Initial evidence for the link between activities and health: Associations between a balance of activities, functioning and serum levels of cytokines and C-reactive protein

Mona Dür [a,b,c], Günter Steiner [b,d], Michaela Alexandra Stoffer [e], Veronika Fialka-Moser [f,1], Alexandra Kautzky-Willer [g], Clemens Dejaco [h], Cem Ekmekcioglu [i], Birgit Prodinger [j], Alexa Binder [b], Josef Smolen [b,k], Tanja Alexandra Stamm [l,b,d,*]

[a] IMC University of Applied Sciences, Department of Health Sciences, Bachelor Program Occupational Therapy, Piaristengasse 1, 3500 Krems, Austria
[b] Medical University of Vienna, Department of Internal Medicine III, Division of Rheumatology, Währinger Gürtel 18-20, 1090 Vienna, Austria
[c] Medical University of Vienna, Department of Pediatrics and Adolescent Medicine, Division of Neonatology, Pediatric Intensive Care and Neuropediatrics, Währinger Gürtel 18-20, 1090 Vienna, Austria
[d] Ludwig Boltzmann Society, Cluster Rheumatology, Balneology and Rehabilitation, Nussdorfer Strasse 64, 1090 Vienna, Austria
[e] University of Applied Sciences for Health Professions Upper Austria, Bachelor Program Occupational Therapy, Niedernharter Straße 20, 4020 Linz, Austria
[f] Medical University of Vienna, Department of Physical Medicine and Rehabilitation, Währinger Gürtel 18-20, 1090 Vienna, Austria
[g] Medical University of Vienna, Department of Internal Medicine III, Division of Gender Medicine, Währinger Gürtel 18-20, 1090 Vienna, Austria
[h] Medical University of Vienna, Department of Internal Medicine III, Division of Gastroenterology and Hepatology, Währinger Gürtel 18-20, 1090 Vienna, Austria
[i] Medical University of Vienna, Institute of Environmental Health, Kinderspitalgasse 15, 1090 Vienna, Austria
[j] Swiss Paraplegic Research ICF Unit, Guido A. Zäch Strasse 4, 6207 Nottwil, Switzerland
[k] Hospital Hietzing and Neurological Centre Rosenhügel, Wolkersbergenstraße 1, 1130 Vienna, Austria
[l] Medical University of Vienna, CeMSIIS—Center for Medical Statistics, Informatics and Intelligent Systems, Section for Outcomes Research, Spitalgasse 23, 1090 Vienna, Austria

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ABSTRACT

Growing evidence shows interrelations of psychological factors, neurological and immunological processes. Therefore, constructs like a balance of activities, the so called "occupational balance", could also have biological correlates. The aim of this study was to investigate potential associations between occupational balance, functioning, cytokines and C-reactive protein (CRP) in patients suffering from a chronic inflammatory disease like rheumatoid arthritis (RA) and healthy people. Moreover, we wanted to explore potential differences in gender and employment status.

A descriptive study in patients with RA and healthy people was conducted using the Occupational Balance-Questionnaire (OB-Quest) and the Short-Form 36 Health Survey (SF-36). Serum levels of cytokines, such as interleukin 6 (IL-6) and 8 (IL-8), interferon alpha (INFα), tumour necrosis factor alpha (TNFα), rheumatoid factor (RF) and of CRP were measured. Descriptive statistics, as well as Mann-Whitney U tests and Spearmen's rank correlation coefficients (r_s) were calculated.

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One-hundred-thirty-two patients with RA and 76 healthy people participated. Occupational balance was associated with functioning, cytokines and CRP. The strongest associations were identified in the unemployed healthy-people sample with cytokines and CRP being within the normal range. For example, the OB-Quest item *challenging activities* was associated with IL-8 ($r_s = -0.63$, $p = 0.04$) and the SF-36 sub-scale *bodily pain* was associated with IFNα ($r_s = -0.69$, $p = 0.02$). The items *rest and sleep* ($r_s = -0.71$, $p = 0.01$) and *variety of different activities* ($r_s = -0.74$, $p < 0.01$) correlated with the SF-36 sub-scale *social functioning*. Employed and unemployed people differed in their age and CRP levels. Additionally, gender differences were found in two OB-Quest items in that fewer women were able to adapt their activities to changing living conditions and fewer men were overstressed. In conclusion, we found preliminary biological evidence for the link between occupation and health in that the concepts encompassed in the construct of occupational balance were associated with functioning, cytokines and CRP.

1. Introduction

Occupational balance is defined as a positive evaluation of the amount and variation of activities (Wagman et al., 2012). Although there is almost no empirical evidence for such constructs, they largely guide the clinical practice of occupational therapists. Occupational therapists are health professionals who focus on activities of daily living as a means, but also as an outcome of therapy. For example, occupational balance was found to be associated with quality of life (Bejerholm, 2010), life satisfaction (Hakansson et al., 2011; Wagman et al., 2014; Wagman and Hakansson, 2014) and subjective health (Wagman and Hakansson, 2014; Wilcock, 1997). However, none of the existing studies (Anaby et al., 2010; Bejerholm, 2010; Hakansson et al., 2011; Wilcock, 1997) searched for biological evidence on the link between occupational balance and health.

Occupational balance extends the construct of work-life balance as it includes also "neither-work-nor-life" activities such as caring for one's own children or self-care activities that may become more difficult in case an individual has a chronic disease like rheumatoid arthritis (RA). However, paid work was found to impact the experience of occupational balance in employed (Forhan and Backman, 2010), unemployed (Primdahl et al., 2011) and retired people (Jonsson et al., 2000) including those who retired early (Stamm et al., 2010). For example, occupational balance was associated with work limitations in RA patients (Forhan and Backman, 2010). The experience of occupational balance was confined by retirement, in that the meaning of certain activities changed or even got lost (Jonsson et al., 2000). In addition, people with mental health illness who were unemployed tended to have more self-care and leisure activities which again could cause a lack of occupational balance (Crist et al., 2000). Occupational balance has been explored in RA patients with paid and unpaid work previously (Backman, 2004a). However, differences of occupational balance in employed and unemployed RA patients and healthy people have not been explored so far.

