

Working time and upper limb musculoskeletal symptoms: a longitudinal study among assembly line workers

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Abstract: This study followed assembly line workers during 7 months, comprising a 4-wk season holidays. The main purposes were to determine the potential effect of working time on the presence and intensity of upper limb musculoskeletal symptoms, as to verify the effect of 4 wk of job interruption in the upper limb musculoskeletal symptoms presence and intensity. Data was collected during 6 moments. Generalized estimating equations analyses were used. For the effect estimates, odds ratio with corresponding 95% confidence intervals were reported for each outcome/model. The upper limb musculoskeletal symptoms showed a significant increase ($p=0.001$), especially after the 4 wk off. In all data collection points there was a significant positive association between the upper limb musculoskeletal symptoms and general health status ($p<0.001$). Considering symptoms' intensity, significant relations were found ($p<0.001$). Work time had a negative effect on the work-related upper limb musculoskeletal symptoms over 7 months (OR 0.909, 95% CI 0.861–0.960, $p=0.001$). For the intensity of upper limb symptoms, the effect of time was also statistical significant (OR 0.115, 95% CI 1.031–1.220, $p=0.008$). A 4-wk job interruption did not show an immediately positive effect on upper limb musculoskeletal symptoms presence.

Key words: Work-related upper limb musculoskeletal disorders (WRULMSD), Musculoskeletal symptoms, High-demanding jobs, Automotive assembly, Occupational health

Introduction

Automotive assembly line work is characterized by standardized tasks, frequently addressed as high demanding jobs¹. The highly repetitive work (the same move-

ment two to four times a minute or in cycles below thirty seconds²) with short recovery periods are often related to neck, shoulder, elbow and forearm musculoskeletal disorders^{3, 4}. Repetition and force exertion are common in these settings and when both occur over a significant period of time, may lead to cumulative biomechanical loading, causing reduced functional capacity to continue performing the task and maintaining force^{5, 6}.

That biomechanical exposure, for itself, is an important factor for the development of musculoskeletal

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disorders^{7, 8}). This exposure to physically demanding work with insufficient recovery periods may result in the development of the work-related upper limbs musculoskeletal disorders (WRULMSD), one of the most common health problems in automotive assembly lines^{9–14}).

A study on newly employed manufacturing workers found that most of the musculoskeletal disorders (including upper limb disorders) developed in the first twelve months¹⁵). Other study, in the early 90's, compared a part-time job with a full time (8 h), reporting that a 5 h working day could delay the development of some of the musculoskeletal disorders¹⁶). Although there is still a lack of evidence on how long exposure should be for the onset of musculoskeletal disorders in assembly lines^{14, 15}) it appears, among other variables, that the duration of the exposure (as a working time period) is critical for time of recovery.

Pauses or other job interruptions are supposed to allow the musculoskeletal system to recover, maintaining the worker productive and avoiding fatigue development¹⁷). Nevertheless, time variation, as the effects of duration, type, and frequency of rest periods are still poorly studied⁸), especially in employees working in assembly lines. Regarding the relationship between job interruptions and the effects on upper limb (UL) musculoskeletal symptoms and WRULMSD, there is even less evidence, being unclear whether there is any dependency between its' length and the effect of a long-term period off, as a vacations' period¹⁸).

The uncertainty surrounding the interactions between time in and out of work and the development of musculoskeletal disorders in high demanding jobs highlights the importance to follow workers with symptoms as a substantial measure to better understand work interactions and manage occupational health issues. This implies the assessment of early perceptions of pain, as musculoskeletal discomfort³), which has been reported as an initial stage of WRULMSD^{3, 19–21}). Both musculoskeletal discomfort and pain are the most prevalent symptoms in work settings²²) and its intensity should be related to changes in worker's functional status²³). Although there is no strong evidence regarding work context, musculoskeletal symptoms scoring intensity values over 4 in a 10-point scale have been established as significant and requiring intervention²²). This is an important suggestion to take into account when we are referring to assembly lines work and to the management of workers' health issues during working time periods.

Considering the insufficient evidence for the distribution, frequency and changes on intensity of the UL mus-

culoskeletal symptoms over time^{24, 25}) in the automotive industry, the present study followed a group of assembly line workers during 7 months, before and after a 4-wk off period, with the specific aims: 1) to determine the potential effect of working time on the presence and intensity of upper limb musculoskeletal symptoms; 2) to verify the potential effect of 4 wk of job interruption in the upper limb musculoskeletal symptoms presence and intensity; 3) to describe the general health status and its relation to musculoskeletal symptoms intensity over time.

