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ABSTRACT


Objective: To evaluate the effect of the self-monitoring approach (SMA) on self-efficacy for physical activity (SEPA), exercise maintenance, and objective physical activity level over a 6-mo period after a supervised 6-mo cardiac rehabilitation (CR) program.

Design: We conducted a randomized, controlled trial with 45 myocardial infarction patients (38 men, seven women; mean age, 64.2 yrs) recruited after completion of an acute-phase, exercise-based CR program. Patients were randomly assigned to an SMA group (n = 24) or control group (n = 21). Along with CR, the subjects in the SMA group self-monitored their weight and physical activity for 6 mos. The SMA used in this study was based on Bandura’s self-efficacy theory and was designed to enhance confidence for exercise maintenance. The control group participated in CR only. All patients were evaluated with the SEPA assessment tool. Exercise maintenance, SEPA scores, and objective physical activity (average steps per week) as a caloric expenditure were assessed at baseline and during a 6-mo period after the supervised CR program.

Results: Mean period from myocardial infarction onset did not differ significantly between the SMA and control groups (12.1 ± 1.3 vs. 12.2 ± 1.2 mos, P = 0.692). All patients maintained their exercise routine in the SMA group. Mean SEPA score (90.5 vs. 72.7 points, P < 0.001) and mean objective physical activity (10,458.7 vs. 6922.5 steps/wk, P < 0.001) at 12 mos after myocardial infarction onset were significantly higher in the SMA than control group. SEPA showed significant positive correlation with objective physical activity (r = 0.642, P < 0.001).

Conclusions: SMA during supervised CR may effectively increase exercise maintenance, SEPA, and objective physical activity at 12 mos after myocardial infarction onset.

Key Words: Exercise Maintenance, Cardiac Rehabilitation, Objective Physical Activity, Self-Efficacy for Physical Activity
Exercise maintenance after cardiac rehabilitation (CR) programs for patients with myocardial infarction (MI) is important to maintain exercise capacity and caloric expenditure, which are both associated with reduced mortality.\(^1,\)\(^2\) Regular physical activity produces significant improvements in many risk factors for cardiovascular disease, increases functional capacity, and reduces the risk of hospitalization among cardiac patients, and it improves the prognosis of patients with coronary artery disease.\(^3\) Niebauer et al.\(^3\) reported subjective leisure-time physical activity as a predictor of the halt of cardiac artery disease progression. Long-term maintenance of exercise compliance is still a major problem in CR for patients after MI. Attrition rates for CR in patients with MI have been reported as 25% for the first 3 mos and to increase up to 50% during the following 3 mos.\(^4\)

Oldridge and Spencer\(^5\) used a self-reported questionnaire and found that >20% of MI patients who participated in a CR program for 6 mos relapsed to a sedentary lifestyle during the subsequent 6 mos. CR in Japan is covered by national health insurance for the first 6 mos after MI onset; thereafter, patients must then continue exercise of their own volition.

It has been reported that self-efficacy is associated with the adoption and maintenance of exercise behaviors.\(^6,\)\(^7\) Compared with standard exercise indices, the self-monitoring approach improves short-term physical activity levels and maintains physical activity behavior in sedentary people with diabetes.\(^8,\)\(^9\) We hypothesized that a self-monitoring approach in addition to exercise training would increase exercise maintenance, self-efficacy, and objective leisure-time physical activity in patients with MI. To our knowledge, exercise maintenance rate, self-efficacy, and leisure-time physical activity level for Japanese patients with MI undergoing a CR program have not been reported. In addition, comparison of subjective physical activity in cardiac patients with that in healthy people has been reported in previous studies; however, objective physical activity has not been evaluated sufficiently. Therefore, we conducted a randomized, controlled trial to evaluate the effect of the self-monitoring approach on exercise maintenance, self-efficacy for physical activity (SEPA), and leisure-time objective physical activity during the 6-mo period after a supervised 6-mo CR program.

**METHODS**

**Study Design and Subjects**

This study was a randomized, controlled trial in which subjects were selected from among 68 consecutive patients admitted to St. Marianna University School of Medicine Hospital for evaluation of MI between October 2002 and April 2003. Of the 68 patients, 59 patients were recruited after successful completion of an acute-phase inpatient CR program and were included in the present study. The remaining nine patients were excluded due to inability to complete the acute-phase inpatient CR program because of cerebrovascular disease, orthopedic disorder, severe heart failure, or because they had experienced uncontrolled arrhythmia.

Of these 59 patients, 50 patients chose participation in the recovery-phase CR program; the other nine patients declined to participate and chose to undergo testing only. Patients were eligible to participate in the study if they successfully completed both exercise testing at 1 mo after MI onset and a routine 1-mo acute-phase CR program. Objective physical activity level, SEPA, and readiness for exercise were measured at baseline and during the 6-mo period after the completion of the supervised 6-mo CR program (i.e., at 12 mos after MI onset). Participant flow through the trial is detailed in Figure 1.

**Ethics**

The ethics committee of the St. Marianna University School of Medicine institutional committee on human research approved the study, and written informed consent was obtained from all patients.

**Clinical Characteristics of the Patients**

Peak serum creatine kinase-myocardial band and left-ventricular ejection fraction as an index of cardiac function were assessed by a cardiologist. We also evaluated several patient characteristics: age, sex, body mass index (BMI), education (<12 yrs or ≥12 yrs of schooling), marital status, MI location, and medications.

**Evaluation of Readiness for Exercise at Baseline and Exercise Maintenance During the 6-mo Period After the Supervised CR Program**

Baseline readiness for exercise and exercise maintenance during the 6 mos after completion of the supervised CR program were evaluated according to the transtheoretical model of exercise behavior change.\(^10,\)\(^11\) This model suggests a progression through five stages as an individual changes his or her exercise behavior: (1) precontemplation: not physically active and does not intend to change; (2) contemplation: not active but intends to change; (3) preparation: doing some activity; (4) action: regularly active but only within the previous 6 mos; and (5) maintenance: regularly active for >6 mos.

Patients were classified according to this transtheoretical model over the 6 mos after stopping the supervised CR program. Patients classified in the

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\(^1\) Oldridge, B.N., Spencer, S. J. Exercise maintenance: regularly active for >6 mos.

\(^2\) H11022

\(^3\) H11021

\(^4\) H11350

\(^5\) H11022

\(^6\) H11021

\(^7\) H11350

\(^8\) H11022

\(^9\) H11021

\(^10\) H11022

\(^11\) H11021
preparation, action, or maintenance stages were assigned to an exercise group, and patients classified in the precontemplation or contemplation stages were assigned to a nonexercise group.

**Physiologic Outcomes**

**Physiologic Outcomes at 1 and 6 mos After MI Onset**

Peak oxygen uptake (Peak \(\dot{V}O_2\)), handgrip strength, and knee extension muscular strength were measured to assess physiologic outcomes of each patient at 1 and 6 mos after MI onset.

**Exercise Capacity**

Subjects underwent cardiopulmonary exercise testing under a ramp treadmill protocol at 1 and 6 mos after MI onset. Peak \(\dot{V}O_2\) was measured as an index of exercise capacity. Measurements made from expired gasses were used as indices of cardiovascular dynamics during exercise. Symptom-limited exercise testing was performed on a MAT-2500 treadmill (Fukuda Denshi, Tokyo, Japan). Throughout the test, a 12-lead electrocardiogram was monitored continuously, and heart rate was measured from the R-R interval of the electrocardiogram (ML-5000, Fukuda Denshi). Peak \(\dot{V}O_2\) was measured during the exercise period with an AE-300S aero monitor (Minato Ika-gaku, Tokyo, Japan) and calculated with a personal computer (Pentium Processor, Windows 98 SE, EPSON, Nagano, Japan). The endpoint of exercise testing was determined according to the criteria of the American College of Sports Medicine. Anaerobic threshold was determined by the original V-slope method. Prescribed cardiac medications were continued on the day of the exercise testing.

**Measurement of Handgrip Strength**

A standard adjustable-handle JAMAR dynamometer (Bissell Healthcare, Grand Rapids, MI) was used for the measurement of handgrip strength as an index of upper limb muscle power and was set at the second grip position for all subjects. Attention was paid to a possible Valsalva effect, and measurements were made three times each on both hands. We used the highest value measured as the index of handgrip strength.

**Measurement of Knee Extension Muscular Strength**

A Biodex System 2 isokinetic dynamometer (Biodex Medical Systems, New York, NY) was used for measurement of knee extension muscular strength as an index of lower limb muscular strength. Testing was performed at a maximum of five repetitions for knee extensors at isokinetic speeds of 60 degrees/sec. Test results were analyzed with the Biodex System 2 software. We measured the knee extension muscular strength peak torque per body weight value for both knees and used the maximum value obtained as the index of knee extension muscular strength.

**SEPA**

General SEPA was measured with the (blinded) version of the SEPA evaluation for its reliability and validity. The SEPA evaluation consists of four subscales: domains of walking, stair climbing, weight lifting, and push off. The domain of walking was used as the index of SEPA in the present study. Subscale scores range from 0 to 100, in which lower scores indicate poorer and higher scores indicate better levels of SEPA. SEPA was measured at baseline and again at 12 mos after MI onset.

**Objective Physical Activity**

Number of steps taken was used as an index of objective physical activity in this study and was measured at baseline and again at 12 mos after MI onset. This index was derived from steps counted by an electronic pedometer (Kenz Lifecorder, Suzuki, Nagoya, Japan). We chose the Kenz Lifecorder because of the reliability and validity of the data output. The Kenz Lifecorder records the number of steps taken on the basis of physical characteristic data (age, sex, height, and weight) entered into the unit by the physical therapist. All patients were instructed to put on the Lifecorder by themselves and to use it 24 hrs a day for 1 wk, except while bathing and sleeping, from the time they received it. Patients were asked to keep a log...
of all physical activity during the 1-wk measurement period. The Lifecorder was then returned to us, and mean daily step count (total step count over 7 days/7) was calculated.

**Supervised CR Program**

The supervised CR program involved an interdisciplinary team approach to rehabilitation and included a cardiologist, nurse, physical therapist, dietician, and pharmacist. At the end of the acute phase of supervised CR, diet and medication instructions were given to each patient at discharge by a dietician and pharmacist, respectively. In addition, patients received individual education at discharge by a nurse regarding cardiovascular risk factors and smoking cessation. Exercise training performed during this phase included low-intensity treadmill walking with upper and lower limb stretches and body stretches.

The supervised recovery-phase CR and exercise training program continued until 6 mos after MI onset and was customized for each patient on the basis of results of cardiopulmonary exercise testing and muscle strength testing performed at the end of the acute-phase CR program. Patients participated in supervised combined aerobic and resistance exercise twice a week for 1 hr. Each exercise session was composed of a warmup, aerobic exercise, resistance training, and cool-down period. Exercise intensity during aerobic exercise was maintained at anaerobic threshold heart-rate level during treadmill walking. For resistance training, four sets of a series of two upper limb exercises (shoulder flexion and abduction from anatomic position) were performed with an iron weight array at a resistance that allowed completion of five repetitions with a rating of perceived exertion of 11–13 (according to the Borg 6–20 scale). Four sets of a series of knee extensions and calf raises comprised the lower limb exercises. Knee extension was performed with a weight strapped to the ankle and at a resistance that allowed completion of five repetitions with 50% of a one-repetition maximum. Exercise intensity for calf raises was maintained at a perceived exertion rating of 11–13. Each session was preceded and followed by series of upper and lower limb stretches and body stretches.

**Self-Monitoring Approach**

Patients were asked to record body weight, objective physical activity derived from the pedometer, blood pressure, and heart rate during the supervised recovery-phase CR program. Each patient was then asked to continue this self-monitoring after the completion of this program. The goal in the self-monitoring approach group was to promote SEPA in relation to exercise maintenance and leisure-time physical activity. The self-monitoring approach used in this study was based on Bandura’s self-efficacy theory and was designed to enhance confidence for exercise maintenance. This theory addresses four components of self-efficacy: verbal persuasion, physiologic states, vicarious learning, and performance accomplishments. Verbal persuasion promotes the motivation of regular exercise and other health behaviors. For example, the physical therapist praised the patient if he or she attained the target of physical activity. Thus, the target of physical activity for each patient was initially set at a low level by the therapist. Vicarious learning encourages the patient through discussion, breaking barriers that prevent patients from exercising and adopting other positive health behaviors. Performance accomplishments were addressed by written feedback on exercise, muscle strength test results, body composition test results (percentage of fat), and discussion of the self-monitoring log. Physical states were addressed by reviewing normal and abnormal physiologic responses to exercise during CR. Patients completed information on the rate of exercise maintenance, SEPA, and objective physical activity during the 6-mo period after the end of the supervised recovery-phase CR program (12 mos after MI onset).

**Statistical Analysis**

Results are expressed as mean ± 1 standard deviation. Nonparametric and χ² tests were used to analyze differences in clinical factors and readiness for exercise between groups. Two-way analysis of variance (ANOVA) of physiologic outcomes was computed to determine if any differences occurred for dependent variables with regard to differences at 1 and 6 mos during the supervised CR period and for interaction effects. ANOVA of SEPA and objective physical activity were computed between the self-monitoring approach and control groups to determine if any differences occurred for each dependent variable with regard to time after supervised CR and interaction effects. Spearman’s correlation coefficients were used to analyze SEPA and objective physical activity data obtained during the 6 mos after completion of the supervised recovery-phase CR program for all subjects. Statistical analyses were performed with SPSS 12.0J statistical software (SPSS Japan, Tokyo, Japan), and a P value of <0.05 was considered significant.

**RESULTS**

**Subjects and Response Rate to Questionnaire**

Of the 50 patients studied, one patient dropped out of the control group for reasons unrelated to the present study. One patient in the self-monitoring approach group and one patient in the control group were excluded because of failure to return the ques-
tionnaire to us. Thus, 47 of 49 patients (94%) returned the questionnaire and Lifeocorder. However, two patients in the control group returned incomplete questionnaires and were excluded from the present study. Therefore, the study sample consisted of 45 patients. Of these 45 patients, 24 patients comprised the self-monitoring approach group, and 21 patients comprised the control group. Mean time from MI onset did not differ significantly between the self-monitoring approach group and the control group (12.1 ± 1.3 vs. 12.2 ± 1.2 mos, P = 0.692) (Table 1).

**Clinical Factors Between Groups**

Patient characteristics were almost identical between the two groups. Medications did not differ significantly between the two groups (Table 2).

**Exercise Maintenance at 12 mos After MI Onset**

Twenty-four of 24 patients (100%) in the self-monitoring approach group continued to exercise at 12 mos after MI onset, whereas 17 of 21 patients (80.9%) in the control group continued exercise. The remaining four patients (19.1%) had quit exercise at 12 mos after MI onset (Table 2).

**Physiologic Outcomes at 1 and 6 mos After MI Onset**

The endpoint of the exercise test was defined as leg fatigue, shortness of breath, or gas exchange ratio of ≥1.20. No patient showed ischemic ST changes or experienced chest pain or serious arrhythmia during exercise testing. Repeated-measures ANOVA showed improvement for all physiologic outcomes at 6 mos after the completion of the CR program (12 mos after MI onset) compared with baseline results for SEPA outcomes. The effects of the self-monitoring approach on SEPA over the two time periods are presented in Figure 2. Significant period by group interactions (F[1,43] = 42.9, P < 0.001) were detected, and post hoc analyses focused on the main effects of period (F[1,43] = 49.8, P < 0.001). Although there were no significant differences in SEPA scores between the groups before treatment (72.0 ± 25.6 vs. 70.2 ± 18.8 points), SEPA at 12 mos after MI onset in the self-monitoring approach group was significantly higher than that in the control group (72.7 ± 25.8 vs. 90.5 ± 13.3 points, P < 0.001).

**Differences in Objective Physical Activity According to Exercise Maintenance**

Differences in objective physical activity values in the self-monitoring approach and control groups were evaluated with repeated two-way ANOVA. Repeated-measures ANOVA showed improvement in objective physical activity outcomes during the 6 mos after the completion of the CR program (12 mos after MI onset) compared with baseline results. The effects of the self-monitoring approach on objective physical activity over the two time periods are presented in Figure 3. Significant period by group interactions (F[1,43] = 20.5, P < 0.001) were detected, and post hoc analyses focused on the main effects of period (F[1,43] = 30.5, P < 0.001). Although there were no

**TABLE 1**

Mean period from myocardial infarction (MI) onset and exercise maintenance during the 6 mos after recovery phase of cardiac rehabilitation

<table>
<thead>
<tr>
<th></th>
<th>SMA Group (n = 24)</th>
<th>Control Group (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean period from MI onset, mos</td>
<td>12.1 ± 1.3</td>
<td>12.2 ± 1.2</td>
</tr>
<tr>
<td>Exercise maintenance after cardiac rehabilitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not doing exercise</td>
<td>0/24 (0%)</td>
<td>4/21 (19.1%)*</td>
</tr>
<tr>
<td>Doing exercise</td>
<td>24/24 (100%)</td>
<td>17/21 (80.9%)</td>
</tr>
</tbody>
</table>

SMA, self-monitoring approach.

<table>
<thead>
<tr>
<th>Mean period from MI onset was not significant between the two groups; however, significant change in measurements of percentage of exercise maintenance during the 6 mos after recovery phase of cardiac rehabilitation in the SMA group was noted at 12 mos vs. those measured at baseline after the onset of MI.</th>
</tr>
</thead>
<tbody>
<tr>
<td>*P &lt; 0.05.</td>
</tr>
</tbody>
</table>
significant differences in objective physical activity values between the groups before treatment (6,564.9 ± 1,114.6 vs. 6,282.6 ± 1,985.9 steps per day for 1 wk), the mean number of steps taken daily during 1 wk at 12 mos after MI onset in the self-monitoring approach group was significantly higher than that in the control group (10,458.7 ± 3,310.1 vs. 6,922.5 ± 3,192.9 steps).

**Relation Between SEPA Scores and Objective Physical Activity for All Subjects**

We also evaluated the correlations between SEPA scores and objective physical activity (average steps per day during 1 wk) at 12 mos after MI onset for all patients. SEPA scores showed significant positive correlation ($r = 0.642, P < 0.01$) with objective physical activity (Fig. 4).

### DISCUSSION

This study is one of the first randomized, controlled trials to investigate the effect of the self-monitoring approach during a supervised CR program on exercise maintenance, SEPA, and objective physical activity after MI onset. We found that the self-monitoring approach group had a higher exercise maintenance rate than did the control group during the 6-mo period after participation in a supervised CR program, despite both groups having identical clinical findings and physiologic outcomes at baseline. These findings are consistent with other randomized, controlled trials showing the effectiveness of exercise maintenance in sedentary healthy individuals and patients with diabetes mellitus.8,9 The present study suggests...

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**TABLE 2 Clinical characteristics of the two study groups**

<table>
<thead>
<tr>
<th></th>
<th>SMA Group (n = 24)</th>
<th>Control Group (n = 21)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD, yrs</td>
<td>63.9 ± 9.7</td>
<td>64.5 ± 10.1</td>
<td>NS</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>21/3</td>
<td>17/4</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>22.9 ± 2.6</td>
<td>21.9 ± 2.5</td>
<td>NS</td>
</tr>
<tr>
<td>Education, yrs</td>
<td>13.6 ± 2.6</td>
<td>13.2 ± 2.4</td>
<td>NS</td>
</tr>
<tr>
<td>Married, %</td>
<td>100</td>
<td>95.2</td>
<td>NS</td>
</tr>
<tr>
<td>Maximum CK-MB, IU/L</td>
<td>198.7 ± 80.3</td>
<td>225.1 ± 151.7</td>
<td>NS</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>51.3 ± 9.8</td>
<td>51.9 ± 7.7</td>
<td>NS</td>
</tr>
<tr>
<td>Location of MI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior</td>
<td>10</td>
<td>8</td>
<td>NS</td>
</tr>
<tr>
<td>Anterior</td>
<td>12</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Medication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>15</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>β-blockers</td>
<td>8</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>ACEI</td>
<td>17</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>ARB</td>
<td>10</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Readiness for exercise, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doing exercise</td>
<td>33</td>
<td>37</td>
<td>NS</td>
</tr>
<tr>
<td>Not doing exercise</td>
<td>67</td>
<td>63</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; CK-MB, creatine kinase–myocardial band; LVEF, left ventricular ejection fraction; MI, myocardial infarction; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

There were no significant differences between groups ($P > 0.05$).

**TABLE 3 Effect of cardiac rehabilitation program on peak oxygen uptake ($\text{VO}_2$), handgrip strength, and knee extension strength**

<table>
<thead>
<tr>
<th>Variable</th>
<th>SMA Group (n = 24)</th>
<th></th>
<th>Control Group (n = 21)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mo</td>
<td>6 mos</td>
<td>1 mo</td>
<td>6 mos</td>
</tr>
<tr>
<td>Peak $\text{VO}_2$, ml/kg/min</td>
<td>21.3 ± 3.2</td>
<td>26.8 ± 4.2*</td>
<td>21.6 ± 3.4</td>
<td>26.1 ± 6.8*</td>
</tr>
<tr>
<td>Handgrip strength, kg</td>
<td>33.8 ± 10.2</td>
<td>37.8 ± 9.3*</td>
<td>34.1 ± 9.8</td>
<td>36.9 ± 9.7*</td>
</tr>
<tr>
<td>Knee extension strength, Nm/kg</td>
<td>1.5 ± 0.6</td>
<td>2.1 ± 0.8*</td>
<td>1.5 ± 0.3</td>
<td>1.9 ± 0.7*</td>
</tr>
</tbody>
</table>

SMA, self-monitoring approach.

Significant improvements in measurements of peak $\text{VO}_2$, handgrip strength, and knee extension strength in both groups was noted at 6 mos vs. those at 1 month during the cardiac rehabilitation program. These improvements were significantly different from initial values within each group, but there were no statistically significant interaction periods by group.

*P < 0.05.
that such intervention may be applied to the CR setting to assist with exercise behavior. Exercise maintenance rate in the self-monitoring approach group was 100% for the 6-mo period after the supervised CR program. Importantly, the exercise maintenance rate in the control group was also >80% for this same period. Oldridge and Spencer\(^5\) previously reported an exercise maintenance rate of 80% during the 6 mos after a 6-mo CR program in patients with MI. The exercise maintenance rate in the present study was higher than that in the study from Oldridge and Spencer.\(^5\) Although the time frame and cohort were different in these two studies, the exercise maintenance rate in the present study seems relatively high.

Prior readiness for exercise has been reported to be effective in maintaining adherence to exercise in healthy people.\(^21\) In the present study, prior readiness for exercise did not differ between the two groups; therefore, it may not be an essential prerequisite for better exercise maintenance during the 6 mos after supervised CR. The self-efficacy theory posits that the performance of a specific behavior is strongly influenced by the individual’s confidence in his or her ability to perform that behavior.\(^16\) Although there were no significant differences in SEPA between the groups at baseline, SEPA during the 6 mos after supervised CR was significantly higher in the self-monitoring approach group than in the control group. We encouraged the patients to self-monitor their physical activity, body weight, and blood pressure during the supervised CR program and to continue this monitoring thereafter. We think that his self-monitoring approach may have improved the rate of exercise maintenance in our patients. Because long-term maintenance of physical activity habits and lifestyle changes after a supervised CR program is generally difficult,\(^22\) further studies to evaluate the effectiveness of the self-monitoring approach over a longer period after supervised CR are necessary.

Objective physical activity reported in the self-monitoring approach group during the 6-mo period after the supervised CR program finished was higher than that in the control group. Berlanga et al.\(^22\) previously investigated the effect of focused individualized advice vs. routine advice on physical activity level over a 1-yr period in patients with diabetes. They reported a significant increase in total weekly energy expenditure measured via a physical activity questionnaire; however, physical activity was not measured objectively. In the present study, objective physical activity was measured as an average of 10,000 steps per day in the self-monitoring approach group after the 6-mo supervised CR program. This number seems to favorably agree with the level of physical activity recommended for management of patients with diabetes mellitus or hyperlipidemia.\(^23,24\) Thus, the amount of physical activity performed by the self-monitoring approach group patients may be effective in the secondary prevention of MI.