Furthermore, the ability to maintain or regain occupational balance after (early) retirement was found to differ between women and men. For example, men had difficulties to find new meaningful activities and therefore to maintain or regain occupational balance after retirement. In contrast, women were more likely to adapt former or to find new meaningful activities, and thereby to maintain their occupational balance after they had retired (Forhan and Backman, 2010; Jonsson et al., 2000; Stamm et al., 2008, 2010). However, occupational balance was explored in women and men in studies with quantitative designs, but gender aspects of this construct were explored in qualitative studies only (Stamm et al., 2010; Wada et al., 2015, 2014).

Associations of occupational balance and self-reported health, more specifically functioning, have been found previously, in that more occupational balance was associated with more functioning (Backman et al., 2004; Bar and Jarus, 2015; Forhan and Backman, 2010). Functioning is defined in the *"International Classification of Functioning, Disability and Health"* (ICF) as an umbrella term referring to all *"body structures and functions"* and *"activities and participation"* (WHO, 2001). For example, high scores of social functioning, general health and pain were associated with high scores of occupational balance in terms of performance, time and accomplishment (all favourable scores) (Forhan and Backman, 2010). However, none of these studies explored associations between occupational balance and functioning in female and male, and employed and unemployed RA patients and healthy people. Consequently, a quantitative description of differences of occupational balance with employed and unemployed women and men, could provide further information for the need to consider these differences in the clinical practice of RA patients and healthy people.

According to the growing evidence for the interrelations of psychological factors, neurological and immunological processes (Dobkin et al., 1998; Irwin, 2008; Miehsler et al., 2008; Steptoe et al., 2009), occupational balance could have biological correlates (Stamm et al., 2009; Wilcock, 2006). Immunological processes are humoral or cell-mediated responses from the immune system to pathogens or endogenous antigens as it occurs in autoimmune diseases such as RA. Besides others, immunological responses include blood and cell expressions, such as C-reactive protein (CRP) levels or number of CD4+ T cells (Calder, 2007). Some of these are of particular interest due to the findings of previous studies, which indicated a potential effect of certain activities on cytokine and CRP levels. For example, physical activity could impact CRP and interleukin 6 (IL-6) levels (Nader and Lundberg, 2009), and mediate CD4+ T lymphocyte levels (Creswell et al., 2009). Dog petting was found to have an effect on immunoglobulin A (IgA) levels (Charnetski et al., 2004), laughter on natural killer cells (Bennett et al., 2003) and Tai Chi on varicella-zoster virus specific cell-mediated immunity (Irwin et al., 2003). In addition, elevated serum levels of IL-6, interleukin 8 (IL-8), tumour necrosis factor alpha (TNFα), interferon alpha (INFα) and CRP were found to reflect inflammatory processes and damage of the rheumatic joints, and were associated with functioning in healthy people and RA patients (Alishiri et al., 2011; Beydoun et al., 2015; Bugatti et al., 2014; Garvin et al., 2015; Lipsky, 2006).

Thus, measuring cytokines, acute phase proteins or even antibodies may reveal some biological evidence for the link between occupational balance and health. This may help to answer the question whether or not a theoretical subjective construct, such as occupational balance, is associated with objective, observable variables such as biological parameters of health (Nersessian, 2008).

Therefore, the aim of this study was to investigate potential associations between occupational balance, functioning, cytokines and CRP in patients suffering from a chronic inflammatory dis-

ease like RA and healthy people. Moreover, we wanted to explore potential differences in gender and employment status.

Thus, the primary research question of this study was whether there are associations between occupational balance, functioning, cytokines and CRP in RA patients and healthy people. The secondary research question was whether the identified associations are different in terms of gender and employment status.

2. Method

We conducted a descriptive study in RA patients and healthy people to explore associations between occupational balance, functioning and serum levels of cytokines and CRP. Thereby, occupational balance was investigated as it "occurred" in the subjects of interest. The Ethical Committee of the Medical University of Vienna approved this study. All participants were informed about the study and gave oral and written informed consent. The current study was partly funded by the Austrian Science Fund (FWF): [P21912-B09].

2.1. Inclusion criteria and recruitment

Patients diagnosed with RA (Arnett et al., 1988) and healthy people were included in the study. Healthy people were defined as having no chronic disease or laboratory abnormalities such as anaemia or elevated liver enzyme levels. People with abnormal liver function tests were therefore excluded. Participants had to be ≥18 years of age. Exclusion criteria were pregnancy (due to the extra blood samples that had to be taken in the study) and restricted reading skills. Consecutive patients from the Rheumatology outpatient clinic of the Medical University of Vienna were asked to participate via personal invitation. Healthy people were invited via announcements on public places such as supermarkets and universities, but also at the hospital.

2.2. Data collection and assessments

Socio-demographic information was obtained regarding sex, age and employment status. Additionally, disease duration was extracted from patient records, where appropriate. Different self-reported measurements were used to systematically assess participants' perspectives and experiences of occupational balance, functioning, subjective health, fatigue and pain. The same was true for disease activity in RA patients.

Firstly, participants were asked to fill in two generic self-reported questionnaires: The self-developed *Occupational Balance-Questionnaire* (OB-Quest) (Dür et al., 2014) was applied to assess occupational balance. The OB-Quest consists of seven items assessing the following components of occupational balance important to people with chronic autoimmune diseases: *challenging and relaxing activities*, *activities with acknowledgement*, *health impact on activities*, *stress in activities*, *rest and sleep*, *variety of activities* and *adaptation of activities*. In the OB-Quest, all items are scored on a three-point numerical rating scale. "1" indicates the best score (e.g. receiving a lot acknowledgement for activities), while "3" indicates the worst score (e.g. receiving no acknowledgement for any activities) (Dür et al., 2014). Every single item was used for analyses. The German version of the *Short-Form 36 Health Survey* (version 2.0; SF-36) (Bullinger, 1995; Ware and Sherbourne, 1992) was used to assess functioning. The SF-36 consists of 36 items and comprises a total of eight scales on *physical functioning*, *role physical functioning*, *bodily pain*, *general health*, *vitality*, *social functioning*, *role emotional functioning* and *mental health*. These scales encompass concepts which were most frequently assessed in medical studies in the 1980s. A total score of 100 indicates the best score and thus a state of "complete" functioning without the experience of restrictions or limitations due to a health condition (Ware and Sherbourne, 1992).

