149.7 (5.3)	50.6 (7.9)	22.6 (3.2)	16; 4; 8; 26
	80's	48	144.6 (5.9)	48.3 (7.9)	23.1 (3.3)	11; 0; 5; 32
	All	210	151.3 (7.1)	51.6 (8.4)	22.5 (3.2)	53; 12; 59; 86

Notes: Table cited from a previous study: [8] Uehara M, Takahashi J, Ikegami S, Tokida R, Nishimura H, Sakai N, Kato H (2018) Sagittal spinal alignment deviation in the general elderly population: A Japanese cohort survey randomly sampled from a basic resident registry. Spine J 8; 18: 30625-30629.

Values represent the mean (standard deviation).

Abbreviations: BMI, body mass index; Pri, primary industry; Sec, secondary industry; Ter, tertiary industry.

Table 2. Spinal sagittal alignment distributions.

Sex	N	SVA (mm)	GT (degrees)	CSVA (mm)	CL (degrees)	TK (degrees)	LL (degrees)	PT (degrees)
Male	203	22 (41)	19 (11)	28 (15)	11 (12)	29 (10)	43 (12)	16 (7)
Female	209	22 (46)	23 (14)	17 (11)	12 (11)	30 (12)	45 (16)	20 (10)
All	412	22 (44)	21 (13)	22 (14)	12 (12)	30 (11)	44 (14)	18 (9)

Note: Values represent the mean (standard deviation).

Abbreviations: SVA, sagittal vertical axis; GT, global tilt; CSVA, cervical sagittal vertical axis; CL, cervical lordosis; TK, thoracic kyphosis; LL, lumbar lordosis; PT, pelvic tilt.

Table 3. Cognitive function test scores and prevalence rates of cognitive impairment.

Sex	Age	N	MoCA		MMSE	
			Score	< 26 points	Score	< 24 points
Male	50's	50	27 (2)	14 subjects, 28%	29 (1)	0 subjects, 0%
	60's	53	26 (3)	22 subjects, 42%	28 (2)	1 subject, 2%
	70's	55	24 (3)	35 subjects, 64%	27 (2)	4 subjects, 7%
	80's	45	21 (4)	39 subjects, 87%	26 (3)	8 subjects, 18%
Female	50's	47	27 (2)	8 subjects, 17%	29 (1)	0 subjects, 0%
	60's	61	26 (3)	25 subjects, 41%	28 (2)	2 subjects, 3%
	70's	54	25 (3)	29 subjects, 54%	28 (2)	2 subjects, 4%
	80's	48	21 (4)	39 subjects, 81%	26 (2)	5 subjects, 10%

Notes: Values represent the mean (standard deviation). The maximum MoCA score is 30 points, with a score of 26 or above considered normal. The maximum MMSE score is 30 points, with a score of 24 or above considered normal.
Abbreviations: MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination.

Table 4. Pearson correlation coefficients between cognitive function tests and age.

Test	Male	Female
MoCA	-0.58	-0.56
MMSE	-0.52	-0.47

Note: All p values for the coefficients are < 0.01.
Abbreviations: MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination.

