Abstract

Objective. To demonstrate an immune response to multiple low back pain risk factors as well as to interactions between risk factors.

Background. Biomechanical, individual and psychosocial risk factors for low back pain have been identified. However our understanding of how these risk factors act and interact to contribute to the etiology of low back pain is still poorly understood.

Methods. This study quantified the immune and spinal load responses of twenty subjects split evenly between the sensor and intuitor personality types when they were exposed to repetitive lifting tasks with a high and low mental workload component.

Results. Spinal loads and immune responses were altered in response to mental load, personality and the combination of mental load and personality. Some immune responses were still significantly different the day following exposure.

Conclusions. An immune inflammatory response to low back pain risk factors is present following exposure for up to 20 hours. This suggests a potential cumulative effect that may influence the development of low back pain.

Relevance

The presence of an inflammatory response to low back pain risk factors and interactions between risk factors indicates an inflammatory component to the development of low back pain.
1. Introduction

Health care systems world-wide experience massive economic costs resulting from occupationally-related low back pain (LBP)–particularly work involving heavy lifting. The direct costs of LBP in the United States has been estimated at up to $90 billion annually [1]. In the state of Ohio, the Ohio Bureau of Worker's Compensation ranked LBP as the most costly and frequent musculoskeletal disorder claim between 1999 and 2004 [2].

A primary cause of low back pain is related to risk factors found in the workplace [3]. The National Academies have identified three primary categories of low back pain risk factors: biomechanical, psychosocial and individual (Figure 1) [4]. Briefly, biomechanical factors relate to manual load handling (e.g. lifting) that transmits force to the tissues inside the body. Psychosocial risk factors involve the social environment the subject is exposed to and the mind-body response to exposure. Individual risk factors are subject-specific such as personality and genetic makeup.

Implicit in Figure 1 is the concept that risk factors interact. Recent, research indicates that risk factors in different categories interact to influence the tissue loads arising from biomechanical risk factors [5]. The evidence suggests the impact of risk factor interactions on risk are quite powerful–potentially more powerful than the main effects of the risk factors themselves.
This risk factor research shows that exposure is associated with LBP. However, it does not tell us how exposure might cause LBP. Unfortunately, the etiology of LBP is poorly understood. The prevailing theory for LBP causation is that lifting transmits biomechanical forces to the spinal tissues. If these forces exceed tissue tolerance, there is a risk that the tissue will fail resulting in LBP (Figure 2) [6]. Unfortunately, diagnostic images of LBP patients seldom show such obvious mechanical tissue damage. In medical practice, only 15% of patients with low back pain have specific diagnoses [7]. The remainder are deemed ‘nonspecific’ low back pain cases.

Recent work has demonstrated an inflammatory response to repetitive lifting [8]. Inflammation is the basic process whereby tissues of the body respond to injury and initiate repair. This process is tightly regulated as inflammation brings macrophages to the site of injured tissue. Macrophages are powerful defensive agents. However, they also release toxins that can damage the body's own tissues. Therefore prolonged inflammation is almost always destructive to the body's tissues. The presence of an inflammatory response to LBP risk factors suggests we need to incorporate the biological response to loading in our model of injury development.

LBP risk factors belonging to the psychosocial and individual categories are known to interact to alter both spinal tissue loading and the body's inflammatory responses. Mental load, personality and mental stress interact to alter muscle activation during lifting [9, 10]. This alters spinal loading which would be expected to alter the body's inflammatory response. Further, mental stress has been shown to alter inflammation in the body resulting in slowed wound
healing [11]. This further underscores the potentially interactive nature of the effect of low back pain risk factor exposure on the body's inflammatory response.

Therefore, the goal of this study was to demonstrate and quantify the influence of interactions between biomechanical, psychosocial and individual risk factors on inflammation in a simulated manual materials handling task.

2. Methods

2.1. Subjects

Twenty male subjects were recruited from the local community. Subjects were screened to only include subjects with: no history of jobs requiring heavy manual materials handling in the past year, intense exercise such as weight training or jogging, no past history of low back pain within the previous year, carpal tunnel syndrome, fibromyalgia or other musculoskeletal disorders, no history of endocrine, immune or metabolic disorders, no history of cancer, coronary artery disease, psychiatric disorders, or current use of psychotropic medications. Subject anthropometric characteristics are presented in Table 1.