In the present study, objective physical activity showed a positive correlation with SEPA scores for all patients. Longer exercise maintenance due to SEPA improvement may be related to this result. As SEPA improved in the self-monitoring approach group, objective physical activity may have been mediated by a change in SEPA improvement in exercise maintenance, or the improvements in perceived SEPA may have been responsible for the improvements in objective physical activity. Thus,
high SEPA detected in patients may have resulted in improved objective physical activity. There may also be an unrecognized predictor of improvement of objective physical activity in the present study for which further detection and study is required.

**Study Limitations**

First, the present study comprised a small sample population; thus, we were unable to determine predictors for dropout from exercise. A previous study suggested that patients who drop out from a CR program have higher levels of depression, neuroticism, and physical symptoms and are less optimistic than those who complete CR.\(^{25}\) We did not ascertain the reasons for exercise discontinuation after completion of the supervised CR program. These reasons may also affect SEPA.

Second, we did not assess peak \(V_{\text{O}}_2\) over the long term after CR; therefore, the difference in exercise capacity between the two study groups was not assessed precisely. Further study is needed to evaluate exercise tolerance relative to the self-monitoring approach over the long term after a supervised CR program.

Third, we did not assess repeated hospitalization of patients in our study or cost-effectiveness of CR. Further study is needed to address these issues. Finally, we did not evaluate coronary risk factor indicators such as lipid cholesterol level. Further study is needed to validate these outcomes over the long term after supervised CR.

**CONCLUSION**

At 12 mos after MI onset, the rate of exercise maintenance in the self-monitoring approach group was relatively high in comparison with that in the control group, and exercise maintenance contributed to improvement in leisure-time physical activity. Therefore, we conclude that use of the self-monitoring approach during supervised CR may effectively increase exercise maintenance, SEPA, and objective physical activity after supervised CR. The present study provides further evidence for the efficacy of exercise maintenance and suggests that such intervention may be applied to the supervised CR setting to assist with exercise behavior. Future trials should be conducted for longer periods, and long-term follow-up will be required to evaluate whether these benefits continue over time.

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Low-Dose Interleukin-1 Partially Counteracts Osteogenic Protein-1–Induced Proteoglycan Synthesis by Adult Bovine Intervertebral Disk Cells

ABSTRACT


Objective: Low back pain associated with degenerative disk disease is a common clinical problem that has enormous socioeconomic impact in today's aging population. As an alternative to the surgical removal of the diseased intervertebral disk, the direct application of a purified growth factor into the intervertebral disk may provide physiatrists a valuable tool to halt or slow down disk degeneration. Our goal here is to determine if low levels of interleukin-1 (IL-1), a proinflammatory cytokine present in the degenerating disk, could interfere with the potentially beneficial effects of growth factors on proteoglycan synthesis. New knowledge gained from this study will prove useful in the development of new treatment modalities that take advantage of the stimulatory effects of growth factors such as osteogenic protein-1 (OP-1).

Design: This was an in vitro study of proteoglycan accumulation and synthesis by cells from the nucleus pulposus, inner annulus fibrosus, and outer annulus fibrosus in the bovine intervertebral disk.

Results: In cells cultured with serum and no additional exogenous growth factor, treatment with low-dose IL-1 does not result in a significant decrease in proteoglycan synthesis. However, in the case of cells stimulated with OP-1, treatment with IL-1 resulted in a statistically significant decrease in sulfur-35–proteoglycan synthesis by cells derived from all three zones of the bovine intervertebral disk (nucleus pulposus, 60.3% \( P < 0.0001 \); inner annulus fibrosus, 18.4% \( P = 0.0330 \); outer annulus fibrosus, 12.3% \( P = 0.0255 \)). Proteoglycan accumulation over the 12-day culture period also decreased significantly (nucleus pulposus, 26.8% \( P < 0.0001 \); inner annulus fibrosus, 15.8% \( P = 0.0276 \); outer annulus fibrosus, 16.8% \( P = 0.0102 \)). It is worth noting that cells cultured in the presence of both OP-1 and IL-1 synthesized proteoglycan at a faster rate than cells cultured in the presence of IL-1 alone (nucleus pulposus, 58.5% \( P < 0.0001 \); inner annulus fibrosus, 39.7% \( P = 0.0055 \); outer annulus fibrosus, 45.1% \( P = 0.0164 \)). Likewise, cells treated with OP-1 and IL-1 accumulated more proteoglycan in their newly formed matrix than cells cultured in the presence of IL-1 alone (nucleus pulposus, 65.3% \( P < 0.0001 \); inner annulus fibrosus, 60.5% \( P = 0.0034 \); outer annulus fibrosus, 19.4% \( P = 0.0840 \)).

Conclusions: Intervertebral disk cells that are stimulated by the growth factor OP-1, to increase the rate at which they produce a proteoglycan-rich matrix become more susceptible to the inhibitory effects of the proinflammatory cytokine IL-1 on the rate of proteoglycan synthesis and accumulation in the matrix over time. This notwithstanding, IL-1 at the low dose used did not totally obliterate the stimulatory effects of OP-1 on matrix formation. Consequently, this growth factor may remain partially effective in stimulating disk repair in vivo even when proinflammatory cytokines such as IL-1 are present.

Key Words: Low Back Pain, Nucleus Pulposus, Annulus Fibrosus, Degenerative Disk Disease
Low back pain is a common clinical problem that has enormous socioeconomic impact in today’s aging population. In the United States, estimates of medical costs attributable to back pain exceed $50 billion annually.1 Although the cause of back pain is most likely multifactorial, lumbar intervertebral disk (IVD) degeneration is associated, perhaps causally, with low back pain.2,3 Despite the high prevalence of degenerative disk disease, treatment is limited to addressing symptoms. Most of the surgical methods performed to obtain pain relief are destructive to the IVD structure and eventually may cause instability of the motion segment.4 As an alternative to the surgical removal of the diseased disk, biological treatment with a growth factor capable of promoting matrix repair and restoring physiologic function has been considered.5,6 Biological approaches have certain advantages; these advantages include restoration of the physiology and structure of the IVD, low morbidity, and the possibility of being adopted by physiatrists interested in providing exciting new treatment modalities.

The IVD can be separated into three distinct zones: a set of tough outer rings rich in collagen (outer annulus fibrosus [outer-AF]), a gelatinous inner core rich in proteoglycan (nucleus pulposus [NP]), and, between them, a transitional zone (inner annulus fibrosus [inner-AF]).7 The major proteoglycan, aggrecan, confers properties of resilience and resistance to deformation necessary for the normal functions of the IVD. With the development of degeneration, the NP is transformed from a turgid gel into a more desiccated fibrocartilaginous structure.8,9 Degenerative disks are characterized by altered matrix composition and, during late stages of degeneration, reduced cell numbers.10,11 Recent metabolic studies have suggested that the synthesis of proteoglycans by chondrocytes decreases markedly with age and degeneration.12,13 This alteration in the metabolism of proteoglycans is thought to contribute to the development and progression of disk degeneration.13

One potential treatment for low back pain is to replenish the proteoglycan and collagen loss associated with degenerative disk disease. The synthesis of proteoglycan and collagen macromolecules by cartilage and IVD cells can be stimulated by human recombinant osteogenic protein-1 (OP-1), one of the most effective known stimulators of aggrecan synthesis. OP-1, also known as bone morphogenetic protein-7, is a member of the transforming growth factor superfamily that exerts potent effects on chondrocyte and osteocyte differentiation and metabolism.14 Our research group has previously shown that OP-1 stimulated the accumulation of proteoglycan and matrix proteins by cells from bovine and rabbit IVDs.5,6

The amount of proteoglycan in normal adult IVD tissues remains relatively constant over time: proteoglycans degraded during turnover are immediately replaced by newly synthesized molecules. The extracellular matrix is in a state of homeostasis (i.e., the cells maintain a balance between matrix synthesis and degradation). Alterations in both anabolic and catabolic processes are thought to play a key role in the onset and progression of IVD degeneration, but the biochemical processes that regulate these changes are poorly understood. Interleukin-1 (IL-1), a proinflammatory cytokine, is thought to contribute significantly to the loss of matrix homeostasis in articular cartilage in joint disease.15,16 However, the effects of IL-1 on matrix homeostasis in disk tissues are less clear. Low concentrations of inflammatory cytokines (e.g., IL-1, IL-6, tumor necrosis factor-α, and granulocyte-macrophage colony stimulating factor) are present in degenerated or herniated IVDs.17–19 Some authors have suggested that proinflammatory cytokines such as IL-1 may disturb matrix homeostasis, thus contributing to IVD degeneration, at least in part, by inhibiting matrix repair and promoting matrix degradation.20,21 The purpose of this study was to compare the effects of low doses of IL-1 and OP-1, alone or in combination, on proteoglycan synthesis and accumulation by IVD cells cultured in vitro.

METHODS
Cell Cultures

Bovine IVDs were isolated from tails, purchased at a local slaughterhouse, of young adult animals (15 to 18 mos old). The IVD at levels coccygeal 1–4 were isolated from four tails, separated into the NP, the outer two thirds of the AF (the outer-AF), and the inner-AF (between the NP and the outer-AF) and separately pooled for each experiment. The cells were first released by enzymatic digestion (0.2% pronase for 1 hr and 0.025% collagenase-P for 18 hrs) and then suspended in 1.2% low-viscosity alginate (Keltone LVCR, ISP Alginates, San Diego, CA) at 2,000,000 cells/ml. The beads were cultured as previously described, using conditions under which bovine adult articular chondrocytes retained their phenotype for up to 8 mos.22,23

Briefly, the cultures containing nine beads per well in a 24-well plate were maintained in 400 μl of complete media (Dulbecco’s modified Eagle medium [DMEM] and Ham’s F-12 medium [DMEM/F-12 ratio of 1:1; Mediatech, Herndon, VA] containing 20% fetal bovine serum [Hyclone, Logan, UT], 25 μg/ml ascorbic acid [Sigma Chemical, St. Louis,
MO], 360 μg/ml l-glutamine [Mediatech], and 50 μg/ml gentamicin [Gibco BRL, Grand Island, NY]). From day 0 to day 6, the beads were cultured under these conditions at 37°C with daily changes of medium. On day 6 of culture, the beads encapsulating NP, inner-AF, and outer-AF cells were separately subdivided into four groups (triplicate cultures of nine beads each): control, IL-1 treated, OP-1 stimulated, and OP-1 plus IL-1 treatment (Fig. 1). Beads in the control group and IL-1 group were maintained in complete medium, whereas beads in the OP-1 group and OP-1 plus IL-1 group were cultured in the presence of OP-1 (100 ng/ml) for 3 days. From day 9 to day 12 of culture, beads in the control group and IL-1 group were maintained in complete medium, whereas beads in the OP-1 group and OP-1 plus IL-1 group were cultured in the presence of IL-1α (0.1 ng/ml), beads in the OP-1 group were cultured in the presence of OP-1 (a gift from Stryker Biotech, Hopkinton, MA) at 100 ng/ml, and beads in the OP-1 plus IL-1 group were cultured in the presence of OP-1 at 100 ng/ml plus IL-1α at 0.1 ng/ml. In all cases, the medium was replaced daily. Each experiment was repeated 3–4 times.

In the control group, cells were cultured in complete medium for the entire 12 days (Fig. 1). Beads in the IL-1 group were cultured in complete medium during the first 9 days; IL-1α (0.1 ng/ml) was included during days 9–12. For the OP-1 group, beads were cultured in complete medium during the first 6 days; OP-1 (100 ng/ml) was included during days 6–12. In the OP-1 and IL-1 group, beads were cultured in complete medium for the first 6 days; OP-1 was included during days 6–12, and IL-1 was included during days 9–12.

Measurement of Proteoglycan Accumulation

At the end of each culture period, alginate beads were collected, dissolved, and treated with papain as previously described.24 The papain digests were analyzed for content of total sulfated proteoglycan by the dimethylmethylene blue (Polysciences, Warrington, PA) dye-binding method.24 The amount of proteoglycan in the culture medium was below the threshold of detection of this method and thus was not included in the total proteoglycan content. Alginate gives a minor positive reactivity with the dye that is constant over a broad range of values. Consequently, alginate was maintained at a minimum concentration of 0.03% in all solutions.25 Purified bovine nasal septum-D1 proteoglycan was used as a standard.

Measurement of the Rate of Proteoglycan Synthesis

During the last 4 hrs of culture on day 12, sulfur-35 (35S)-sulfate (20 μCi/ml; Perkin Elmer/New England Nuclear, Boston, MA) was added to each medium. At the end of each culture period, alginate beads were collected, dissolved, and treated with papain. Conditioned media were also collected for analysis. The amount of 35S-sulfate incorporated into proteoglycans recovered from the medium and papain digest was measured in each case. To do so, 35S-proteoglycans were first separated from unincorporated 35S-sulfate by a rapid filtration assay, and the radioactivity present in macromolecules was then measured by scintillation counting.26

Measurement of DNA Content as an Indicator of Cell Proliferation

The papain digests were analyzed for DNA content using the Hoechst dye method (Hoechst 33258: Polysciences), as previously described.24 Briefly, 100 μl of the papain-digested samples was mixed with 1 μg/ml Hoechst dye solution. The dye/sample complex was excited with ultraviolet light (wave length, 360 nm), and the emission at 460 nm was measured on a fluorescence microplate reader. Calf thymus DNA type I (Sigma Chemical) was used as a standard.

Statistical Analyses

Each experiment was repeated 2–5 times with triplicate cultures for each condition. Therefore,
the sample number is the number of experiments multiplied by three (representing triplicate culture). The results are expressed as the mean ± standard error of the mean. Analysis of variance was used to assess the differences among cells from the three distinct zones of the IVD, and the effects of OP-1 on 35S-proteoglycan synthesis, accumulation, and DNA content values were obtained by unpaired t test. The level of statistical significance was set at P < 0.05.

RESULTS

Hyperanabolic IVD Cells Are More Sensitive to the Inhibitory Effect of IL-1 on 35S-Proteoglycan Synthesis

As we recently reported, exposure to OP-1 markedly stimulated cells from all three zones of the IVD to produce proteoglycan at a faster rate (Fig. 2). Recent studies on IVD cells have suggested that OP-1 also stimulates the synthesis by these cells of other matrix constituents (i.e., collagen type II; Zhang et al., unpublished data). Consequently, it can be said that IVD cells exposed to OP-1 become hyperanabolic. In this study, OP-1 was more effective in stimulating proteoglycan synthesis by NP cells than by either group of AF cells.

IVD cells that entered this state of hyperanabolism became more susceptible to the inhibitory effects of a subsequent exposure to IL-1 on proteoglycan synthesis. Again, this was most readily evident in the case of NP cells (60% decrease, P < 0.0001), but it also was evident, although less so, in the case of inner-AF (18% decrease, P = 0.0330) and outer-AF cells (12% decrease, P = 0.0255) (Fig. 2). Other results are worth noting. First, IL-1 at 0.1 ng/ml was relatively ineffective in inhibiting proteoglycan synthesis by NP cells not previously exposed to OP-1 (P = 0.3775). In the case of inner-AF and outer-AF cells not exposed to OP-1, the treatment with IL-1 actually moderately stimulated proteoglycan synthesis (inner-AF: 45% increase, P = 0.0045; outer-AF: 30% increase, P = 0.0038).

Second, at the concentration used, IL-1 was unable to totally obliterate the OP-1–induced stimulation of proteoglycan synthesis by any of the IVD cell types studied. Cells stimulated with OP-1 and subsequently exposed to IL-1 (OP-1 plus IL-1 group) synthesized proteoglycan at a significantly faster rate than cells exposed to IL-1 only (NP: 81% faster, P < 0.0001; inner-AF: 45% faster, P = 0.0138; outer-AF: 90% faster, P = 0.0011).

The results in each case reflect 35S-proteoglycan synthesized by cells encapsulated in nine alginate beads during the last 4 hrs of the culture period (Fig. 2). When compared with their counterparts maintained in the presence of OP-1 alone, cells from all three zones of the IVD exhibited a decrease in the rate of proteoglycan synthesis when they were treated additionally with IL-1 during the last 3 days of culture.

The results show, in each case, the amount of radioactivity in 35S-proteoglycan synthesized by the cells during the last 4 hrs of culture. After

FIGURE 2

Hypermetabolic cells from the bovine nucleus pulposus (NP), inner-annulus fibrosus (inner-AF), and outer-annulus fibrosus (outer-AF) are more sensitive to the inhibitory effect of interleukin-1 (IL-1) on sulfur-35 (35S)-proteoglycan synthesis. The results in each case reflect 35S-proteoglycan synthesized by cells encapsulated in nine alginate beads during the last 4 hrs of the culture period. When compared with their counterparts maintained in the presence of osteogenic protein-1 (OP-1) alone, cells from all three zones of the intervertebral disk exhibited a decrease in the rate of proteoglycan synthesis when they were treated additionally with IL-1 during the last 3 days of culture. Error bars represent standard error of the mean.
culture for 6 days in the presence or absence of OP-1, the cells were cultured in the presence or absence of IL-1, as outlined in Figure 1.

**Hyperanabolic IVD Cells Are More Sensitive to the Inhibitory Effect of IL-1 on Proteoglycan Accumulation**

The IVD cells maintain matrix homeostasis by balancing the synthesis and degradation of matrix macromolecules. Inflammatory cytokines such as IL-1 are known to disturb the state of matrix homeostasis. Thus, it is important to study the total proteoglycan content at the end of the 12-day culture period, during which IL-1 was present for the last 3 days. Proteoglycan accumulation represents the portion of proteoglycans entrapped in alginate beads; this is the net result of proteoglycans synthesized by the cells less proteoglycans degraded during this period and secreted into the culture media (Fig. 3). Among the results with four combinations of treatment (with and without OP-1 and with and without IL-1), several points are worth noting. First, as expected, accumulation of proteoglycan during the 12-day period was clearly greater in cultures exposed for six of those 12 days to OP-1. Treating those cultures with IL-1 between days 9 and 12 resulted in decreased proteoglycan accumulation by cells derived from all three zones of the IVD.

**Cell Proliferation in Response to IL-1 After OP-1 Stimulation by Cells from Three Zones of the Bovine IVD**

It is known that OP-1 has mitogenic effects on bovine and rabbit IVD cells. However, the effects of the cytokine IL-1 on cell proliferation have not been previously studied. As a measurement of cell number, the total DNA content of the culture (nine beads) at the end of the 12-day culture period in all treatment groups was measured.
four groups was measured. At the beginning of the culture period, the cell number was the same (2,000,000 cells/ml alginate) for each group, as verified by cell particle counting before encapsulating the cells in alginate.

In the absence of the growth factor OP-1, the addition of IL-1 had little effect on cell proliferation in any of the groups studied (Table 1). When administered to cells cultured in the presence of OP-1, IL-1 caused a reduction in the marked OP-1–induced cell proliferation.

**DISCUSSION**

We have previously demonstrated that the growth factor OP-1 up-regulates proteoglycan synthesis by cells in three zones: the NP, inner-AF, and outer-AF of the bovine IVD.5 This led us to suggest that the injection of this growth factor into the disk (under fluoroscopic guidance) has potential as a modality in the treatment of IVD degeneration by physiatrists. It is also known that low concentrations of inflammatory cytokines (e.g., IL-1), present in herniated IVDs, may adversely affect the metabolism of IVD cells.20,21 Herein, we report, for the first time, that exposure of IVD cells to OP-1 can counteract, in part, the deleterious effects of IL-1 on proteoglycan synthesis.

The bovine IVD was selected for this study because it is large in size and is therefore easily separated into three distinct zones as described by Thompson et al.;7: the NP, inner-AF, and outer-AF. Tails from bovine animals aged between 15 and 18 mos are readily available from the local slaughterhouse at little cost as a source of mature IVD cells.27 The alginate bead culture system used in this study was originally developed by Guo et al.22 to study the metabolism of chondrocytes, but recently, it has been used principally, in a modified form, to identify differences in the organization and turnover of two distinct compartments of the matrix formed by phenotypically stable articular chondrocytes.24 The same approach was recently used to show that, like articular chondrocytes, IVD cells entrapped in these alginate beads reform an extracellular matrix made up of at least two distinct compartments.6 The results presented above suggest that it also is well suited to study metabolic differences among cells derived from different zones of the IVD.

After OP-1 treatment, a short exposure to IL-1 resulted in a dramatic decrease (by 60.3%) in the rate of proteoglycan synthesis by NP cells and a less impressive, but statistically significant, decrease in inner-AF cells (by 18.4%) and outer-AF cells (12.3%). Proteoglycan accumulation, which represents the net difference between what is synthesized and degraded by these cells over the culture period, was also decreased significantly (NP, 26.8% decrease; inner-AF, 15.8% decrease; outer-AF, 16.8% decrease); this is remarkable given that the cells pre-exposed to OP-1 were exposed to IL-1 only during 3 days of the 12-day culture. We predict that a longer culture period in the presence of IL-1 will result in an even more profound decrease in proteoglycan accumulation.

It is worth noting that proteoglycan accumulation by cells not exposed to OP-1 was not significantly compromised by including IL-1 at 0.1 ng/ml during the last 3 days of culture. This is not really surprising for two reasons. First, IL-1 at concentrations considered close to those measured around and in herniated disks17 has been found to have little propensity to up-regulate catabolic processes in articular chondrocytes.28 Second, this low dose of IL-1 actually stimulated, rather than inhibited, 35S-proteoglycan synthesis by annulus cells (inner-AF: 45.2% increase, P = 0.0017; outer-AF: 30.2% increase, P = 0.0038). IL-1, at a very low concentration, also has been shown to have a similar stimulatory effect on proteoglycan synthesis by articular chondrocytes.28

In summary, in the absence of growth-factor stimulation, low-dose proinflammatory cytokine (IL-1) treatment does not have a negative effect on proteoglycan accumulation or rate of proteoglycan synthesis by cells derived from all three zones of the IVD. After stimulation with the growth factor OP-1, IL-1 resulted in a significantly decreased proteoglycan synthesis and accumulation. This effect is more profound in NP cells than in AF cells. Our results demonstrate that after stimulation with a growth factor such as OP-1, IVD cells are more sensitive to the negative effects of IL-1, even at very low concentrations that normally do not negatively affect proteoglycan metabolism. Based on these findings, clinicians should be aware that

| TABLE 1 | Ratios of DNA content in the different treatment groups |
|-----------------|-----------------|-----------------|-----------------|
| NP: IL-1/control | 0.95 | 0.1658 | 0.8330 |
| Inner-AF: IL-1/control | 1.10 | 0.0970 | 0.3657 |
| Outer-AF: IL-1/control | 0.93 | 0.0383 | 0.6864 |
| NP: OP-1/control | 1.79 | 0.4328 | 0.0018 |
| Inner-AF: OP-1/control | 2.00 | 0.2058 | <0.0001 |
| Outer-AF: OP-1/control | 1.73 | 0.1747 | 0.0004 |
| NP: OP-1 + IL-1/control | 1.50 | 0.3036 | 0.0464 |
| Inner-AF: OP-1 + IL-1/control | 1.54 | 0.1807 | 0.0005 |
| Outer-AF: OP-1 + IL-1/control | 1.36 | 0.1222 | 0.0306 |

NP, nucleus pulposus; IL-1, interleukin-1; inner-AF, inner annulus fibrosus; outer-AF, outer annulus fibrosus; OP-1, osteogenic protein-1.
although treatment with growth factors may promote matrix repair, this response might be less than optimal when proinflammatory cytokines are present.

