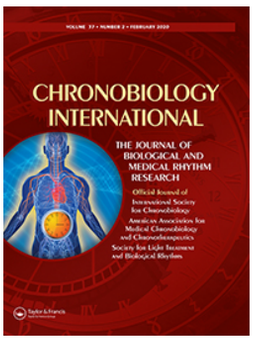

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Time of day effect on balance performance, functional capacities and risk of fall in women with rheumatoid arthritis

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ABSTRACT

Objective: This study explored the time of day effect of balance performance, functional capacities and risk of fall in three different times in patients with rheumatoid arthritis (RA) and the association between these variations and those of RA symptoms.

Methods: A "discontinual" protocol, composed of three test sessions, carried out at 6 am, 2 pm and 10 pm was set up, in order to investigate the time of day effect of balance performance, functional capacities, risk of fall, stiffness, range of motion, swollen and painful joints in women with RA.

Results: Time Up and Go Test (TUGT), Functional Reach Test (FRT) and tinetti test scores were significantly higher ($p < .01$) at 6 am and at 10 pm compared to 2 pm. Stiffness, range of motion, swollen and painful joints values were significantly higher ($p < .01$) at 6 am and at 10 pm compared to 2 pm. A significant difference was observed on the stiffness, range of motion and swollen joints values between 6 am and 10 pm that were higher at 6 am ($p < .05$).

Using Pearson's coefficient, correlations were found between RA symptom values; and TUGT, FRT and Tinetti test scores.

Conclusion: Results showed a time of day effect of balance performance, functional capacities and risk of falls in women with RA. This variation indicates an alteration of performance at 6 am and 10 pm. Fluctuations of stiffness, limited range of motion, swollen and painful joints noted are concomitant to those of balance performance, functional capacities, and risk of fall.

Abbreviations: RA: rheumatoid arthritis; H&O questionnaire: Horne and Ostberg questionnaire; PSQI: Pittsburgh sleep quality index; HAQ: health assessment questionnaire; SF-36: the short form-36; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; TUGT: Time Up and Go Test; FRT: Functional Reach Test

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Postural balance; time of day; rheumatoid arthritis; RA symptoms; women

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by synovial inflammation and progressive articular destruction (Goksel Karatepe et al. 2010). Tendons, ligaments, cartilage, and the joint capsule are all subject to inflammation and destruction, leading to symptoms of pain, stiffness, swollen joints and fatigue (Epstein and Harris 1990). Foot deformity is common in RA, with 75% of patients reporting foot involvement within four years of diagnosis, increasing to 90% as the disease progresses (Silvester et al. 2010). An association between foot deformity and foot function in people with RA has been shown in previous studies (Bal et al. 2006; Khazzam et al. 2007; Turner et al. 2006, 2008; Turner and Woodburn 2008). Functional changes, such as painful joints (Platto et al. 1991), reduced muscle strength (Ha¨kkinen et al. 1995), limited range of motion (Laroche et al. 2006), disease activity (Hamilton et al. 2001), fatigue (Epstein and Harris 1990) and fear of falling (Jamison et al. 2003), can affect everyday activities requiring postural control (Aydoğ et al. 2006; Ekdahl 1992). The restricted locomotor ability in patients with RA is typically manifest as reduced gait velocity, increased double support period, reduced stride length, and reduced cadence (Turner et al. 2003). In fact, many RA patients have long-standing disease and are often forced to resign from their jobs, which cause disability in daily life. Indeed, a high incidence of falls in people with RA has been reported in the literature (Armstrong et al. 2005; Fessel and Nevitt 1997). Armstrong et al. (2005) found that 33% of 253 patients with RA reported

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falls in the previous year, with 52% of these patients falling more than once. Similarly, Fessel and Nevitt (1997) reported that 31% of their sample of 570 RA participants fell once per year and 16% fell twice or more. Balance and gait disorders have been consistently identified among the strongest risk factor of falls (Deandrea et al. 2010). Therefore, individuals with an increased risk of falling need to be identified at an early stage to prevent future falls.

Several studies investigated the time-of-day effect on postural balance and gait in healthy older and young adults (Gribble et al. 2007; Jorgensen et al. 2012). There is controversy about the influence of circadian rhythms on postural balance in healthy adults. In normal conditions without sleep deprivation, some studies in young adults showed that postural balance is better in the morning (Gribble et al. 2007; Kwon et al. 2014). The circadian fluctuations of gait and postural balance have been linked to that of body temperature or sleepiness (Bougard and Davenne 2014; Forsman and Hæggström 2013).

