Postural control and disability in patients with early rheumatoid arthritis

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Abstract

Objective

Rheumatoid arthritis (RA) may affect the postural control through abnormal sensory inputs and impaired motor responses. Sensory Organization Test (SOT) objectively evaluates contribution of different sensorial afferences in postural control. The aim of the study is to assess mechanisms of postural instability and their relations with disability and disease characteristics in an early RA(ERA) cohort.

Methods

The equilibrium scores were assessed in 30 ERA patients and 30 age- and sex-matched controls. The somatosensory (SOM), visual (VIS) and vestibular (VEST) ratios were computed to assess the use of different sensory and the composite equilibrium score (CES) as a measure of global balance performance.

Results

ERA patients had lower CES (78.4±6.0% vs. 83.4±5.0%, p=0.002), SOM ratio (98.5±1.8% vs. 99.6±2.1%, p=0.035), VIS ratio (85.2±7.6% vs. 91.5±6.0%, p=0.001) and VEST ratio (70.8±10.0% vs. 80.3±7.8%, p<0.001) compared to controls. The presence of ankle arthritis correlated negatively to both SOM (r=-0.369, p=0.045) and VIS ratio (r=0.470, p=0.009), pain severity to CES (r=-0.389, p=0.045) and VIS ratio (r=-0.385, p=0.048) and HAQ-DI to CES (r=-0.591, p=0.001), SOM (r=-0.510, p=0.004) and VIS ratio (r=-0.390, p=0.033.). Patients-reported postural instability was associated with lower CES (75.4±5.4% vs. 80.7±5.5%, p=0.016) and VEST ratios (66.5±10.1% vs. 74.1±8.8%, p=0.036). SOT outcomes did not differ according to acute phase reactants, disease activity or autoantibody positivity.

Conclusion

RA patients showed an early impairment of postural control related to the degree of disability and subjective postural instability. Our data suggest that the lack of balance could result from both impaired motor response and abnormal sensory organisation.

Key words

rheumatoid arthritis, postural balance, psychomotor performance, musculoskeletal pain

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Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that causes joint inflammation, not infrequently accompanied by extra-articular manifestations (1). RA patients may experience postural instability with episodes of loss of balance and falls that may have crucial consequences in term of long-term loss of confidence, restriction of everyday activities and disability (2). Moreover, injuries are a primary concern since the annual incidence of falls in RA patients ranged from 10 to 50% (3) that is significantly higher than matched controls and even groups of elderly people (4). Previous studies about postural impairment in RA focused on patients with a long-standing disease in which superimposed secondary osteoarthritis, ageing, comorbidities, atherosclerosis of labyrinthine arteries, drug-induced ototoxicity may play confounding effects. Therefore, early RA (ERA) patients – defined as having joint symptoms duration less than 12 months (5) – may be the ideal clinical setting in which early and direct consequences of the disease can be observed.

Postural control is an automated process that requires visual, vestibular and somatosensory information, central integration and motor response (6). Sensory organization test (SOT) is a protocol of the computerised dynamic posturography (DP) that assesses how the balance system uses individual sensory components by either removing or distorting the visual and/or somatosensory inputs (7). Based on this, the study aims were (i) to evaluate by SOT a cohort of ERA patients, naive to immunosuppressant drugs, and (ii) to establish the prevalence of balance impairment, the role of vestibular, visual and somatosensory systems in the maintenance of postural control, and the relationship with disability and subjective postural instability.

Patients and methods

Patient enrolment

The study had a comparative cross-sectional design. Eligible patients with newly diagnosed ERA were enrolled at the outpatient clinic of the Division of Rheumatology of the Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore in Rome, from January to December 2019. Patients were consecutively included in the study if they were aged 18–65 years, met ACR/EULAR classification criteria for RA (8) had a disease duration less than 12 months from the onset of articular symptoms and were naive to corticosteroids and disease-modifying antirheumatic drugs. A control group of health volunteers matched for age, sex, height and body mass index (BMI), without known concomitant oto-vestibular, neurologic or rheumatologic diseases, were enrolled. Patients with previous lower extremity joint surgery or major trauma, visual impairment uncorrectable with eyeglasses, diabetes, ongoing treatment with salicylates, diuretics, sedatives, antidepressants or antipsychotics and using walking aids were excluded from both groups. The study protocol was approved by our institutional Committee on Research Ethics and written informed consent was obtained from each enrolled subject.

Rheumatological assessment

A comprehensive medical history was collected and physical examination, including tender and swollen joint count, was performed for each RA patient during the rheumatologic assessment. Demographics, BMI, joint symptoms duration, positivity of Rheumatoid Factor (RF) and/or anti-citrullinated protein antibodies (ACPA), pain intensity on a visual analogue scale (VAS pain), patient general health on VAS (VAS GH), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values were recorded. Disease activity score on 28 joints (DAS28) (9) and the Health Assessment Questionnaire Disability Index (HAQ-DI) (10) were also collected. Patients were specifically asked for subjective postural instability defined as a perceived difficulty to keep steady or move with an adequate amount of weight on each side of the body. This difficulty has been put in the record only if associated with a reported limitation in daily-life activity or with the occurrence of at least one episode of fall during the following six months.