Secondly, 10 cm visual analogue scales (VAS) were used to assess levels of pain, fatigue and disease activity (only for patients). Thirdly, a so called composite score, a combination of subjective and objective measurements, the *Clinical Disease Activity Index* (CDAI) was used to measure disease activity in RA patients. The CDAI is the simple linear sum of swelling and tender of 28 joints, and the evaluator and patient global disease activity visual analogue scales (Aletaha and Smolen, 2005). The CDAI scores range from 0 to 76, remission was defined as CDAI below 2.8, indicating a comparatively healthy state of RA patients (Aletaha et al., 2005).

Blood samples were collected from all participants and stored frozen at $-80\,^\circ$C for further analysis. The following cytokines were measured: IL-6, IL-8, TNFα and INFα. These cytokines were measured by commercial enzyme linked immune sorbent assay (ELISA, high sensitivity kits *Quantikine HS®* obtained from *R&D Systems*). In addition, CRP and rheumatoid factor (RF) were measured. CRP is an unspecific acute phase reactant which is expressed in the course of immune reactions. Furthermore, several health risks are associated with elevated levels of CRP (Carpenter et al., 2012). RF is an antibody which is in RA patients a predictor of clinical manifestations and erosions (Bas et al., 2002). CRP and RF levels were measured by routine laboratory. RF was specified only above the detection limit 12 (IU/ml). Since this would affect the correlation coefficients of the associations between RF and occupational balance and functioning, respectively, RF levels were not used for further analyses.

2.3. Data analysis

For statistical analyses the Statistical Package for Social Sciences (SPSS) was used. Data were summarized with descriptive statistics. All variables showed a non-normal distribution. Consequently, medians and interquartile ranges were used to describe the data. Before starting the sub-group analyses, we explored the associations between occupational balance, functioning, cytokines and CRP in all participants. Based on regression analyses of the whole sample, there were few and weak statistically significant correlations between these factors. However, there was a considerable range in the cytokines and functional parameters in the RA patients (data not shown). We assumed that these differences may be due to the fluctuation of immunological and functional parameters in the course of these health conditions. Thus, we considered sub-group analyses for different health conditions being appropriate in addition to analysing the whole sample together. Consequently, non-parametric Mann–Whitney U Tests for independent samples were calculated to identify statistically significant differences regarding health conditions, gender and employment status. Hodges–Lehmann estimate was used to determine the difference between group medians and the confidence interval of 95%.

Spearman's rank correlation coefficients (r_s) were calculated to assess potential relationships between OB-Quest items, SF-36 scales, cytokine and CRP levels. Correlation coefficients up to 0.30 were interpreted as low, between 0.31 and 0.69 as moderate and of 0.70 or above as strong correlation (Machin et al., 2007). The level of statistical significance was set by $\alpha = 0.05$.

3. Results

3.1. Participants

Two-hundred eight people participated in the study, including 132 RA patients and 76 healthy people. Characteristics of the participants, cytokine and CRP levels are shown in Table 1. As expected, all cytokines, CRP as well as perceived pain and fatigue differed significantly between RA patients and healthy people.

Table 1
Sample characteristics.

Characteristics	Samples		Differences	
	Healthy	Rheumatoid arthritis	*p*-values	
Participants per group	76	132		
n (%)				
Female	48 (63)	116 (88)	**0.01***	
Employed/self-employed	65 (86)	42 (32)	**0.01***	
Non-smoker (lifelong)	40 (53)	55 (42)	0.15	
ß-Blocker/ACE inhibitors/statins	–	43 (35)	–	
DMARD	–	70 (54)	–	
Biologic	–	54 (42)	–	
Cortisone	–	47 (36)	–	
Remission	–	96 (72)[a]	–	
Median (IQR)			HL [CI 95%]	*p*-values
Disease duration (years)	–	10 (4–16)	–	–
Age (years)	38 (27–49)	59 (48–65)	18 [14–22]	**0.01***
IL-6 level (pg/ml)	1.3 (0.8–2.1)	2.9 (1.2–8.2)	1.6 [0.9–2.4]	**0.01***
IL-8 level (pg/ml)	15.0 (6.0-31.6)	29.1 (19.6–60.6)	14.8 [9.8–20.4]	**0.01***
IFNα level (pg/ml)	3.7 (0.1–6.7)	4.1 (0.9–8.6)	0.6 [0–1.9]	**0.03***
TNFα level (pg/ml)	5.1 (3.8–7.9)	8.0 (4.3–13.1)	2.5 [1.3–3.8]	**0.01***
CRP (mg/l)	0.8 (0.5–2.0)	2.5 (1.0–6.0)	0.1 [0.1–0.2]	**0.01***
VAS pain	0 (0–.25)	16.0 (3.5–31.0)	13 [8–20]	**0.01***
VAS fatigue	4.00 (0–24.0)	16.50 (2.25–40.0)	8 [2–14]	**0.01***
VAS disease activity	–	14.0 (4.0–35.0)	–	–

Abbreviations: *n* (%) = number (percentage); ß-Blocker/ACE inhibitors/statins = took Beta-blocker, ACE-inhibitors and/or statins; DMARD = disease-modifying anti-rheumatic drugs; Biologic = biologic DMARDs; [a] = Clinical Disease Activity Index (CDAI) was ≤ 2.8; IQR = interquartile range; HL [CI 95%] = Hodges-Lehman estimated difference between medians with a [confidence interval of 95%]; IL–6 = interleukin 6; IL–8 = interleukin 8; IFNα = interferon alpha; TNFα = tumour necrosis factor alpha; CRP = C-reactive protein; VAS = visual analogue scale; – not applicable; pg/ml = picograms per millilitre; mg/l = milligrams per litre; U/ml = units per millilitre; bold* = statistically significant differences between the RA and the healthy sample ($p \leq .05$).

Values of all cytokines and CRP of the healthy people were within the normal range (data not shown). The correlations between the cytokine and CRP levels are depicted in the Appendix A.

Statistically significant differences were found between employed and unemployed people in both, the RA and the healthy-people sample concerning age, CRP levels, the OB-Quest items *rest and sleep* and the SF-36 scale *physical functioning*. Table 2 shows only those median values of the variables that differed statistically significantly between employed and unemployed subjects. Cytokine levels did not differ statistically significantly between employed and unemployed people.