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Personality Trait</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>10</td>
</tr>
<tr>
<td>Age (years)</td>
<td>28.7 (10.6)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>182.9 (7.2)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77.8 (11.5)</td>
</tr>
<tr>
<td>Spine Length (cm)</td>
<td>59.4 (2.0)</td>
</tr>
<tr>
<td>Torso Depth at Pelvis (cm)</td>
<td>21.0 (3.0)</td>
</tr>
<tr>
<td>Torso Breadth at Pelvis (cm)</td>
<td>28.6 (3.3)</td>
</tr>
<tr>
<td>Torso Circumference (cm)</td>
<td>83.2 (6.4)</td>
</tr>
<tr>
<td>Acromion-Knuckle Length (cm)</td>
<td>66.8 (4.2)</td>
</tr>
<tr>
<td>Nasion-Inion Length (cm)</td>
<td>36.4 (1.6)</td>
</tr>
</tbody>
</table>

2.2 Experimental Design

A repeated measures within-subjects experimental design was employed. Subjects completed two bouts consisting of two hours of repetitive lifting with a simultaneous high- or low- mental workload task. An additional bout was collected for to provide baseline cytokine
levels. The Ohio State University Institutional Review Board approved the experimental protocol.

Independent variables were subject personality trait and mental load level.

Dependent variables were blood and saliva biological markers (White Blood Cell counts, creatine kinase, IL-1, TNF, IL-6, IL-10, and cortisol), spinal loads determined by an EMG assisted biomechanical model (compression, lateral shear, anterior-posterior shear) and

2.4 Apparatus

Torso kinematics was collected using a Lumbar Motion Monitor (LMM) worn by the subject [12]. Subjects stood on a forceplate and a set of goniometers was used to measure external moments about the L5/S1 intervertebral joint [13].

Electromyographic (EMG) activity of the right and left muscle pairs of the latissimus dorsi, erector spinae, rectus abdominus and external and internal obliques were collected using standardized techniques from previous studies [14, 15]. EMG signals were band pass filtered between 30 and 1000 Hz, rectified and integrated through a 20 ms sliding window filter.

2.5 Experimental Procedure

After obtaining subject consent, subjects completed the Myers-Briggs Type Indicator (MBTI) questionnaire [16]. Subjects completed three experimental bouts separated by at least one week. There were two lifting bouts and one baseline bout. The lifting bouts consisted of a blood and saliva collection at 8:00AM followed by incrementing the

Figure 3. Experimental lifting task.
subject for EMG data collection. The subject then performed maximal voluntary contractions in six directions used for normalizing the later EMG data [17]. Subjects completed the bouts in randomized order. Subjects then performed 2 hours of repetitive lifting immediately followed by another blood and saliva collection (approximately 1PM). 2 hours later, another blood and saliva collection was performed. The following morning at 8 AM a final blood and saliva collection was performed. Lifting bouts differed by the high or low mental workload presented to the subject during lifting. The baseline bout consisted of blood and saliva collections at the same time points without the lifting or mental load exposure.

The lifting task consisted of repetitive lifting controlled by a computer timer. At the sound of a tone the subject would lift a 6.8kg box located on an 88cm high platform at a distance equal to the subject's acromion-knuckle length in front of the subject. The subject would then place the box on a destination located 90° clockwise, at the subject's hip height and acromion-knuckle length from the midline of the subject's body (Figure 3). At the next tone, the subject would reverse the lift from the clockwise location back to the location in front. Subjects performed a lift every 5.4 seconds with a 6 second break every 48.6 seconds. Subjects performed a mental task every time the lift origin was in front of the subject.