Before clinical trials can be conducted, the effect of OP-1 should be investigated on both healthy and degenerated human disk tissues, and the dose of OP-1 and duration of its effect should be optimized. This study suggests that under those optimized conditions, OP-1 will exert its positive effects in humans even when proinflammatory cytokines such as IL-1 are present. Inhibition of IL-1 may become a viable strategy for the treatment of degenerative disk disease. Recombinant human IL-1 receptor antagonist protein (IRAP, anakinra, or Kinrem) was recently approved by the United States Food and Drug Administration for the treatment of rheumatoid arthritis. Additional studies on the effects of IL-1 receptor antagonists on IVD-cell extracellular matrix metabolism may prove useful in preventing matrix catabolism.

CONCLUSIONS

Bioengineering or surgical approaches are likely to be favored in the late stages of IVD degeneration, when cells are present in the disk tissues in much reduced numbers. On the other hand, injection of growth factors into the IVD under fluoroscopic guidance could provide physiatrists with an exciting new treatment modality during the early stages of IVD degeneration, when viable cells still are present in significant numbers. Although low concentrations of inflammatory cytokines such as IL-1 do not down-regulate proteoglycan synthesis to any significant degree, they have a more profound inhibitory effect after cells have been stimulated with a growth factor, such as OP-1. This notwithstanding, IL-1 at the low dose used did not totally obliterate the stimulatory effects of OP-1 on matrix formation. Consequently, this growth factor may remain partially effective in stimulating disk repair in vivo, even when proinflammatory cytokines such as IL-1 are present.

REFERENCES


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Abstract


Objective: In subjects with unilateral vestibular malfunction, running is associated with less departure from the straight-ahead path than walking. The purpose of this study was to broaden the scope of these observations by investigating whether they can be generalized to healthy subjects.

Design: Healthy blindfolded subjects were asked to traverse a 10-m straight path while walking at a self-selected slow speed, walking at a fast speed, or running. Gait speed and mediolateral feet placement were monitored, and departure from the straight-ahead path (path integration) was determined.

Results: In healthy subjects, similar to subjects receiving unbalanced vestibular information, departures from the straight-ahead trajectory (namely, path integration) were larger in slow walking than in running.

Conclusions: In healthy subjects, variation in foot placement between the acts of walking and running seem to account for the enhanced path integration found during running. Perhaps consideration of these findings is also relevant for the interpretation of speed-dependent path integration in subjects receiving abnormal unilateral vestibular inputs.

Key Words: Walking, Running, Balance, Vestibular, Path Integration
Subjects with acute unilateral vestibular disorders have balance impairments. Characteristically, they walk slower than healthy, aged-matched controls and manifest larger side-to-side deviations and a larger base of support than healthy individuals. These subjects tend to deviate excessively from their starting position when walking in place blindfolded (Fukuda's stepping test) and to veer sideways when walking blindfolded. Similarly, in healthy adults, vestibular galvanic stimulation causes blindfolded subjects to deviate from the straight-ahead trajectory while walking.

Recently, Brandt et al. and Jahn et al. compared the effects of walking and running on path integration (operationally defined as the ability to maintain a straight-ahead progression line) in patients with acute unilateral vestibular hypofunction and in healthy subjects who had been subjected to unilateral vestibular stimulation. Their major finding was that faster progression speed (i.e., running) is associated with decreased departure from the straight-ahead intended path. This was explained by differential regulation of vestibular inputs by the central nervous system, which is dependent on the speed of locomotion. Subsequently, they argued against the working hypothesis that slower walking speed provides more safety than faster speeds in patients with acute unilateral vestibular deficits and claimed that their findings may have important consequences for the physical therapy and rehabilitation of patients with vestibular pathologic gait.

In addition, it has further been demonstrated that deviations from the straight-ahead path are also smaller in running than in walking among healthy adults subjected to distorted optic flow by inverting prisms. Once more, these findings were interpreted by speed-dependent differential regulation of sensory inputs by the central nervous system.

Path integration is a direct consequence of foot placement in successive steps. Step-width variability, which is a characteristic of mediolateral foot placement, increases with age and with the absence of vision. Walking velocity in the elderly may also be associated with an increase in step-width variability. Changing step width of an upcoming step was shown to be a strategy of overcoming mediolateral foot perturbation during midstance in both healthy subjects and in subjects with unilateral vestibular hypofunction.

Whereas most observations of mediolateral foot placement pertain to a constant pace of locomotion or to a single velocity, the relationship between gait trajectory (as determined by successive mediolateral foot placement) and forward locomotion speed is not well documented. The goal of this study was therefore to examine the effect of forward speed on mediolateral foot placement in healthy subjects. Its main question was whether the effect of speed on path integration in healthy adults is comparable with the effect reported in subjects receiving unilateral vestibular or distorted visual stimulation (namely, better path integration in running than in walking).

METHODS

Subjects and Procedure

Participants were 12 healthy volunteers, including seven men and five women, with a mean age of 32.8 yrs (range, 18–58 yrs). Subjects were independent community dwellers (ten students and two physical therapists), all declaring good health and unaware of any malfunction of the vestibular, visual, or somatosensory system. None of them were professionally engaged in sports; however, they all declared having an active lifestyle, including participation in leisure sport activities, mainly in walking.

Before commencement of data collection, thin inked pads of two different colors (i.e., one color for each foot) were adhered underneath the heel of each of the subjects' shoes. Each subject was tested in six trials in which three speed conditions—slow walking, fast walking, and running—were applied twice in a random order. The first of each of the two trials of identical speed was considered as a familiarization trial and the second was used for inferential data analysis.

The trials were conducted in a large open space (about 100 m²). Subjects were instructed to stand facing the straight-ahead 10-m path. They were subsequently blindfolded to prevent the use of vision for mediolateral foot alignment and to force reliance on egocentric vestibular or somatosensory information for path integration. In accordance with the prerandomized order, subjects were then directed to use a self-selected speed for walking slowly (walk slowly and directly to the finish line of the route that you face), walking fast (walk rapidly and straight to the finish line), or running (run straight ahead to the finish line) to the end of the path. Because data were compared only within subjects, no attempts were made to attain comparable speeds between the participants. Complete silence was maintained throughout the subjects' locomotion, with the exception of instructing them when they could stop after passing the finish line.

Gait speed from the starting point of locomotion to the moment when subjects passed over the finish line was measured with a stopwatch, and foot position was determined by the distance of the midpoint of the medial margin of each heel ink print from the midline straight-ahead path.
Analysis

For each stride, the midpoint of the horizontal distance (in centimeters) between the medial border of the two heels, called the mean mediolateral feet placement, was used for establishing the location of the subject along the walking path, with negative and positive signs assigned to leftward and to rightward deviations from the midline, respectively. Deviation from the straight-ahead path was determined every 2.5 m by calculating the distance between the mean mediolateral feet placement of the nearest step and the straight line originating from the starting point of locomotion (Fig. 1).

The following variables were extracted for the analysis: (1) the angle of deviation at 10 m, defined as the final angle; (2) the angle of veering per step, derived from the division of the value of the final angle by the number of steps in the corresponding trial; (3) the root mean square (RMS) of deviations from the 10-m path, calculated by measuring the respective mean feet placements at the four successive points of 2.5, 5, 7.5, and 10 m along the straight midline trajectory; (4) the RMS deviation per step obtained by dividing the RMS of the whole trajectory into the number of the corresponding steps; (5) the total sum of deviations along the 10-m course obtained by summing the absolute mediolateral distances between the mean feet placement at the four successive measurement points along the progression line (note that the summed deviations were of the distance between successive mean feet placement and not of their distance from the midline path); and (6) deviation per step, obtained by dividing the total sum of deviations into the number of steps in the corresponding trial.

Analysis of variance with repeated measures was used to determine the difference between the effects of the three tested speeds, measured in the second trial, on the six variables of interest. Significant results were followed by pair-wise paired t-test comparisons. Statistical significance was established at $P \leq 0.05$, whereas marginal significance was indicated by $P$ values of 0.06–0.08.

The number of steps and the time taken to traverse the 10-m path in each trial were also used to calculate cadence and mean step length. Analysis of variance followed by pair-wise t-test comparisons was also used to describe differences between the three speeds in each of the trials.

RESULTS

The information for speed, step length, and step frequency—representing the self-selected temporal and spatial gait variables of the healthy blindfolded adults in each of the two trials—are presented in Figures 2–4. The difference between the three speeds was significant ($F = 82.8, P < 0.0001$), as were the separate pair-wise comparisons in each trial ($P$ values were between 0.001 and 0.03). Note that subjects increased their locomotion speed in the second trial relative to the first in each of the three speeds (Fig. 2), probably reflecting an increase in confidence of task performance. The increase in gait speed was associated with increased step length (Fig. 3) and cadence (Fig. 4). Mean step length was 0.60 and 0.65 m, and 0.83 and 0.90 m for slow walking and running, during the first and second trial, respectively. Obviously, step length in all speed conditions increased when performing the trial the second time. The differences in step length between the three speeds were significant ($F = 34.25, P < 0.0001$), with all pairwise comparisons within each trial pointing to significant differences in step length between the different speeds ($P$ values between 0.0001 and 0.01). The one exception was that the difference between step length during fast locomotion and running in the second trial was not significant ($P > 0.08$). Step frequency ranged from 1.76 to 3.1 steps/sec and from 1.9 to 3.5 steps/sec during slow locomotion and running for the period of the first and second trial, respectively. Thus, once more, the second trial was characterized by increased cadence in all three speeds relative to the first trial. The differences in cadence between the three
speeds were significant \( F = 23.1, P < 0.0001 \), with pair-wise comparisons indicating significant differences between each pair of speeds in each of the trials \( (P \) values between 0.0001 and 0.01). The one exception was for the comparison between fast walking and running in the second trial, which yielded a nonsignificant difference \( (P > 0.08) \).

The RMS deviations in each of the two trials consistently decreased with the increase in progression speed (Fig. 5). The decrease in RMS deviation was especially prominent during running in the second trial, presumably indicating greater comfort in performance relative to the first trial. The raw data of the slow walking and running measurements during the second trial of all subjects are presented in Figure 6.

The final angles of deviation for slow walking, fast walking, and running speeds were 4.6 ± 2.4, 3.1 ± 2.9, and 1.8 ± 1.2 degrees, respectively. These differences were significant \( F = 6.65, P < 0.01 \) insofar as the angles of deviation for slow walking were significantly larger than those for running \( (t = 3.59, P < 0.004) \), whereas the deviations in fast locomotion were not statistically different from those of either slow locomotion or running. When the final angle of deviation was converted to veering per step, the deviations for slow walking, fast walking, and running speed were 0.29 ± 0.16, 0.24 ± 0.2, and 0.16 ± 0.12 degrees per step, respectively. Veering per step was almost significantly smaller for running than for slow locomotion \( (t = 2.07, P < 0.06) \), whereas the com-
FIGURE 4  Mean and standard deviation of the cadence of the subjects at self-selected speed during each of two trials of slow locomotion, fast locomotion, and running.

FIGURE 5  Mean and standard deviation of the root mean square (RMS) deviation from the straight-ahead 10-m trajectory in the six trials. The left three bars represent the first trial of three speeds (slow1, fast1, run1), and the right three bars represent the second trial of three speeds (slow2, fast2, run2).
parisons involving fast locomotion again yielded nonsignificant findings.

The RMS deviations (Fig. 5) were significantly smaller in the running speed than in the fast and slow walking speeds ($F = 8.48, P \leq 0.007$). A significant difference was found between slow walking and running ($t = 3.86, P \leq 0.003$) rather than between fast walking and either slow walking or running. The RMS deviations per step for the slow walking and running speeds were $3.1 \pm 1.5$ and $1.7 \pm 1.0$ cm, respectively, with these values being significantly different from each other ($t = 2.61, P \leq 0.024$).

The total deviations for slow walking, fast walking, and running speeds were $86 \pm 40, 76 \pm 63,$ and $41 \pm 16$ cm, respectively. Significant differences were found between slow walking and running ($t = 3.31, P < 0.007$), and marginally significant differences were indicated between fast walking and running ($t = 1.9, P < 0.08$). The total deviations per step were $5.7$ and $3.7$ cm for the slow walking and running speeds, respectively. The differences in the total deviations per step between these two speeds were significant ($t = 2.2, P \leq 0.05$), whereas the analysis involving fast walking yielded nonsignificant findings.

DISCUSSION

The findings indicate that in healthy blindfolded individuals, larger departures from the straight trajectory are associated with slow overground walking than with running. It seems, therefore, that the scope of observations applied only to conditions of unbalanced vestibular or misleading visual information$^8,9,11$ should be broadened to include healthy subjects as well. Similar to the results for subjects with distorted optic flow, which were shown to be valid in relation to time and to distance variables,$^11$ our results for healthy individuals point to changes in cadence and step length. The fact that normalization by cadence alone was not shown in previous research to depict differences in path integration in healthy subjects$^9$ indicates that enhancing cadence without increasing step length does not necessarily affect path integration in healthy individuals.

One limitation of this study is that the results are based solely on one trial of task performance in

![FIGURE 6 Raw data of the 12 subjects while slowly walking (triangles) and while running (circles) with their eyes closed along the 10-m path. Data are from the second trial in each speed.](image-url)
each speed, as the first trial was used to familiarize the subjects with the difficult task of forward ambulation in the absence of vision. These results underscore the need to include more trials in future studies. In addition, although the differences between the slow locomotion and running speeds were obvious in all comparisons, the results pertaining to the fast locomotion speed were not unequivocal. Perhaps the orders given to adopt a fast speed were somewhat ambiguous, as the subjects were not explicitly instructed to walk as fast as possible. Thus, the large range and variability associated with the fast locomotion speed (Fig. 5) are probably the main reasons behind the nonsignificant findings related to that speed. Worthwhile mentioning in this regard is a recent study showing that patients who had acute unilateral vestibular deficits with their eyes open were able to maintain a straight-ahead direction of locomotion when adopting a fast speed but not when walking at their normal speed.20

Progression speeds of the current blindfolded individuals during slow walking and running speeds were comparable with those of subjects wearing prisms that distorted optic flow11 (about 1 and 3 m/sec for slow walking and running, respectively). The values of the final angle of deviation found in the present study were smaller than those reported for subjects who received unilateral galvanic stimulation.9 Thus, these results seem to indicate lesser deviations from the straight-ahead path of our healthy subjects as compared with subjects receiving unilateral vestibular stimulation. Although this comparison is obviously flawed due to the differences in the experimental settings and designs, it does provide a reasonable indication of larger deviations in subjects with abnormal vestibular stimulation. However, it must be considered that the final angle in subjects with unilateral sensory malfunctions seems to reflect the endpoint of a continuous trajectory,4,9 whereas the final angle of the current healthy subjects was measured at the termination point of a less smooth progression course with occasional rightward or leftward deviations between successive steps. For this reason, the RMS distance from midline and the total mediolateral deviations, especially when compared per step, seem to be a stronger indication of the speed-associated differences in path integration.

Lateral foot placement is a control mechanism for lateral balance13,15 and is proportional to the mediolateral acceleration of the center of mass.18 Although a biomechanical analysis of the acts of walking and running is beyond the scope of the present study, the relative differences in mediolateral accelerations of the body between walking and running may clarify the associated differences in lateral foot placement. A simple explanation to better path integration with increased forward speed is the lack of double stance in running, which enables the foot to be placed closer to the midline. Conversely, the occurrence of double support in walking means that the feet have to be placed further away from the midline.21 Further research including kinetic measurements is obviously needed for better elucidation of the mechanism behind speed-dependent path integration in locomotion.

Generalization of the current findings is hampered by the small number of subjects taking no more than 20 steps in either trial. Considering the fact that accurate estimation of step kinematic variability during treadmill walking requires at least 400 steps,14 the scope of this work is obviously limited. Furthermore, as can be seen in Figure 6, the differentiation between the trajectories of slow walking and running is gradually enhanced with the increase in forward speed. Because subjects started from a standing position, it was only at a point about 5 m from the initiation of locomotion that the slow walking trajectory started to substantially deviate from that of running. Therefore, it is recommended that similar studies with longer progression lines available for testing be conducted in the future.

Brandt et al.8,10,22 offered a neurophysiologic explanation for the relationship between path integration and forward ambulation speed, arguing that vestibular or visual inputs are differentially weighted by the central nervous system, depending on the speed of locomotion. Consequently, they maintained that these stimuli become progressively more inhibited with faster progression speeds, allowing more automatic control by lower spinal centers to take place. The current similar findings in healthy individuals show that a disregard of the differences between step characteristics in walking vs. running speeds is unjustified. It is clear that a biomechanical analysis, with the monitoring of mediolateral acceleration of the center of mass in several locomotion speeds and concurrent foot placement, is required to deepen our understanding of the relationship between path integration and locomotion speed in subjects with unilateral vestibular deficits.

REFERENCES


Effect of Plantar Micromechanical Stimulation on Cardiovascular Responses to Immobility

ABSTRACT


Objective: We investigated the cardiovascular responses of adult women to the influence of extended quiet sitting and the extent to which these responses may be reversed by micromechanical stimulation of the plantar surface.

Design: The cardiovascular responses of 20 healthy adult women (mean age, 55.9 ± 4.45 yrs) were observed during quiet sitting with and without exposure to a plantar-based micromechanical stimulation. Beat-to-beat heart rate via electrocardiogram was acquired along with preexposure and postexposure blood pressures, from which heart rate variability and mean arterial pressure were determined. Seven stimulus frequencies (0, 15, 22, 44, 60, 90, and 120 Hz, all at 0.2 × g, peak to peak) were tested on each subject.

Results: Over one-half of the women tested (11/20) exhibited a significant resting tachycardia (mean, 8.3 ± 0.5 beats/min) with a corresponding decline in their systolic blood pressure (9.45 ± 1.8 mm Hg) after 20 mins of quiet sitting. Plantar stimulation at 44 Hz (25 μm, peak to peak) was able to completely reverse the effect of immobility in this group, resulting in a heart rate decline of 2.5 beats/min (P < 0.0001) and a decrease of only 1 mm Hg in systolic pressure (P = 0.006).

Conclusion: We interpret these results to suggest that the immobility of quiet sitting has a profound effect on the cardiovascular systems in a large fraction of otherwise healthy women, perhaps due to inadequate muscle tone leading to venous insufficiency. Simple external stimulation of the plantar surface seems to be capable of preventing these cardiovascular stress-based responses.

Key Words: Immobility, Postural Stress, Cardiovascular System, Plantar Stimulation
Immobilization exerts profound stresses on numerous physiologic systems. The ability of extended bed rest to instigate significant muscle wasting (sarcopenia) and bone loss (osteopenia), for example, has long been known. In addition, the effect of the orthostatic stresses associated with quiet standing has been well documented. Upright posture significantly elevates the hydrostatic pressure in the peripheral vascular supply, resulting in both increased fluid extravasation and caudal venous blood collection. This blood pooling is, in part, compensated for by reflex-mediated vasoconstriction, and, at least in young healthy individuals, venous and lymphatic pooling is reduced by the actions of the skeletal muscle pump, without which systemic cardiac output declines substantially, resulting in tachycardia and compromising orthostatic tolerance.

For the majority of the American population, extended bed rest or long bouts of quiet standing are not common, although in some occupations, extended periods of relatively quiet standing can be required. Instead, modern life involves extended periods of sitting during the typical day, in the office, in cars and airplanes during long-distance travel bouts, and at home due to the ubiquity of passive entertainment options. The immobility of quiet sitting as a physiologic stress has undergone far less investigation as compared with bed rest or the orthostatic stress of standing; nonetheless, studies of quiet sitting suggest similar effects to those of other forms of immobility. In recent tilt-table studies investigating the influence of a 35-degree upright tilt (equivalent to sitting upright) on blood and interstitial fluid flows, we observed that plantar micromechanical stimulation was able to normalize blood flow in immobile individuals. We hypothesized, therefore, that a similar plantar stimulation may serve as an effective means to prevent peripheral fluid accumulation in individuals during quiet sitting, particularly those with inadequate compensatory mechanisms, thereby enhancing cardiovascular function in these afflicted individuals.

To address this hypothesis, we investigated cardiovascular responses to quiet sitting and the extent to which plantar micromechanical stimulation could prevent fluid pooling and, correspondingly, the deleterious cardiovascular responses to this stress. Because orthostatic intolerance is more common in women, we focused our investigation on an adult female population. Furthermore, we utilized a range of plantar stimulation frequencies in this study to determine whether the observed cardiovascular responses could be optimized.

MATERIALS AND METHODS

This investigation conformed with the principles outlined in the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board’s Committee on Research Involving Human Subjects at the State University of New York, Stony Brook, and was performed in the University Health Sciences Center in Long Island, NY, from March through early August 2002. During screening, subjects’ age, height, and weight were obtained.

Subjects and Study Design

The entrance criteria for this clinical study were healthy adult women with no current fractures, peripheral vascular disease or systemic illness, and the capability of providing informed consent. From an initial upright mobile position, lasting for a minimum of 5 mins, the subjects sat down in a relaxed position with their spine against a chair back. The subjects’ feet (shoeless) were positioned on a stimulation platform that was raised approximately 8 cm above floor level, and chair height was positioned so that the subjects’ knees were at an approximate 90-degree angle. The stimulation platform permitted exposure of the plantar surface of the subjects’ feet to micromechanical stimulation at any one of six frequencies at a time, 15, 22, 44, 60, 90, and 120 Hz, this frequency range being selected so as to be centered around the normal receptive range of somatosensory cutaneous mechanoreceptors of the foot. Stimulus acceleration was kept constant as a function of frequency so as to keep the applied dynamic force constant, though this resulted in different displacements of the stimulus platform at each stimulus frequency. Peak-to-peak accelerations of \( \sim 0.2 \times g \) (\( g = 9.8 \text{ m/sec}^2 \)) were used throughout the study, corresponding to peak displacements of approximately 110 \( \mu \text{m} \) at the lowest frequency utilized (15 Hz) and a peak displacement of approximately 1.7 \( \mu \text{m} \) at the highest frequency utilized (120 Hz). Correspondingly, peak displacements at 22, 44, 60, and 90 Hz were 50, 13, 7, and 3 \( \mu \text{m} \), respectively. Each subject also completed a 0-Hz (no vibration) control exposure.

The experiment was executed using a randomized, one-factor design to eliminate any potential effect of the training. The study subjects returned once each week for testing, with the seven test frequencies being randomized and conducted with one exposure frequency each week. To ensure that variations in biorhythmic dynamics did not influence the results, the tests were performed on each respective subject at approximately the same time of the day.

Cardiovascular responses were recorded for a...
period of 20 mins to provide adequate time for plasma volume to equilibrate after a change in stance. Subjects were asked to minimize their arm and leg movements during the recording period, though conversation was permitted. Heart rate was recorded continuously by an electrocardiograph by using wrist electrodes (Heart Rhythm Scanner, Version 2.0, Biocom Technologies, Poulsbo, WA). Blood pressure values were measured from the arm using a semiautomatic digital blood pressure monitor (HEM 741C, Omron Health Care, Vernon Hills, IL). To minimize the perturbations of the subjects during the therapy, blood pressures were obtained, in duplicate, only at the beginning and end of the 20-min treatment duration. The first set of previbration measurements was acquired within 1 min after the subject sat from the standing position and removed her footwear. A graphical illustration of the recording protocol is presented in Figure 1.