Concerning gender differences, cytokines, CRP and SF-36 scales did not differ between women and men within the RA and the healthy people-sample. However, in the healthy people-sample, two OB-Quest items were found to differ statistically significantly between women and men: These were *feeling overstressed* and *the ability to adapt activities*. Seventy percent of the men ($n = 19$) perceived rarely or never periods in which they *felt overstressed*, compared to 29% of the women ($n = 14$, $p \leq 0.01$). Sixty-five percent of the women ($n = 32$) found to have a very good *ability to adapt activities* to changing living conditions compared to 89% of the healthy men ($n = 24$, $p \leq 0.05$).

3.2. Occupational balance, cytokines and CRP

Regarding the primary research question, there were few and weak statistically significant associations between occupational balance, cytokines and CRP in the whole sample, as depicted in Table 3.

The secondary research question focused on sub-group analyses for different health conditions and employment status. In the sub-groups, some associations between occupational balance, cytokines (IL-6, IL-8, IFNα) and CRP were found, as shown in Table 4. The OB-Quest item *challenging and relaxing activities* was moderately associated with IL-8 levels ($r_s = -0.63$, $p = 0.04$) in healthy, unemployed people. OB-Quest items, cytokines and CRP correlated most frequently in the data of healthy, employed people, as compared to the other sub-groups.

Interestingly, in the RA patient sample all associations between OB-Quest items, cytokines and CRP were found in unemployed subjects. For example, little or no *acknowledgement* for *activities* ($r_s = 0.22$, $p = 0.04$) and less *variety of activities* ($r_s = 0.25$, $p = 0.02$) were associated with high CRP levels. A similar trend could be identified in the associations between IFNα and *rest and sleep* ($r_s = -0.21$, $p = 0.04$) and the perceived *ability to adapt activities* to changing living conditions such as a changed state of health ($r_s = -0.24$, $p = 0.02$). Finally, little or no *variety of activities* was associated with high IL-6 ($r_s = 0.25$, $p = 0.01$) and CRP levels ($r_s = 0.25$, $p = 0.02$). The item *impact of a health condition on activities* did not correlate with any cytokine or with CRP at all.

3.3. Functioning, cytokines and CRP

Regarding the primary research question, there were few and weak statistically significant associations between functioning, cytokines and CRP in the whole sample, as depicted in Table 3. Further to the secondary research question, in the sub-groups, some associations between functioning, cytokines and CRP could be found. Seven of the eight SF-36 scales correlated with CRP. High CRP levels (within the normal range) were associated with high *vitality* ($r_s = 0.26$, $p < 0.04$) and *mental health* scores ($r_s = 0.27$, $p < 0.03$) in healthy, employed people and with high *bodily pain* scores (low pain) in healthy, unemployed people ($r_s = 0.71$, $p < 0.01$). Additionally, low CRP levels were associated with high *general health* scores ($r_s = -0.71$, $p = 0.02$) in healthy, unemployed people. Compared to that, low CRP levels were associated with high *physical functioning* ($r_s = -0.21$, $p < 0.05$), *vitality* ($r_s = -0.22$, $p < 0.04$) and *role emotional functioning* ($r_s = -0.34$, $p < 0.01$) scores in unemployed RA patients, as shown in Table 5.

3.4. Occupational balance and functioning

Regarding the primary research question, there were weak and moderate statistically significant associations between occu-

Table 2
Identified differences between employed and unemployed participants.

Sample	Healthy		Differences	
Employment status	Employed	Unemployed	HL [CI 95%]	*p*-values
n (%)	65 (85)	11 (15)		**0.01***
Median (IQR)				
Age	36 (26.5–44)	61 (47-64)	21 [11–30]	**0.01***
CRP levels (mg/l)	0.7 (0.4–1.2)	2.6 (0.7–2.9)	0.1 [0–0.2]	**0.01***
Amount of rest and sleep[a]	2 (1–2)	1 (1–2)	0 [0–1]	**0.04***
Physical functioning[b]	100 (95–100)	92.5 (90–96.3)	5 [0–10]	**0.03***

Sample	Rheumatoid arthritis		Differences	
Employment status	Employed	Unemployed	HL [CI 95%]	*p*-values
n (%)	42 (32)	90 (68)		**0.01***
Median (IQR)				
Age	45 (35.3–51.3)	63 (58–67)	17 [14–21]	**0.01***
Subjective disease activity	7 (2–22)	21 (6-41.3)	8 [2–17]	**0.01***
Disease activity[c]	3.9 (1.5–8.5)	6.1 (2.5–11.8)	1.9 [0.2–3.9]	**0.03***
CRP levels (mg/l)	1.9 (0.8–5.9)	3.1(1.4–6.9)	0.1 [0–0.2]	**0.03***
Amount of rest and sleep[a]	2 (1–2)	1 (1–2)	0 [0–0.1]	**0.01***
Physical functioning[b]	80 (65–90)	70 (45–80)	10 [5–20]	**0.01***
Role physical functioning[b]	75 (50–100)	50 (0–100)	25 [0–50]	**0.01***

Abbreviations: Employed = employed/self-employed; bold* = statistically significant differences between employed and unemployed ($p \leq .05$) calculated with independent samples Mann–Whitney *U* tests; HL [CI 95%] = Hodges-Lehman estimated difference between medians with a [confidence interval of 95%]; CRP = C-reactive Protein; mg/l = milligrams per litre.
[a] Items of the Occupational Balance-Questionnaire.
[b] Scales of the Short-Form 36 Health Survey.
[c] Clinical Disease Activity Index (CDAI).

Table 3
Spearman's rank correlation coefficients of OB-Quest items, SF-36 scales, cytokines and CRP of the whole sample.