Symptoms of RA frequently show circadian variation, with exacerbations in the morning (Ingpen 1968). This variation in disease expression is accompanied by daily oscillations in circulating concentrations of disease-mediating cytokines (Perry et al. 2009). In particular, fluctuations in serum IL-6 levels correlate with changes in disease symptoms such as stiffness, limited range of motion, painful and swollen joints (Arvidson et al. 1994). These symptoms' fluctuations may result in functional impairment, adversely affecting normal activities of daily living and working life (Da et al. 2011).

Based on these considerations, exploring the time of day effect of balance performance, functional capacities and risk of falls seems to be crucial in the management of RA not only for the quality of daily life activities but also for prevention of serious injuries and fractures due to the risk of falls in RA patients. If these fluctuations were observed, at which time of day these parameters would be more perturbed?

We hypothesized that in patients with RA all of these parameters could fluctuate during the day following the time of day variation of RA symptoms such as stiffness, limited range of motion, painful and swollen joints. Moreover, we hypothesized that balance performance could be more altered early in the morning and late in the evening. Therefore, this study aimed to investigate balance performance, functional capacities and risk of fall circadian variations in patients with RA and to explore if there is an association between these variations and those of RA symptoms.

Methods

Participants

Fifteen RA women and 15 healthy women participated in this study. All participants agreed with the testing protocol and gave their consent to participate in accordance with the National Medical Ethical Committee of our Medical School. RA patients were recruited from the department of rheumatology of a hospital. All patients with RA were classified as having functional classes I and II, based on the criteria of the American College of Rheumatology (1987) (Arnett et al. 1988). These patients received ongoing medications and had not received intra-articular steroid injections at least 3 weeks prior. None of the RA patients used walking aids. Women in both groups were matched in age, weight, and height. Participants with vestibular difficulties with any visual disorder, musculoskeletal or neurological disease, aftereffects from diabetes type I and II and with a history of injuries or of falls within the last 6 months requiring medical attention were excluded from the study.

In order to guarantee sample homogeneity, all participants were selected according to their chronotype using the circadian typology questionnaire of Horne and Ostberg (1976) and the Pittsburgh sleep quality index (PSQI) (Buysse et al. 1989). The health assessment questionnaire (HAQ) (Ferraz et al. 1990), the short form-36 (SF-36) (Ciconelli et al. 1999) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Bellamy 2002) were also used to evaluate the quality of their everyday life activities (Table 1).

Study design

The time of day effect of Functional capacities, balance, range of motion, painful and swollen joints were assessed in the two groups at 6 am, 2 pm and 10 pm. Participants perform one test session per day. All test sessions are randomized and separated by a period of rest (more than 36 hours) in order to eliminate the learning effect.

Table 1. Baseline characteristics of the two groups.

	RA group, $n = 15$	Control group, $n = 15$	p
Age	50 ± 2	50 ± 3	NS
Weight	73 ± 4	77 ± 4	NS
Height	162 ± 5	164 ± 4	NS
Chronotype	"moderately morning"	"moderately morning"	
PSQI	"poor sleepers"	"good sleepers"	
HAQ	1.2	2.5	0.01
SF-36	41%	70%	0.01
WOMAC	28	17	0.05

Before 6 am test session, participants were instructed to get up at 5 a.m. to prevent sleep-induced inertia (Baxter and Reilly 1983). Before 10 pm, the participants were required to remain awake and perform standard activities (reading, TV, …). In order to avoid post-prandial effects, such as an increase in body temperature, the subjects were only allowed to drink one glass of water (15–20 cl) prior to the 6 am tests session and eat at least 4 hours before the 2 pm., 6 pm. and 10 pm., test sessions (Reilly and Bambaeichi 2003).

During the 24 hours before each test session, participants were prohibited from eating or drinking any stimulant, e.g. caffeine or any other ergogenic drug that could enhance wakefulness. Participants did not engage in any tiring exercise during the testing period (Reilly and Bambaeichi 2003), and they were instructed to adhere as closely as possible to their usual sleeping habits for at least one week before the start of the testing period.

Balance performance, functional capacities, and risk of fall assessment

Time Up and Go Test (TUGT)

Balance and risk of fall were assessed using the Time Up and Go Test (TUGT). It is internationally accepted functional dynamic test of balance with known reliability and validity, as well as being low cost and easy to apply (Podsiadlo and Richardson 1991). The TUGT test measures the time in seconds that takes a participant to stand up from a chair, walk 3 meters at a comfortable and safe pace, turn around, walk back to the chair and sit down (Podsiadlo and Richardson 1991).