Table I. Sensory organisation test outcomes.

Description		LLN*	Significance
C1	None	90%	Vision, vestibular and somatosensory inputs available
C2	Eyes closed	85%	Vestibular and somatosensory input available (no vision)
C3	SR surround	86%	Vestibular and somatosensory inputs available (vision altered)
C4	Eyes opened, SR platform	70%	Vision and vestibular inputs available (somatosensory altered)
C5	Eyes closed, SR platform	52%	Vestibular input available (no vision, somatosensory altered)
C6	SR surround, SR platform	48%	Vestibular input available (vision and somatosensory altered)
CES	(C1+C2+3 • C3+3 • C4+3 • C5+3 • C6)/14	70%	Global balance performance
SOM	C2/C1	90%	Use of somatosensory input
VIS	C4/C1	74%	Use of visual input
VEST	C5/C1	55%	Use of vestibular input
PREF	C3+C6/C2+C5	86%	Denial of wrong visual input

*LLS was defined according to published NeuroCom norms of the 20–59-year-old group by subtracting 1.64 times the standard deviation from the mean of the reference population (Balance ManagerVR Systems Clinical Operations Guide, D102376-00 Rev H 2014).
LLN: lower limit of normal; C1-C6: condition 1-6; SR: sway-referenced; CES: composite equilibrium score; SOM: somatosensory ratio; VIS: visual ratio; VEST: vestibular ratio; PREF: preferential ratio.

Audiovestibular assessment with computerised dynamic posturography (DP)

Audiovestibular assessment was carried out by a single experienced otolaryngologist blinded to the rheumatological data. The evaluation included audiovestibular history, otoscopy, laryngoscopy, assessment of spontaneous nystagmus and Romberg test, tympanometric test, pure tone audiometry and computerised DP with SOT protocol. Air conduction pure tone average (PTA) thresholds at frequencies 0.5-1–2-4 kHz (PTA.0.5–4 kHz) were calculated for each ear and were used to assess hearing function. Hearing loss was present if the average thresholds was >20 dB. Tympanometry test was evaluated by means of tympanometer system, measuring the tympanic membrane's response to changes in pressure, and its output, the tympanogram. The tympanograms were classified as types A, As, Ad, B, and C (11). Acoustic Reflex Threshold test was performed eliciting the contraction of stapedial muscles at sounds between 65 dB and 95 dB. Postural control was evaluated using Computed DP, performed by Equitest, Neurocom Int. Inc., Clackamas, Oregon, USA. The tests were performed with the subject standing on a dual forceplate enclosed by a visual surround. The dual forceplate records the vertical forces between feet and ground, as well as horizontal shear forces, thereby allowing estimation of the position of the swaying body. The SOT protocol consisted of three trials for each of six experimental sensory conditions with increasing difficulty. The tested conditions were: eyes open with fixed platform (condition 1), eyes closed with fixed platform (condition 2), eyes opened with sway-referenced (SR) surround (condition 3), eyes opened with SR platform (condition 4), eyes closed with SR platform (condition 5), and eyes open with SR platform and surround (condition 6), respectively. The mean equilibrium score was calculated to for each condition with the formula [12.5° - (θ_{max}- θ_{min}) • 100/12.5°] where 12.5° is the theoretical limits of stability and θ is the angle between the vertical and the ideal line that joins the centre of the platform to the gravity centre of the patient. The somatosensory ratio (SOM = condition 2/condition 1), visual ratio (VIS = condition 4/condition 1) and vestibular ratio (VEST = condition 5/condition 1) were computed to assess the ability to use inputs from each sensory system to control balance. Moreover, the composite equilibrium score was a weighted average of the six conditions and it was related to the individual equilibrium scores (CES = 0.07 • condition 1 + 0.07 • condition 2 + 0.21 • condition 3 + 0.21 • condition 4 + 0.21 • condition 5 + 0.21 • condition 6). Finally, the preference ratio (PREF = condition 3 + condition 6/condition 2 + condition 5) was computed to assess the ability to deny wrong visual inputs (12). The lower level of the range of normality (LLN) was defined according to the cut-off provided by the manufacturer for the 20–59-year-old group by subtracting 1.64 times the standard deviation from the mean of the reference population (Balance Manager VR Systems Clinical Operations Guide, D102376-00 Rev H 2014) (Table I). Finally, a strategy score (SS) for each SOT condition has been calculated, in particular scores close to 100 indicated the use of an ankle strategy and scores close to 0 indicated a hip strategy.