Figures

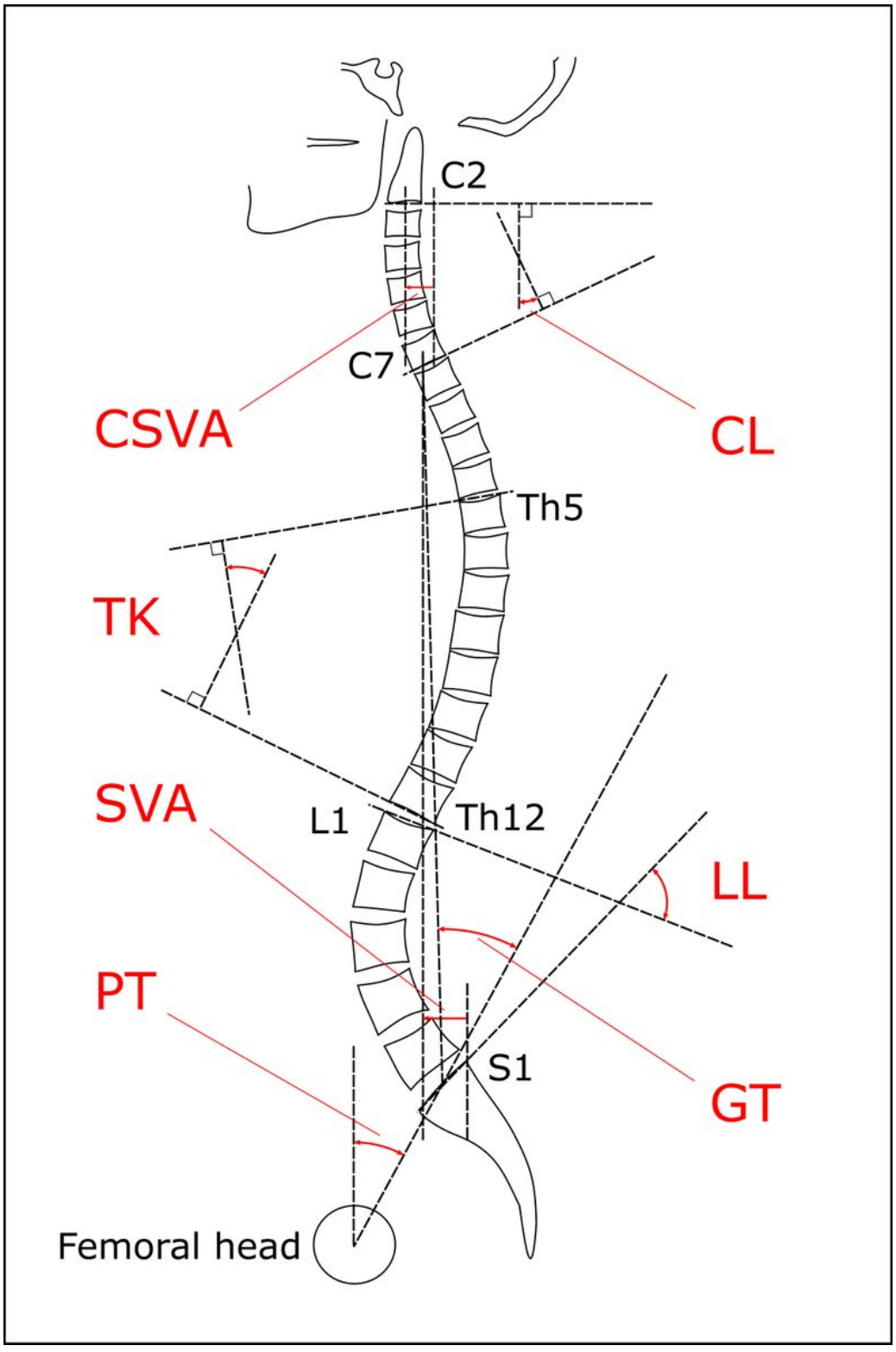

Figure 1

Radiographic spinal sagittal parameters. Abbreviations: SVA, sagittal vertical axis; GT, global tilt; CSVA, cervical sagittal vertical axis; CL, cervical lordosis; TK, thoracic kyphosis; LL, lumbar lordosis; PT, pelvic tilt.