OB-Quest items	Cytokines and CRP				
	IL-6	IL-8	IFNα	TNFα	CRP
Challenging and relaxing activities	**0.14***	−0.03	0.10	−0.04	0.04
Activities with social acknowledgement	0.03	−0.01	**0.14***	**0.20***	**0.14***
Feeling overstressed	−0.08	−0.04	0.02	0.08	−0.03
Impact of a health condition on activities	−0.02	0.04	−0.06	0.04	0.08
Rest and sleep	−0.12	−0.05	−0.10	−0.12	−0.01
Variety of activities	0.02	0.20	−0.07	−0.04	**0.18***
Ability to adapt activities	−0.03	0.02	−0.05	**0.16***	0.06
SF-36 scales					
Physical functioning	−0.03	−0.02	**−0.15***	−0.10	**−0.25***
Role physical functioning	−0.04	−0.03	0.03	**−0.20***	**−0.17***
Bodily pain	−0.03	−0.05	−0.12	**−0.21***	**−0.19***
General health	−0.06	0.06	−0.05	−0.10	**−0.15***
Vitality	0.06	0.04	0.01	−0.12	−0.07
Social functioning	0.10	0.04	−0.02	**−0.15***	−0.05
Role emotional functioning	0.00	−0.01	0.07	−0.07	**−0.19***
Mental health	0.09	0.06	0.08	−0.11	0.01

Abbreviations: OB-Quest = Occupational Balance-Questionnaire; IL-6 = interleukin 6; IL-8 = interleukin 8; IFNα = interferon alpha; CRP = C-reactive protein; SF–36 = Short-Form 36 Health Survey; bold* = statistically significant associations ($p \leq .05$); Inverse correlations, as given in TNFα or CRP, indicate that lower scores in functioning relate to increased TNFα or CRP values, respectively.

pational balance and functioning in the whole sample, as shown in Appendix B.

Concerning the secondary research question, OB-Quest items correlated with the SF-36 scales, particularly in RA patients. However, strong correlations were found in healthy, unemployed people only (Table 6). For example, the OB-Quest items *rest and sleep* ($r_s = − 0.71$, $p = 0.01$) and a *variety of activities* ($r_s = -0.74$, $p < 0.01$) correlated with the SF-36 scale *social functioning*. All items, showed inverse correlations, indicating that low scores on the OB-Quest items relate to high scores on the SF-36 scales (both the favourable scores, respectively). Significant r_s varied between |0.23| and |1.00|, as shown in Table 6. A perfect correlation ($r_s = − 1.0$, $p < 0.01$) was found between the OB-Quest item *variety of activities* and the SF-36 scale *role physical functioning* in healthy, unemployed people.

4. Discussion

The data obtained in this study seem to provide some biological evidence for the link between activities and health. With regards to the primary research question, we found only few statistically significant associations between OB-Quest items, SF-36 scales, cytokine and CRP levels in the whole sample. These associations were weak, which might be related to the considerable range in the cytokines and functional parameters in RA patients and the relatively small sample size. Furthermore, the number of RA patients receiving biological treatment could have impacted the associations between occupational balance, functioning, cytokines and CRP (Alishiri et al., 2011; Baturone et al., 2009; Berliner et al., 2007; Beydoun et al., 2015; Forhan and Backman, 2010; Garvin et al., 2015).

Table 4
Spearman's rank correlation coefficients of OB-Quest items, cytokines and CRP in employed and unemployed healthy people and RA patients.

OB-Quest items	Cytokines and CRP				
	IL-6	IL-8	IFNα	TNFα	CRP
Challenging and relaxing activities					
Healthy—employed	**0.26***	0.11	0.10	0.03	0.16
Healthy—unemployed	−0.57	**−0.63***	−0.54	−0.53	0.21
Rheumatoid arthritis—employed	−0.18	0.16	−0.11	−0.11	−0.12
Rheumatoid arthritis—unemployed	−0.02	0.05	−0.12	0.10	0.08
Activities with social acknowledgement					
Healthy—employed	−0.09	−0.12	−0.06	0.08	0.01
Healthy—unemployed	0.15	0.00	0.20	−0.32	−0.06
Rheumatoid arthritis—employed	−0.08	0.08	0.30	−0.03	0.12
Rheumatoid arthritis—unemployed	0.12	0.09	0.09	0.17	**0.22***
Feeling overstressed					
Healthy—employed	0.16	0.05	0.10	0.13	−0.05
Healthy—unemployed	−0.51	0.00	0.12	−0.30	−0.60
Rheumatoid arthritis—employed	−0.26	−0.16	−0.03	−0.06	−0.04
Rheumatoid arthritis—unemployed	−0.12	0.12	−0.11	−0.06	−0.08
Impact of a health condition on activities					
Healthy—employed	0.07	0.22	0.18	−0.12	−0.07
Healthy—unemployed	−0.35	−0.35	−0.26	−0.40	0.15
Rheumatoid arthritis—employed	−0.14	−0.02	0.16	0.05	−0.11
Rheumatoid arthritis—unemployed	−0.18	−0.17	−0.01	0.00	0.09
Rest and sleep					
Healthy—employed	0.05	−0.04	0.06	−0.06	−0.10
Healthy—unemployed	−0.51	0.26	0.03	−0.24	−0.26
Rheumatoid arthritis—employed	−0.16	−0.23	−0.05	−0.22	0.03
Rheumatoid arthritis—unemployed	0.03	0.02	**−0.21***	−0.06	0.17
Variety of activities					
Healthy—employed	−0.14	0.10	−0.16	0.01	−0.19
Healthy—unemployed	−0.40	0.20	0.25	−0.35	−0.20
Rheumatoid arthritis—employed	−0.04	0.13	0.24	−0.12	−0.07
Rheumatoid arthritis—unemployed	**0.25***	0.11	−0.08	0.01	**0.25***
Ability to adapt activities					
Healthy—employed	−0.01	0.06	0.06	0.08	−0.14
Healthy—unemployed	0.08	−0.08	−0.04	−0.15	0.23
Rheumatoid arthritis—employed	−0.17	−0.10	0.19	0.05	0.03
Rheumatoid arthritis—unemployed	0.08	0.08	**−0.24***	0.13	0.10

Abbreviations: OB-Quest = Occupational Balance-Questionnaire; IL–6 = interleukin 6; IL–8 = interleukin 8; IFNα = interferon alpha; CRP = C-reactive protein; bold* = statistically significant correlation coefficients ($p \leq .05$); Inverse correlations, as given in IL-8 or IFNα, indicate that lower scores in occupational balance relate to increased IL-8 or IFNα values, respectively; employed = employed/self-employed.