Table II. Characteristics of ERA patients.

n	30
Age, years, mean±SD	48.6 ± 13.6
Height, m, mean±SD	1.66 ± 0.77
BMI, kg/m^2, mean±SD	25.5 ± 4.1
Female, n (%)	27 (90.0)
RF positive, n (%)	20 (66.7)
ACPA positive, n (%)	21 (70.0)
TJC, median (IQR)	3.0 (1.0-9.0)
SJC, median (IQR)	3.0 (1.0-7.0)
Hip involvement, n (%)	2 (6.7)
Knee involvement, n (%)	14 (46.7)
Ankle involvement, n (%)	10 (33.3)
Feet involvement, n (%)	16 (53.1)
CRP, mg/l, median (IQR)	6.7 (2.0-14.2)
ESR, mm/h, median±SD	37.8 ± 21.3
VAS pain, cm, median (IQR)	6.0 (2.5-8.0)
VAS GH, cm, mean±SD	5.6 ± 2.1
DAS28, mean±SD	3.4 ± 1.8
HAQ-DI, mean±SD	1.138 ± 0.643

ERA: early rheumatoid arthritis; SD: standard deviation; BMI: body mass index; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; TJC: tender joints count; IQR: interquartile range; SJC: swollen joints count; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: visual analogue scale; GH: general health; DAS28: Disease Activity Score for 28 joints; HAQ-DI: Health Assessment Questionnaire Disability Index.

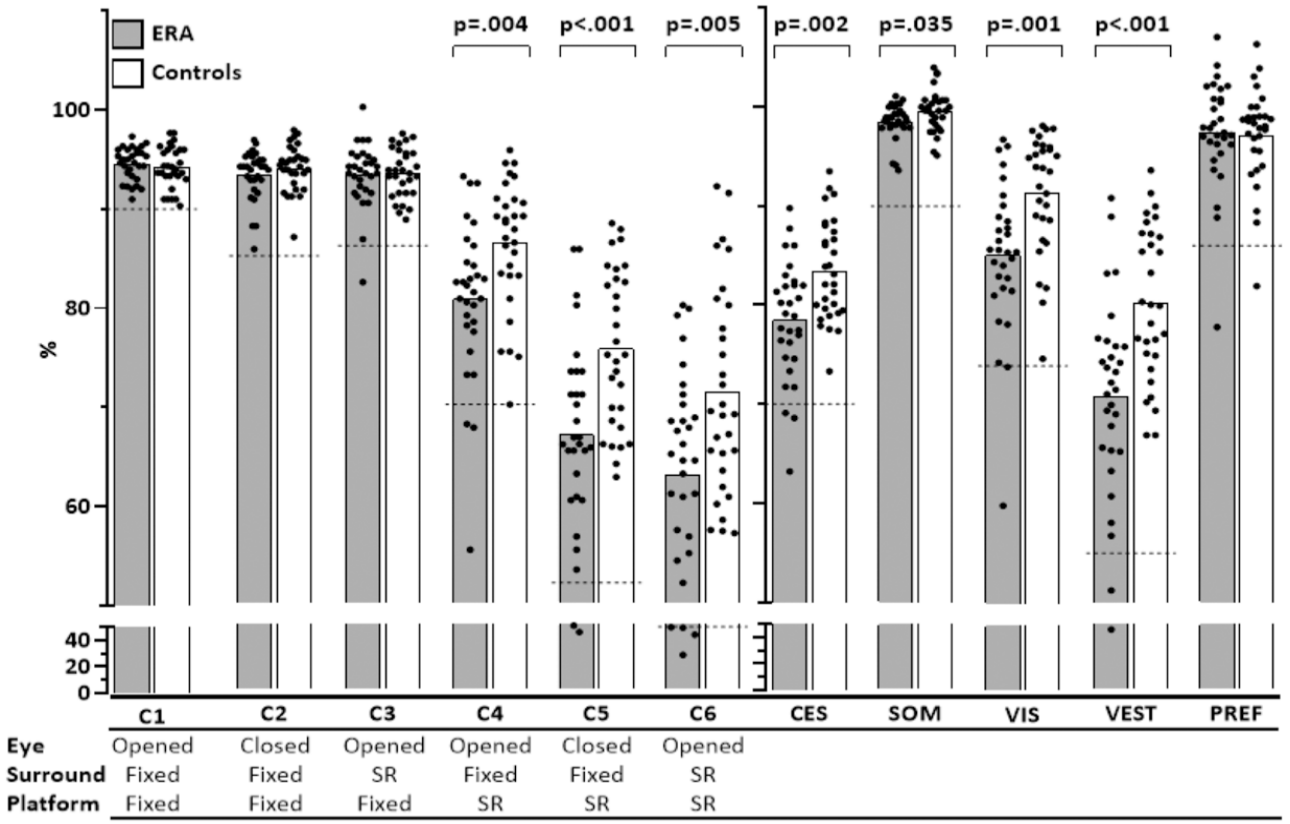

Fig. 1. Comparison of SOT outcomes between ERA patients and controls.
ERA: early rheumatoid arthritis; C1-C6: condition 1-6; CES: composite equilibrium score; SOM: somatosensory ratio; VIS: visual ratio; VEST: vestibular ratio; PREF: preferential ratio; SR: sway-referenced; SOT: sensory organisation test.
Dotted lines indicate lower limits of normal for each condition or ratio.