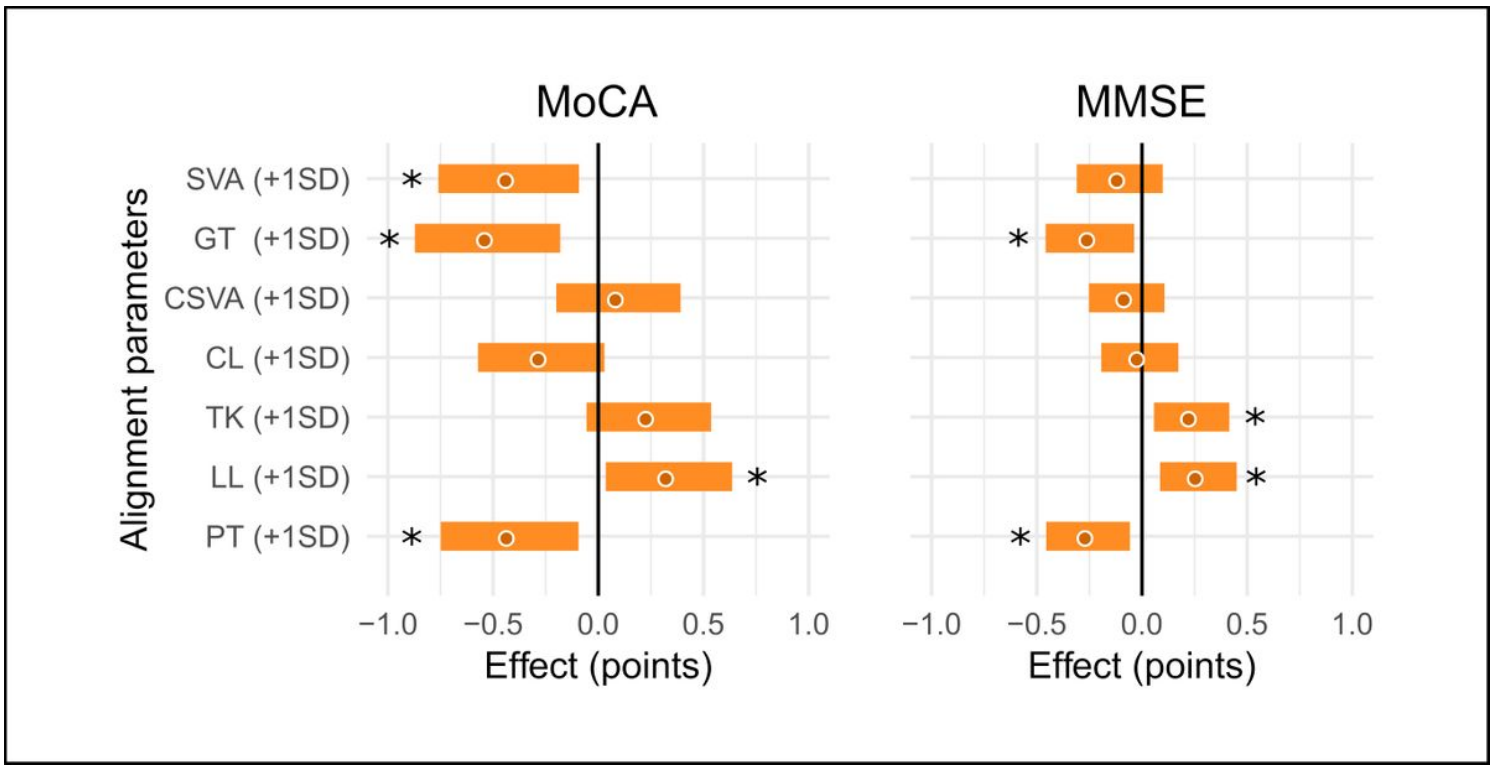

Figure 2

Impact on cognitive function score of a shift of +1 standard deviation of sagittal spinal alignment parameters. Notes: Error bars represent 95% confidence intervals of effect. All values were adjusted by age and sex. *statistically significant. Abbreviations: MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; SVA, sagittal vertical axis; GT, global tilt; CSVA, cervical sagittal vertical axis; CL, cervical lordosis; TK, thoracic kyphosis; LL, lumbar lordosis; PT, pelvic tilt; SD, standard deviation.