2.6 Personality Trait Identification

Subjects were separated into Sensor or Intuitor personality traits using the Myers-Briggs Type Indicator (MBTI) questionnaire [16]. The MBTI Sensing or intuition scale indicates the preferred mode of perceiving and gathering information. In physical lifting situations, sensors have been described as enjoying order at work and being good at precision work, whereas intuitors dislike repetition and prefer to work in spurts [18]. The MBTI sensing or intuition scale is a linear scale which assigns 26 points to either the sensor or intuitor category. To ensure clear
differentiation between personality types, subjects scoring 13-16 in either the sensor or intuitor category, classified as ‘slight’ sensor/intuitor by the MBTI, were excluded from the study.

2.7 Spinal Load Assessment

An EMG-assisted biomechanical model employed the EMG, and kinematic data to compute dynamic loads on the spine [19]. This model has been validated in three dimensions, accounts for gender, muscle coactivation and anthropometric differences between subjects and has been widely reported in the spine biomechanics and ergonomics literature [19-24].

2.8 Mental Loading

Mental load was controlled by presenting the subject with a mental task to perform while lifting. On lifts where the origin was in front of the subject, a computer display would ask the subject and experimental question. The subject was instructed to formulate the answer to the question and respond by pressing the appropriate key located at the lift destination.

The low mental load task consisted of a random up or down arrow displayed on the computer screen. At the lift destination, the subjects pressed the corresponding up or down arrow on the keyboard.

The high mental load task was a modified Stroop color-word task [25] (Figure 4). The Stroop color-word task presents the subject with a word that is a color (such as the word white) presented in a font color that is a different color from the word (green in Figure 4). The subject was instructed to choose the answer corresponding to the color of the font in which the text of the word is written. Visually we read words before we process font colors so this task requires
the subject to mentally focus and discard the meaning of the word in favor of the color of its font. To add additional complexity to the task, the response buttons were arranged perpendicularly to their arrangement on the computer screen. This poor cognitive mapping requires the user to make an additional translation so that the left arrow on the computer screen corresponds to the up arrow on the response pad.

2.9 Blood and Saliva Biomarkers

Plasma white blood cell counts (WBC), Creatine Kinase (CK), IL-1β, TNF-α, IL-6, IL-10 and salivary cortisol collected before, after, 2 hours after and 20 hours after lifting. Venous blood samples were drawn and collected into sterile EDTA tubes containing aprotinin (bovine lung 15-30 units/ml; Sigma at 0.67 unit/ml). Serum was separated from cells and platelets by centrifugation at 400g for 7 min, and then at 10,000g for 7 min at 4°C. Commercially available Enzyme Linked Immunosorbant Assay (ELISA) (e-Bioscience, San Diego, CA) kits were used to quantify circulating levels of cytokines. Cortisol was collected by a cotton salivette (Salivette, Sarstedt, Nümbrecht Germany) held in the mouth to stimulate saliva flow. Saliva was collected before the blood draws to reduce any anxiety effects.

2.10 Statistical Analysis

Analysis of Variance (ANOVA) tests were used to test the main effects of personality trait, mental load and time as well as the personality*mental load, personality*time and mental load*time interactions. The response variables tested were total WBC count, percentage of total WBC count that was granulocytes, CK, IL-1β, TNF-α, IL-6, IL-10, cortisol, spinal compression, lateral shear and anterior-posterior shear.

3. Results
Table 2 shows the results of the ANOVA models. As expected, there were many significant effects and interactions. For spinal loading, anterior-posterior shear and compression responded to personality and mental loading. As markers of overall immune activity, white blood cell counts changed over time after exposure to repetitive loading., CK and several cytokines responded to combinations of mental load, time the interaction between personality and mental load.