Statistical analysis

Data were analysed using IBM SPSS Statistics version 26.0 for Windows (IBM Corp., Armonk, NY, USA). Distribution of continuous variables was assessed by the Shapiro-Wilk test. Categorical variables were reported as number and percentage and continuous variables as mean ± standard deviation (SD) or median with interquartile range (IQR), according to the distribution of the data. Continuous and categorical variables were compared between subjects according to the diagnosis of ERA. Analysis of categorical variables was performed with the Chi-square test or Fisher's exact test, as appropriate, and comparisons between groups of continuous variables were performed by the Mann-Whitney U-test or Student t-test, according to the data distribution. Spearman's correlation coefficient was calculated to measure the relationship between oto-vestibular variables and patients characteristics. The Bias Corrected and accelerated bootstrapped analyses (BCa) were performed in line to the dimension of the population to estimate the 95% confidence intervals of Spearman's correlation coefficient by means of two thousand samples (13). Statistical significance was defined as a $p<0.05$.

Results

Characteristics of ERA patients

Thirty patients with ERA (age 48.6±13.6 years, 90.0% female, height 1.65±0.08 m, BMI 25.5±4.1 kg/m^2) and 30 matched controls (age 46.8±9.8 years, 86.7% female, height 1.64±0.07 m, BMI 24.0±2-4 kg/m^2) were enrolled. The demographic, clinical and immunological characteristics of ERA patients are summarised in Table II. Twenty (66.7%) RA patients were RF positive, 21 (70.0%) were ACPA positive, and five (16.7%) were negative for both autoantibodies. The median number of tender and swollen joints were 3.0 (IQR 1.0–9.0) on 68 and 3.0 (IQR 1.0–7-0) on 66, respectively. All ERA patients had at least one joint affected in the lower limbs on physical examination, in particular, 2 (6.7%), 14 (46.7%), 10 (33.3%) and 16 (53.1%) patients had hip, knee, ankle and foot arthritis, respectively. The mean value of DAS28 was 3.4±1.8 and – according to this index – 10 (33.3%) patients had low disease activity, 14 (46.7%) moderate disease activity and 6 (20.0%) high disease activity. The mean value of HAQ-DI was 1.138±0.643 and 27 (90.0%) ERA patients had a score higher than 0.500 (14). Thirteen (43.3%) ERA patients complained of postural instability with restriction of daily activities. Of these, 7 (23.3%) patients reported at least one episode of fall during follow-up.

Audiovestibular findings in ERA patients and controls

None of the ERA patients and controls showed abnormal otoscopic or laryngoscopic examinations. No spontaneous nystagmus or positive Romberg test were detected. Four (13.3%) pa-

Table III. Correlation between SOT outcomes and disease-related characteristics.