**Analysis**

Changes in heart rate over the 20 mins of exposure were determined by converting the interbeat R–R interval data stream into beat-to-beat heart rate. These were averaged for the first and the last 3 mins of the session, and the difference was calculated. Heart rate variability (HRV) was characterized using the standard deviation of cardiac cycle length, which was calculated from each 2-min interval of the acquired real-time, beat-to-beat interval data using custom software code in Matlab V 6.5 (Math Works, Natick, MA). Time-dependent changes in the standard deviation of cardiac cycle length (HRV) were then evaluated by linear regression. These changes in HRV were used in a quadratic regression model to estimate the frequency dependence of the physiologic response to the plantar stimulation. HRV data were also utilized to evaluate changes in respiratory rate through detection of the spectral peak in the 0.18- to 0.4-Hz range of the HR power spectrum. The duplicate systolic and diastolic blood pressure values were averaged, and the respective variations over the treatment duration were plotted as a function of stimulation frequency. Mean arterial pressure (MAP) was calculated as diastolic pressure + 1/3 × pulse pressure, and the change in MAP over the 20-min exposure period was determined. Changes in the mean preexposure and postexposure values of systolic pressure and MAP were also evaluated by polynomial (quadratic) regression against vibration frequency. Regression analyses were carried out utilizing Origin Version 7.0 (Origin Lab, Northampton, MA) and statistical analyses were confirmed with Sigma Stat Version 10.0 for Windows (SPSS, Chicago, IL). Within-group multiple comparisons were performed using analysis of variance. Data are expressed as mean ± standard error of mean. Statistical significance was accepted at \( P < 0.05 \).

**RESULTS**

A total of 20 healthy adult female volunteers aged 30–75 yrs (mean age, 55.9 ± 4.45 yrs) were recruited for the study and completed the experimental protocol, having undergone a minimum of four of the seven recording sessions. Of the possible 140 trials for these 20 volunteers for the seven stimulus frequencies, a total of 105 trials were accomplished due to missed sessions by some participants. Randomization resulted in the highest participation for the 22-Hz test frequency, and the lowest participation at the test frequency of 120 Hz. The plantar stimulation was readily perceived by the participating subjects, except for the 120-Hz stimulus, which was reported to be barely perceptible. In all of the cases, the subjects reported a “pleasant” stimulus sensation. The subjects had no difficulty remaining seated quietly for the 20 mins, and no experimental complications were observed in any of the trials in this investigation.

Changes in heart rate during quiet sitting were dependent neither on subject body mass index \((P = 0.1)\) nor on subject age, but a distinct bipolar distribution in heart rate changes was evident (Fig. 2). Gaussian curve fitting indicated that these results were unlikely to reflect simply normal variation but rather a bimodal distribution \((R^2 = 0.05, \text{ unimodal}; R^2 = 0.66, \text{ bimodal})\). Approximately one
half (n = 9) of the subjects demonstrated a slight decrease in heart rate (mean, 2.8 ± 0.74 beats/min) after their assuming a seated position. The remaining subjects (n = 11) demonstrated a significant increase in heart rate (mean increase, 8.3 ± 0.5 beats/min) over the 20 mins of quiet sitting. As both these subgroups had similar heart rates and blood pressures at the start of the sitting regimen (Table 1), we defined the group with a declining heart rate as normal, given the reduction in muscular activity after cessation of locomotion would be expected to result in decreased cardiac output and therefore heart rate, and the group with the significantly increased heart rate as manifesting resting tachycardia. Given these two distinct responses, in subsequent analyses we evaluated the normal and tachycardia subpopulations separately.

Micromechanical plantar surface stimulation had essentially no effect on heart rate in the normal subpopulation (Fig. 3, left). However, the plantar stimulation significantly inhibited the elevation in heart rate in the tachycardia group at all frequencies tested (Fig. 3, right). Moreover, at 44 Hz, plantar stimulation was able to completely inhibit the tachycardia, resulting in a decrease in the average heart rate by 2.5 beats/min (P < 0.0001).

Although no effect of plantar stimulation on heart rate was observed in the normal population, HRV was significantly influenced by this stimulation (Fig. 4, left). Indeed, at all frequencies of vibration, HRV was elevated to levels at or above the HRV calculated at the start of the recording period. Similarly, plantar vibration prevented the depression in HRV observed in the tachycardia cohort (Fig. 4, right). In this latter subpopulation, efficacy of the plantar stimulation to inhibit the depression in HRV was limited to the 44-Hz frequency (P = 0.002).

In the normal subpopulation, a significant decrease in the systolic blood pressure of 7.75 ± 1.6 mm Hg (P < 0.01) (Fig. 5, left) and a decrease of 2.5 mm Hg in diastolic pressure were observed (data not shown), resulting in an average decrease of 6 mm Hg in MAP (Fig. 6, left). Plantar vibration at 44 Hz inhibited these decreases in blood pressure, resulting in normalization of the systolic pressure (P = 0.03) and preventing the MAP from decreasing >2 mm Hg (P = 0.003).

In the tachycardia subpopulation, average systolic blood pressure declined 9.5 mm Hg (Fig. 5, right) and diastolic pressure decreased 2.7 mm Hg (data not shown), resulting in a depression in MAP of 6.2 mm Hg (Fig. 6, right). Plantar stimulation at all frequencies mitigated these depressions in blood pressure, with efficacy peaking at the 44-Hz stimulus frequency. Systolic pressure was essentially normalized with the 44-Hz stimulus (P = 0.002), with the overall response showing a significant frequency dependence (P = 0.006, R² = 0.96). Correspondingly, the 44-Hz stimulus resulted in a depression in MAP of only 1.5 mm Hg (P = 0.03) and again demonstrated a significant frequency dependence of the stimulus (P = 0.05, R² = 0.85).

Analysis of the HRV spectrum to extract respiratory frequency showed that respiration rates were identical for both the normal and tachycardia group during the control exposures (0.25 ± 0.01 Hz). Plantar stimulation, even at 44 Hz, the stimulus at which the largest cardiovascular responses were observed, had no significant effect on respiration rate in either the normal (0.24 ± 0.01 Hz) or the tachycardia group (0.25 ± 0.01 Hz).

**DISCUSSION**

In previous studies on cardiovascular responses to upright tilt, we observed that a plantar-

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**TABLE 1** Demographic and baseline characteristics of subjects

<table>
<thead>
<tr>
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<th>Normal Subjects</th>
<th>Tachycardia Subjects</th>
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</thead>
<tbody>
<tr>
<td>No. of subjects, n</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Age, yrs (mean ± SE)</td>
<td>52 ± 4</td>
<td>54 ± 4</td>
</tr>
<tr>
<td>Initial systolic pressure, mm Hg</td>
<td>Control 122.9 ± 2.1</td>
<td>122.4 ± 4.4</td>
</tr>
<tr>
<td></td>
<td>44 Hz</td>
<td>122.3 ± 3.4</td>
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<tr>
<td>Initial diastolic pressure, mm Hg</td>
<td>Control 77.1 ± 1.7</td>
<td>79.4 ± 2.2</td>
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<tr>
<td></td>
<td>44 Hz</td>
<td>77.9 ± 2.1</td>
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<tr>
<td>Initial heart rate, beats/min</td>
<td>Control 77.7 ± 3.8</td>
<td>77.2 ± 3.1</td>
</tr>
<tr>
<td></td>
<td>44 Hz</td>
<td>77.1 ± 3.8</td>
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Based micromechanical stimulus was capable of inhibiting the reduction in peripheral blood flow commonly associated with this orthostatic stress. This observation may have implications for the prevention of orthostatic intolerance in individuals undergoing long periods of quiet standing; however, the usual remedy for such problems is simply to have the individual sit down. Of greater practical concern are those individuals who find the immobility associated with quiet sitting a significant stress, and so we focused this investigation on characterizing the responses of the cardiovascular system to the influences of both quiet sitting and the extent to which plantar-based micromechanical stimulation was able to inhibit the influence of this stress. Quiet sitting is not normally thought of as a significant orthostatic stress. The transition from ambulatory activity to quiet sitting results in decreased muscle demand for oxygen and therefore cardiac output, which should be evidenced in a decreased heart rate. Consistent with this expectation, we observed that approximately one half of the women tested demonstrated a decreased heart rate during the 20 mins of quiet sitting. However, sitting upright posture still leads to the translocation of thoracic blood volume into the lower limbs, requiring both peripheral venoconstriction and skeletal muscle pump activity to maintain normal systemic blood pressure and heart rate, such that lack of either or both of these adaptive processes can lead to resting tachycardia. Correspondingly, over one half of the adult women we tested developed a pronounced tachycardia (>8 beats/min), concomitant with a substantial (~10 mm Hg) decrease in systolic blood pressure. The transition from upright to quiet sitting results in decreased muscle vasoconstriction and increased blood pooling in the lower extremities, leading to a decreased systemic blood pressure and heart rate. Correspondingly, over one half of the women tested demonstrated a decreased heart rate during the 20 mins of quiet sitting. However, sitting upright posture still leads to the translocation of thoracic blood volume into the lower limbs, requiring both peripheral venoconstriction and skeletal muscle pump activity to maintain normal systemic blood pressure and heart rate, such that lack of either or both of these adaptive processes can lead to resting tachycardia.

**FIGURE 3** Influence of quiet sitting and plantar stimulation on heart rate during extended sitting. Top, plantar stimulation had minimal effects on heart rate in the normal group. Bottom, in the tachycardia group, plantar stimulation reduced the tachycardia at all stimulus frequencies and normalized the heart rate response at 44 Hz.

**FIGURE 4** Influence of quiet sitting and plantar stimulation on heart rate variability. Heart rate variability, as calculated by the standard deviation of cardiac cycle length (SDNN), shows a distinct depression in both the normal and tachycardia groups during the 20 mins of quiet sitting. Top, plantar stimulation returns heart rate variability to levels similar to those when the subjects first sit down, with all stimulus frequencies being equally effective. Bottom, in the tachycardia group, the efficacy of the plantar stimulation to inhibit the decrease in heart rate variability was frequency dependent ($P = 0.002$, $R^2 = 0.98$), with the 44-Hz stimulus frequency significantly increasing heart rate variability as compared with the controls ($P = 0.002$).
crease in systolic blood pressure. The distribution of heart rate shifts we observed does not seem to represent a normal distribution around a mean change in heart rate but a distinct bimodal distribution. The cardiac response data, therefore, leads us to suggest that, for a significant fraction of adult women, the immobility associated with quiet sitting represents a significant orthostatic challenge with peripheral regulatory mechanisms incapable of providing full compensation.

Numerous physiologic mechanisms could be responsible for these observed cardiovascular responses to immobility, including increased venous capacitance, depressed autonomic function, decreased cardiac function, and reduced skeletal muscle tone. Given the low level of muscle activity during quiet sitting, it is reasonable to consider lack of skeletal muscle pump activity as playing a significant role in the responses of the tachycardia group. It is reasonable to hypothesize, therefore, that the plantar stimulation we found to be capable of preventing this cardiovascular response is serving to enhance the efficiency of the skeletal muscle pump. Because the stimuli we utilized provided a continuous neuromuscular stimulus in the range of 15–120 Hz, it is unlikely that muscle contraction at these frequencies could serve to directly increase muscle pump activity. More likely, these stimuli enhance low-level tonic muscle activity in the postural muscle fibers, thereby enhancing the efficacy

FIGURE 5 Influence of quiet sitting and plantar stimulation on systolic blood pressure. Top, the normal population experienced an average decrease of 7.8 mm Hg in systolic blood pressure during 20 mins of quiet sitting, and plantar stimulation at 44 Hz significantly inhibited this decrease (P = 0.03), although no clear frequency dependence was observed (R^2 = 0.84, P = 0.06). Bottom, the tachycardia group experienced an average decrease of 9.5 mm Hg in systolic pressure. Systolic pressure in the tachycardia group responded to plantar stimulation in a highly frequency-dependent manner (R^2 = 0.96, P = 0.006), with the 44-Hz stimulus essentially eliminating the decrease in systolic pressure (P = 0.002).

FIGURE 6 Influence of quiet sitting and plantar stimulation on mean arterial blood pressure. The declines in mean arterial pressure as a result of quiet sitting were remarkably similar (~6 mm Hg) for both the normal (top) and tachycardia (bottom) groups. Plantar stimulation inhibited this decrease in mean arterial pressure in a frequency-dependent manner (normal group: R^2 = 0.91, P = 0.02; tachycardia group: R^2 = 0.85, P = 0.05).
of skeletal muscle pump activity by improving venous sufficiency.

Consistent with the suggestion that the plantar stimulus may be triggering muscle activity is our observation that the 44-Hz stimulus is particularly efficacious in preventing the tachycardia and blood pressure decrease. The stimulus of 44 Hz is very near the central response frequency of the Meissner’s corpuscles, an afferent cutaneous mechanoreceptor, well distributed on the plantar surface, that play a critical role in the neuromuscular feedback necessary for maintaining upright posture. Moreover, the muscle fiber groups most commonly associated with stimulation in this frequency range (15–50 Hz) are the fast oxidative-glycolytic fibers (type II-A). Because of the high level of vascularization of type-II-A fibers and because of their chronic contractile activity, this fiber group has been implicated in playing a critical role in skeletal muscle pumping during postural activities. Electromyographic measurements would be required to confirm the possible involvement of this fiber group.

Despite the remarkable similarity between the observed frequency responses in our studies and the frequency response characteristics of Meissner’s sensory corpuscles, alternative coupling mechanisms may be responsible for the observed results. Primary muscle spindle receptor endings show a distinct increase in sensitivity near 30 Hz, with thresholds well below the displacements utilized in this study, and thus, muscle spindles may be directly detecting the vibrational stimulus. Because we utilized a constant peak acceleration as a function of frequency, the decreased responsiveness at increasing frequency may be a result of the decreasing amplitude of the stimulus at higher frequency. Alternatively, it is also possible that this stimulus has regional effects on tissue blood flow or vascular resistance. Finally, it is possible that the vibrational stimulus travels sufficiently far up into the body to directly influence vagal activity and thereby the cardiac function. Studies are underway to determine the role of cutaneous reception in this response and the changes in lower limb skeletal muscle activity during plantar stimulation.

Although the cardiovascular response to orthostatic stress is usually measured in subjects moving from supine to upright standing, representing, for example, waking and rising from bed, the transition from walking/standing to sitting is a far more common daily activity. The cardiovascular responses we observed here may have profound implications given the decreased venous flow, particularly in the lower limbs, is considered a major cause of pulmonary emboli, the primary cause of death in as many as 200,000 individuals each year in the United States. Hypotension has also been implicated in a variety of other common clinical conditions, including syncope, chronic fatigue syndrome, and osteoporosis. Hence, these outcomes may have important implications from the perspective of occupational health maintenance and preventative medicine. That the tachycardia and depressed systolic pressure can so readily be inhibited by a simple intervention such as plantar stimulation is encouraging in light of the very high fraction of individuals who seem to manifest a lack of tolerance to quiet sitting.

Although these results are supportive of our initial hypothesis, certain aspects of the experimental design limit the interpretation of these results. First, although neither age nor body mass index of our subjects distinguished the tachycardia group from the normal group, the correlation to body mass index suggested a trend that should be pursued through study of a larger population of women, as the existence of such a relationship may provide an easily obtained indicator of those most at risk of orthostatic tachycardia. Also, we only looked at this response in women, knowing to what extent men exhibit similar responses would be an important extension of this work. In addition, only previbration and postvibration blood pressures were acquired in this investigation. Continuous blood pressure recordings would provide additional insight into the dynamics of the systemic response to the plantar stimulus. Similarly, extending recordings beyond 20 mins would provide knowledge of the ability of plantar vibration to maintain normal heart rate and blood pressure in response to a sustained seated activity, such as encountered during long-distance travel. In addition, it would be useful to know whether the plantar stimulation is effective in reversing the effects of sitting on the cardiovascular system or is only capable of inhibiting the development of these effects. Further studies will be required to address these issues.

CONCLUSION

We suggest that these initial findings are consistent with the hypothesis that the immobility associated with quiet sitting can produce qualitatively similar stresses to those associated with quiet standing, resulting in a significant depression in systolic pressure and tachycardia in a large fraction (~50%) of adult women. Furthermore, the results support the hypothesis that plantar-based micro-mechanical stimulation at the appropriate frequency can largely eliminate the effects of this cardiovascular stress. We suggest that these observations may have significant implications given the extended durations over which many Americans remain seated and relatively immobile during the course of their day in the workplace, during passive
entertainment options, and during long-distance travel.

ACKNOWLEDGMENTS

We thank the volunteer subjects and the financial supporters.

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Effect of Trunk Flexion on the Occupant Neck Response to Anterolateral Whiplash Impacts

ABSTRACT

Objective: The purpose of this study was to determine the response of the cervical muscles to increasing low-velocity anterolateral impacts with the volunteer’s trunk flexed to the right and left.

Methods: A total of 20 healthy volunteers were subjected to left anterolateral impacts of 4.0, 7.6, 10.7, and 13.4 m/sec² and, sequentially, with trunk flexed either left or right. Bilateral electromyograms (EMGs) of the sternocleidomastoids, trapezius, and splenii capitis were recorded.

Design: At an acceleration of 13.4 m/sec², with the trunk flexed left, the left trapezius generated 48% of its maximal voluntary contraction EMG, whereas the right trapezius (contralateral to the left anterolateral impact) generated 38% of this variable. All other muscle generated ≤23% of their maximal voluntary contraction EMG, a significant difference from the trapezius (P = 0.005). Similarly, with the trunk flexed to the right under these same conditions, the left trapezius generated 26% and the right trapezius 35% of their maximal voluntary contraction EMG. Again, all other muscles generated significantly less EMG activity, ≤22% (P = 0.009). Overall, the EMG responses were of low magnitude compared with known data with the trunk in neutral posture in this direction of impact.

Conclusions: When the subject sits with trunk flexed out of neutral posture at the time of an anterolateral impact, the cervical muscle response is reduced compared with anterolateral impacts with the trunk in neutral posture.

Key Words: Neck Muscles, Electromyography, Accidents, Traffic, Whiplash Injuries
Previously in this journal, Fast et al.\(^1\) conducted a cadaveric study and reported on lumbar spinal strains associated with whiplash injury. As they note, many whiplash claims arise out of low-velocity collisions, but there is a paucity of biomechanical data concerning the biomechanics of spinal injury in low-velocity collisions. Physiatrists and other medical specialists are frequently involved in providing opinions dealing with a number of controversial topics concerning whiplash injury, a problem that costs billions of dollars each year in the United States alone and is an internationally recognized economic and healthcare burden.\(^2\) One question encountered by physiatrists asked to give medicolegal opinions is, “Did the accident cause the whiplash syndrome?” or “Are the patient’s symptoms consistent with the collision injury mechanisms?” As difficult as these questions may seem, one source of information for the clinician may come from engineering studies. A problem that has long been encountered, however, is that the pathology of the acute whiplash injury remains unknown, although the mechanism of acceleration and deceleration of the head is commonly used in the definition of the “whiplash injury mechanism.”\(^2\) Because the acute whiplash injury is not readily demonstrated in most cases in patients or volunteers in studies, engineering studies of low-velocity impacts often rely on outcome measures such as symptoms\(^3\) as a surrogate of injury, although this may be unreliable because symptoms may be nonspecific and, in fact, can arise in placebo collisions.\(^4\) Still, from available data of volunteers subjected to impacts,\(^3,5–13\) it seems likely that muscle responses to acceleration of the head are reasonable candidates for injury mechanisms.\(^15–18\) Although cadaveric and animal studies can define damage to tissue, muscle responses cannot be tested in cadaveric studies and thus require volunteers for study.

Given ethical concerns with subjecting volunteers to injurious neck perturbations, however, to conduct investigations elucidating the kinematics and electromyographic response in volunteers, we have used surface electromyography (EMG) combined with regression techniques modeled on very-low-velocity collisions. Using this approach, the results of the impact studies and the regression models are in good agreement with the available data concerning biomechanical response that has been gathered in previous, small studies of higher-velocity collisions.\(^14\)

Although this solves the ethical concerns, additional problems in deriving conclusions from volunteer impact studies arise from the fact that most research with volunteers concerns rear or frontal impacts, with few considering other directions of impact. Moreover, even rear and frontal impacts may be offset by some angle so that they are, for example, anterolateral or posterolateral impacts. Furthermore, patients often report that they were turned or twisted to one side at the time of impact, yet impact studies are conducted with the head and trunk in the neutral posture (i.e., the recommended driving posture).

Therefore, considering these more complicated impact scenarios is increasingly relevant in understanding what happens to people in road collisions. Previous volunteer studies of the cervical muscle response and head–neck kinematics to frontal impacts have indicated, for example, that the exact direction of frontal impact is relevant to the measured responses.\(^15–18\) In straight-on frontal impacts, the trapezius muscles show the greatest muscle response to head acceleration, bearing a greater proportion of the force of the neck perturbation than other neck muscles.\(^16\) It has also been shown, however, that anterolateral impacts (offset by 45 degrees) result in not only increased EMG generation in both trapezius, but the splenius capitis contralateral to the direction of impact also bears part of the force of the neck perturbation.\(^17,18\)

Again, these studies considered the occupant only in a neutral head and trunk posture. To address a void in current knowledge, we undertook an EMG study to repeat a previous study with anterolateral (45-degree offset) impacts but examined the cervical muscle response when the trunk is flexed forward and to the subject’s right and left to mimic circumstances of “out-of-position” vehicle occupants. To place the magnitude of the muscle response into perspective, with the assumption that a greater muscle contraction in response to impact indicates a greater risk of muscle injury, we compare the EMG responses with the subject’s maximal voluntary contraction EMG. It is assumed that EMG responses lower than the maximal voluntary muscle contractions are less likely to be injurious compared with impacts that cause EMG responses that exceed these physiologic maximum contractions.

**SUBJECTS AND METHODS**

The methods for this study of left anterolateral impacts (frontal impact offset by 45 degrees) with trunk flexed to the left or right are the same as that used for previous anterolateral impact studies.\(^16,17\)

**Sample**

A total of 20 healthy, normal subjects with no history of whiplash injury and no cervical spine pain during the preceding 12 mos volunteered for the study. The 20 subjects (ten women, ten men) had a mean age of 23.6 ± 3.0 yrs, a mean height of 172 ± 7.7 cm, and a mean weight of 69 ± 13.9 kg.
All were right-hand dominant. The study was approved by the University Research Ethics Board. Subjects were asked to report any symptoms at the time of impacts or at the 6-mo follow-up.

**Methods**

Active surface electrodes with ten-times on-site amplification were placed on the belly of the sternocleidomastoids, upper trapezius at C4 level, and splenius capitis in the triangle between sternocleidomastoids and trapezii bilaterally. The fully isolated amplifier had additional gain settings up to 10,000 times, with frequency response of DC-5 kHz and common mode rejection ratio of 92 dB. Before calibrating sled acceleration, the cervical strength of the volunteers was measured to develop a force-EMG calibration factor. The seated and stabilized subjects exerted their maximum isometric effort in attempted flexion, extension, and lateral flexion to the left and the right for force-EMG calibration, as described by Kumar et al.19,20

The acceleration device consisted of an acceleration platform and a sled (Fig. 1). The full details of the device and the EMG data collection are given elsewhere. After the experiment was discussed and informed consent obtained, the age, weight, and height of each volunteer was recorded. The volunteers then were seated on the chair with a lap seatbelt only so that they could then be positioned out of neutral posture. Subjects were then outfitted with triaxial accelerometers (CXL04M3, Crossbow Technology, San Jose, CA) on their glabella and the first thoracic spinous process. Another triaxial accelerometer was mounted on the sled. The accelerometers had a full-scale nonlinearity of 0.2%, dynamic range of ±500 mV/g, resolution of 5 mg within a bandwidth of DC-100 Hz, and a silicon micromachined capacitive beam that was quite rugged and extremely small in die area. Subjects were then exposed to left anterolateral impacts (45-degree offset frontal impact) with their trunk flexed forward and to either their left or right at accelerations of 4.0, 7.6, 10.7, and 13.4 m/sec² generated in a random order by a pneumatic piston (Fig. 2). We did not attempt to have the subjects completely relaxed with the neck fully flexed (i.e., slumped posture), as we expected this would not be typical of road collisions. We positioned each of the volunteers in 45 degrees of flexion and 45 degrees of rotation either to the left or to the right. The subjects were asked to assume a position of trunk flexion (forward and lateral) and to look down at their right or left foot. As shown in previous studies, there is a greater muscle response to impact if all visual and auditory cues are blocked before impact. This is referred to as an unexpected impact status, although even though the volunteers know they will experience an impact at some time. The expected impact status of the previous anterolateral impact study to which we are comparing means the subjects did not have any blocking of auditory and visual cues. The impact severity and posture positions were randomly varied between the four levels of acceleration, as was done previously. The accelerations involved in this experiment are again low enough that injury is not expected, but the acceleration impulse is delivered in a way that mimics the time course seen in motor vehicle collisions and occurs fast enough to produce eccentric muscle contractions.