Tinetti test

Tinetti test is a common clinical test for assessing a person's static and dynamic balance. The test is two short sections, one examining static balance abilities in a chair and then standing and the other gait (Tinetti et al. 1986).

Functional Reach Test (FRT)

It is a quick and simple, single-task dynamic test that defines functional reach as "the maximal distance one can reach forward beyond arm's length, while maintaining a fixed base of support in the standing position" (Hill et al. 2013). It is a dynamic rather than a static test and measures a person's "margin of stability" as well as ability to maintain balance during a functional task. The test has been shown by Duncan et al. (1990) to be predictive of falls in older adults.

RA symptom evaluation

The patient's own perception of severity of his general stiffness was captured at each time point using a 100 mm visual analogue scale (VAS) anchored with "no stiffness" and "worst stiffness imaginable" (Backhouse et al. 2014).

In addition, the range of motion of the knee and ankle joint was measured with a goniometer for each participant.

Painful and swollen joints were counted by the 28 joint-index (Fuchs et al. 1989). The 28-joint count evaluates the following joints: shoulder, elbow, wrist, metacarpophalangeal and proximal interphalangeal; knee.

Statistical analyses

The statistical analysis of the results was carried out using the software Statistica 8 (StatSoft, France). Values are expressed as mean ± standard error (M ± ES).

The Shapiro–Wilk test was used to assess the normality of the data and revealed a normal distribution. An analysis of variance (ANOVA) with two factors (group, time) with repeated measurements was applied to the TUGT, Tinetti and FRT scores in the 3 times. The time factor has three levels: 6 am/2 pm/10 pm. We applied two-way repeated measures ANOVA also on the stiffness, range of motion, painful and swollen joints.

When significant differences were observed ($p < .05$), a post-hoc analysis was then performed with a Bonferroni significant difference test.

Significance was set as $p < .05$. Effect sizes were calculated as partial eta-squared ηp2, to assess the practical significance of our findings.

Pearson product moment correlations were performed to ascertain the correlation between each TUGT, Tinetti and FRT scores and those of RA symptoms. Correlations coefficients (r) were interpreted using the following qualitative descriptors: trivial (<0.1), small (<0.3), moderate (0.3–0.5), large (0.5–0.7), very large (0.7–0.9), nearly perfect (>0.9), perfect (1.0).

Results

The two-way repeated measures ANOVA revealed a significant main effect of group, of time and a significant interaction (group* time) on the balance and risk of falls tests values (TUG, Tinetti and FRT). Post-hoc analysis showed that these values were significantly higher in the RA group in the three sessions ($p < .001$; ηp2 = 0.82) compared to control group. Regarding the time of day effect, in the RA group, the post-hoc analysis showed that the TUGT, FRT and tinetti test scores were significantly higher ($p < .01$; ηp2 = 0.91) at 6 am and at 10 pm compared to 2 pm. No significant difference was observed between the balance and risk of falls test values at 6 am and 10 pm. However, in the control group, no significant difference was revealed between all times for the balance and risk of fall tests values (Figure 1).

In addition, the two-way repeated measures ANOVA, applied on stiffness, range of motion, swollen and painful joints values, revealed a significant main effect of group, of time and a significant interaction (group* time). The post-hoc analysis showed that these values were significantly higher in the RA women compared to healthy ones in the three test sessions ($p < .001$; ηp2 = 0.77). Regarding the time day effect, in the RA group, the post-hoc analysis showed that the stiffness (Figure 2), range of motion (Figure 5), swollen (Figure 3) and painful joints (Figure 4) values were significantly higher ($p < .01$; ηp2 = 0.71) at 6 am and at 10 pm compared to 2 pm. A significant difference was observed on the stiffness (Figure 2), range of motion (Figure 5) and swollen joints (Figure 3) values between 6 am and 10 pm that were higher at 6 am ($p < .05$). However, no significant difference was observed between 6 am and 10 pm on the painful joints (Figure 4) values. In the control group, no significant difference was revealed between all times.