However, the findings of the sub-group analyses confirm previous assumptions of occupational therapists and scientists regarding the theoretically developed construct of occupational balance which was found to be associated with functioning, cytokines and CRP. Identified correlations between OB-Quest items and IL-6, IL-8, IFNα and CRP levels, show that the associations between occupational balance and immunological activities exist. In line with our findings, previous studies reported associations between three of the seven components of occupational-balance (*feeling overstressed*, the *impact of a health condition on activities and [rest and] sleep*), cytokines and CRP. For example, associations between stress and cytokines and CRP, respectively, were found. While acute high psychosocial and work-related stress levels were found to be associated with high IL-6 or CRP levels (Nakata, 2012; Rohleder, 2012), chronic stress was found to down regulate pro-inflammatory cytokines, such as IL-6 and TNFα (Tian et al., 2014). Additionally, *feeling overstressed* has been associated with high levels of CRP and TNFα (Straub and Kalden, 2009). Several studies indicate an association of the *impact of a health condition on activities* with CRP in RA patients in that, a high impact is associated with high CRP levels (Combe et al., 2003).

Patients treated with IFNα therapy were found to have poor sleep quality and sleep disruption (Prather et al., 2009). However, these studies focused on patients with other health conditions than RA. In RA, associations between sleep and IFNα, as found in our study, have not been reported previously. Moreover, rest has not been taken into account concerning cytokines and CRP before. Associations of single concepts, such as *sleep* (Prather et al., 2009) or *feeling overstressed* (Straub and Kalden, 2009) and cytokines and CRP were investigated. However, a synopsis of these concepts, such as the construct of occupational balance and their associations with cytokines and CRP has not been researched before.

Three components of occupational balance have not been associated with cytokines and CRP previously. These are *challenging and relaxing activities* (IL-6 and IL-8), a *variety of activities* (IL-6 and CRP) and the *ability to adapt activities* (IFNα). However, previous studies found associations between activities, which could be challenging or relaxing, cytokines and CRP, in that high levels of physical, leisure time and mental activities were associated with low levels of IL-6, TNFα and CRP (Lin et al., 2012; von Kanel et al., 2014). Since most of the components of occupational balance which were meaningful to people with and without chronic autoimmune diseases (Dür et al., 2014; Stamm et al., 2009), correlated with IL-6, IL-8, IFNα or CRP, further research on these associations and their meaning in the clinical practice is needed.

Surprisingly, better (higher) SF-36 scores (little or no *bodily pain*, good *vitality* and *mental health*) were associated with high CRP levels (though, still within the normal range) in healthy people. Previous studies showed that CRP levels increase with age (Rumley et al., 2006; Woloshin and Schwartz, 2005). However, since the

Table 5
Spearman's rank correlation coefficients of SF-36 scalescytokines and CRP in employed and unemployed healthy people and RA patients.

SF-36 scales[†]	Cytokines and CRP				
	IL-6	IL-8	IFNα	TNFα	CRP
Physical functioning					
Healthy—employed	0.02	−0.05	−0.13	0.03	−0.14
Healthy—unemployed	−0.25	−0.20	−0.32	−0.01	0.05
Rheumatoid arthritis—employed	0.05	−0.07	0.06	−0.03	−0.28
Rheumatoid arthritis—unemployed	−0.16	−0.07	0.09	−0.06	**−0.21***
Bodily pain					
Healthy—employed	−0.08	−0.10	0.01	−0.04	0.05
Healthy—unemployed	0.10	−0.49	**−0.69***	0.35	**0.71***
Rheumatoid arthritis—employed	0.15	0.01	0.02	−0.10	**−0.38***
Rheumatoid arthritis—unemployed	−0.16	0.03	0.10	0.21	−0.11
General health					
Healthy—employed	0.04	0.19	0.25	−0.06	0.16
Healthy—unemployed	−0.41	0.16	−0.02	−0.28	**−0.71***
Rheumatoid arthritis—employed	0.22	**0.31***	−0.03	0.19	−0.22
Rheumatoid arthritis—unemployed	−0.13	0.08	0.20	−0.09	−0.09
Vitality					
Healthy—employed	0.15	0.20	0.05	0.00	**0.26***
Healthy—unemployed	−0.02	−0.03	−0.10	0.21	0.06
Rheumatoid arthritis—employed	0.26	0.16	−0.02	−0.04	−0.08
Rheumatoid arthritis—unemployed	0.01	0.02	0.12	0.00	**−0.22***
Social functioning					
Healthy—employed	0.18	0.08	0.06	0.06	0.14
Healthy—unemployed	0.26	−0.23	−0.37	0.18	0.06
Rheumatoid arthritis—employed	**0.33***	0.18	0.01	0.14	−0.22
Rheumatoid arthritis—unemployed	0.13	−0.03	0.16	0.15	−0.16
Role emotional functioning					
Healthy—employed	0.20	0.10	0.15	0.09	0.17
Healthy—unemployed	−0.25	−0.40	−0.50	0.35	0.50
Rheumatoid arthritis —employed	0.17	0.06	0.15	−0.09	0.01
Rheumatoid arthritis—unemployed	−0.03	−0.08	0.10	−0.04	**−0.34***
Mental health					
Healthy—employed	−0.01	0.05	0.04	0.08	**0.27***
Healthy—unemployed	0.17	0.34	0.15	0.20	−0.01
Rheumatoid arthritis—employed	**0.38***	0.27	−0.01	0.03	0.08
Rheumatoid arthritis —unemployed	0.02	−0.07	0.19	0.13	−0.13

Abbreviations: SF–36 = Short-Form 36 Health Survey; IL–6 = interleukin 6; IL–8 = interleukin 8; IFNα = interferon alpha; CRP = C-reactive protein mg/l; bold* = statistically significant correlation coefficients ($p \leq .05$); † = only those scales which correlated statistically significantly with cytokines and/or CRP; employed = employed/self-employed; Inverse correlations, as given in IFNα or CRP, indicate that lower scores in functioning relate to increased IFNα or CRP values, respectively.

healthy-people sample had a median age of 38 years, relating these findings to age appears unreasonable. Some of our findings differ from the observations of other studies. For example, inverse correlations between cytokines (like IL-6), erythrocyte sedimentation rate and CRP, respectively, and the SF-36 subscales (like *physical functioning*, *social functioning*, *general health* and *bodily pain*) were found in patients with RA and healthy people (Alishiri et al., 2011; Garvin et al., 2015). Furthermore, high levels of IL-6 and CRP were associated with decreased quality of life and a risk for depression in healthy people (Ekmekcioglu, 2012; Garvin et al., 2015). While cytokines are generally not considered to be useful single biomarkers for monitoring disease activity, CRP reflects ongoing immunological processes and thus is used as a marker for increased immunological activation, especially inflammation. Consequently, further research on the association of functioning and cytokines and CRP in healthy people is needed.