The data on the peak and average accelerations in all three axes of the sled, shoulder, and head for all four levels of accelerative impacts were measured. In the analysis, the sample of volunteers was collapsed across sex because preliminary analysis showed no statistically significant differences in the EMG amplitudes between the men and women. The sled velocity and its acceleration subsequent to the pneumatic piston impact were measured. All timing data were referred to the solenoid firing.
The time of the peak acceleration was measured. Also, the time relations of the onset and peak of the EMG were measured and analyzed. The time to onset was determined when the EMG perturbation reached 2% of the peak EMG value. This method was chosen to avoid any false positives due to tonic EMG. This method was in agreement with projection of the line of slope on the baseline. EMG amplitudes were normalized against the subjects’ maximal voluntary contraction EMG recorded before accelerative impacts.\(^{19,20}\) The ratio percentage of the EMG amplitude vs. the maximal contraction normalized EMG activity for that subject allowed us to determine the force equivalent generated due to the impact for each muscle.

Statistical analysis was performed using the SPSS statistical package (SPSS, Chicago, IL) to calculate descriptive statistics, correlation analysis between EMG and head acceleration, analysis of variance of the time to EMG onset, time to peak EMG, average EMG, and the force equivalents. In addition, a linear regression analysis was performed for the kinematic variables of head displacement, head velocity, head acceleration, and EMG variables. Initially, all regressions were carried out to the level of exposure, and subsequently, they were extrapolated to twice the applied acceleration. Significance is defined at a \(P\) value of \(<0.01\); this level was chosen to correct for the fact that we conducted multiple comparisons. A trend is considered when the \(P\) value lies between 0.01 and 0.05.

**RESULTS**

The kinematic response of the head to the four levels of applied acceleration are shown in Figure 3. As anticipated, an increase in applied acceleration resulted in an increase in excursion of the head and accompanying accelerations. The accelerations in these impacts were not associated with any reported symptoms in the volunteers after the experiment and up to 6 mos later.

In a left anterolateral impact, with the trunk flexed 45 degrees to the right or left, the trapezius were the most active of all muscles (\(P = 0.004\)). That is, in left trunk flexion at the time of impact, the left trapezius generated 48% of its maximal voluntary contraction EMG, whereas the right trapezius (contralateral to the left anterolateral impact) generated 38% of this variable. All other muscles generated \(<23%\) of their maximal voluntary contraction EMG, a significant difference from the trapezius (\(P = 0.005\)). Similarly, with the trunk flexed to the right under these same conditions, the left trapezius generated 26% and the right trapezius 35% of their maximal voluntary contraction EMG. The remaining muscles generated \(\approx 22\%\) of their maximal voluntary contraction EMG, a significant difference from the trapezius (\(P = 0.009\)).

Although the magnitude of the right splenius capitis was numerically higher, than the left splenius capitis, this was not statistically significant. This trend suggests that the splenius capitis contralateral to the direction of impact has a greater EMG response.

The normalized EMG for the sternocleidomastoid, splenius capitis, and trapezius muscles are shown in Figure 4. As the level of applied acceleration in the impact increased, the magnitude of the EMG recorded from the trapezius increased progressively and disproportionately compared with other muscles (\(P = 0.009\)). With trunk flexed to the right or left, the sternocleidomastoid muscles were the least active in response to the EMG (\(P = 0.008\)).

To place the magnitude of the EMG responses in perspective, in Figure 5 we show the normalized EMG percentages of the trapezius for two conditions (all data from impacts in which the impact was expected): head and trunk in neutral posture and trunk flexed forward and laterally right or left. The comparison data are from a previous left anterolateral impact study.\(^{18}\) With the head and trunk in neutral posture in an anterolateral impact, the right trapezius EMG contraction was 74% of the maximal voluntary contraction and the left trapezius contraction was 55% of the maximal voluntary contraction. In the current study, the corresponding values are 38% and 48%, respectively. Thus, trunk flexion significantly reduces the trapezius EMG response (\(P = 0.009\)).

The time to onset of the sled, torso, and head acceleration decreased with increased applied acceleration (\(P = 0.05\)), though this trend was not statistically significant at the \(P = 0.01\) level. Similarly, the time to onset of the EMG decreased with increased applied acceleration. The mean times at which peak EMG occurred show a trend to earlier times of peak activity with increasing acceleration, but this again did not reach statistical significance.

To obtain the force equivalency of a muscle response due to impact, we first performed a linear regression analysis on the graded EMG data obtained in the maximal voluntary contraction trials. This resulted in an equation for force/EMG ratio. EMG values from each muscle as measured in this impact study were then entered into the equation, giving us a force equivalent value for each muscle. This helps to gauge the magnitude of the response compared with physiologic force exertions. The kinematic responses show that very–low-velocity impacts produce less force equivalent than the maximal voluntary contraction for the same subject, and thus, this experimental approach allows us to gather valuable data without exposing subjects to any foreseeable injury. The head acceler-
tions were correspondingly lower than the sled accelerations in this experiment. For very–low-velocity impacts, this is to be expected, as it is usually only when the sled acceleration exceeds \(5 \times g\) (5 times acceleration due to gravity) that head acceleration begins to exceed sled acceleration. This experiment involved \(<2 \times g\) accelerations.

We used a linear regression model to plot the available data and extrapolate from the experimental accelerations to accelerations on the order of 30 m/sec\(^2\). Initially, regression analyses were performed only up to 13.4 m/sec\(^2\) using a linear function. The kinematic variables of head displacement, velocity, and acceleration in response to applied acceleration were calculated (Fig. 1). In addition, we also regressed the EMG magnitudes on acceleration. The responses of the left and right trapezius muscles were extrapolated to more than twice the

FIGURE 3  Trunk flexed to left and right. Head acceleration in the x-, y-, and z-axes of one subject in response to the level of applied acceleration. The z-axis is parallel, the x-axis orthogonal, and the y-axis vertical to the direction of travel. Head X, head acceleration in the x-axis; Head Y, head acceleration in the y-axis; Head Z, head acceleration in the z-axis.
applied acceleration value (Table 1). It is of note that the EMG magnitudes remain low over this range compared with previous studies with the head and trunk in neutral posture.18 In particular, the sternocleidomastoid muscles show little increase in EMG activity despite increasing acceleration.

DISCUSSION

In this study, in which volunteers underwent impacts from the frontal direction offset by 45 degrees to the left (i.e., left anterolateral impacts), we found that if the subjects are flexed to the left or right at the time of impact, then the muscle EMG response is highest from the trapezii, with the contralateral splenius capitis being the next most active muscle. From a biomechanical perspective, we suspect that with the trunk flexed forward and laterally, the out-of-position condition activates the trapezii more because of their role in maintaining this position. In this experiment, we kept the

FIGURE 4  Trunk flexed to left and right. Normalized peak and average electromyogram (EMG, percentage of isometric maximal voluntary contraction), force equivalent of EMG, and applied acceleration. lscm, left sternocleidomastoid; lspl, left splenius capitis; ltrp, left trapezius; rsbm, right sternocleidomastoid; rspl, right splenius capitis; rtrp, right trapezius.
direction of impact constant (left anterolateral) but had the subjects out of position, with the trunk flexed to the right or left about 45 degrees. This was done to determine if the occupant position itself amplified or mitigated the magnitude of cervical muscle response already shown for frontal and anterolateral impacts.\textsuperscript{15–18} In a straight-on frontal impact, for example, the burden of the impact is primarily responded to by the trapezii, and the sternocleidomastoids are not significantly active.\textsuperscript{16} When the frontal impact is offset 45 degrees to the subject's left or right, however, part of the impact burden is experienced more by the contralateral splenius capitis.\textsuperscript{17,18} Thus, direction of impact determines which muscles respond and the proportionality of the response among the different muscle groups. In this experiment, trunk flexion alters the muscle response significantly.

FIGURE 5 Trunk flexed to left and right. Normalized peak electromyogram (EMG, percentage of isometric maximal voluntary contraction) at the highest level of acceleration for two conditions: head and trunk in neutral posture and trunk flexed forward and laterally left or right. The example shown here is for the left and right sternocleidomastoid (lscm and rscm) and trapezius muscles (ltrp and rtrp).
TABLE 1  Trunk flexed to left and right. Extrapolated regression equations of the effect that applied acceleration has on the left and right trapezius and sternocleidomastoid muscles for the variables of force equivalent of electromyogram (EMG), normalized peak EMG (percentage of isometric maximal voluntary contraction), and the peak EMG.

<table>
<thead>
<tr>
<th></th>
<th>Equation</th>
<th>( R^2 )</th>
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<tbody>
<tr>
<td><strong>Left flexion</strong></td>
<td>LTRP</td>
<td>0.75a + 19.94</td>
<td>0.94</td>
<td>2.40a + 15.40</td>
<td>0.98</td>
<td>2.16a + 11.77</td>
</tr>
<tr>
<td></td>
<td>RTRP</td>
<td>0.64a + 17.35</td>
<td>0.96</td>
<td>1.89a + 12.58</td>
<td>0.98</td>
<td>1.96a + 9.69</td>
</tr>
<tr>
<td></td>
<td>LSCM</td>
<td>0.29a + 5.21</td>
<td>0.88</td>
<td>0.24a + 1.23</td>
<td>0.96</td>
<td>0.47a + 5.54</td>
</tr>
<tr>
<td></td>
<td>RSCM</td>
<td>0.25a + 4.95</td>
<td>0.95</td>
<td>0.22a + 1.25</td>
<td>0.91</td>
<td>0.43a + 6.40</td>
</tr>
<tr>
<td><strong>Right flexion</strong></td>
<td>LTRP</td>
<td>0.65a + 13.53</td>
<td>0.90</td>
<td>0.61a + 17.03</td>
<td>0.95</td>
<td>0.41a + 15.22</td>
</tr>
<tr>
<td></td>
<td>RTRP</td>
<td>0.63a + 15.42</td>
<td>0.93</td>
<td>1.61a + 12.27</td>
<td>0.95</td>
<td>1.48a + 13.72</td>
</tr>
<tr>
<td></td>
<td>LSCM</td>
<td>0.20a + 4.28</td>
<td>0.80</td>
<td>0.10a + 1.28</td>
<td>0.97</td>
<td>0.08a + 7.25</td>
</tr>
<tr>
<td></td>
<td>RSCM</td>
<td>0.40a + 2.48</td>
<td>0.98</td>
<td>0.30a + 1.68</td>
<td>0.95</td>
<td>0.98a + 4.92</td>
</tr>
</tbody>
</table>

LTRP, left trapezius; A, applied acceleration; RTRP, right trapezius; LSCM, left sternocleidomastoid; RSCM, right sternocleidomastoid.

The biomechanical rationale for reduced EMG response, implying lesser torque on the cervical spine, is strong. The postural configuration, in which the trunk is flexed, brings it closer to the direction of the force vector of the impact. Although this may increase the axial compression on spinal units, for which they are well adapted, the magnitude of this compression remains minor compared with their tolerance. This posture then reduces the magnitude of the moment arm significantly, which acts as multiplier for the force to develop torque, causing a forced postural perturbation. With a considerably smaller moment arm, the torque is reduced to a large extent. Because the torque tending to cause postural perturbation of the cervical spine is small, the EMG response of the cervical muscles is also small, mitigating risk of injury. The observation in the current study of significantly lower cervical muscle EMG supports this reasoning.

There are limitations to this study. First, we are using results from a previous impact study\(^{18}\) with the trunk in neutral posture (historical controls) in comparing the effect of trunk flexion on the cervical response. We believe this is a reasonable approach given that we have used the exact methodology and equipment in both studies and that there is no difference in the mean ages, sex distribution, or mean weight of volunteers between the studies. Furthermore, the data were normalized and are thus comparable across the subjects. A second limitation may be that the overall EMG activity is lower partly because the impacts were expected (no blocking of visual or auditory cues), and this is known to reduce EMG responses.\(^{15–18}\) Here again, however, when we compare muscle responses between this study and that of a previous study with the trunk in neutral posture, in both cases we are comparing volunteers in the expecting state. Trunk flexion reduces the EMG response when compared with the neutral posture due to a decrease in the moment arm of the impacting force. Third, we only used a lap belt in this study, and the results may have been different if we used a lap and shoulder belt. We argue, however, that when occupants lean over from their driving position, for example, or try to pick up something from the vehicle floor, they are sliding out from behind the restraint of the shoulder strap and effectively are restrained only by the lap portion. Still, we are now conducting additional studies comparing the effect of different restraint systems on cervical muscles response because this may remain relevant. Finally, we are assuming, in extrapolating our results into the low-velocity impact range that the muscle behavior remains linear. Nonlinear regressions were developed as well, but they did not significantly better the linear ones. All extrapolations are approximations of the truth, and the only way to confirm them is to make measurements at the extrapolated ranges. We do know, however, that our extrapolations closely match those from small volunteer studies in which higher velocities were used with symptoms produced.\(^{8,11–14}\) This suggests that regression techniques may allow for extrapolations into low-velocity ranges and may obviate the need for exceeding ethical concerns with experimental designs that could cause volunteer injury. It is recognized that extrapolation may lead one into an erroneous realm if they are not confirmed with available data and exceed the physiologic range. In this instance, neither is the case.

Although we cannot measure injury in this experiment, we have no indication of any significant muscle response, even in the extrapolations that would exceed the normal physiologic limits of strength of these muscles. There are no studies in
animals in which EMG responses to impact are compared with maximal voluntary EMG. This is not surprising because maximal effort cannot be produced in animals. As we have no other means by which to measure injury potential, we are proceeding on the assumption that the more a muscle’s EMG response exceeds the physiologic maximal voluntary contraction level, the more likely it is to be injured. If the EMG response to an impact is well within the envelope of maximal voluntary contraction, then it is assumed that injury is less likely to occur to that muscle.

This is the first study to document the cervical muscle response to impact when the occupant is out of the neutral posture, and we are unable to compare with any other approaches to this problem. There has been a review of data from dummy experiments suggesting that being out of position at the time of impact may increase the risk of injury in a frontal impact, not only from impact with the vehicle interior, but through effects of increased cervical extension when the occupant is seated with most of the torso away from the seat and rebounds into the seat after the impact.21 Obviously, it is difficult to extrapolate these results to humans, and our results would not support an increased risk of injury. It may be that at higher velocities, the biomechanics are quite different, and our results likely hold for only very–low-velocity impacts or low-velocity impacts, as confirmed with published data.8,11–14

CONCLUSIONS

Unless the trunk-flexed posture increases the risk of interior vehicle impact, it is likely protective in low-velocity impacts. Compared with occupants sitting with head and neck in the neutral posture, when they are out of position at the time of impact, EMG responses to impact are lower. Thus, the current study finds no evidence to indicate that being out of position at the time of a low-velocity frontal impact amplifies injury risk. If anything, this positioning probably lowers injury risk. It remains unclear, therefore, why it is assumed, as it often seems to be in medicolegal reports, that being out of the neutral posture is more likely to cause injury. There are, to date, no data to support this for low-velocity impacts, and more studies are warranted to determine how occupant position affects whiplash injury risk.

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Botulinum Toxin Treatment of Spastic Equinus in Cerebral Palsy
A Randomized Trial Comparing Two Injection Sites

ABSTRACT

Objective: To explore the clinical relevance of injection site by comparing two different injection techniques in children with cerebral palsy who have spastic equinus gait.

Design: A total of 19 children (13 boys, 6 girls; range, 1 yr 6 mos to 7 yrs; nine hemiplegics, eight diplegics, two quadriplegics; levels I to IV with the Gross Motor Function Classification System) participated in the study. The children were randomized into two groups: the proximal group received a botulinum toxin A injection into the proximal part of both heads of the gastrocnemius, and the distal group received a botulinum toxin A injection into the mid-belly of the muscle bulks. A single-point injection of BOTOX, 3 units/kg per site, was used. Assessments of active and passive range of motion, dynamic muscle length (modified Tardieu scale), calf tone (modified Ashworth scale), and video gait analysis (Observational Gait Scale) were performed before treatment and 3, 8, and 16 wks posttreatment.

Results: Active and passive dorsiflexion and calf tone in both groups and Observational Gait Scale total scores in the distal group improved at all time points. The median change from baseline values in Observational Gait Scale initial foot contact and total scores at 8 wks showed a significant difference favoring the distal group, but the clinical relevance remained tenuous.

Conclusions: Using the methods described, no major changes in main outcome measures were associated with changing the injection site.

Key Words: Botulinum Toxin Type A, Cerebral Palsy, Spastic Equinus, Injection Site
Botulinum toxin A (BTX-A), an acetylcholine-blocking, denervating chemical when injected into a muscle, has been used in children since 1993 in the management of spasticity in cerebral palsy. The most common indication is spastic equinus gait. Botulinum toxin is an expensive and potentially toxic agent. The reduction in muscle tone should be effective and selective, which requires both optimal dosage and injection site for each muscle—not yet clearly defined factors, even for the most commonly injected gastrocnemius muscles.

Various techniques to improve verification of needle placement in the correct muscle comprise palpation and anatomic landmarks, neurophysiologic methods (nerve or motor-point stimulation, electromyographic guidance), ultrasound, and computed tomography. Furthermore, the importance of localizing the neuromuscular junctions (NMJs) within the muscle has been stressed.

In humans and experimental animals, BTX-A spreading occurred into nearby muscles or into contralateral muscles through fascia and bony structures, leading to undesired excessive weakening. These results suggest that a dosage of 2–3 units/kg body weight of BTX-A (BOTOX; concentration, 1.25 units/0.1 ml injected into rabbit long-gissimus dorsi muscle) spreads up to 4.5 cm from the injection site. Quantification of BTX-A–induced muscle paralysis with varying injection sites in rat tibialis anterior muscle showed that injection directly into the NMJ zone gave the best results: when the toxin was injected 0.5 cm from the NMJ zone, paralysis was decreased by 50%. To avoid excessive spread, the authors recommended toxin administration into the center of a muscle, as near the NMJ zone as possible.

In the 1950s, Coers in Belgium and Christensen in Denmark studied dissected mammalian and fetal striated muscles, staining them with cholinesterase. They noticed that the NMJs were situated in the middle of each extrafusal muscle fiber. Depending on the structure of the muscle, the NMJs were either scattered diffusely or formed one or multiple detectable zone-like patterns. Gastrocnemius is a bipennate muscle and, according to work of Christensen, the NMJ zones form oval patterns (Fig. 1). NMJ zones can be detected with electromyography needles (miniature end-plate potentials), but this procedure can be painful.

Childers et al. conducted a double-blind, placebo-controlled study comparing two different BTX-A injection techniques in 15 ambulant adults (aged 19–76 yrs) with spastic hemiplegia. One group received a single-point injection of 50 units of BTX-A (BOTOX) into the proximal part (near motor point) and another group received 50 units divided at three sites into the mid-belly part (near the NMJ zone) of the gastrocnemius. No difference in reduction in muscle tone or functional outcome was detected. Only one (the largest) of the two heads of the gastrocnemius was injected, which may have affected the results.

Little is known about the importance of injection site in children. Compared with adults, the muscles are smaller in size, and the toxin may diffuse more easily throughout the muscle. Therefore, it might be enough to inject into the target muscle. In pediatric clinical practice, the gastrocnemius is the most often treated muscle in cerebral palsy, and due to its clear anatomic appearance, it is also mostly injected by palpation. In the present randomized study, we used the model described by Childers et al., modified for children. A standard dose of BTX-A (6 units/kg/gastrocnemius, BOTOX) was injected either as near to the NMJ zone as possible or into the proximal part of each gastrocnemius muscle near the origin to discover whether the injection site is of clinical relevance in regard to tone reduction and walking pattern.

**METHODS**

**Patient Sample**

Patients were recruited over a 39-mo period from Tampere University Hospital and Central
Hospital of Kanta-Häme, Hämeenlinna, both in Finland. Inclusion criteria were: 1) diagnosis of cerebral palsy verified by a child neurologist, 2) ambulation with or without devices, and 3) spastic equinus gait. Exclusion criteria were: 1) age of >7 yrs, 2) previous serial casting or BTX-A treatment within 6 mos before enrolment, and 3) previous surgery on the lower limbs.

Patient characteristics are presented in Table 1. Two patients, one from each treatment group, failed to attend the 4-mo posttreatment assessment and were assessed 6 mos postinjection. Their 6-mo data are included in the intention-to-treat analysis. Three children were enrolled twice, with 1 yr between the treatments. The study was approved by the local Research Ethics Committees and the National Agency for Medicines.

After the baseline measurements, informed written consent was obtained from parents or guardians. Patients meeting the study criteria were randomized into one of the two treatment groups. The treating physician (H. Sätilä) allocated each child by tossing a coin with predetermined sides for each treatment group (heads for the proximal group and tails for the distal group). Unilaterally involved (hemiplegic) vs. bilaterally involved (diplegic and quadriplegic) subjects were enrolled in separate categories and then paired on calf tone spasticity grade measured by the Ashworth scale so that after randomization, both treatment groups had the same amount of hemiplegics/diplegics with the same spasticity grade to begin with. The proximal group received BTX-A injection into the proximal part of both heads of the gastrocnemius (near the muscle origin or motor point where the motor nerve enters the muscle), and the distal group received BTX-A injection into the mid-belly of the muscle bulk (near the assumed NMJ zone) (Fig. 1).

Location of the injection site was determined according to anatomic landmarks and palpation. No electromyography or motor-point stimulation was used. In addition to gastrocnemius injections, five patients received hamstring injections due to excessive spasticity. All injections were administered by the same physician (H. Sätilä). Site of injection was not entered in any official record, and the therapists involved in assessment and parents were blinded to the injection site throughout the study.

Clinical assessments were performed at baseline and at 3, 8, and 16 wks posttreatment by one of the two research physiotherapists (T. Pietikäinen or T. Iisalo) in Tampere University Hospital or one research physiotherapist (M. Salo) in Central Hospital of Kanta-Häme, Hämeenlinna, all having 7–15 yrs experience with handicapped children. The same examiner continued with the child throughout the research period.
Throughout the study, the content and frequency of physiotherapy continued unchanged. Parents and personal physiotherapists were instructed not to introduce any new programs or activities. At the 3-wk assessment, every child received night splints (Fig. 2) on the treated limb to potentiate the BTX-A effect. If the participant already had a splint, he or she was asked to have at least a 2-mo pause in wearing it before entering the trial (three legs in the proximal group, four legs in the distal group).

Injection Technique

A constant dose (100 units in 1 ml of 0.9% saline, BOTOX, Allergan, Irvine, CA) was used for every patient: 3 units/kg per site (6 units/kg per gastrocnemius), making the total dose 12 units/kg for the diplegics and 6 units/kg for the hemiplegics. A single-point injection was used except for doses of >50 units, which were divided into two nearby sites (distance, 0.5–1.0 cm) corresponding to the single-point injection (five children in the proximal group, four children in the distal group).

With local lidocaine cream applied to the injection sites and light oral sedation with midazolam (0.3 mg/kg, maximum of 10 mg per child), the injections were performed with a 22-gauge needle and 1-ml syringes under sterile conditions. The needle was inserted into the muscle (depth, 5–7 mm) with the ankle in neutral position. The needle position was checked by flexing-extending both knee and ankle joint as described by Corry et al.14 After injection, the flexing-extending movement was continued to enhance the spreading of BTX-A in the muscle bulk. Treatments were given on an outpatient basis; no immediate side effects were observed.