Subjects and Methods

Study design

This was a longitudinal study that followed assembly line workers from an automotive industry from September 2014 to April 2015, which included a job interruption of 4 wk for season holidays (between 15th December and 12th January). Data was initially assessed every month however, considering the interruption for holidays, the initial 6-month follow up turned into a 7-month longitudinal study. Considering this, data collection occurred in six different moments: three moments separated by one month before the 4-wk off period—T0 (baseline, September), T1 and T2, and three moments after the 4-wk off period (January, March and April—T3-T4-T5—respectively).

Assembly line work

In this area of the automotive industry, the car is assembled with other parts into a complete vehicle. The assembly line is divided into different areas; each area has a unit, constituted by different stations. In a typically 8 h's working day, the worker changes to other station every 2 h.

There are stations with powertools and handling devices, others requiring snap-fits (manual attachment of pre-shaped plastic flexible parts) and in several positions it is necessary to work under the car, above shoulder's line. It is usual to acknowledge an assembly line as a workplace with noise, vibrations and machines, as vehicles of parts transport or garbage collection.

The cycle for a car to be assembled is short and that means that every 90 s a new car comes down to the line. The present industry had a morning shift (from 7.00 h to 15.30 h) and an evening shift (15.30 h to 23.00 h). The lunch/dinner break was of 30 min and for both shifts there were 2 additional breaks of 7 min each.

Participants

This study was in agreement with the recommendations

of the Declaration of Helsinki and submitted and accepted by the Portuguese Data Protection Authority (authorization nr 8602/2014). The workers attended an informative session to invite for participation. Individuals who agreed to participate signed an informed consent and provided their email address and number of employee.

Inclusion criteria were: (i) female and male workers, (ii) working at the assembly line, (iii) volunteers, (iv) age between 18 and 65 yr, (v) workers performing the same activity in the last 3 months, (vi) not having medical restrictions (as examples: not working with powertools, not performing movements above shoulder line or repetitive movements of the elbow joint).

There was no compensation for participating in this study; the company allowed the participation during working hours.

Participant flow

After the information session, there were 400 workers with intention to participate. From these, 270 completed the baseline survey (Fig. 1). After applying the inclusion criteria, only those participants whom completed the survey at least in one collection point besides T0 were selected (n=225) (Fig. 1).

The 225 workers considered in this study showed some fluctuations on their response during the follow-up period (Fig. 2). After 1 month, 2.2% did not answer to the survey and, in the last reply, a loss to follow up of 23.1% was found. This non response increased in time, although for T4 there was an exception.

Outcomes

For every collection points the work-related musculoskeletal symptoms (discomfort and pain), location and symptoms' intensity were determined as the outcomes to analyze during the follow-up. A secondary outcome was general health status.

Data collection

Each point of follow up collected information through an online survey (SurveyMonkey.inc). The participants received by email a link to the questionnaire, which should be answered within 2 wk. If the participant failed to return

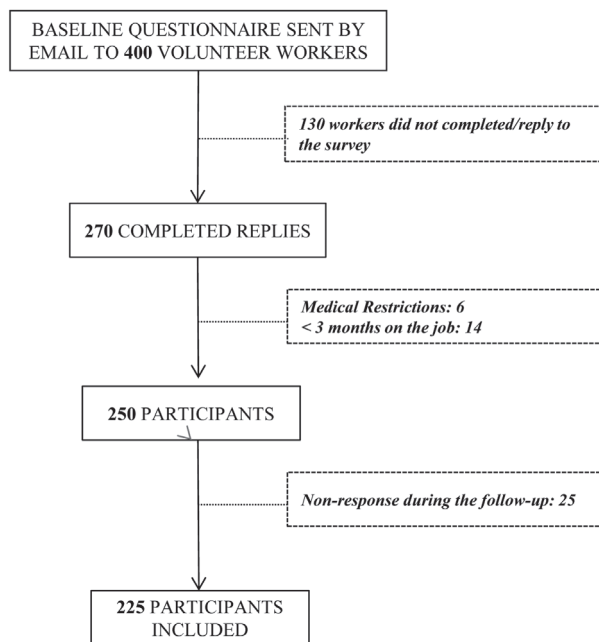


Fig. 1. Flow chart of the participants in study.

a completed questionnaire within 10 d after the initial email, a second email with the questionnaire was sent. In the case of no response, a text message was sent to inform that the survey was closing in 24 h and the participation was important.