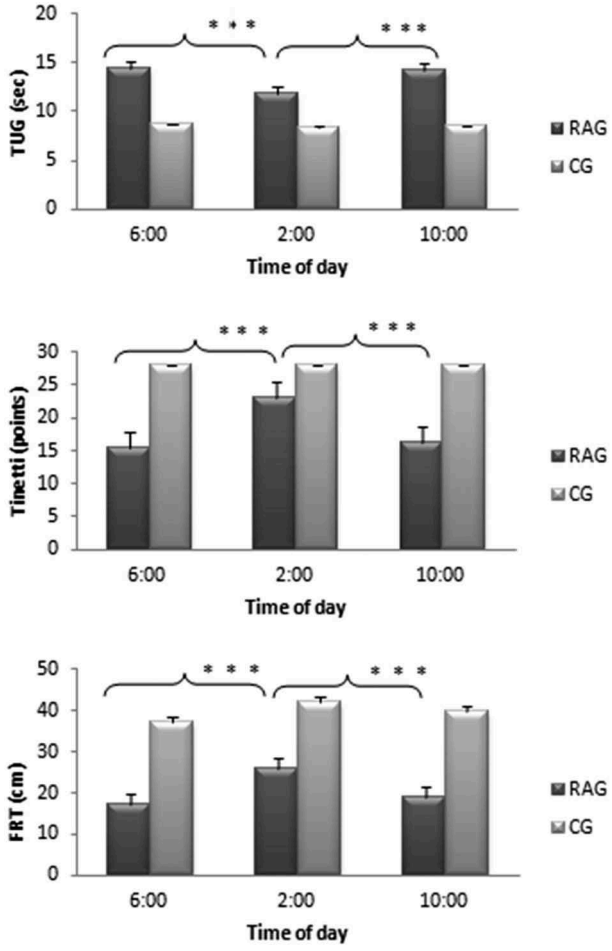

Figure 1. TUGT, tinetti test, and FRT scores in three sessions in rheumatoid arthritis and healthy participants.
***: significant difference at $p < .001$.

Using Pearson's coefficient of correlation, moderate positive correlations were found between the TUGT values and those of stiffness (r = 0.47; $p < .01$), swollen and painful joints values (r = 0.46; $p < .01$). No correlations were obtained between the TUGT and range of motion values. In addition, large positive correlations were obtained between the Tinetti and range of motion values (r = −0.46; $p < .001$). Negative large correlations were revealed also between the Tinetti values and those of stiffness (r = −0.58; $p < .001$) as well as those of swollen and painful joints (r = −0.64; $p < .001$). Large positive correlations were obtained between the FRT and range of motion values (r = −0.51; $p < .01$) and large negative correlations were obtained also between

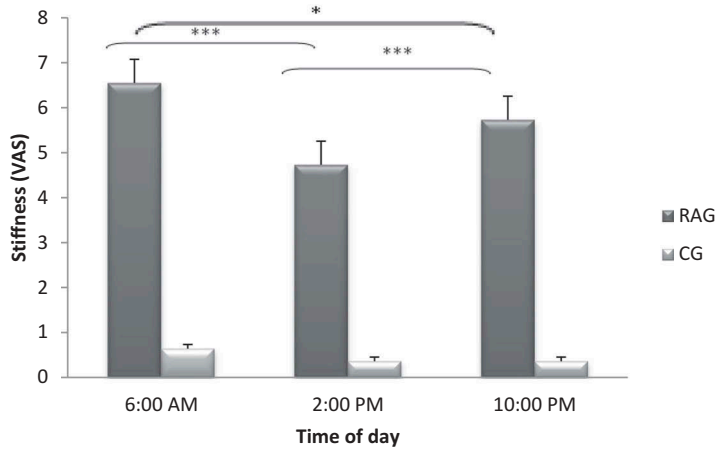

Figure 2. Stiffness values in the three sessions in rheumatoid arthritis and healthy participants.
***: significant difference at $p < .001$; *: significant difference at $p < .05$.

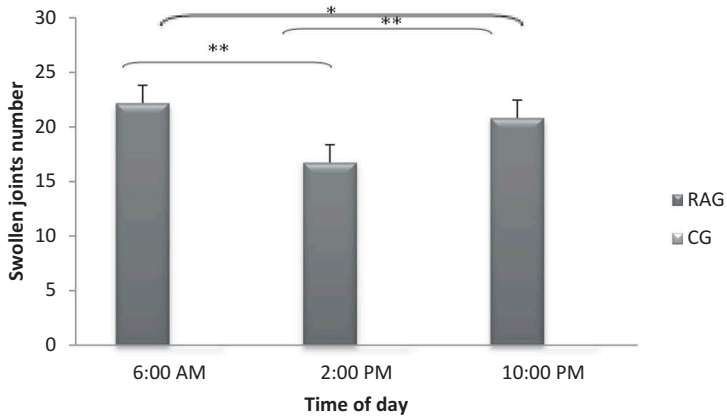

Figure 3. Swollen joints number in the three sessions in rheumatoid arthritis and healthy participants.
**: significant difference at $p < .01$; *: significant difference at $p < .05$.