		CES, %	SOM, %	VIS, %	VEST, %	PREF, %
SOM, %	r	**0.381 [0.046, 0.681]**	-	-	-	-
	p	**0.038**	-	-	-	-
VIS, %	r	**0.816 [0.637, 0.909]**	0.186 [-0.192, 0.616]	-	-	-
	p	**<0.001**	0.325	-	-	-
VEST, %	r	**0.770 [0.614, 0.910]**	0.295 [-0.017, 0.586]	**0.382 [0.118, 0.628]**	-	-
	p	**<0.001**	0.114	**0.037**	-	-
PREF, %	r	**0.392 [0.195, 0.704]**	0.067 [-0.447, 0.633]	**0.564 [0.036, 0.806]**	-0.180 [-0.614, 0.175]	-
	p	**0.032**	0.725	**0.001**	0.342	-
Age, years	r	-0.175 [-0.511, 0.270]	-0.153 [-0.422, 0.147]	-0.242 [-0.000, 0.000]	-0.007 [-0.460, 0.512]	-0.097 [-0.349, 0.189]
	p	0.356	0.420	0.198	0.970	0.610
Male sex, n	r	0.061 [-0.257, 0.323]	0.149 [-0.318, 0.584]	-0.049 [-0.641, 0.419]	0.014 [-0.272 0.257]	0.183 [-0.061, 0.435]
	p	0.751	0.433	0.797	0.941	0.334
Height, m	r	-0.099 [-0.403, 0.179]	-0.057 [-0.318, 0.384]	-0.026 [-0.481, 0.341]	-0.304 [-0.755, 0.075]	-0.265 [-0.042, 0.493]
	p	0.623	0.777	0.896	0.123	-0.182
BMI, kg/m^2	r	-0.143 [-0.450, 0.203]	0.182 [-0.184, 0.511]	-0.075 [-0.438, 0.327]	-0.255 [-0.536, 0.075]	0.228 [-0.079, 0.548]
	p	0.478	0.363	0.709	0.199	0.254
RF positive, n	r	-0.317 [-0.589, 0.024]	-0.242 [-0.486, 0.066]	-0.319 [-0.559, -0.052]	-0.220 [-0.551, 0.156]	0.028 [-0.284, 0.416]
	p	0.099	0.198	0.086	0.242	0.884
ACPA positive, n	r	-0.018 [-0.354, 0.385]	-0.309 [-0.150, 0.658]	-0.200 [-0.481, 0.170]	-0.015 [-0.297, 0.363]	-0.036 [-0.342, 0.411]
	p	0.925	0.097	0.290	0.936	0.851
TJC, n	r	-0.151 [-0.527, 0.262]	-0.074 [-0.513, 0.300]	-0.185 [-0.470, 0.062]	-0.231 [-0.651, 0.224]	0.047 [-0.354, 0.427]
	p	0.452	0.715	0.355	0.247	0.814
SJC, n	r	-0.169 [-0.544, 0.196]	-0.125 [-0.532, 0.236	-0.176 [-0.467, 0.074	-0.218 [-0.590, 0.128	-0.050 [-0.379, 0.358
	p	0.400	0.536	0.379	0.275	0.803
Hip involvement, n	r	-0.065 [-.269, 0.053]	-0.144 [-0.238, 0.513]	-0.165 [-0.574, 0.110]	-0.021 [-0.190, 0.107]	-0.082 [-0.216, 0.378]
	p	0.732	0.446	0.383	0.913	0.667
Knee involvement, n	r	0.039 [-0.331, 0.362]	0.109 [-0.258, 0.429]	0.143 [-0.208, 0.394]	-0.109 [-0.458, 0.220]	0.067 [-0.373, 0.362]
	p	0.839	0.565	0.452	0.567	0.724
Ankle involvement, n	r	-0.183 [-0.496, 0.179]	**-0.369 [-0.671, 0.002]**	**0.470 [-0.676, -0.181]**	-0.022 [-0.359, 0.247]	-0.036 [-0.450, 0.459]
	p	0.332	**0.045**	**0.009**	0.910	0.850
Feet involvement, n	r	-0.060 [-0.377, 0.345]	0.040 [-0.377, 0.403]	-0.056 [-0.377, 0.347]	-0.089 [-0.449, 0.269]	-0.061 [-0.372, 0.468]
	p	0.753	0.836	0.771	0.639	0.749
CRP, mg/l	r	-0.166 [-0.528, 0.083]	-0.131 [-0.533, 0.344]	-0.174 [-0.415, 0.026]	-0.179 [-0.435, 0.039]	-0.024 [-0.419, 0.272]
	p	0.330	0.506	0.375	0.362	0.905
ESR, mm/h	r	-0.204 [-0.493, 0.040]	-0.230 [-0.564, 0.019]	-0.208 [-0.486, 0.000]	-0.013 [-0.305, 0.210]	-0.215 [-0.493, 0.029]
	p	0.294	0.240	0.289	0.950	0.294
VAS pain, cm	r	**-0.389 [-0.628, 0.065]**	-0.198 [-0.499, 0.199]	**-0.385 [-0.635, 0.022]**	-0.200 [-0.497, 0.128]	-0.176 [-0.499, 0.307]
	p	**0.045**	0.323	**0.048**	0.317	0.380
DAS28	r	-0.207 [-0.572, 0.266]	-0.042 [-0.464, 0.411]	-0.250 [-0.620, 0.218]	-0.061 [-0.447, 0.316]	-0.199 [-0.525, 0.314]
	p	0.300	0.883	0.208	0.761	0.320
HAQ-DI	r	**-0.591 [-0.783, -0.317]**	-0.316 [-0.572, 0.021]	**-0.510 [-0.709, -0.245]**	**-0.390 [-0.620,- 0.159]**	-0.264 [-0.119, 0.392]
	p	**0.001**	0.088	**0.004**	**0.033**	0.059

Bias corrected and accelerated bootstrap 95% Confidence Intervals are reported in square brackets. Bold indicates variables with p-value <0.05.
CES: composite equilibrium score; SOM: somatosensory ratio; VIS: visual ratio; VEST: vestibular ratio; PREF: preferential ratio; BMI: body mass index; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibodies; TJC: tender joints count; SJC: swollen joints count; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; VAS: visual analogue scale; DAS28: Disease Activity Score for 28 joints; HAQ-DI: Health Assessment Questionnaire Disability Index.