The survey was constituted by 5 topics at T0: 1- **sociodemographic data** (age, gender, weight, height), education, exercise – *Do you perform regular physical exercise at least twice a week?*; 2- **health data** (previous musculoskeletal injury – *type and anatomical location of the injury, time of the last episode* – diseases – *Do you have any of the following diseases: a) Diabetes; b) Hypertension; c) Gout; d) Osteoporosis; e) Osteoarthritis; f) Herniated disc; g) Carpal tunnel syndrome; h) Other (please specify)* – and medication data- *Do you take any medication regularly?*); 3- **self-reported general health status**(the first question of the Portuguese version of the 12-item short form Health Survey – Sf-12:v2); 4- **work-related musculoskeletal symptoms** (presence of discomfort/pain – and its' intensity and location); 5- **work-related information** (job designation, job tenure and perceived occupational risk hazards – yes/no. If the worker replied

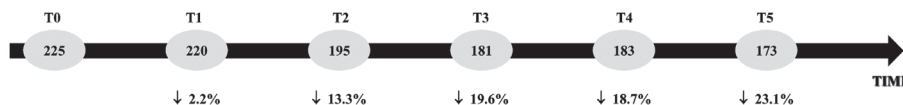


Fig. 2. Loss to follow up.

Table 1. Baseline survey: explanatory of the physical hazards

	Question	Possible answers for each hazard:
	<i>Considering your daily work activities:</i>	
	<i>Please identify the main characteristic(s) that describe your function by referring the average time you spend in the following situation(s):</i>	
Physical hazards	1. Manual Material Handling	1- 100%/d
	2. Repetitive movements/gestures	2- 75%/ d
	3. Force application	3- 50%/ d
	4. Static work	4- 25%/ d
	5. Use of powertools	5- 0%/ not applicable

“yes” to one or more hazards, the daily percentage was determined (Table 1). Answer as *never/not applicable* and 25% of the day were considered as low physical exposure, as the other possibilities were considered as high physical exposure.)

For the following data collection points—T1 to T5—the survey only collected the outcomes in study: the presence of musculoskeletal symptoms—discomfort/pain—and its intensity and location and the self-reported general health status.

Work-related UL musculoskeletal discomfort and pain

The presence of UL musculoskeletal symptoms was assessed considering a dichotomic question (yes/no answer) – *At the present, or at least for 4 d during the last 7 d, have you experienced any musculoskeletal discomfort or pain?* The temporal criteria had as referential the SALTSA criteria, a screening tool that takes into account the time-frame (symptoms at the present), duration (during at least 1 wk) and frequency (at least 4 d during the last 7 d)^{2, 26}.

Anatomical area and intensity of UL symptoms

A body map²⁷) was available with each data collection; the participants were expected to select the affected anatomical area. It was possible to select the right or left side of the body, and each body region was flagged (head, cervical, dorsal, lumbar, shoulder, arm, elbow, forearm, wrist, hand, hip, thigh, knee, leg, ankle, foot). Due to the heterogeneity and often multisite pain of the reported musculoskeletal symptoms in these settings²⁸), in case there was more than one complaint the selection was to be based only on the highest intensity symptom.

For symptoms’ intensity, a 10-point scale was used—pain intensity numeric rating scale (PI-NRS)—where 0 represents “no pain” and 10 “unbearable pain”. This scale is easier to score and is validated to measure both pain and discomfort^{29, 30}), as was shown for sensitivity to changes in pain^{31, 32}), reinforcing its use in reassessments and follow-up’s.

General health status

To analyze the dependency between the variations in general health status (GHS) and the symptoms’ intensity scores over time, GHS assessment was made through the first question of the Portuguese version of the 12-item short form SF-12³³) – *How do you rate your overall current health?* The workers should reply on a 5-point Likert scale ranging from 1 (excellent) to 5 (poor). This single global health-rating question has been previously used³⁴), considering a relation of the self-reported general health to chronic pain^{35, 36}).