In the current study, numerous associations between OB-Quest items and SF-36 scales were found. Favourable scores of the OB-Quest items were associated with favourable scores of the SF-36 scales. These findings add further evidence for the previously identified associations between occupational balance and self-reported functioning (Backman, 2004b; Forhan and Backman, 2010). In addition, the validity of the SF-36 (Bullinger, 1995; Linde et al., 2008; Stoll et al., 1997) and the number of correlations with the OB-Quest, strengthen the credibility of the identified associations between

occupational balance and cytokines and CRP, respectivley. The perfect correlation of -1 between *role physical functioning* and a *variety of activities* in unemployed, healthy people indicates that a good *variety of activities* are associated with high *role physical functioning*. Since employed and unemployed, healthy people did not differ statistically significantly in their *variety of activities* and *role physical functioning* the reason remains unclear. However, due to small sample size of the unemployed healthy people, these findings should be interpreted with caution.

Occupational balance, functioning, cytokines and CRP have not been compared between employed and unemployed people before. Anyway, employment, cytokines and CRP have been previously associated. For example, associations between CRP levels and work, work exposure and stress have been identified (Bellingrath et al., 2009; Loucks et al., 2010). The treatment of RA with TNF antagonists was found to improve patients' workability, employability and to reduce workday losses (Furuya et al., 2013).

The differences between women and men identified in the current study need to be interpreted with caution, due to unequal proportions of these subgroups. Healthy men were less frequently *overstressed* and perceived more frequently a good *ability to adapt their activities* than healthy women. This might relate to previous findings, where women and men with similar average stress levels were found to differ in their expressions about their stress experiences (Lee et al., 2014).

Table 6
Spearman's rank correlation coefficients of the OB-Quest items and SF-36 scales in employed and unemployed healthy people and RA patients.

Measures of theoretical concepts	SF-36 Scales							
OB-Quest items	PF	RP	BP	GH	VT	SF	RE	MH
Challenging and relaxing activities								
Healthy—employed	−0.08	−0.07	−0.06	**−0.26***	0.50	**−0.26***	−0.14	0.01
Healthy—unemployed	0.10	−0.43	0.23	−0.22	−0.18	−0.42	0.32	−0.43
Rheumatoid arthritis—employed	**−0.35***	−0.23	0.08	−0.25	−0.14	−0.12	0.10	−0.12
Rheumatoid arthritis—unemployed	**−0.38***	**−0.41***	**−0.39***	**−0.45***	**−0.50***	**−0.27***	**−0.27***	**−0.31***
Activities with social acknowledgement								
Healthy—employed	−0.12	−0.24	−0.01	−0.04	**−0.26***	0.03	−0.09	−0.21
Healthy—unemployed	**−0.66***	−0.29	−0.40	−0.41	−0.31	0.01	−0.29	0.03
Rheumatoid arthritis—employed	−0.15	**−0.29***	−0.14	−0.09	**−0.40***	**−0.29***	**−0.44***	**−0.47***
Rheumatoid arthritis—unemployed	−0.12	0.04	−0.14	−0.09	**−0.30***	**−0.27***	**−0.40***	**−0.44***
Feeling overstressed								
Healthy—employed	−0.10	−0.23	−0.18	−0.13	**−0.42***	**−0.35***	**−0.35***	**−0.50***
Healthy—unemployed	0.03	−0.42	−0.52	0.42	−0.44	−0.18	0.24	−0.57
Rheumatoid arthritis—employed	−0.15	−0.28	−0.03	**−0.38***	**−0.51***	**−0.39***	**−0.34***	**−0.57***
Rheumatoid arthritis—unemployed	**−0.39***	**−0.33***	**−0.50***	**−0.39***	**−0.54***	**−0.40***	**−0.30***	**−0.47***
Impact of a health condition on activities								
Healthy—employed	−0.15	−0.05	−0.19	−0.10	−0.14	−0.22	**−0.39***	**−0.28***
Healthy—unemployed	0.09	−0.35	−0.24	−0.32	−0.43	−0.51	−0.29	−0.47
Rheumatoid arthritis—employed	**−0.33***	**−0.32***	−0.22	−0.20	**−0.57***	**−0.38***	−0.81	**−0.32***
Rheumatoid arthritis—unemployed	**−0.33***	−0.17	−0.17	**−0.30***	**−0.35***	**−0.35***	−0.23	**−0.34***
Rest and sleep								
Healthy—employed	0.03	−0.09	−0.02	−0.11	**−0.29***	−0.15	−0.19	−0.16
Healthy—unemployed	−0.06	−0.59	−0.02	0.12	−0.34	**−0.71***	0.24	0.03
Rheumatoid arthritis—employed	−0.28	−0.25	−0.07	−0.18	**−0.46***	**−0.43***	**−0.42***	**−0.46***
Rheumatoid arthritis—unemployed	**−0.24***	**−0.24***	**−0.26***	**−0.32***	**−0.38***	**−0.24***	**−0.28***	**−0.36***
Variety of different activities								
Healthy—employed	−0.02	−0.23	−0.12	−0.20	**−0.38***	**−0.25***	−0.24	**−0.44***
Healthy—unemployed	−0.53	**−1.00***	0.52	−0.30	−0.53	**−0.74***	0.10	−0.25
Rheumatoid arthritis—employed	−0.06	−0.01	−0.09	−0.19	−0.07	−0.23	−0.01	−0.16
Rheumatoid arthritis—unemployed	**−0.39***	**−0.33***	**−0.27***	−0.20	**−0.52***	**−0.38***	**−0.28***	**−0.33***
Ability to adapt activities								
Healthy—employed	−0.06	−0.20	−0.11	−0.19	**−0.31***	**−0.30***	**−0.30***	**−0.42***
Healthy—unemployed	−0.58	**−0.67***	−0.22	−0.52	**−0.63***	0.44	−0.15	−0.49
Rheumatoid arthritis—employed	**−0.37***	−0.23	−0.24	**−0.32***	**−0.51***	**−0.54***	−0.17	**−0.42***
Rheumatoid arthritis—unemployed	**−0.42***	**−0.40***	**−0.48***	**−0.49***	**−0.54***	**−0.49***	**−0.32***	**−0.47***

Abbreviations: OB-Quest = Occupational Balance-Questionnaire; SF-36 = Short-Form 36 Health Survey; PF = physical functioning; RP = role physical functioning; RE = role emotional functioning; VT = vitality including energy and fatigue; MH = mental health; SF = social functioning; BP = bodily pain; GH = general health; bold* = statistically significant correlation coefficients ($p \leq .05$); employed = employed/self-employed.