<table>
<thead>
<tr>
<th></th>
<th>Personality</th>
<th>Mental Load</th>
<th>Time</th>
<th>Personality*Mental Load</th>
<th>Mental Load*Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Blood Cell Count</td>
<td>0.2966</td>
<td>0.0279</td>
<td>0.0094</td>
<td>0.9404</td>
<td>0.0439</td>
</tr>
<tr>
<td>Granulocyte % of WBCs</td>
<td>0.1473</td>
<td>0.7883</td>
<td>&lt;.0001</td>
<td>0.0404</td>
<td>0.9557</td>
</tr>
<tr>
<td>Creatine Kinase</td>
<td>0.3537</td>
<td>&lt;.0001</td>
<td>0.0212</td>
<td>&lt;.0001</td>
<td>0.0717</td>
</tr>
<tr>
<td>IL-1β</td>
<td>0.0427</td>
<td>0.172</td>
<td>0.9742</td>
<td>0.0004</td>
<td>0.9147</td>
</tr>
<tr>
<td>TNE-α</td>
<td>0.2577</td>
<td>&lt;.0001</td>
<td>0.6914</td>
<td>0.1136</td>
<td>0.0036</td>
</tr>
<tr>
<td>IL-6</td>
<td>&lt;.0001</td>
<td>0.7705</td>
<td>&lt;.0001</td>
<td>0.024</td>
<td>0.1278</td>
</tr>
<tr>
<td>IL-10</td>
<td>0.9412</td>
<td>0.1541</td>
<td>0.242</td>
<td>0.5223</td>
<td>0.1559</td>
</tr>
<tr>
<td>Cortisol</td>
<td>0.5206</td>
<td>0.0062</td>
<td>0.0816</td>
<td>0.397</td>
<td>0.0014</td>
</tr>
<tr>
<td>Spinal Lateral Shear</td>
<td>0.1624</td>
<td>0.641</td>
<td>-</td>
<td>0.5712</td>
<td>-</td>
</tr>
<tr>
<td>Anterior-Posterior Shear</td>
<td>0.0089</td>
<td>&lt;.0001</td>
<td>-</td>
<td>0.2185</td>
<td>-</td>
</tr>
<tr>
<td>Compression</td>
<td>&lt;.0001</td>
<td>0.0011</td>
<td>-</td>
<td>0.8201</td>
<td>-</td>
</tr>
</tbody>
</table>

**Bold:** Significant at $P<0.05$

4. Discussion

The majority of white blood cells found in the plasma are normally granulocytes and
lymphocytes. Granulocytes are primary actors during innate immune system activity. Generally, innate immune activity is indicative of a bodily response to infection or tissue trauma. In this study, the shift in percentage of total white blood cells towards granulocytes indicates the body was responding to tissue trauma through innate immune system activation. The general trend for granulocyte counts was for the percentage of WBCs that were granulocytes to peak 2 hours after each bout and return to baseline the day after exposure. However, when we examine the interaction of personality with mental load (Figure 5) the personalities significantly differed 20 hours post exposure in both the high and low mental load exposures. The trends indicate that intuitors' immune systems have returned to homeostasis with respect to white blood cell balance while the sensors were still in an adaptive immune system state the day after exposure.

Creatine kinase is used clinically as a marker of muscle tissue damage, commonly as a marker of heart attacks and muscle breakdown. In this experiment CK responded to personality and mental load (figure 6). From Figure 6, the CK data indicates differential responses attributable to the interaction between personality and mental loading. Under low mental load conditions (Figure 6B), sensors' CK levels did not differ from baseline indicating low levels of muscle breakdown. Intuitor CK levels, however, steadily increased and remained elevated the
day following exposure. The low mental load task presented a relatively monotonous working environment and the observed intuitor CK response is in keeping with their previously observed dislike of repetition.

The high mental load task was stressful for both groups of subjects as indicated by the elevation in cortisol in the high mental load bout. Effects of this were observed through an overall increase in spinal loading as has been found in other studies [9]. Figure 6A also shows an elevation in CK levels for the high mental load task for both personality types.

5. Conclusions

This study demonstrates for the first time an immune response to multiple LBP risk factors in an occupational lifting setting. Personal and individual LBP risk factors interact to dynamically alter the body's immune response to loading. Further, this immune response is ongoing the day following exposure indicating the potential for cumulative immune activation with repeated exposure. This line of research opens up new approaches for interventions to minimize LBP risk. For example, some personality types demonstrated opposite responses to mental loading during lifting. This suggests that a ‘one size fits all’ approach of lowering the mental load is not appropriate for all workers. Further, the immune response to risk factor exposure suggests potential biomarkers for injury development and thresholds above which a worker's risk of injury is elevated.

References