Statistical methods

Descriptive statistics were used to describe the participants’ characteristics, as well as the outcomes during the follow-up (presence of symptoms, location and intensity).

Spearman’s rank correlation was used when analyzing the UL symptoms variations in time. To determine the UL symptoms’ mean intensity variation over the follow-up, a repeated-measures analysis of variance (ANOVA) was performed. An alpha level of 0.05 or less was accepted as statistically significant.

To study the outcomes *presence of work-related UL symptoms and intensity* during the 7 months, generalized estimating equations analysis was used^{37, 38}). Two models were determined: Model **one**, a logistic regression model, measured the effect of time (0, 1, 2, 4, 6, 7 months) on the outcome *presence of work-related UL musculoskeletal symptoms* (binary variable). The analysis was carried out with binomial distribution and a correlation structure autoregressive 1st order [AR (1)], with subjects measured repeatedly with time as repeated measures factor within subjects. For the effect estimates, odds ratio (OR) with corresponding 95% confidence intervals (CI) were reported.

In model **two**, a linear regression model measured the

effect of time (0, 1, 2, 4, 6, 7 months) on the *intensity of work-related symptoms* (numerical variable), with normal distribution, correlation structure autoregressive 1st order [AR (1)], with subjects measured repeatedly with time as repeated measures factor within subjects. The estimation of the effect considered the linear regression coefficient with corresponding 95% confidence intervals (CI).

All analyses were performed using the SPSS software (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY, USA).

Results

T0

Sociodemographic, health-data, self-reported job characteristics and self-reported musculoskeletal symptoms are listed in Table 2. The study population was mostly constituted by male workers (88.9%), predominantly in the age band 31–40 yr, with average job tenure of 15.49 yr.

There were 20.8% of the individuals reporting diseases. Among these, the majority selected *other* conditions (such as hearing problems, respiratory chronic conditions, associated conditions—as HTA with diabetes or asthma—gastritis, gout) or did not specify any disease. Regarding *having a previous musculoskeletal injury*, 57.8% of the workers answered *yes*, being the *upper limb* the most reported (20.4%). The last episode occurred at least 1 yr before the survey. The *self-reported general health status* was mainly stated as *good* (57.3%).

Regarding work characteristics, *repetitive motion* and *force application*, were the most selected (93.8 and 85.8%, respectively), both with high frequency of exposure/day (Table 2).

For work-related musculoskeletal symptoms, there were 68.4% of the participants reporting discomfort or pain at baseline, with mean intensity was 5.04 on the PI-NRS (Table 2). The majority of the reports considered the UL (35.6%) and the mean intensity was 5.31.

The follow-up study

Frequency of self-reported UL musculoskeletal symptoms

During the follow-up study the number of reported musculoskeletal symptoms had some variations. This was not statistical significant ($p=0.072$) and followed the loss of participations frequencies during the 7 months (Fig. 3).

The UL symptoms were the most frequently reported and increased significantly over time ($p=0.001$). Comparing the time points before and after the 4 wk off (T3) there was an increase of UL musculoskeletal symptoms imme-

diately after the season holidays (Fig. 3).

Intensity of self-reported UL musculoskeletal symptoms

The mean intensity of the UL symptoms reported during the follow-up was always ≥ 5 in the PI-NRS scale (Fig. 4) ($M=5.40$, $SD=2.08$). The data collection after the 4-wk off (T3) was the time point with a higher value ($M=5.5$, $SD=2.05$).

During the study, there were statistical significant differences in intensity mean values ($F_{1,1174}=251.011$, $p<0.001$).

Self-reported general health status and the association to UL symptoms

Over time, the general health status was mainly reported as “good”. It is possible to verify that after the vacations period both “very good” and “fair” categories increased (Fig. 5).

For all collection points, there was a significant positive association between the reported UL musculoskeletal symptoms and general health status ($p<0.001$). Considering symptoms’ intensity, the same positive and significant relations were found ($p<0.001$).

Time effect on work-related UL musculoskeletal symptoms and its intensity

Time had a statistical significant effect on having UL symptoms and on the intensity of the reported symptoms during the study (Table 3).

For having UL musculoskeletal symptoms the $OR<1$ shows a decrease of this outcome during time. Regarding the effect of time in the UL symptoms’ intensity, the GEE model shows an increase odds of 1.121 in symptoms intensity values (Table 3).