Outcome Measures

Primary outcome measures were:

1. Active and passive ankle dorsiflexion with knee extended and flexed measured by manual goniometry with the “neutral-null” method: dorsiflexion angle over the neutral position was counted in positive degrees, under the neutral in negative degrees.

2. Calf muscle tone measured by modified Ashworth scale.15 The scoring was as follows: 0 =
no increase in muscle tone; 1 = slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion; 2 = slight increase in muscle tone shown as a catch and followed by minimal resistance throughout less than half the range of motion; 3 = marked increase in muscle tone through most of the range of motion, the affected part being easily moved; 4 = considerable increase in muscle tone, with passive movement difficult; and 5 = affected part remaining rigid.

Secondary outcome measures were:

1) Dynamic ankle range of motion with knee extended assessed by modified Tardieu scale. The ankle was dorsiflexed as fast as possible and the catch angle was measured by manual goniometry.

2) Video gait analysis by Observational Gait Scale (Table 2). Video recordings were performed in sagittal and coronal planes, with the child walking barefoot. A senior pediatric physiotherapist (R. L. Seppänen) not involved with the measurements and unaware of the treatment groups or time sequences scored each treated leg from compiled video recordings. The initial foot contact and total scores were noted.

A questionnaire for parents asked them to report timing and duration of beneficial effects and side effects of the BTX-A treatment. The physician actively asked about adverse events at each assessment, and classified them as severe, moderate, or mild.

**Statistical Analysis**

The needed sample size was estimated when each group had 6–8 treated limbs. Because of the skew continuous distributions, calculations were done within groups using Friedman’s test and between groups at the 8-wk assessment using the \( t \) test (as an estimate of Mann-Whitney \( U \) test), with alpha of 0.05 and power of 80%. Sample size of 11 legs per group was required to detect a difference in passive dorsiflexion. The changes of skew continuous and ordinal data within groups were tested using Friedman’s test and paired comparisons us-

### TABLE 2 Observational Gait Scale

<table>
<thead>
<tr>
<th>Gait Parameter</th>
<th>Definition</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee position in midstance</td>
<td>Crouch: Severe, &gt;15 degrees</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Moderate, 10–15 degrees</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mild, &lt;10 degrees</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Recurvatum: Mild, &lt;5 degrees</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Moderate, 5–10 degrees</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Severe, &gt;10 degrees</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Initial foot contact</td>
<td>Toe</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Forefoot</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Foot-flat</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Heel</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Foot contact at midstance</td>
<td>Toe/toe (equinus)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Foot-flat/early heel rise</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Foot-flat/no early heel rise</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Occasional heel/foot-flat</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Heel/toe (normal rollover)</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Timing of heel rise</td>
<td>No heel contact (fixed equinus)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Before 25% stance (very early)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Between 25% and 50% (slightly early)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>At terminal stance</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>No heel rise (after foot-flat, i.e., crouch)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hindfoot at midstance</td>
<td>Varus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Valgus</td>
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<td>1</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
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<td>2</td>
</tr>
<tr>
<td>Base of support</td>
<td>Frank scissoring</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Narrow base (poor knee clearance)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Wide base</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Normal base (width of shoulders)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Gait assistive devices</td>
<td>Walker (forward/posterior) with assistance</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Walker (independent)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Crutches, sticks</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>None, independent for 10 m</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Overall change</td>
<td>Worse</td>
<td>-1</td>
<td>-1</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Better</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Total score maximum: 23 points
ing Wilcoxon’s test. Mann-Whitney U test was used to compare differences of the same type of data between groups. Differences in cross-tables were tested using Fisher’s exact test. Significance was assumed at $P < 0.05$. Statistical analysis was performed using SPSS for Windows (version 11.5) and Solo Power Analysis (version 1.0).

**RESULTS**

**Clinical Examination Data**

The treatment groups were similar in age, sex, diagnosis, and Gross Motor Function Classification System score (Table 1). At baseline, the difference between the groups approached significance only in passive dorsiflexion with knee extended ($P = 0.065$) (Table 3). At all time points, the active dorsiflexion with knee extended (proximal group, $P = 0.030$; distal group, $P = 0.014$), passive dorsiflexion both with knee extended (proximal group, $P = 0.004$; distal group, $P = 0.004$) and flexed (proximal group, $P = 0.000$; distal group, $P = 0.006$), and modified Ashworth scale scores (proximal group, $P = 0.000$; distal group, $P = 0.001$) improved significantly in both groups. The dynamic muscle length increased significantly at all assessment points in the distal group ($P = 0.048$) but not in the proximal group ($P = 0.074$). Table 3 shows the changes in absolute scores from baseline to those at 3, 8, and 16 wks after treatment. A significant difference between the treatment groups was detected in passive dorsiflexion with knee extended at 3 wks and in passive dorsiflexion with knee flexed at 16 wks, favoring the distal group. However, no differences between the groups were detected when median changes from baseline were used (Table 4). The calf tone decreased slightly later in the proximal group (peak at 8 wks) compared with the distal group (already low at 3 wks) (Table 3).

**Observational Gait Scale**

No significant differences between baseline values existed. A significant improvement was found at all measurement points in total scores in the distal group (proximal group, $P = 0.122$; distal group, $P = 0.014$) but not in initial foot contact subscore (proximal group, $P = 0.548$; distal group, $P = 0.075$). Table 3 shows the Observational Gait Scale variable absolute score changes from baseline to those at 3, 8, and 16 wks after treatment. No differences between the groups existed. However, in median changes from baseline, a significant difference between the groups was detected in initial foot contact and total scores at 8 wks, favoring the distal group (Table 4). This difference disappeared by 16 wks.

**Subgroup Analysis**

A subgroup of eight children had passive dorsiflexion of $<0$ degrees at baseline. Five of these children (six treated legs: two hemiplegics, two quadriplegic, one diplegic) were enrolled into the proximal group and three children (three treated legs; two hemiplegics, one diplegic) into the distal group (difference between groups, $P = 0.226$). No significant differences between groups were detected in any variable. In the subgroup of children having passive dorsiflexion of $\geq 0$ degrees at baseline, the only significant difference between groups was found in median change of active dorsiflexion knee extended at 16 wks, favoring the distal group ($P = 0.044$). When comparing the less involved children (Gross Motor Function Classification System I–II) with more severely involved (Gross Motor Function Classification System III–IV) ones, significant differences between groups were found in median change of passive dorsiflexion knee extended at 3 wks ($P = 0.011$), active dorsiflexion knee extended at 8 wks ($P = 0.021$), total scores ($P = 0.037$), and foot contact at 3 wks ($P = 0.022$), favoring the less involved children.

**Parental Perception and Adverse Events**

Parents noticed a change in muscle tone within a few days: mean of 4.1 days (range, 2–7 days) in the proximal group and mean of 5.8 days (range, 1–20 days) in the distal group. An increase in muscle tone started between 3 and 8 wks in two children (one child in both groups) and between 8 and 16 wks in 11 children (five in the proximal group, six in the distal group). A good response was still being observed in six children at 16 wks (three in both groups). Parents reported a total of 19 adverse events (proximal group, nine events; distal group, ten events), out of which 16 events were considered mild and only three moderate. Adverse events were: tenderness in calf ($n = 8$), tiredness ($n = 3$), irritability ($n = 3$), clumsiness ($n = 3$), and fever or flu-like symptoms ($n = 2$). Moderate symptoms were irritability ($n = 2$) and tenderness in calf ($n = 1$). All symptoms resolved within 1–7 days, except in one child in the proximal group who experienced clumsiness for 16 days. Three adverse events were judged not to relate to the treatment: flu and fever ($n = 2$; both children having the common cold in their family) and calf pain ($n = 1$) occurring after 1 wk, following a long walk. No one withdrew because of these symptoms. No difference between the groups was detected in parental perception or adverse event variables. After the trial period, ten children required a new BTX-A treatment during the following 8 mos (five in both groups), eight children continued with conservative treatment (three in the proximal group, five in...
TABLE 3 Clinical examination and Observational Gait Scale results in proximally (PROX) and distally (DIST) injected groups (absolute scores)

<table>
<thead>
<tr>
<th></th>
<th>PROX Group</th>
<th></th>
<th>DIST Group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Median (Range)</td>
<td>P Value</td>
<td>n</td>
</tr>
<tr>
<td>Active dorsiflexion knee extended</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pretreatment</td>
<td>10</td>
<td>-25 (-40 to -10)</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>3 wks</td>
<td>10</td>
<td>-20 (-35 to -10)</td>
<td>0.017 a</td>
<td>11</td>
</tr>
<tr>
<td>8 wks</td>
<td>10</td>
<td>-15 (-35 to 0)</td>
<td>0.049 a</td>
<td>11</td>
</tr>
<tr>
<td>16 wks</td>
<td>10</td>
<td>-15 (-45 to 0)</td>
<td>0.313</td>
<td>11</td>
</tr>
<tr>
<td>Passive dorsiflexion knee extended</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pretreatment</td>
<td>12</td>
<td>-1 (-15 to +15)</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>3 wks</td>
<td>12</td>
<td>+5 (-10 to +20)</td>
<td>0.018 a</td>
<td>13</td>
</tr>
<tr>
<td>8 wks</td>
<td>12</td>
<td>+7.5 (-5 to +35)</td>
<td>0.003 a</td>
<td>13</td>
</tr>
<tr>
<td>16 wks</td>
<td>12</td>
<td>+10 (-10 to +25)</td>
<td>0.007 a</td>
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<tr>
<td>Passive dorsiflexion knee flexed</td>
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<td></td>
</tr>
<tr>
<td>Pretreatment</td>
<td>12</td>
<td>+3 (-10 to +30)</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>3 wks</td>
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<td>+19.5 (-3 to +30)</td>
<td>0.005 a</td>
<td>13</td>
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<td>8 wks</td>
<td>12</td>
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<td>0.002 a</td>
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<td>16 wks</td>
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<td>+15 (0 to +30)</td>
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<td>13</td>
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<td>Calf tone</td>
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<td></td>
</tr>
<tr>
<td>Pretreatment</td>
<td>12</td>
<td>3 (2 to 4)</td>
<td></td>
<td>13</td>
</tr>
<tr>
<td>3 wks</td>
<td>12</td>
<td>2 (1 to 3)</td>
<td>0.011 a</td>
<td>13</td>
</tr>
<tr>
<td>8 wks</td>
<td>12</td>
<td>1.8 (1 to 3)</td>
<td>0.002 a</td>
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<tr>
<td>16 wks</td>
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<td>2 (1 to 3)</td>
<td>0.010 a</td>
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<td>Dynamic muscle length</td>
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<tr>
<td>Pretreatment</td>
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<td>-12.5 (-35 to 0)</td>
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<td>3 wks</td>
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<td>-15 (-20 to 0)</td>
<td>0.878</td>
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<td>8 wks</td>
<td>12</td>
<td>-8.5 (-19 to 0)</td>
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<td>16 wks</td>
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<td>-10 (-30 to 0)</td>
<td>0.440</td>
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<td>Initial foot contact</td>
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<tr>
<td>Pretreatment</td>
<td>12</td>
<td>0.5 (0 to 2)</td>
<td></td>
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<tr>
<td>3 wks</td>
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<td>1 (0 to 2)</td>
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<td>16 wks</td>
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<td>1 (0 to 3)</td>
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<tr>
<td>Total score</td>
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<td></td>
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</tr>
<tr>
<td>Pretreatment</td>
<td>12</td>
<td>9 (3 to 17)</td>
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<tr>
<td>16 wks</td>
<td>11</td>
<td>11 (4 to 19)</td>
<td>0.044 a</td>
<td>11</td>
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</tbody>
</table>

Median and range at 3, 8, and 16 wks with significance of difference from pretreatment values (W, Wilcoxon’s test) and significance of difference between groups (MWU, Mann-Whitney U test).

a Significant difference from pretreatment values (W) and between treatment groups (MWU).
TABLE 4  Clinical examination and Observational Gait Scale results in proximally (PROX) and distally (DIST) injected groups (median change from pretreatment values)

<table>
<thead>
<tr>
<th></th>
<th>PROX Group</th>
<th></th>
<th>DIST Group</th>
<th></th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n$</td>
<td>Median (Range)</td>
<td>$n$</td>
<td>Median (Range)</td>
<td>MWU</td>
</tr>
<tr>
<td>Active dorsiflexion knee extended</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pretreatment</td>
<td>10</td>
<td>$-25$ ($-40$ to $-10$)</td>
<td>11</td>
<td>$-20$ ($-35$ to $-15$)</td>
<td>0.943</td>
</tr>
<tr>
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<td>10</td>
<td>$+5$ ($-2$ to $+10$)</td>
<td>11</td>
<td>0 ($-10$ to $+15$)</td>
<td>0.490</td>
</tr>
<tr>
<td>8 wks</td>
<td>10</td>
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Median and range at 3, 8, and 16 wks, with significance of difference between groups (MWU, Mann-Whitney U test).

* Significant difference between treatment groups (MWU).
the distal group), and one child in the proximal group was referred to surgery.

Intention to Treat
The intention-to-treat analysis with the same variables did not alter the results.

DISCUSSION
We are not aware of any studies on BTX-A diffusion in human muscles, but we predicted that if toxin diffusion occurs parallel to gastrocnemius fibers, the effect on calf tone and passive dorsiflexion will occur in both groups but be more pronounced in the distal group. The two injection sites were chosen because of their clear anatomic appearance, easy accessibility, and the in-between distance being long enough (4–5 cm, despite the size of the child). Our findings demonstrated that both groups benefited from the treatment in terms of passive and active dorsiflexion, dynamic muscle length, calf tone reduction, and function (initial foot contact per treated leg) and that the differences between groups were not robust. In the distal group, the video gait analysis showed a slightly better improvement in equinus gait at 8 wks, declining by 16 wks. These results did not support the hypothesis that BTX-A injections directed as near the NMJ zone as possible are more effective in reducing the muscle tone and produce far better functional results in spastic equinus gait than injections given into a remote site.

The nearly significant difference between the treatment groups in passive dorsiflexion knee extended pretreatment values was unexpected. However, it is unlikely that this affected the results, as median changes from baseline were used, showing similar changes in both injection groups. An extended analysis revealed that the legs with baseline values of <0 degrees accumulated to the most severely involved children (Gross Motor Function Classification System IV) and into the proximal group (three out of four legs). They all benefited in terms of passive dorsiflexion and foot contact. When analyzing the whole group, the less involved children had better change in passive dorsiflexion at 3 wks, active dorsiflexion at 8 wks, and foot contact and total scores at 3 wks, but they were equally distributed between the treatment groups.

Because of different outcome measures, our results are not directly comparable with the animal models. Our findings did not agree with those of Childers et al.,12 who found no significant differences in muscle tone and functional variables between treatment groups. They injected only one of the two heads of gastrocnemius and studied hemiplegic adults with varying pathogeneses and duration of central nervous system injury, which makes the comparisons of these two study results complex. Our findings correlate well with the clinical observations of Westhoff et al.,5 who under ultrasound guidance injected the iliopsoas muscle from the groin, a site far from the NMJ zone.

Our study population comprised both hemiplegics and diplegics. Equinus gait in hemiplegia is usually due to spasticity in the gastrocnemius, whereas in diplegia, the involvement of hamstrings is more frequent.2 The hemiplegics might have benefited from soleus injections, which the study protocol did not allow. Eight children had passive dorsiflexion of <0 degrees at baseline—a group not so often treated with BTX-A only. All three children in the distal group and three children (one hemiplegic and two quadriplegics) in the proximal group benefited from the injection. In children with cerebral palsy, the reduction in muscle excursion may rather be progressive than sud-
den, having a transition period of coexisting spasticity and mild shortening of muscle. Thus, these children may benefit from BTX-A injections, but the effect is not long lasting. Combining the treatment with serial casting is thought to be more effective than BTX-A alone. Examination of these children after sedation could have revealed whether the stiffness in the ankle was because of fixed shortening.

BTX-A reduces muscle tone and increases dynamic muscle length, and the outcome measures were chosen to detect changes in these variables. Different gait rating scales have been used in previous studies. The interrater and intrarater reliability of the Observational Gait Scale subscales were found to be moderate to substantial in diplegics aged ≥6 yrs. We found the foot contact at midstance and timing of heel rise subscores to be difficult to rate from the video recordings of our young children lacking compliance and decided to stay with the initial foot contact section, which would be comparable with previous studies.

The measurements of the three research physiotherapists are a possible source of variation. The reliability of the modified Tardieu scale, passive range of movement, and the modified Ashworth scale were recently assessed in the lower limb of children with cerebral palsy. Considering the subjectivity of the measurement tools used and differences in interrater and intrarater reliabilities, we tried to maximize the reliability by having the same physiotherapist assess the same children throughout the study.

The dosage of 3 units/kg body weight for each muscle half was chosen according to recommendations and was thought to be effective enough to reduce muscle tone. Higher dosage might have increased BTX-A spreading but also might have resulted in better functional improvement. Despite the rather low dosage, the prevalence of adverse events (68% of participants) in this present study was unexpectedly high. This may be related to injection technique but also to the methodologic reason of the physician actively asking the parents about any events that they thought could be connected to the injections. This may increase reporting symptoms not related to the treatment but decrease the chance of forgetting. Adverse events have varied between 5% and 85% in children, and the most frequent symptoms have been leg pain or bruising, falling, flu-like symptoms, and transient weakness. Adverse events, like pain at the injection site, may be underreported. In this study, all adverse events occurred within 3 wks, and the majority resolved within a week. The hemiplegic child with prolonged clumsiness had poor active range of movement, and the modified Ashworth scale were recently assessed in the lower limb of children with cerebral palsy.

The Innervation of Muscle

REFERENCES

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**How to Obtain CME Category 1 Credits**

To obtain CME Category 1 credit, this educational activity must be completed and postmarked by December 31, 2006. Participants may read the article and take the exam issue by issue or wait to study several issues together. After reading the CME Article in this issue, participants may complete the Self-Assessment Exam by answering the questions on the CME Answering Sheet and the Evaluation pages, which appear later in this section. Send the completed forms to: Bradley R. Johns, Managing Editor, CME Department-AAP, *American Journal of Physical Medicine & Rehabilitation*, 7240 Fishback Hill Lane, Indianapolis, IN 46278. Documentation can be received at the AAP National Office at any time throughout the year, and accurate records will be maintained for each participant. CME certificates are issued only once a year in January for the total number of credits earned during the prior year.
Self-Assessment Exam Questions

CME Article Number 3: H. Satila, et al.

1. Experimental animal studies with rats have shown that botulinum toxin A injected 5 mm from the neuromuscular junction zone:
   A. Increases the paralysis by 5%.
   B. Decreases the paralysis by 5%.
   C. Increases the paralysis by 50%.
   D. Decreases the paralysis by 50%.

2. The modified Tardieu Scale measures:
   A. Flexibility.
   B. Flaccidity.
   C. Dynamicity.
   D. Spasticity of muscle.

3. Which of the following statements does NOT apply to botulinum toxin A treatment with children?
   A. The toxin decreases muscle tone and dynamic muscle length.
   B. Combining the treatment with other modalities like casts and splints may potentiate the effect.
   C. The toxin spreads into adjacent muscles and causes excessive weakening.
   D. The most frequent side effect has been pain and tenderness at the injection site.

4. After botulinum toxin A treatment the subjects in this study in both groups significantly improved in all of the following parameters except:
   A. Active dorsiflexion with knee extended.
   B. Passive dorsiflexion with knee extended.
   C. Dynamic muscle length with knee extended.
   D. Muscle tone.

5. After botulinum toxin A treatment the median changes between groups in this study were significant in one of the following parameters:
   A. Active dorsiflexion with knee extended.
   B. Passive dorsiflexion with knee extended.
   C. Dynamic muscle length with knee extended.
   D. Initial foot contact.
The answers to any essay questions must be typed or computer printed on a separate piece of paper and attached to this page.

After finishing this exam:
1. Check your answers with the correct answers on page 392.
2. Complete the CME Evaluation and Certification on the following page and mail to Bradley R. Johns, Managing Editor, CME Dept.-AAP, American Journal of Physical Medicine & Rehabilitation, 7240 Fishback Hill Lane, Indianapolis, IN 46278.
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CME Article Number 3: H. Satila, et al.
Circle the appropriate answers.

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Suggestions for future topics: ____________________________

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SCUBA Diving for Individuals with Disabilities

ABSTRACT


Self-contained underwater breathing apparatus (SCUBA) diving has become an increasingly popular recreational activity, enjoyed by millions of individuals. There has also been a growing interest in SCUBA diving in the disabled population for rehabilitation and recreation. This review discusses medical issues relevant to individuals with disabilities who wish to participate in SCUBA diving. In addition, specialized equipment, adaptations in techniques, and additional precautions will be presented. SCUBA diving can be an enriching experience, potentially helping to improve self-image and quality of life. Knowledgeable healthcare professionals can help to guide their patients who are interested in SCUBA diving.

Key Words: SCUBA, Diving, Disability, Sport, Adaptive, Hyperbaric

Self-contained underwater breathing apparatus (SCUBA) diving is a rapidly growing sport in the United States and around the World. Since the advent of SCUBA equipment by Jacques Cousteau and Emily Gauyon in 1943, advances in technology have allowed the exploration of the marine environment to develop into a recreational sport enjoyed by millions of individuals. Currently, the number of recreational divers in the United States alone has been estimated to be between 3 and 9 million strong.1–4 SCUBA diving has become popular for people with disabilities as well. The buoyancy of the marine environment is appealing to some mobility-challenged individuals.

Although there is a significant body of medical literature in the field of dive medicine, the number of publications addressing issues related to disabled divers is scarce.5–7 A general discussion of dive medicine and emergencies is beyond the scope of this review. Rather, issues pertinent to the diver with disabilities will be discussed.

CASE REPORTS

Case 1 is a 15-yr-old girl with paraparesis due to high lumbar spina bifida. Her lesion was closed at birth, and she had a ventriculoperitoneal shunt placed at 1 wk of age, revised 1 wk afterward. She had soft-tissue release of the left ankle at age 6 and right hip surgery for dislocation at age ten. She had a distal right femoral pathologic fracture at age 13 with poor healing and an episode of cellulitis of the right foot.

She successfully completed a 3-day Professional Association of Diving
Instructors course in an outdoor pool and open ocean, using webbed gloves to increase propulsion ability (Fig. 1). Her training was complicated only by sunburn on her lower legs that went unnoticed due to sensory deficit, as she wore a “shorty” neoprene wetsuit that covered only to mid-thigh (Fig. 2). She had not used sunscreen.

Case 2 is a 14-yr-old girl with paraparesis due to poliomyelitis. She has had bilateral soft-tissue releases at the ankles and utilizes hip-knee-ankle orthoses with forearm crutches for therapeutic ambulation. She uses a wheelchair for community mobility. She successfully completed a 3-day Professional Association of Diving Instructors course. Her training was complicated by transient dizziness in the evening of the first day due to dehydration.

Both girls fulfilled all requirements for Professional Association of Diving Instructors Open Water SCUBA Diver certification and undertook several open-water dives independently. Although neither diver had significant medical problems during their training, what are the potential complications they and other individuals with disabilities may encounter while SCUBA diving?

**DISCUSSION**

**Potential Medical Problems in Divers with Disabilities**

**Osteoporosis and Fractures**

Some individuals with disabilities are at risk for osteoporosis due to factors such as immobilization and paralysis.°° Divers at risk for pathologic fractures should seek dive boats with access platforms near water level for easier transfers in and out of the water. The lifts commonly found in accessible pools are less widely available on boats.

Because of compromise of sensation in many neurologic disorders, fractures may go unrecognized. Anyone with localized and otherwise unexplained lower limb edema or erythema should be evaluated for possible pathologic fracture.