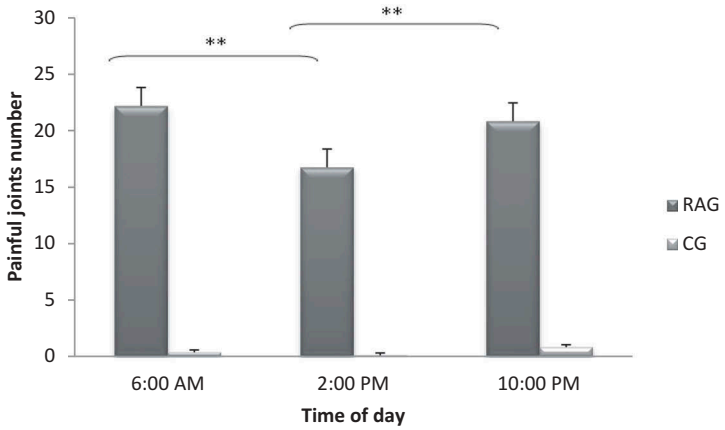

Figure 4. Painful joints number in the three sessions in rheumatoid arthritis and healthy participants.
**: significant difference at $p < .01$.

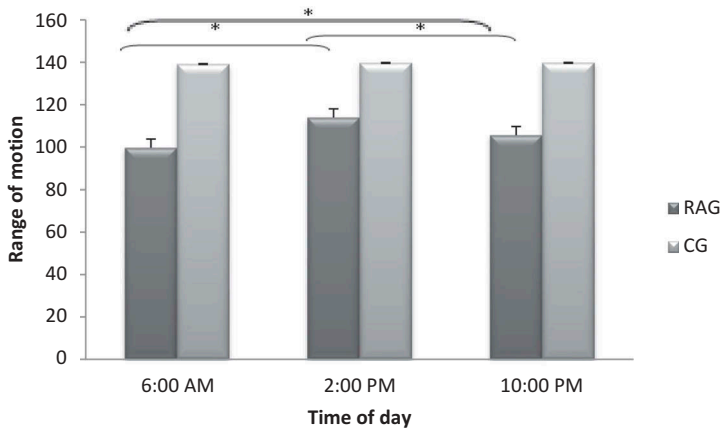

Figure 5. The range of motion values in the three sessions in rheumatoid arthritis and healthy participants.
*: significant difference at $p < .05$.

the FRT and stiffness values (r = −0.53; $p < .01$). Moderate negative correlations were found between FRT values and those of swollen and painful joints (r = −0.47; $p < .01$).

Discussion

The aim of our study was to investigate the time of day effect fluctuations of balance performance, functional capacities, and risk of fall in women with RA and to explore the association between these fluctuations and that of the major clinical symptoms of RA: stiffness, limited range of motion, swollen and painful joints.

The major result of this study showed a time of day effect on balance performance, functional capacities, and risk of fall in patients with RA. Indeed, performance is significantly altered at 6 am and at 10 pm compared to 2 pm. No previous study has analyzed the circadian variations of balance performance, functional capacities, and risk of fall in these patients. There is only one study that explored the diurnal variation of gait in patients with RA (Backhouse et al. 2014). In this study, 31 patients (male and female) with ≥30 minute morning stiffness were recruited from the rheumatology ward. These participants showed a marked diurnal variation in gait. This diurnal variation corresponded to gait velocity and stride length increase; and double support decrease, consistent with improving function throughout the day. In order to explain balance performance, functional capacities and risk of fall fluctuations in woman with RA, we assessed the major RA symptoms: stiffness, limited range of motion, painful and swollen joints at the same time of the day.