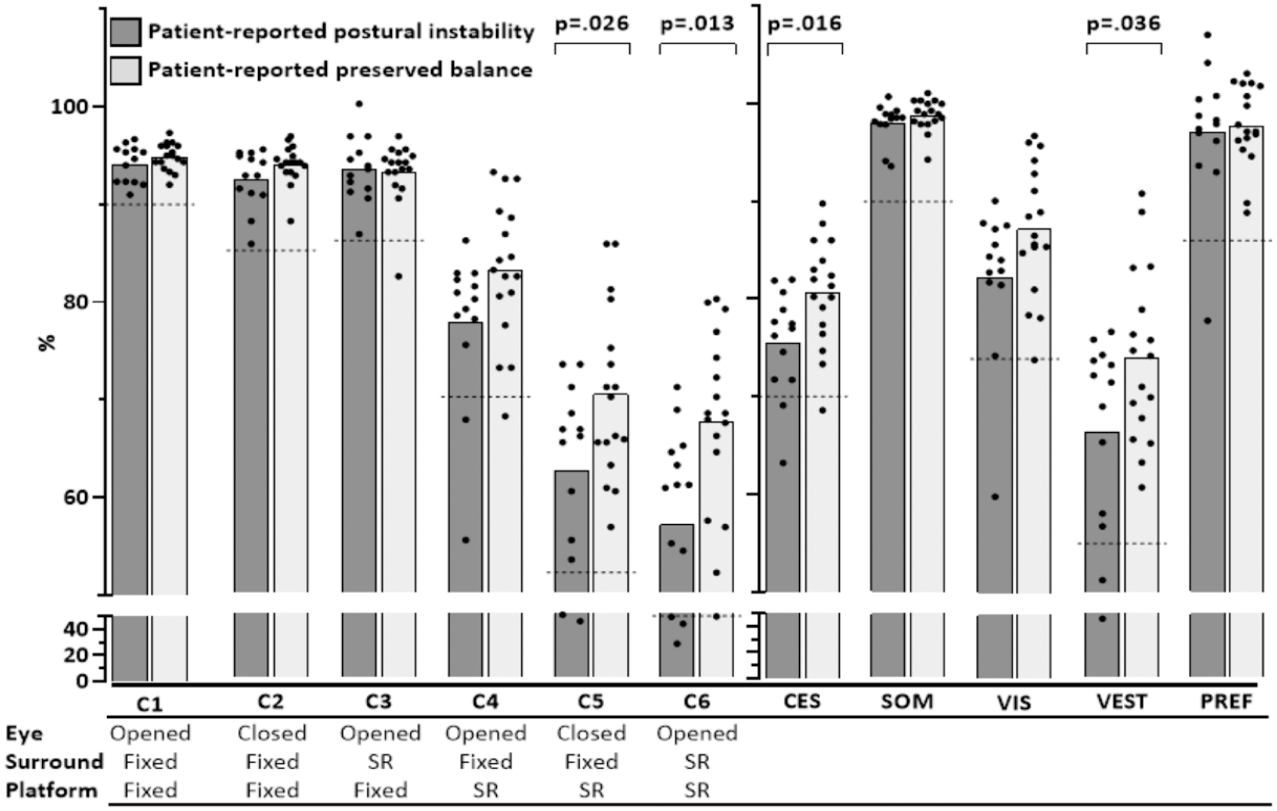

Fig. 2. Comparison of SOT outcomes in ERA patients according to report of subjective postural instability.
ERA: early rheumatoid arthritis; C1-C6: condition 1-6; CES: composite equilibrium score; SOM: somatosensory ratio; VIS: visual ratio; VEST: vestibular ratio; PREF: preferential ratio; SR: sway-referenced; SOT: sensory organisation test.
Dotted lines indicate lower limits of normal for each condition or ratio.

tients had an abnormal tympanogram, in particular, one patient had a bilateral As type, one a bilateral Ad type, and two a monolateral Ad type while the remaining ERA patients and all the controls showed physiological bilateral A type tympanograms. The prevalence of abnormal tympanogram did not significantly differ between ERA patients and controls. Ipsilateral and contralateral acoustic reflexes were elicitable in all evaluated ears with a comparable threshold between the two groups. Lastly, Air and bone conduction pure tone average (PTA) threshold was not statistically significant between ERA patients and controls (Supplementary Table S1).

The results of SOT in the two groups of patients are shown in Figure 1. In the ERA group, the equilibrium score was abnormal in one patient in condition 3, 3 (10.0%) patients in condition 4, 2 (6.7%) patients in condition 5 and 4 (13.3%) patients in condition 6. The mean equilibrium score was lower in ERA patients compared to controls in condition 4 (80.6±7.9% *vs*. 86.3±6.5%, $p<0.001$), condition 5 (66.9±9.7% *vs*. 75.7±8.0%, $p=0.001$) and condition 6 (62.9±11.8% *vs*. 71.3±10.5%, $p=0.005$) while was comparable in condition 1, condition 2 and condition 3 between the two groups. CES was abnormal in 3 (10.0%) patients. VIS and VEST ratios were abnormal in 2 patients (6.7%), PREF ratio in one patient and SOM ratio in none of the patients. ERA patients had lower CES (78.4±6.0% *vs*. 83.4±5.0%, $p=0.002$), SOM ratio (98.5±1.8% *vs*. 99.6±2.1%, $p=0.035$), VIS ratio (85.2±7.6% *vs*. 91.5±6.0%, $p=0.001$) and VEST ratio (70.8±10.0% *vs*. 80.3±7.8%, $p<0.001$) compared to controls while PREF ratio was comparable between the two groups (Fig. 1). Lastly, strategy scores do not differ between ERA patients and control in any condition (Suppl. Table S1).