**Medical Implants**

As more individuals with disabilities become interested in SCUBA diving, questions will be posed concerning the integrity of medical appliances when exposed to the increased barometric pressures associated with SCUBA diving. Many individuals with disabilities such as spina bifida have ventriculoperitoneal shunts for the treatment of hydrocephalus. Huang et al.°° subjected four ventriculoperitoneal shunts to one and four atmospheres absolute in a hyperbaric chamber and found that all shunts performed according to manufacturers’ specifications. They reasoned that any increase in pressure will compress all fluid-filled compartments. Therefore, there would be no significant change in gradient between intracranial and intraperitoneal pressures.

Preliminary studies have been carried out for cochlear implants in a hyperbaric chamber, illustrating that the implantable components of various cochlear implants can withstand pressures of up to six atmospheres without damage or failure of critical seals.°°

![FIGURE 1 Webbed gloves assist disabled individuals with paraparesis to negotiate the marine environment.](image1)

![FIGURE 2 Wetsuits assist in thermal regulation and protect from abrasions, lacerations, puncture wounds, and pressure ulcers.](image2)
Intrathecal baclofen pumps are increasingly being utilized in the management of spasticity and dystonia. Akman et al. described a case of retrograde leakage of cerebrospinal fluid (CSF) into the infusion pump reservoir of an intrathecal baclofen pump (Medtronic SynchroMed, Medtronic, Minneapolis, MN) during hyperbaric oxygen therapy. Medtronic does not recommend exposing their intrathecal baclofen pumps to pressures of $\geq 2.0$ atmospheres absolute (SynchroMed II Technical Manual, Medtronic).

Thermal Regulation

Thermal regulation is compromised in many disabling conditions. For individuals with this deficit, diving should be undertaken in warm water regions and neoprene wetsuits should be utilized. Greater depths will cause increased compression of the neoprene of wetsuits. Because a large component of the insulating quality of wetsuits is provided by the air trapped in the material, compression of these garments will decrease their insulating capabilities. When diving to greater depths, the need for increased thermal protection should be anticipated due to the compression of neoprene and the much colder water.

Peripheral vasoconstriction, as an adaptation to minimize the strain caused by loss of body heat, may compromise circulation to the limbs and may need to be minimized. This vasoconstriction may decrease already tenuous circulation to the limbs of some individuals with paraplegia. For example, Boot et al. found that individuals with spina bifida and spinal cord injury have peripheral arterial vasculature that was of smaller diameter, lower flow, and higher shear stress when compared with controls. These changes may compromise optimal regulation of the peripheral vasculature.

For individuals with spinal cord injury at the neurologic level of T6 and above, exposure to cold water may increase sympathetic nervous system activity, inducing or exacerbating autonomic dysreflexia. Development of autonomic dysreflexia at greater depths may become life-threatening. The need for slow ascent and safety stops may prevent the individual from receiving needed medical care quickly. Individuals with spinal cord injury who are at risk for autonomic dysreflexia should be monitored for common symptoms such as headache, vision changes, and flushing.

Atrophy and Hypotrophy

One should note that due to atrophy and hypotrophy of the lower limbs associated with paraplegia and tetraplegia and other disorders, regular wetsuits may not fit properly. Custom wetsuits may be necessary to ensure proper fit and optimal heat retention.

Decreased muscle mass in the lower limbs may result in increased buoyancy. This may be worsened when a full wetsuit is worn. Paraplegic individuals may therefore need to utilize ankle weights to establish neutral buoyancy in the lower limbs.

Cardiovascular Issues

Individuals with paraparesis and some amputees must rely on the upper limbs for propulsion. Various physiologic factors need to be considered when the upper limbs alone are used for propulsion. Activities performed with the upper limbs compared with the lower limbs require higher myocardial oxygen consumption at the same total oxygen consumption. Also, the rate pressure product ($\frac{\text{heart rate} \times \text{systolic blood pressure}}{100}$) is increased for upper limb exercise compared with lower limb exercise for a given exercise level due to a greater increase in systolic blood pressure. Therefore, the stress induced by upper limb propulsion underwater is greater than that of propulsion by lower limbs.

Cardiac disorders are a feature of many neurologic and muscular conditions such as the muscular dystrophies/myopathies, Friedreich’s ataxia, and many syndromes. The shift of blood into the central circulation resulting from water immersion may aggravate congestive heart failure. There is also increased myocardial demand in diving due to increased exertion. In addition, immersion in cold water can also cause a significant increase in metabolic rate. Given these potential stresses on the cardiovascular system during diving, cardiac function should be evaluated carefully in those individuals who have documented cardiac disorders or conditions that predispose them to cardiac pathology.

The use of webbed gloves can help facilitate propulsion with the upper limbs (Fig. 1). Disabled divers may also opt for the use of motorized propulsion devices that are available from several manufacturers and utilized by many nondisabled divers as well (Fig. 3).
Decompression Sickness

The brain and spinal cord contain myelin, which is very susceptible to excess nitrogen supersaturation after ascent. Symptoms of air embolism affecting the brain or spinal cord include unconsciousness with stroke-like symptoms, paralysis, seizures, bowel/bladder dysfunction, sensory abnormalities, fatigue, personality change, poor concentration, irritability, and changes in vision.

The cortical gray matter is more efficient at releasing nitrogen compared with the spinal cord. Therefore, the spinal cord is at particular risk for decompression sickness. Venous bubbles can cause thrombosis of the venous plexus surrounding the spinal cord, resulting in venous stasis and spinal cord ischemia. However, there is no direct evidence that individuals with spinal cord dysfunction or cortical neurologic disorders are at greater risk of decompression sickness of the brain or spinal cord.

Boot et al. found that individuals with spina bifida had common femoral arteries that were smaller, with decreased blood flow, compared with normal controls. It is unknown if these arterial characteristics increase the risk of decompression sickness. There are currently no studies investigating the appropriateness of the use of current dive tables by the disabled population.

Individuals with disabilities may be at increased risk in the context of decompression sickness because neurologic impairment caused by the decompression sickness can be confused with or masked by the neurologic signs and symptoms associated with the divers’ disease processes. Therefore, it is very important for the disabled diver and his or her dive companions to be familiar with the signs and symptoms of decompression sickness and be able to contrast them with the disabled individual’s baseline state.

Seizure

Many individuals with disabilities have seizure disorders related to their disease processes. Any seizure underwater would result in severe drowning risk and would also be a danger to that diver’s partner. Therefore, seizure disorder requiring ongoing medical management is a strict contraindication to SCUBA diving. Some certifying agencies, however, will allow divers who have been seizure-free without medications for 5 yrs to participate in their diving programs.

Pneumothorax

Pneumothorax can be spontaneous or result from trauma. Spontaneous pneumothorax can be associated with structural abnormalities and lung disease. It is a strict contraindication for SCUBA diving because the underlying cause may still be present at the time of diving. Many individuals who have disabilities resulting from traumatic events have had pneumothoraces. Traumatic pneumothorax, however, is not a contraindication provided that the injury is well healed.

Latex

Latex allergy is rare in the general population, with a prevalence of <1%. However, it is a concern for individuals with spina bifida and other disorders. Latex allergy is very common in these populations, with up to 60% of individuals with spina bifida having allergies to latex. It is an immunoglobulin E–mediated hypersensitivity reaction to natural rubber latex that can result in urticaria, rhinitis, bronchospasm, and anaphylaxis.

Bernardini et al. found that 25% of subjects with spina bifida had latex sensitization, and only 33% of those individuals had had clinical reactions to latex. Although severe reactions are rare, such reactions at greater depths would present a life-threatening event. Therefore, previous screening is important. Individuals at risk for latex allergies, especially people with spina bifida, may wish to consult an allergist for skin prick or serum latex-specific immunoglobulin E antibody testing before considering SCUBA diving. Those individuals who are at risk may wish to have antihistamines and intramuscular epinephrine available in case of a serious reaction.

It may also be prudent to contact the manufacturers of the equipment to be used to determine the precise material content to further decrease the risk. The majority of modern diving masks and snorkels are made from silicone. Also, there is...
usually no natural latex in neoprene wetsuits. However, certain seals and tubing may contain latex, as may seams in certain wetsuits. Latex seals are much more common in dry suits in which water-tight seals are required. Wetsuits manufactured from neoprene rarely have latex seals. Air tubing may contain natural latex, but the latex is usually vulcanized with other materials and therefore would not likely cause a hypersensitivity reaction. However, it may be best to contact individual manufacturers to confirm the latex content in their air hoses. Alternatively, silicone tubing can be utilized to further reduce the risk.

**Skin**

Many conditions resulting in paraplegia are also associated with sensory deficits. Because of insensate skin, these individuals are at risk for developing pressure ulcers and injuries from trauma. Muscle atrophy also results in decreased protection normally afforded by muscle mass and therefore increases the risk of pressure ulcers. In addition, these individuals are at risk for unrecognized burns from sun exposure.

Wetsuits may provide a certain level of protection from skin injury. During the dive, they may protect from abrasions and lacerations while preventing sunburn while on the surface.

**Bladder Management**

Water immersion and cold exposure have been found to cause diuresis by increasing plasma volume and increasing the release of factors such as atrial natriuretic peptide. Changes in urine production can become a factor in individuals requiring catheterization because of a neurogenic bladder. Individuals whose bladder programs include clean intermittent catheterization may be required to catheterize more often to address the increased diuresis. This may be difficult given the limited space of a dive boat. It would be an important consideration to identify dive boats that have private spaces available for bladder management and a means of washing hands to maintain the aseptic nature of the procedure.

Individuals who are on clean intermittent catheterization programs may regularly limit their intake of fluids to reduce the frequency of catheterizations throughout the day. While SCUBA diving, the sources of fluid loss as previously described and those associated with increased exertion and ambient temperature may predispose the diver to dehydration. In addition, wetsuits provide significant thermal protection while in the water. However, prolonged wetsuit wearing may result in hyperthermia, increased sweat production, and dehydration. Therefore, careful monitoring of fluid intake and output balance and monitoring for symptoms of dehydration are very important in this population. Also, bladder distention can be of particular concern for spinal cord–injured patients with a neurologic level above T6 who are at risk for autonomic dysreflexia.

**Ear Barotrauma**

Problems associated with middle-ear spaces and paranasal sinuses are the largest source of morbidity among SCUBA divers. As a diver descends, external pressure increases and pushes on the tympanic membrane. This pressure needs to be equalized in the middle ear through the oropharynx via the eustachian tube. Equalization involves forcefully exhaling against closed (pinched off) nares. Inability to properly equalize will cause barotrauma and may result in pain, acute hemorrhagic otitis media, or tympanic membrane rupture. Therefore, before diving, each individual should be evaluated for the ability to perform this maneuver independently or with the assistance of another diver.

**Asthma**

Asthma affects 6–7% of the general population in the United States, often with childhood onset. Some have supported that any history of asthma is a strict contraindication. However, asthma varies greatly in severity and in its triggers across individuals. Bove states that individuals with mild asthma should not be prohibited from diving. Neuman et al. suggests that individuals with normal airway function at rest with little airway reactivity to exercise or cold air inhalation may have risks of pulmonary barotrauma similar to nonasthmatic individuals. However, air-trapping at depth while breathing compressed air in individuals with

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**TABLE 1** Levels of certification available from the Handicapped SCUBA Association

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level A</td>
<td>Able to provide equal assistance to a fellow diver in case of an emergency. Qualified to dive with another certified diver, including a level A diver.</td>
</tr>
<tr>
<td>Level B</td>
<td>Able to care for self in case of an emergency but cannot provide a fellow diver equal assistance in case of an emergency. Qualified to dive with two certified divers who may be level A.</td>
</tr>
<tr>
<td>Level C</td>
<td>Able to safely use SCUBA underwater but unable to effectively care for self or a fellow diver in case of an emergency. Must dive with two certified divers, one of whom has been trained by a nationally recognized diver training agency in diver rescue. In most cases, this would be an instructor, assistant instructor, or dive master.</td>
</tr>
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</table>
asthma can lead to serious pulmonary barotrauma. Therefore, subjects with a history of asthma should be screened carefully. Additional research may be helpful to better describe the risks for different asthma severities and triggers as opposed to using a history of asthma as a strict contraindication for diving.

Certification

Certifying bodies for recreational SCUBA diving such as the Professional Association of Diving Instructors and the National Association of Underwater Instructors have requirements for swimming and fitness. For example, Professional Association of Diving Instructors requires that an individual be able to tread water for 10 mins and swim for 200 meters independently, even though these skills are rarely needed in SCUBA diving. The authors advocate that for full certification, individuals with disabilities should be held to the same requirements and standards as their able-bodied peers. This is to ensure the highest level of safety for the disabled diver. In addition, an important component of SCUBA certification is the ability to perform skills necessary to assist a dive partner. Any disabled individual who is to be a candidate for full certification should be able to carry out these responsibilities.

The Handicapped SCUBA Association has established a hierarchical certification structure based on each diver’s abilities. This system allows individuals with disabilities to participate in SCUBA diving at different levels of independence based on their level of function (Table 1).

CONCLUSIONS

SCUBA diving is an adventurous sport that allows participants to explore a diverse, exciting marine environment. Guidelines have been established by SCUBA certification organizations to minimize injury. Often times, injuries occur when these guidelines are violated. However, some individuals may experience injury even when diving conservatively. Mortality rates in recreational SCUBA diving are estimated to be one to nine in 100,000 divers.

The authors advocate that SCUBA diving be made available to as many interested individuals as possible. It can be a great source of self-discovery and a means of building confidence and independence. However, individuals with disabilities present with many medical conditions that need to be considered carefully by their physicians before guiding them in this venture. Recognizing and addressing risk factors can help to limit morbidity and mortality. Additional research into how the unique anatomy and physiology of individuals with disabilities interact with a hyperbaric, marine environment would help to better refine guidelines and allow safer diving in the least restrictive framework.

REFERENCES


Enthesitis of Biceps Brachii Short Head and Coracobrachialis at the Coracoid Process
A Generator of Shoulder and Neck Pain

ABSTRACT


This series describes the outcome of diagnostic block at the coracoid process’s common origin of the biceps brachii short head and coracobrachialis for anterior shoulder pain and cervical myofascial pain syndrome in six patients. All showed significant tenderness over the tip of the coracoid process. All underwent diagnostic injection with Marcaine at the coracoid process, followed by therapeutic injection with Marcaine and DepoMedrol. All reported complete relief of pain after local injection. Enthesitis at the coracoid process needs to be considered as a causative or contributing factor in patients presenting with shoulder and neck symptoms. No study was found in the literature describing this association. Whether tendonitis of the common origin is a primary cause or result of chronic neck and shoulder dysfunction remains to be established.

Key Words: Shoulder Pain, Neck Pain, Coracoid Process, Enthesitis, Injection

We describe a series of cases of shoulder pain due to enthesitis at the coracoid process’s common origin of the biceps brachii short head and coracobrachialis in six patients who did not respond to conservative treatment but who did respond to a diagnostic block at the coracoid process. No study was found in the literature describing this association between coracoid process enthesitis and cervical and shoulder pain. Most of the literature found describing the differential diagnosis of shoulder pain (including physical medicine and rehabilitation, orthopedic, and physical diagnosis texts) mention the coracoid process but not as a site causing pain. No literature suggested the tendons of the short head of the biceps brachii or coracobrachialis as cause of pain. No study was found in the literature describing therapeutic injections over the coracoid process for the treatment of anterior shoulder pain.

Literature was found that describes the coracoid impingement syndrome. This syndrome is hypothesized to be due to encroachment of the lesser tuberosity on to the coracoid process because of overuse in flexion–internal rotation, which can lead to displacement of normal centering of the humeral
head. Symptoms of coracoid impingement syndrome include anterior shoulder pain, occasionally radiating down to the upper arm/forearm. Shoulder impingement signs are negative. Pain is made worse with passive flexion. On palpation, there is tenderness over the coracoid process. The literature does not describe conservative treatment but rather describes confirmation of the diagnosis with a local anesthetic injection between the coracoid process and the humeral head. This site of injection was different from ours, which was centered over the coracoid process. No conservative treatment was recommended or described in these studies. According to the studies, definitive treatment is coracohumeral decompression surgery, such as resection of the coracoid tip. This syndrome seems to be similar to what we found in our patients in whom conservative treatment with steroid injection over the coracoid process improved or resolved our patients' symptoms.

Other diagnoses to be considered for shoulder pain included, but were not limited to, impingement syndrome and long head of the biceps tendonitis. Tendonitis of the long head of the biceps brachii often exists with rotator cuff tendonitis and presents with anterior shoulder pain that is worse with shoulder flexion and lifting activities that involve elbow flexion. Physical examination usually reveals a positive Speed's test and pain to palpation over the long-head tendon (significantly greater than for the contralateral side). Shoulder impingement syndrome usually presents with posterior lateral shoulder pain that is exacerbated with activities above the shoulder level. Provocative tests such as the empty can test may be positive, along with tenderness to palpation over the rotator cuff tendons with the shoulder in extension.

We describe six patients who responded well to diagnostic and therapeutic injections of the tendons over the coracoid process. All patients had minimal or no signs or symptoms on examination that were consistent with impingement syndrome or tendonitis of the long head of the biceps brachii. Several patients had undergone therapy to address either of these entities without resolution of their symptoms.

**METHODS**

In the following cases, we describe the injury or repetitive use (if known) and pertinent positive findings on the physical examination. All of the patients complained of anterior shoulder pain that increased with shoulder flexion and abduction but not with activities above the level of the shoulder. Pain was lessened with rest. No patient complained of weakness or sensory changes in the ipsilateral upper limb. Half of the cases also complained of ipsilateral neck pain. All underwent palpatory examination of bones, joints, soft tissue of the cervical, upper thoracic, and proximal arm; provocative testing including the empty can test, Speed's test, and anterior and posterior drawer for glenohumeral stability; passive and active range of motion (ROM) assessment of shoulders in all planes; active ROM of the neck in all planes; and neurologic examination of upper limbs. Unless noted in individual cases, these tests were negative. All underwent shoulder impingement series radiography on the affected side, which consists of anteroposterior, lateral, and Y view of the scapula. Unless noted, the radiographs were reported as normal. Diagnostic injections with Marcaine were done before therapeutic injections with steroids to aid in the diagnosis so that no patient would undergo an unnecessary steroid injection. The risks of the injections that were explained to each patient included bleeding, infection, tendon weakening with rupture, pneumothorax, and increased blood sugars (with the steroid, if diabetic). To perform the injections, the patient was supine, and the coracoid process was palpated. The examiner's fingers were placed on either side of coracoid process for localization, the needle was placed between the fingers, and the tip was advanced to the coracoid process. If pain improved with injection of Marcaine, it was followed with DepoMedrol either the same day or 1 wk later. All of the patients underwent diagnostic injection with 3–4 ml of 5% Marcaine at the coracoid process over the common tendon origin of the biceps brachii and coracobrachialis muscles followed by therapeutic injection with 2–3 milliliters of 0.5% Marcaine and 40–50 milligrams of DepoMedrol. All noted improvement or resolution of symptoms at the noted follow-up times, and all were able to resume their vocational (if applicable) or avocational activities.

**Case 1**

The patient was a 62-yr-old, heavily built man who underwent right acromioplasty and rotator cuff repair 9 mos before his evaluation. He had been pain free for 3 mos after surgery, then gradually noted an increase in pain in the right shoulder over several months. He participated in daily water exercises that included pushing water forward with his hands outstretched, an activity that exacerbated his pain. For 2 mos before being evaluated in our clinic, he participated in physical therapy at an outside hospital, which included phonophoresis and preventative health education followed by a trial of transcutaneous electrical nerve stimulation for bicipital tendonitis. He noted a moderate improvement in his pain initially, but the improvement did not last. He also complained of ipsilateral neck and intermittent el-
bow pain. Shoulder radiographs were consistent with history of acromioplasty and supraspinatus repair.

On physical examination, palpatory examination of the right shoulder was significant for very mild tenderness over the tendon of the long head of the biceps brachii and very severe tenderness at the coracoid process over the common tendon origin of the biceps brachii and coracobrachialis muscles, which reproduced his pain. Shoulder abduction, extension, and internal rotation were limited. The patient underwent the standard procedure of diagnostic injection at the coracoid process over the common tendon origin, followed by the therapeutic injection 1 wk later. He reported immediate and complete relief of neck and shoulder pain and no tenderness to palpation over the coracoid process. At 24 wks after the therapeutic injection, the patient still reported complete relief of his pain. His shoulder ROM was within normal range and palpation over the coracoid process revealed no tenderness.

Case 2

The patient was a 79-yr-old man with a history of a neck injury in 1942, bilateral partial rotator cuff tears, and cervical degenerative disk disease. He was referred for evaluation of right shoulder and neck pain that had gradually increased during the previous 10 yrs. He participated in physical therapy at an outside hospital, which consisted of ultrasound, phonophoresis, and transcutaneous electrical nerve stimulation. He was also given a home exercise program for stretching and strengthening of his rotator cuff muscles. He reported no improvement in his neck and shoulder pain. His radiographs showed minimal spurring along the inferior aspect of his glenoid and acromioclavicular joint, with a slight decrease in the acromiohumeral space.

On physical examination, he had significant tenderness of the right coracoid process over the common tendon origin of biceps brachii and coracobrachialis and moderate tenderness of the right lateral epicondyke, with painful and limited ROM of neck and shoulders in all planes. The patient underwent the standard procedure of diagnostic injection at the coracoid process over the common tendon origin, followed by the therapeutic injection on the same day. The patient reported immediate relief of neck and shoulder pain and relief of tenderness over the coracoid process. At 16 wks after the therapeutic injection, the patient still reported no pain. On examination, his shoulder ROM was within the normal range and palpation over the coracoid process revealed no tenderness.

Case 3

The patient was a 45-yr-old woman who worked as a dental technician and complained of right shoulder and neck pain. Her job involved repeated flexion and adduction of her right arm while holding a tray in a fixed position for a prolonged period. She was referred by her primary care clinic for a steroid injection for right rotator cuff tendonitis because 3 wks of conservative treatment (ice, nonsteroidal anti-inflammatory drugs, rest) had failed to improve her symptoms. Pain was increased by flexion and adduction and better because she was off work.

On physical examination, she had limited active and passive ROM of her right shoulder in all directions except for flexion, which was normal. With palpation, she complained of mild tenderness of her subacromial bursa and significant tenderness over the right coracoid process. She could not tolerate manual muscle testing or provocative testing for rotator tendonitis due to pain. She underwent the diagnostic and therapeutic injections at the coracoid process over the common tendon origin on the same day. She reported immediate and complete relief of neck and shoulder pain. On re-examination, she had full active and passive ROM, with mild limitation of active abduction. Work modification and regular gentle stretching were introduced because of mild symptoms that recurred 1 wk after she resumed normal work. She continued to be without symptoms at a 6-mo follow-up examination. Her shoulder ROM was within the normal range, palpation over the coracoid process revealed no tenderness, neurologic examination was normal, and provocative testing for impingement was negative.

Case 4

The patient was a 59-yr-old man referred for evaluation of left shoulder pain that developed after he performed back bench press exercises. He received physical therapy for 9 mos at an outside hospital, which included modalities and strengthening and stretching exercises. He also had multiple trigger point injections in the posterior shoulder girdle muscles and injection of the tendon of the biceps brachii long head. He reported temporary relief of his symptoms with some of the treatments. The anterior shoulder symptoms never improved.

On physical examination, he had limited active and passive ROM of the left shoulder in all directions except for flexion. He had significant tenderness with palpation of the left coracoid process. He could not tolerate manual muscle testing or provocative testing for rotator cuff impingement because of pain. He underwent the standard diagnostic injection at the coracoid process, followed by a
therapeutic injection 1 wk later. After both injections, he noted relief of pain. He continued with physical therapy once a week for stretching and strengthening. He reported continuation of pain relief at his follow-up visit 2 mos later. His shoulder ROM was within the normal range, palpation over the coracoid process revealed no tenderness, neurologic examination of the upper limb was normal, and the provocative test for impingement was negative.