Discussion

The main goal of this study was to follow a group of workers during the course of 7 months, regarding the self-reported UL musculoskeletal symptoms presence and intensity and analyze the possible effects of 4 wk of holidays of the assembly line production.

As key points from the descriptive analysis there were several characteristics to consider, similar to other studies: participants were mostly men^{39–41}, with an average age of 36 yr^{40, 42}, the majority in the 16–20 yr of job tenure^{39, 43} and with a body mass index over 25^{40, 42–44}.

This follow up showed that the variable *time* (as working time in the studied period) had a negative effect on UL musculoskeletal symptoms presence. The reported UL musculoskeletal symptoms increased after the 4-wk off. This goes in line with the cumulative effect of work in

Table 2. Baseline Characteristics

Variable	N (%)	Mean	SD
Gender (male)	200 (88.9)	-----	-----
Age (yr)	-----	36.20	4.99
18–20	1 (0.4)		
20–30	22 (9.8)		
31–40	164 (72.9)	-----	-----
41–50	37 (16.4)		
>50	1 (0.4)		
BMI		25.44	3.33
Normal (<25)	109 (48.4)		
Overweight (25–30)	98 (43.6)	-----	-----
Obese (>30)	18 (8)		
Education			
Basic	57 (25.3)	-----	-----
Upper Secondary	153 (68)		
Higher School	15 (6.7)		
Tenure (yr)	-----	15.49	5.92
0–5	33 (14.7)		
6–10	13 (5.8)		
11–15	21 (9.3)	-----	-----
16–20	152 (67.5)		
21–25	6 (2.7)		
Diseases (Yes)	47 (20.8)		
Diabetes	1 (0.4)	-----	-----
Hypertension	7 (3.1)		
Other/NA	39 (17.3)		
Previous Musculoskeletal injury (Yes)	130 (57.7)		
Last episode			
<1 yr	39 (17.3)		
1–5 yr	33 (14.7)		
6–10 yr	14 (6.2)		
>10 yr	16 (7.1)		
NA	28 (12.5)	-----	-----
Anatomical Area			
Cervical	5 (2.2)		
Lumbar	20 (8.9)		
Upper limb	46 (20.4)		
Lower limb	36 (16)		
Other/NA	23 (10.2)		

SD: standard deviation; NA: no answer.

Variable	N (%)	Mean	SD
Medication (Yes)	47 (20.9)	-----	-----
Regular Exercise (Yes)	112 (49.8)	-----	-----
General Health Status			
Excellent	17 (7.6)		
Very good	36 (16)	-----	-----
Good	129 (57.3)		
Fair	42 (18.7)		
Poor	1 (0.4)		
Work reported risk factors (yes)			
<u>Manual Material Handling</u>	132 (58.7)		
Low physical exposure (0 to 25% d)	64 (28.4)		
High physical exposure (50 to 100% d)	68 (30.3)		
<u>Repetitive movement</u>	211 (93.8)		
Low physical exposure (0 to 25% d)	34 (15.1)		
High physical exposure (50 to 100% d)	177 (78.7)		
<u>Force application</u>	193 (85.8)		
Low physical exposure (0 to 25% d)	68 (30.2)	-----	-----
High physical exposure (50 to 100% d)	125 (55.6)		
<u>Static work</u>	177 (78.7)		
Low physical exposure (0 to 25% d)	70 (31.1)		
High physical exposure (50 to 100% d)	107 (47.6)		
<u>Powertools</u>	122 (54.2)		
Low physical exposure (0 to 25% d)	37 (16.4)		
High physical exposure (50 to 100% d)	85 (37.8)		
Musculoskeletal Symptoms (yes)	154 (68.4)		
Intensity of symptoms (0–10)		5.04	2.07
Upper limb musculoskeletal symptoms (yes)	80 (35.6)		
Intensity of symptoms (0–10)		5.31	1.2

the musculoskeletal system, considering that the temporal characteristics of the exposure—duration and dose—could be more important to the presence of symptoms¹⁴). On the other side, the mean intensity of symptoms increased also after the 4 weeks of job interruption, showing a faint decrease after. This decrease is also present for the

frequencies of reported UL symptoms and our GEE model shows this negative tendency during time (OR<1). It could be the case that if the follow up continued, the frequencies of musculoskeletal symptoms would be reduced.