Swollen and painful joints data demonstrated significant differences between the values obtained in the three sessions. These results showed that the swelling and the pain fluctuate during the day with higher perturbation at 6 am then at 10 pm compared to 2 pm. It has been previously reported that pain appears mainly at the beginning of the day in patients with RA (Backhouse et al. 2014) and at the end of the day in patients with osteoarthritis (Levi et al. 1985). In addition, in RA patients, the morning volume of joints usually exceeded that of the evening (Scott 1960). Furthermore, the correlations between functional capacities and balance values and those of swollen and painful joints calculated in the three sessions argue in favor of this association. Previously, it has been reported that pain and swelling have a significant influence on functional capacities and balance in patients with RA (Backhouse et al. 2014). Hassan et al. (2001) showed that pain has a significant influence on the postural balance in patients with RA. Since pain can inhibit muscle reflex mainly around the knee, rapid and effective motor responses could be compromised resulting in altered postural balance (Bishop and George 2017).

Same results were observed for the knee flexion range of motion showing an accentuated limited range of motion at 6 am then at 10 pm. One could speculate that if pain perception was a mechanism of action for changes in range of motion, associations between their fluctuations would be observed. A limited range of motion measured at each

evaluation session was associated with average pain rating. This result is in line with those of Bishop and George (2017). These authors revealed a relationship between the range of motion of each joint and disability based on HAQ-DI categories in patients with long-standing RA. Interestingly, range of motions of a large number of joints was significantly associated with physical function in daily life (Kojima et al. 2017). The correlation between functional capacities and balance values and those of the range of motion during these sessions of the day can confirm the association between the fluctuations of balance and that of the range of motion in these patients.

Our result revealed that stiffness is significantly accentuated at 6 am and at 10 pm compared to 2 pm and is significantly accentuated at 6 am compared to 10 pm. It has been previously reported that the classic pattern of stiffness in patients with RA is one in which stiffness is worst first thing in the morning but then improves during the day before returning in the evening (Scott 1960). Backhouse et al. (2014) confirm that the improvement in function is sharpest during the first hour after waking, but functional performance continued to improve throughout the day. Functional capacities and balance impairments found at 6 am and at 10 pm could be, therefore, associated to the stiffness exacerbation recorded in these times. Furthermore, the correlations between stiffness values and functional capacities and balance ones calculated in the three sessions are in favor of this association. More recently, some studies showed that stiffness has a significant influence on the functional ability in patients with RA. In fact, this pattern of symptoms and associated functional ability has been shown to correspond to circadian variation in pro-inflammatory cytokines (Gibbs and Ray 2013)

In healthy adults, our data showed that functional capacities, balance, and risk of falls do not fluctuate during the day. Results of the previous studies are controversial. In fact, some studies showed that balance do not fluctuate during the day which is in line with our findings (Zouabi 2013). Results of other studies showed that balance is altered in the morning. It has been reported that the postural control is low between 05:00 and 08:00 h corresponding to the bathyphase of the body temperature rhythm (Forsman et al. 2007) and around 13:00 h (Gribble et al. 2007; Kwon et al. 2014) corresponding to the post-lunch dip observed in the vigilance level (Jorgensen et al. 2012). In this context, it has been established that the postural control of young adults fluctuates according to a rhythm which is close to that of body temperature and/or vigilance (Forsman et al. 2007; Jorgensen et al. 2012). Controversial results between studies may be due to several factors such as age and experimental protocols (timing of the sessions of the balance evaluation, visual sensory and proprioceptive conditions …).

Interesting practical implications could emerge from our study. Balance performance and functional capacities of women suffering from RA is significantly altered at 6 am and 10 pm. Therefore, they should be more careful and take the necessary precautions in the activities of their daily life especially during these periods of the day in order to reduce the risk of falls and injuries. In addition, the best performance in these patients is revealed at 2 pm. It would be important to plan functional rehabilitation programs at this time of day to avoid increased stiffness, pain, swelling and limited range of motion in the execution of these programs and to optimize their beneficial effects.

Study limits

This study faces some limitations that should be considered in subsequent studies. First, the number of RA patients who participated in our study is relatively reduced. Moreover, this disease mainly affects women, which explains the female sex of our study population. In addition, hormones such as cortisol, cytokines could influence balance performance and functional capacities in these patients with RA. Thus, an evaluation of these parameters could further explain the time of day effect of postural control in these patients.

Conclusion

Our major result showed that functional capacities, balance performance and risk of falls fluctuate during the day in women with RA. These variations indicate an alteration of performance at 6 am and 10 pm. Fluctuations of stiffness, pain, swelling and limited range of motion noted in this study are concomitant to those of functional capacities and balance performance.

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Disclosure statement

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