Relationship between SOT outcomes and clinical features of ERA

The relationship between SOT outcomes and both demographic and disease-related characteristics of ERA patients is shown in Table III. SOM ratio seemed independent from all the other ratios when VEST and VIS ratios were positively correlated (r=0.382, BCa CI 95% from 0.118 to 0.681, $p=0.037$). None of the equilibrium scores was related to age, gender, height, BMI, ACPA or RF positivity, total number of tender or swollen joints, serum ESR and CRP or DAS28 respectively. Hip, knee, ankle or foot arthritis was not associated with a significant difference in equilibrium score in any single condition (Suppl. Table S2) or in global postural performance according to CES. Of notice, strategy scores in ERA patients did not differ according to joint involvement.

When looking at sensory analysis, the presence of ankle arthritis negatively correlated to both SOM (r=-0.369, BCa CI 95% from -0.671 to .002, $p=0.045$) and VIS ratio (r=0.470, BCa CI 95% from 0.676 to -0.181, $p=0.009$). Pain severity on VAS was negatively related to CES (r=-0.389, BCa CI 95%

from -0.628 to -0.065, p=0.045) and VIS ratio (r=-0.385, BCa CI 95% from -0.635 to -0.022, p=0.048) and HAQ-DI to CES (r=-0.591, BCa CI 95% from -0.783 to -0.317, p=0.001), SOM ratio (r=-0.510, BCa CI 95% from -0.709 to -0.245, p=0.004) and VIS ratio (r=-0.390, BCa CI 95% from -620.0 to -0.159, p=0.033). ERA patients who reported postural instability had lower C5 (62.5±9.4% *vs*. 70.3±8.8%, p=0.026), C6 (56.9±12.2% *vs*. 67.5±9.5%, p=0.013), CES (75.4±5.4% *vs*. 80.7±5.5%, p=0.016) e VEST ratio (66.5±10.1% *vs*. 74.1±8.8%, p=0.036) compared to the other (Fig. 2). Moreover, the former had higher disability according to HAQ-DI (1.451±0.496 *vs*. 0.899±0.652, p=0.022) compared to controls, but the two groups do not differ for any disease characteristic (Suppl. Table S3).

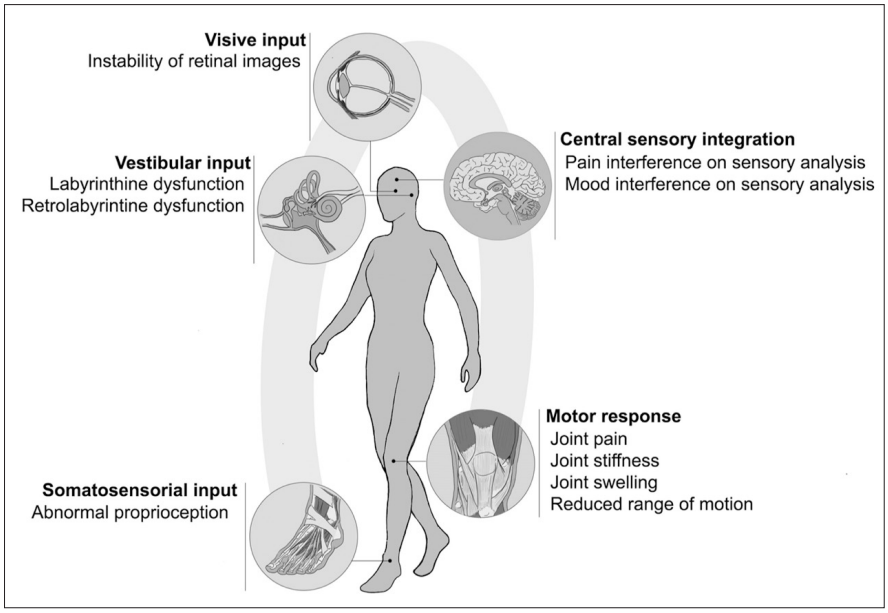

Fig. 3. Possible mechanisms of postural imbalance in patients with early rheumatoid arthritis.

Discussion

Balance control is an automatic process that could be affected in ERA patients through multiple mechanisms (Fig. 3). We observed that global equilibrium performance evaluated by CES was worse in ERA patients compared to controls and it was related to the degree of disability according to HAQ-DI. The last observation was predictable since most of the activity investigated in the questionnaire – namely dressing, arising, eating, walking, hygiene, reach, grip, and common activities (10) – are closely related to an efficient postural control. Coherently, we also found in our cohort that subjective postural instability with restriction of daily activities was associated with lower CES rather than to disease activity indexes or specific joint involvement. Lasty, ERA patients and controls seemed to use similar strategies for maintaining their balance.