Larger sample size and less variance could have led to stronger associations between occupational balance, functioning, cytokines and CRP. Furthermore, the use of other occupational balance measurements could have led to different findings. Interestingly, in both the RA and the healthy-people sample, unemployed people had considerably higher CRP levels than the employed, which did not differ between the two groups, in contrast to the employed. Since CRP levels increase with age (Rumley et al., 2006; Woloshin and Schwartz, 2005) this might have been a confounding factor. Thus, in both samples unemployed people were older (median age 61 years in healthy people and 63 years in RA patients) than employed people (median age 36 and 45 years, respectively), had worse *physical functioning* and in the RA sample had higher disease activity. A relation between *physical functioning* and age has been reported previously (Christian et al., 2011; Welsing et al., 2001).

This study used a novel approach to search for biological evidence of a theoretically developed construct by determining relations between occupational balance, functioning and the immune system. On the basis of our descriptive preliminary data, further investigations on such relations appear to be justified and should be focused on patients with different disease activity. Moreover, a sample with equal female/male proportions could add further information about occupational balance as a construct that might be perceived differently by women and men. Such research could provide additional insight whether there are associations between occupational balance, functioning, cytokines and CRP in people with other chronic autoimmune diseases. In addition, further research could be used to determine the potential benefits of targeting occupational balance in the treatment of RA patients.

5. Conclusions

This study seems to provide preliminary biological evidence for the link between occupation and health in that occupational balance was associated with functioning, cytokines and CRP. This supports the theoretically developed construct of occupational balance confirming previous assumptions of occupational therapists and scientists.

Conflicts of interest

None.

Contributors

MD, GS, JS, and TAS were involved into conception and design, the acquisition of data, the analysis and interpretation of data, wrote the draft manuscript, and gave final approval of the manuscript. AB assisted the data acquisition, analysis and interpretation, and the draft version, and finally gave advice on editing of manuscript. BP, AK-W, VF-M, and CD gave substantial contributions to conception and design, supported the acquisition of the data, have been involved in revising the draft manuscript critically, and finally approved the manuscript considered for publication. CE, MAS and AB were involved into the conception and design, the acquisition and the interpretation of the data, the writing of the draft manuscript and gave final approval of the manuscript. The authors have taken an active part in the study and take responsibility for its contents. The FWF did not have any influence on the manuscript.

Appendix A.

Spearman's rank correlation coefficients between the different cytokines, CRP and RF per sample and subgroup.

	Employed						Unemployed					
	IL-6	IL-8	IFNα	TNFα	RF	CRP	IL-6	IL-8	IFNα	TNFα	RF	CRP
Healthy												
n (%)	65 (86)						11 (14)					
IL-6	1	**0.41***	**0.42***	**0.33***	−0.15	0.21	1	0.26	0.34	**0.65***	0.5	0.44
IL-8		1	**0.78***	0.11	−0.04	0.16		1	**0.80***	0.33	−0.30	−0.42
IFNα			1	0.17	0.1	0.12			1	0.16	−0.30	−0.44
TNFα				1	−0.15	0.01				1	0.15	0.54
RF					1	−0.17					1	0.50
CRP						1						1
Rheumatoid arthritis												
n (%)	42 (32)						100 (68)					
IL-6	1	**0.31***	0.17	**0.38***	0.22	0.01	1	0.11	0.05	0.15	0.2	**0.42***
IL-8		1	**0.35***	**0.39***	0.21	−0.1		1	0.03	0.16	−0.06	0.02
IFNα			1	0.21	**0.53***	0.2			1	−0.02	**0.48***	0.09
TNFα				1	0.11	−0.07				1	0.07	−0.01
RF					1	0.05					1	0.16
CRP						1						1

Abbreviation: n (%) = number (percentage), IL-6 = interleukin6, IL-8 = interleukin8, IFNα = interferon alpha, TNFα = tumor necrosis factor-alpha, RF = rheumatoid factor assessed in IU/ml, CRP = C-reactive protein assessed in mg/l, bold* = statistically significant correlation coefficients ($p \leq .05$), employed = employed/self-employed.

Appendix B.

Spearman's rank correlation coefficients of the occupational balance-questionnaire items and SF-36 scales whole sample.

Measures of theoretical concepts	SF-36 scales							
OB-Quest items	PF	RP	BP	GH	VT	SF	RE	MH
Challenging and relaxing activities	**0.14***	**0.19***	**0.12**	**0.19***	**0.24***	**0.20***	**0.15***	**0.07**
Activities with social acknowledgement	−0.26*	−0.23*	−0.25*	−0.21*	−0.33*	−0.27*	−0.36*	−0.27*
Feeling overstressed	−0.27*	−0.32*	−0.31*	−0.33*	−0.52*	−0.39*	−0.33*	−0.24*
Impact of a health condition on activities	−0.26*	−0.23*	−0.22*	−0.29*	−0.40*	−0.36*	−0.27*	−0.25*
Rest and sleep	**0.02**	−0.08	−0.05	−0.08	−0.31*	−0.20*	−0.21*	−0.14*
Variety of different activities	−0.18*	−0.21*	−0.18*	−0.19	−0.39*	−0.32*	−0.20*	−0.18*
Ability to adapt activities	−0.30*	−0.34*	−0.33*	−0.40*	−0.49*	−0.48*	−0.28*	−0.33*

Abbreviations: OB-Quest = Occupational Balance-Questionnaire; SF-36 = Short-Form 36 Health Survey; PF = physical functioning; RP = role physical functioning; RE = role emotional functioning; VT = vitality including energy and fatigue; MH = mental health; SF = social functioning; BP = bodily pain; GH = general health; bold* = statistically significant correlation coefficients ($p \leq .05$).

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