Our results show that the expected positive effect from the 4-wk of absence from work was either short

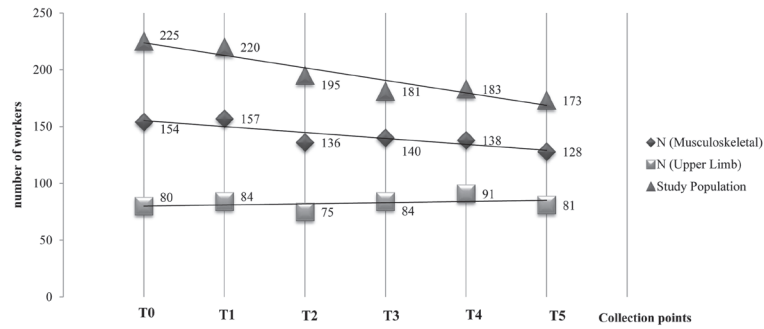


Fig. 3. Number (N) of reported work-related musculoskeletal symptoms VS number (N) of work-related UL musculoskeletal symptoms during the follow-up.

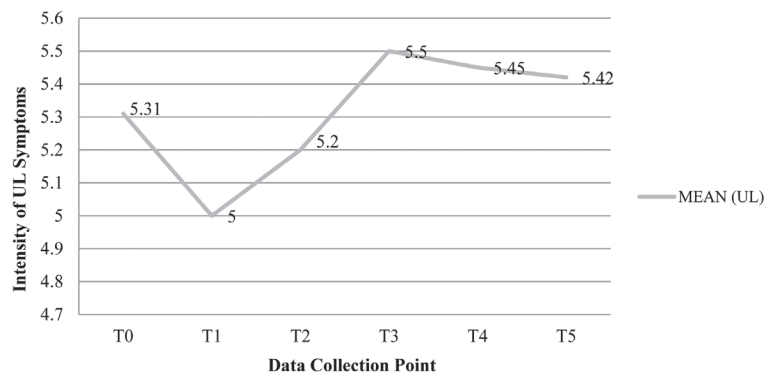


Fig. 4. UL symptoms mean intensity during the study.

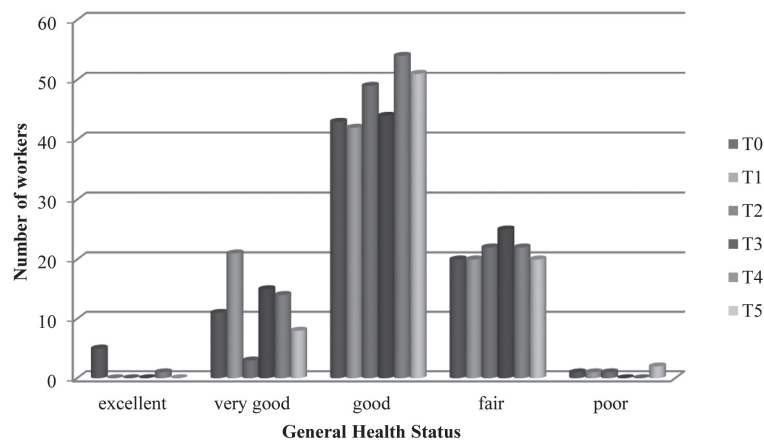


Fig. 5. Reported General Health Status of workers with UL symptoms.

Table 3. GEE analyses of the association between Time and a) having UL symptoms and b) UL symptoms intensity

	B	p-value	OR	CI
Having UL symptoms		0.001	0.909	0.861–0.960
UL Symptoms Intensity	0.115	0.008	1.121	1.031–1.220

OR: odds ratio; CI: 95% confidence interval Wald Test.

Having UL symptoms (yes/no).

UL symptoms (PI-NRS).

or inexistent (considering the number of reported UL symptoms and the decrease of workers with no symptoms both before and after the holidays) and for that its impact was not effective and enough to stop that progression. However, regarding the symptom intensity, it appears that the workers made an adaptation to work demands after the interruption. This could be due to the motor adaptation; a study on assembly lines work reported this *adaptability* as the capacity to modify when performing repetitive work⁴⁵). There are kinematic and kinetic changes of the upper limb, in response to muscle fatigue⁵). Given that our study population can be determined as *experienced*, once the average years in the company is over 16, there is some evidence that for these type of workforce the ability to develop more variability for shorter cycles of work is higher³). Additionally, it could be a hypothesis that in presence of chronic conditions, the return to work after the season holidays would be characterized by pain. After a musculoskeletal adaptation occurs, the symptoms would be decreasing (which can be explained by our GEE results).