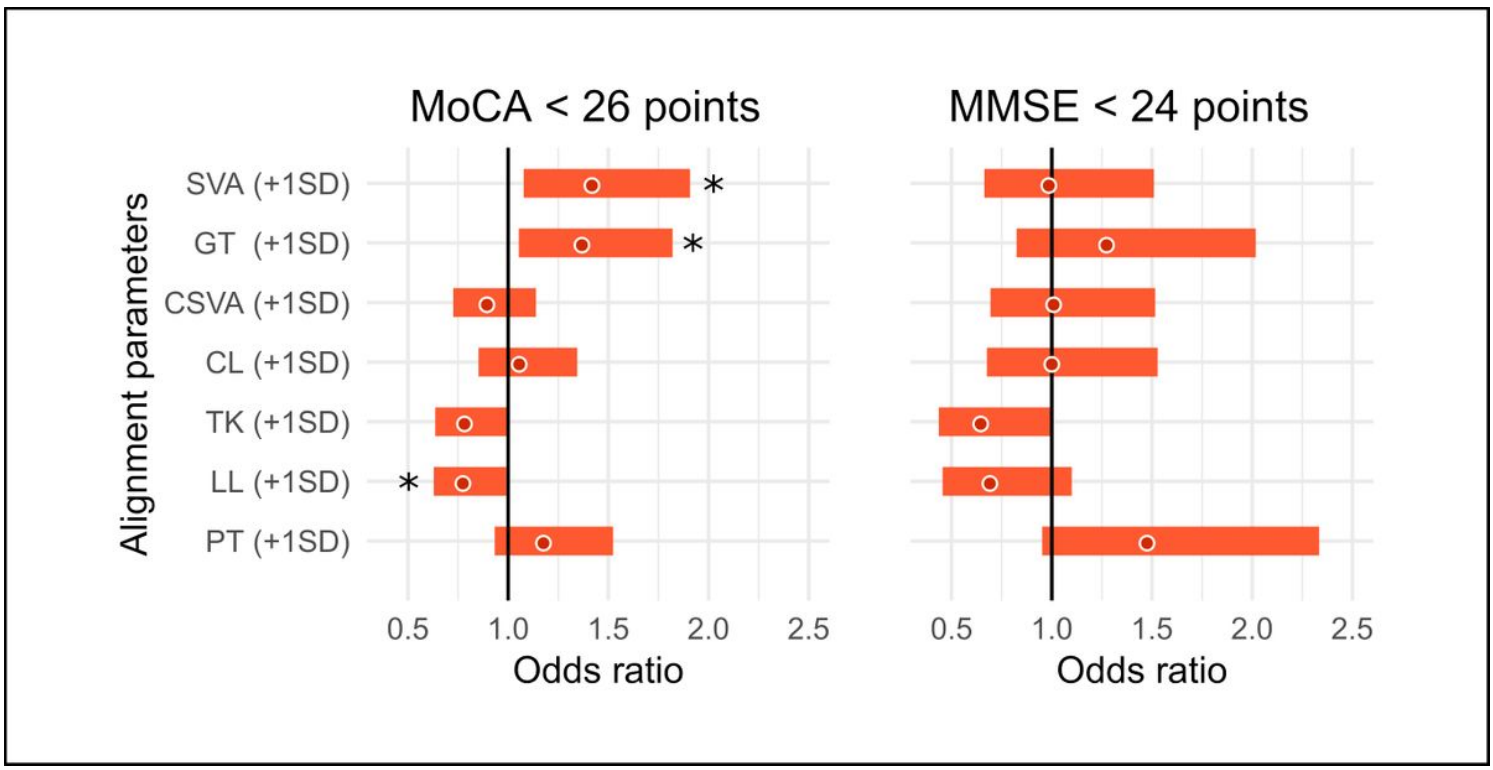

Figure 3

Effect on cognitive hypofunction of a shift of +1 standard deviation of spinal sagittal alignment parameters. Notes: Error bars represent 95% confidence intervals of odds ratio. All values were adjusted by age and sex. *statistically significant. Abbreviations: MoCA, Montreal Cognitive Assessment; MMSE, Mini-Mental State Examination; SVA, sagittal vertical axis; GT, global tilt; CSVA, cervical sagittal vertical axis; CL, cervical lordosis; TK, thoracic kyphosis; LL, lumbar lordosis; PT, pelvic tilt; SD, standard deviation.