Our findings are consistent with previous reports of balance impairment assessed with other devices (15-17) that focused mainly on mechanic consequences of joint involvement. To our knowledge, this is the first description of postural control by DP in ERA patient naive to DMARDs and steroids with two main advantages. The EquiTest® provides a specific assessment of the vestibular, visual, and somatosensory afferences investigating conditions close to daily activity since falls and instability usually occur during movement-related tasks. Moreover, the ERA population is slightly affected by ageing, comorbidities and chronic joint damage, and non-influenced by possible ototoxicity from drug.

The DP showed lower equilibrium scores in condition 4, 5 and 6 in ERA patients compared to controls. This pattern is classified as "surface dependent" (18) since the balance performance is compromised when the support surface is sway-referenced. Subjects with a surface dependent pattern have a strong dependence from vestibular information – even if inaccurate – that becomes critical when proprioception or vision are lost. In our series, SOT indicates a combined poor use of somatosensory, visual and vestibular references in ERA patients compared to controls.

About the use of somatosensorial input, we observed that SOM ratio was slightly but significantly lower in ERA patients compared to controls and had a poor correlation with VIS and VEST ratios. Since SOM ratio had also a poor correlation with CES and HAQ-DI it can be postulated that that alternative sensorial inputs can compensate an impairment of somatosensory information. SOM ratio is the only parameter of sensory organisation analysis that had a relation with joint involvement. In particular, ankle involvement was associated with a low SOM ratio consistently with the known contribution of ankle proprioception to postural stability (19) and the impact of ankle involvement on disability and lower extremities function in ERA patients (20). On the contrary, SOM ratio is not affected by foot involvement suggesting that plantar pressoreceptors of the feet are weakly affected by inflammatory joint disease. Of notice, the lack of correlation between DAS28 and SOM ratio is not surprising since ankles, feet and hips are not included in the related joint count (21).

ERA patients also had a reduced VEST ratio compared to controls, with a wider difference between the two groups than that observed for SOM and VIS ratio and closely related to disability and patient reported postural instability. It may therefore be inferred that vestibular dysfunction plays a role in the poor postural control of ERA patients. Our observation is consistent with previous hypotheses of vestibular impairment (22-26) in long-standing RA (27). Since our ERA patients were not exposed to ototoxic drugs and had a low comorbidity burden, an intralabyrinthine autoimmune process (28) or a microvascular impairment related to systemic inflammation (29) can be postulated as responsible for this impair-

ment. We first described that auditive function is preserved in ERA patients, and cochlear dysfunction could be therefore a late complication of the disease, potentially based on mechanisms distinctive from vestibular impairment. Of notice, the effect of immunosuppressive treatment on both vestibular and acoustic dysfunction in RA is still debated (30).

Finally, the evidence of poor use of visual reference in ERA patients could appear counterintuitive given that these subjects were free from any ophthalmologic disease. It is known that vestibular disorders may interfere with the retinal image stability that is stressed when the platform is unstable (31). Coherently, we found a strong relationship between VIS and VEST ratios. We can hypothesise a visuo-vestibular dysfunction related to an impairment of central nervous pattern network. Noteworthy, we also observed a strong relationship of VIS ratio and CES with pain intensity on VAS. This observation supports the hypothesis of the negative influence of chronic pain on central processing of sensory inputs involved in postural control (32). It has been indeed reported that chronic lumbar pain (33), fibromyalgia (34) and anxiety disorder (35) can affect postural performance independently of the presence and the site of pain, while an experimentally induced acute articular pain does not seem to alter the standing balance in healthy individuals (36). The clinical implication is that treatments aimed at reducing the pain in ERA may not necessarily lead to improvements in balance (37).

It might be questioned if the balance impairment of ERA patients could be mainly the consequence of joint inflammation rather than of a real defect in the use of somatosensory, vestibular and visual reference. Given that SOT cannot directly assess muscular response, SOT data suggest that postural impairment in ERA patients is more than the simple mechanic consequence of joint disease. We indeed reported that global postural performance according to CES, the equilibrium scores and the strategy scores in each condition were independent of specific joints involvement in the lower limbs. Moreover, previous studies about SOT in patients with degenerative or traumatic articular diseases of knees (38), hips (39) or ankles (40) seemed to produce patterns substantially different from ERA patients with a similar joint involvement. In particular, the poor relationship between joint involvement and postural strategy is consistent with the hypothesis of a global impairment of sensory input integration rather than a direct joint-dependent imbalance.

This study is limited by its cross-sectional design which does not allow a determination of causality. Moreover, even if the enrolled patients were specifically selected to look for a clear association between ERA and abnormalities of SOT, their number was relatively small. These results need to be replicated in a larger sample and the potential effect of immunosuppressants and analgesics on postural control has to be assessed in longitudinal studies.

Conclusion

RA patients showed an early impairment of postural control with a proportional degree of disability and subjective postural instability. The lack of balance could be the result of impaired sensory inputs, central processing and motor response. Further studies are needed to assess possible benefits of immunosuppressants and rehabilitation on dynamic postural control in ERA patients.

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