Yet, the intensity of UL symptoms was always over 5 in the PI-NRS and the participants maintained their performance at work. This can reinforce the presence of chronic musculoskeletal diseases and persistent symptoms. Also the positive association of general health status and intensity of UL symptoms can support the relation of health status to chronic diseases^{35, 36}). Regarding that these workers were still performing their job, besides an analysis on the cumulative effect of working days, the hypothesis of workers “neglecting their symptoms” is possible. The miss perception of the onset of pain as sudden and not gradual and the idea that experiencing symptoms is normal⁴⁶), are an example.

High-demand jobs are related to WRULMSD^{3, 4}) and there is existing evidence for the first occurrence of musculoskeletal disorders in the 3 to 6 months¹⁶) or in the first 12 months of newly employed workers¹⁵). Taking this and the *experienced workers* in mind, we are excluding the hypothesis of new cases, once the fluctuations during time were mostly of workers with symptoms since T0 (and probably before). This is a situation already reported—workers with symptoms at baseline are more likely to have/maintain symptoms in follow-up studies^{22, 47}).

To our knowledge, there is no consistent evidence considering a break of 4 wk and its impact on musculoskeletal symptoms in the automotive industry—studies have been reporting data concerning breaks during the workday^{17, 48, 49}) or short vacations, as 2 wk, but in relation

to well-being¹⁸). As working time is strongly associated to the development of musculoskeletal disorders^{14, 50}), it is still inaccurate to determine how long it takes to reduce an inflammation process or what would be the amount of time needed for recovery¹⁷) (and adaptation). The majority of the participants probably already had WRULMSD and the 4-wk off was not enough to reduce symptoms frequencies. A study on low back pain in high demanding jobs showed a cumulative effect of consecutive workdays and its relation to back pain⁵¹). It can be hypothesized for our work population this cumulative effect and a similar result on the upper limb. A plausible justification can be related to WRULMSD development theories and the chronic inflammation process, that leads to changes over time^{52, 53}). It can be predicted that the symptoms reported would be more related to an inflammatory episode of chronic pain rather to an acute injury, even though this is still a multivariable and complex transition⁵¹).

Furthermore, given the fact that the reported UL musculoskeletal symptoms in our study had high intensity values, we consider that it was in fact musculoskeletal pain rather than discomfort, since the latter is likely to be reversed by load reduction or rest⁵⁴).

Study limitations

This study had several limitations and our findings have limited transferability to other automotive assembly lines. Firstly, these were volunteer workers and that could represent a sample bias. Secondly, the outcomes in study were exclusively based on self-reported information that could determine possible misclassification bias or/and underestimation of the associations. A physical assessment in each collection point would be important to overcome this limitation. Thirdly, after the 4-wk off the number of participants dropped 19.6%, contrary to the increase of UL symptoms. Considering the self-reported data, follow up studies can lead to bias, once there is a higher probability of maintain the workers with health complaints⁵⁵). It is also a fact that the 7-month follow up is, by itself, a limitation, once we can question if this time period was enough to understand the development of the UL symptoms over time. Perhaps a longer study, with other season holidays break, would add important information in this topic.

Recommendations

We consider important in the future to develop more studies on job daily rotations in automotive assembly lines, once it can contribute to the cumulative exposure of the upper limbs. One hour rotation, which is not the cur-

rent rotation system for these type of industries⁵⁶), could be more appropriate to muscle activity patterns¹⁶). Also studies on new approaches in the return to high demanding jobs after sickness leave or holidays would be of most importance in chronic musculoskeletal conditions. This highlights the importance of the reorganization of work in high demanding jobs, in order to prevent WRULMSD. Additionally, to be able to follow workers through time can provide important evidence to better understand the transitions between muscle fatigue, musculoskeletal discomfort and pain³).

Availability of Data and Material

All data analyzed during this study are included in this published article.

Authors' Contributions

All authors contributed to the development of this study. All authors participated in revising the article critically for important intellectual content; all authors gave final approval of the version to be submitted.

Conflict of Interest

The authors of this manuscript declare that they have no conflicting interests, financially or non-financially.

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