Case 5

The patient was a 70-yr-old man with a history of a right shoulder dislocation 50 yrs before the examination. Since the injury, he reported constant shoulder pain with very limited and painful ROM. He underwent a subacromial injection and several sessions of physical therapy during the previous 50 yrs with no improvement in his symptoms. His shoulder radiograph showed flattening of the superior and lateral aspect of the greater tuberosity.

On physical examination, he had very limited ROM of his right shoulder in all directions and severe tenderness at the right coracoid process. He had limited ROM in his neck in all planes. He underwent the standard diagnostic and therapeutic block to the coracoid process. He reported dramatic pain relief after the procedures. On examination, there was no tenderness to palpation over the coracoid process. At follow-up 6 wks after the injection, he reported improvement in the ROM in his shoulder and continued improvement in his pain.

Case 6

The patient was a 24-yr-old woman who worked as a nurse and was referred for evaluation of her left shoulder and neck pain. The pain began after she was assisting a patient to sit. After initial conservative treatment that included ice, rest, and nonsteroidal anti-inflammatory drugs, she received physical therapy that included exercises, ultrasound, and phonophoresis. She was diagnosed with bicipital tendinitis, which was treated with steroid injection. This injection improved the tendinitis, but she continued to complain of anterior shoulder pain and intermittent elbow pain.

On physical examination, she had limited ROM of her left shoulder except for forward flexion, which was normal. She was very tender to palpation over the coracoid process. She underwent the standard diagnostic and therapeutic injections at the coracoid process on the same day. She reported immediate relief of her shoulder and neck pain. At follow-up 8 wks after the injection, she continued to report an improvement in her pain. On examination, her shoulder ROM was within the normal range and palpation over the coracoid process revealed no tenderness.

DISCUSSION

All patients in this series presented with primary complaints of anterior shoulder pain. Excluding one patient, all of the patients' pain has been managed by conservative treatment that included physical therapy. None of the patients reported any significant sustained improvement in their symptoms, but the therapy addressed either rotator cuff or biceps brachii long-head dysfunction. Of those with known injury, the movement involved shoulder adduction. On examination, they all had tenderness to palpation over the coracoid process at the common tendon origin of the biceps brachii and coracobrachialis muscles, which reproduced their symptoms. Diagnosis of tendinitis at the coracoid process was confirmed with diagnostic and therapeutic blocks. All patients in this series reported sustained relief at their follow-up appointments up to 6 mos after the blocks, and therapy aimed at treating the dysfunction. No studies were found in the literature that addressed this tendinitis as a cause of shoulder pain.

Shoulder pain or injury may lead to altered mechanics of the shoulder, which may cause myofascial pain syndrome, which includes tendinitis of different muscles. These patients may have started with trigger points in coracobrachialis, pectoralis minor, or biceps brachii muscles. According to Simon7, trigger points in all of these muscles can radiate pain to the anterior shoulder region. Also, trigger points in the pectoralis minor and coracobrachialis can radiate pain to the arm, and trigger points in the biceps brachii can radiate pain to the suprascapular region.7 These pain referral patterns may explain the reason that the patients presented with not only shoulder pain but also arm pain. Persistent trigger points may cause an enthesopathy that can persist and lead to an enthesitis.7 "The enthesopathy (tenderness at the muscle attachment where the taut band terminates) is explained by the inability of the muscle attachment structures to withstand the unrelieved sustained tension produced by the taut band."7 Enthesitis occurs "where recurring concentration of muscle stress provokes inflammation with a strong tendency toward fibrosis and calcification."7 All of the patients in this series except for case 3 had pain for at least 1 yr.

There are biomechanical studies using cadavers assessing the effects of shoulder positions on different anatomic structures of the shoulder. In a study using cadaver models to make biomechanical measurements of the shoulder, Wuelker et al.8 found the highest pressure underneath the acromion at 13.9 N, followed by pressure underneath
the coracoid process at 3.44 N and underneath the coracoacromial ligament (0.43 N). All of these forces increased at the final stage of arm elevation and early reverse elevation. The authors noted that the coracoid process had received little attention in association with impingement. In another cadaver study by Burns and Whipple,9 results indicated that there was increased compression of the supraspinatus tendon against the coracoid process with abduction, along with extension and internal rotation of the bicipital tendon against the coracoid process with abduction and internal rotation.

Few descriptions were found in the literature regarding isolated injuries of the short head of the biceps tendon or injury to the coracobrachialis. Only six case reports describe isolated rupture of the short head of the biceps tendon. The mechanism of action was described as brusque flexion and adduction of the arm with the elbow in extension.10 With this movement, the short head of the biceps is under the greatest strain. This is similar to another study that showed the short head of the biceps most active with arm adduction compared with the long head of the biceps;11 the long head of biceps is more active in fatiguing activities using elbow flexion12 and shoulder flexion and abduction13 compared with the short head of the biceps. Biomechanics of this injury can be inferred from case reports of isolated short-head tear.

We present these cases as additional diagnoses in the differential for shoulder pain. Coracoid enthesopathy should be considered when equivocal impingement test presents, or for bicipital long-head tendon, or when the patient has been treated for the above entities without complete resolution of symptoms. Tendonitis of the common origin of biceps brachii short head and coracobrachialis at the coracoid process needs to be considered as a causative or contributing factor in patients presenting with anterior shoulder and neck symptoms.

CONCLUSION

Shoulder pain or injury may lead to altered mechanics of the shoulder, which may cause myofascial pain syndrome, which includes tendinitis of different muscles. In these cases, these six patients may have developed tendinitis of the common tendon origin, which may be primarily or secondarily caused by their initial injury or altered mechanics. Tendonitis of the common tendon origin is simple to diagnose and treat. It should be considered when a patient presents with shoulder pain with or without symptoms of rotator cuff tendinitis of impingement syndromes. Misdiagnosis may lead to unnecessary procedures such as injections or surgery and the patient being labeled as a malingerer. Mechanics of the shoulder and related occupational ergonomics should be addressed as well. No study was found in the literature describing this association. Whether tendinitis of the common origin is a primary cause or result of chronic neck and shoulder dysfunction remains to be established.

REFERENCES

Spontaneous Recovery from Posttraumatic Hypopituitarism

ABSTRACT


Hypopituitarism is an increasingly recognized complication of traumatic brain injury that can have significant potential to impair recovery and rehabilitation in affected survivors. Although posttraumatic cranial diabetes insipidus is known to be transient in many cases, recovery of established anterior pituitary hormone deficiency is thought to be a very rare event. We report the case of a 25-yr-old man who incurred severe traumatic brain injury in 1997. Sixteen months later, dynamic pituitary stimulation tests revealed severe growth hormone and adrenocorticotropin hormone deficiency. He was treated with recombinant human growth hormone and hydrocortisone. Five years after traumatic brain injury, repeat neuroendocrine assessment, prompted by an increasing serum insulin-like growth factor-1 level, showed normal growth hormone and adrenocorticotropin hormone responses. This is the first case report, to our knowledge, to show that adult posttraumatic growth hormone deficiency can be reversible. The recognition that anterior pituitary dysfunction can recover after traumatic brain injury has implications for the follow-up of patients with hypopituitarism secondary to head trauma to avoid unnecessary, expensive, and potentially harmful therapy.

Key Words: Hypopituitarism, Growth Hormone, Somatotroph Recovery, Adrenocorticotropic Hormone, Cortisol, Rehabilitation

Traumatic brain injury (TBI) is increasingly recognized as an important but underdiagnosed cause of hypopituitarism. Until recently, most of the literature on the occurrence of posttraumatic hypopituitarism was derived from case reports,1,2 but several systematic studies in the last 4 yrs have shown that anterior pituitary dysfunction may be present in 28–68% of TBI survivors,3–8 which is a much higher prevalence than traditionally thought. Although the relative frequencies of different pituitary hormone abnormalities vary depending on the study, growth hormone (GH) deficiency seems to be the most frequent finding in posttraumatic hypopituitarism. The results of these studies may have important public health implications because of the significant potential of undiagnosed hypopituitarism to impair recovery and impede rehabilitation after TBI.

Established posttraumatic anterior hypopituitarism is generally regarded as permanent, although there has been very rare reports of spontaneous recovery...
of hormone deficiency. Because the natural history of posttraumatic hypopituitarism has not yet been defined by prospective studies, there are no reliable data on the frequency of recovery of anterior pituitary hormone deficiency. In this report, we describe the case of a young man whose hypopituitarism was defined some time after TBI but in whom anterior pituitary function recovered spontaneously several years later.

CASE REPORT

Our patient is a 25-yr-old man who, in May 1997, was involved in a road traffic accident and sustained a significant head injury when he was catapulted through the windshield of his car. When he arrived at his local hospital, his Glasgow Coma Scale score was 6/15. Computerized tomography of the brain revealed a large frontoparietal extradural hematoma and bilateral frontal contusions, with associated midline shift and effacement of the basal cisterns. He was transferred to the national neurosurgical unit at Beaumont hospital, where he underwent mass evacuation. He spent 10 days in the intensive care unit and a total of 72 days in the neurosurgical unit before transfer to the rehabilitation hospital. He made a gradual but slow recovery of speech, mobility, and activities of daily living but continued to have significant behavioral and cognitive dysfunction and developed a seizure disorder. While undergoing rehabilitation, he was noted to be polyphagic, with an increase in weight from 64 kg to 84 kg over a 12-mo period. He reported excessive tiredness and global reduction in muscle strength. As a result, he was referred to our unit, in September 1998, for investigation of possible posttraumatic hypopituitarism.

When assessed at our unit, the patient was noted to have impaired cognitive function (Mini-Mental State Examination score, 16/30). His body mass index was 25.8 kg/m² and blood pressure was 120/70 without postural drop. General physical and neurologic examination was otherwise unremarkable. He had normal testicular size and normal secondary sexual characteristics.

Initial biochemical assessment revealed normal plasma glucose, renal function, and plasma sodium. GH and adrenocorticotropic hormone (ACTH) reserve were evaluated using the glucagon stimulation test, and the results are shown in Figure 1. Gonadotrophins were stimulated using gonadotrophin-releasing hormone, and thyrotrophin and prolactin were stimulated using thyrotrophin-releasing hormone. Peak GH response to the glucagon stimulation test was 3 ng/ml, indicating borderline severe deficiency (normal response, >5 ng/ml; severe deficiency, <3 ng/ml). Peak stimulated cortisol was 307 nmol/liter (11 μg/dl), indicating ACTH-cortisol deficiency (normal response, >450 nmol/liter or 16 μg/dl). His insulin-like growth factor-1 (IGF-1) level, a serum marker of GH action, was 164 ng/ml (standard deviation score, −0.9). His gonadotrophins and thyrotrophin responses to stimulation were normal, and basal testosterone, prolactin, and free thyroxine were all within the normal reference range. The 8-hr water deprivation test was normal, therefore, excluding diabetes insipidus.

The patient was commenced on hydrocortisone, 10 mg twice daily, and recombinant-human GH, which was titrated up to a dose of 0.6 mg/day on the basis of plasma IGF-1 concentrations, which increased to 398 ng/ml (IGF-1 standard deviation score, +0.2). He reported increased energy level, improved muscle strength, and enhanced well-being. His Mini-Mental State Examination score, performed 6 wks after commencement of hormone replacement, improved to 23/30. Quality of life, assessed using the Quality of Life Assessment of GH Deficiency in Adults questionnaire, showed an improvement from a score of 17/25 before GH treatment (moderately severe impairment) to a score of 7/15 (mild impairment) 6 wks after GH replacement, which was sustained thereafter.

The patient was followed up with serum IGF-1 measurements every 6 mos, which remained in the

![FIGURE 1](attachment://dynamic_growth_hormone_gh_top_and_cortisol_bottom_response_to_the_glucagon_stimulation_test_gst_at_the_initial_1998_and_repeat_2002_endocrine_assessments_normal_response_is_a_peak_gh_of_5_ng/ml_and_a_peak_cortisol_of_450_nmol/liter_16_microgram/dl).
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age-adjusted normal reference range until July 2001 when it was noted to be elevated at 613 ng/ml (standard deviation score, +2.4). This prompted a gradual reduction in his recombinant-human GH treatment dose, which was eventually discontinued. His IGF-1 level off treatment was 324 ng/ml (IGF-1 standard deviation score, +0.2). He was readmitted for repeat assessment in March 2002. The result of his repeat glucagon stimulation test is shown in Figure 1. This showed normal peak cortisol and GH responses. Hydrocortisone treatment was also discontinued. At 18 mos after cessation of GH and hydrocortisone therapy, he remained well, with no symptoms or signs of hypopituitarism.

**DISCUSSION**

We report the first adult case of recovery of normal GH secretion in posttraumatic hypopituitarism. As TBI is increasingly recognized as a cause for hypopituitarism, clinicians should also be aware of the potential for recovery of established hormone deficiency.

Anterior pituitary hormone production (GH, ACTH, gonadotrophins, thyrotrophin, and prolactin) is primarily regulated by the hypothalamus through several stimulatory and inhibitory peptides, which are released into the portal circulation and transported down the stalk to the anterior pituitary. Therefore, hypopituitarism can result from damage to the hypothalamus, the pituitary stalk, or the pituitary gland itself. There are several mechanisms by which TBI can cause hypothalamic-pituitary dysfunction, including vascular injury to the pituitary or the hypothalamus; compression from edema, skull fracture, hemorrhage, or increased intracranial pressure; hypoxic insult or by direct mechanical injury to the hypothalamus, pituitary stalk, or the pituitary gland. The long hypophysial vessels and the portal capillaries in the pituitary stalk provide 70–90% of the blood supply to the anterior pituitary, and they are particularly vulnerable to traumatic injury, resulting in anterior lobe infarction. Autopsy results showed evidence of injury to the hypothalamus, the pituitary gland, or the pituitary stalk in 26–86% of patients who died of TBI. The site of the injury varies according to the studies, but necrosis of the anterior lobe was more frequent in patients who died within 1 wk of TBI. In the series reported by Crompton, hypophysal lesions were present in 42% of 106 autopsies, and pituitary lesions were present in 28% of the 53 pituitary gland studied.

The assessment of GH and ACTH-cortisol secretion in cases of suspected hypopituitarism requires stimulation tests because basal or random GH and cortisol levels are not adequately reliable to confirm or rule out deficiency. Because our patient had a history of seizures, we were unable to use the insulin hypoglycemia test, which is used as the first-line investigative tool to assess GH and ACTH-cortisol secretion in our unit. Instead, we used the glucagon test, which showed clearly GH and ACTH deficiencies. The glucagon test has been shown to be reliable in assessing GH and ACTH reserves. The normal and reproducible cutoff values, which we use in our unit, for peak stimulated serum GH and cortisol are 5 ng/ml and 450 nmol/liter (16 µg/dl), respectively, and are based on data collected from our own healthy controls. The initial GH response of 3 ng/ml, which was seen in our patient, is indicative of severe GH deficiency and has been shown to offer a 100% sensitivity and specificity for the diagnosis of GH deficiency in adults. Although the pretreatment serum IGF-1 was in the low normal range, Hoffman et al. showed that 70% of GH-deficient patients have serum IGF-1 concentration in the normal age-stratified reference range, although they tended to be lower than serum IGF-1 values in normal subjects. Therefore, a low-normal serum IGF-1 concentration in our patient is consistent with GH deficiency. The diagnosis of GH and ACTH-cortisol deficiencies is also supported by the clinical improvement and improvement in the Mini-Mental State Examination score after treatment. The diagnosis of GH deficiency is further supported by the improvement in quality-of-life scores, assessed using the Quality of Life Assessment of GH Deficiency in Adults questionnaire, which is regarded as specific for GH deficiency after GH replacement.

Because the glucagon stimulation test assesses the integrity of the entire hypothalamic-pituitary axis, it can not identify the exact site of the lesion. However, hypophysal or stalk lesions are usually associated with hyperprolactinemia (due to deficiency of the hypothalamic peptide, dopamine, which exerts a powerful inhibitory effect on prolactin release from the anterior pituitary). Therefore, the normal serum prolactin concentration in our patients is suggestive of a pituitary rather than a hypothalamic lesion.

GH deficiency in adults is associated with abnormal body composition, reduced muscle strength and exercise tolerance, impaired cardiac function, reduced bone mineral density, and impaired quality of life. In addition to all these abnormalities that may have adverse consequences for recovery and rehabilitation, GH deficiency is also associated with several metabolic abnormalities and, possibly, increased overall vascular mortality. GH replacement shows a clear benefit. Cortisol deficiency is associated with lethargy and muscle weakness and can be life threatening during intercurrent illness. Our patient enjoyed a significant clinical improvement after treatment with GH and hydrocortisone.
The suspicion that this patient may be recovering somatotropic function was prompted by the steady increase in serum IGF-1 levels on GH treatment, which developed 4 yrs after the trauma. Repeat glucagon stimulation showed recovery of both somatotropic and corticotrophic function. Recovery of established posttraumatic hypopituitarism has been regarded as an exceptional event. There have only been three previously published case reports of recovery of pituitary function after TBI, two in adults and one in a child.9–11 Table 1 summarizes the details of the case reports. Of the two adult cases, one had recovery of isolated gonadotrophin deficiency,11 the other case developed GH, ACTH, and gonadotrophin deficiencies after TBI, but although ACTH and gonadotrophin deficiency recovered, normalization of GH secretion had not occurred by the time of the case report.10 In the single pediatric case report, the patient was prepubertal and was not primed with gonadal steroids before GH reserves were assessed.9 Although he was found to have normal GH secretion when he was reassessed in the postpubertal stage, many prepubertal children who fail provocative tests for GH secretion are found to have normal GH reserves after the administration of gonadal steroids.27 The low prepubertal gonadal steroid level may therefore have caused the poor GH response to stimulation in this case.

The mechanism underlying recovery of anterior pituitary function after TBI is speculative. Recovery may result from regeneration of portal vessels, which grow down into the surviving parts of the anterior lobe,2 resulting in restoration of function. This hypothesis is supported by postmortem findings showing the presence of mitotic figures15 and repopulated appearance in the anterior lobe16 in patients who died after head injury, suggesting tissue regeneration.

CONCLUSION

This case report illustrates that well-established posttraumatic adult GH deficiency, which is the most common deficiency in adult hypopituitarism, can recover some time after the diagnosis is made and treatment has started. As hypopituitarism after TBI is diagnosed more frequently, clinicians should be aware of the possibility of late recovery of hormonal function and of the need for periodic assessment to avoid unnecessary, expensive, and possibly harmful treatment.

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### Table 1

<table>
<thead>
<tr>
<th>Authors</th>
<th>Subject’s Age at Time of TBI, yrs</th>
<th>Pituitary Hormone Deficiencies</th>
<th>Recovery</th>
<th>Time to Recovery</th>
</tr>
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<tbody>
<tr>
<td>Eiholzer et al.9</td>
<td>7.25</td>
<td>GH, ACTH, TSH</td>
<td>GH, ACTH, TSH</td>
<td>12 yrs</td>
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<tr>
<td>Iglesias et al.10</td>
<td>32</td>
<td>GH, GT, ACTH, partial TSH</td>
<td>GT, ACTH, TSH</td>
<td>6 mos</td>
</tr>
<tr>
<td>Benvenga et al.11</td>
<td>26</td>
<td>GT</td>
<td>GT</td>
<td>10 yrs</td>
</tr>
</tbody>
</table>

TBI, traumatic brain injury; GH, growth hormone; ACTH, adrenocorticotrophin hormone; TSH, thyrotrophin; GT, gonadotrophins.
ABSTRACT


We report a case of an 87-yr-old woman with hemorrhage restricted to the corpus callosum. After conservative treatment at an emergency hospital, she was admitted to our hospital presenting with bilateral lower limb weakness (paraparesis) and abnormal behavior in her left hand, such as pulling at dishes while eating and purposeless “floating” of the hand while walking. We believed these behaviors to represent disconnection syndrome. Six weeks after onset, her abnormal behavior while eating disappeared. The incomplete paraparesis also improved, and she regained the ability to walk, albeit with a T cane. These findings are compatible with previously reported cases. In cases of a corpus callosum lesion, careful observation from the outset is indispensable to avoid misdiagnosis.

Key Words: Corpus Callosum, Cerebral Hemorrhage, Magnetic Resonance Image, Disconnection Syndrome, Rehabilitation

A variety of causes of callosal damage have been reported and include cerebral infarction in the area of the anterior cerebral artery, hemorrhage from a ruptured aneurysm of an arteriovenous malformation,1 brain tumors,2,3 Marchiafava-Bignami disease,2 moyamoya disease,4 multiple sclerosis,5 and surgical section of the corpus callosum (CC) for the treatment of epilepsy.6 However, hemorrhage restricted to the CC is uncommon, and the symptoms and clinical course are not well documented. In the present case, hemorrhage was restricted to the body of the CC, and no other lesions near the CC were detected.

The patient demonstrated paraparesis and abnormal behaviors in her left hand. A variety of abnormal involuntary motor behaviors has been reported after callosal lesions. One example of this is the group of syndromes labeled alien hand,7 anarchic hand,8 wayward hand,9 intermanual conflict,10 and diagonistic dyspraxia.11 We examine the clinical course of the symptoms and signs and discuss their neurologic mechanism.

CASE PRESENTATION

The patient was an 87-yr-old, right-handed woman. Before this brain lesion, her activities of daily living and gait were completely independent. Medical...
history included hypertension and subtotal gastrectomy due to gastric carcinoma 4 yrs earlier.

She noted sudden onset of gait disturbance on October 5, 2000, and was transferred to an emergency hospital. At admission, her consciousness level was 4-4-6 on the Glasgow Coma Scale. She showed incomplete paraparesis, 2/5 on the manual muscle test, and the grasp reflex was present in the left hand. A computed tomographic image revealed hemorrhage restricted to the CC. After conservative treatment, she was transferred to our hospital for rehabilitation on November 22, 2000.

NEUROLOGIC FINDINGS

The patient was alert and well oriented regarding time, place, and people. There were no abnormal findings in the cranial nerves. There was incomplete paraparesis (i.e., 3/5 [bilateral gluteus medius] to 4/5 [bilateral quadriceps and tibialis anterior] in the manual muscle test). Barre’s sign was negative and the upper limbs showed no weakness in any muscle. No motor ataxia was found, but her left arm movements were desynchronized in the pronation-supination diadochokinesis test. Perception of pain, temperature, and touch were almost normal. Deep tendon reflexes were normal and symmetric, and no pathologic reflexes were elicited. She could not remain sitting without a backrest, stand up, or walk due to the muscle weakness. Her Barthel index score was 60.

NEUROPSYCHOLOGICAL FINDINGS

She said that her left hand, against her will, reached for dishes, pulled them, and interfered with eating. She described her left hand as behaving in a “foreign” manner. This behavior was triggered by the right hand’s eating behavior. Thus, she kept her left hand on her left leg intentionally during eating to suppress the unintentional behavior. This peculiar phenomenon occurred only while eating, and we did not observe it on any other occasion. We also noted her left hand floating in the air during walking.

She had no speech disturbance and showed no features of aphasia. She had no symptoms of agnosia or apraxia according to the Standard Performance Test for Apraxia, which is the standard battery for the assessment of apraxia in Japan. There were no deficits in tactile naming of objects and letters drawn by the left hand nor defective cross-replication of hand postures. She was able to write Japanese letters with either hand. Visuomotor ataxia, forced grasping, visual groping, compulsive manipulation of tools, and intermanual conflict were absent. She did not show crossed optic ataxia in either side of her visual field. Results of the neuropsychological evaluation of callosal functions are listed in Table 1, and only the main findings will be described below.

NEURORADIOLOGIC FINDINGS

A computed tomographic image made on the day of onset showed a callosal hemorrhage (Fig. 1a). Magnetic resonance images demonstrated a high signal area (gadolinium-diethylenetriamine pentaacetic acid enhanced) in the caudal part of the body 18 days after onset (Figs. 1, b–d). The lesion was restricted to the body of the CC, and there was no evidence of cortical damage, including cingulated gyri and other cortical areas. Magnetic resonance imaging at admission to our hospital (51 days after onset) no longer showed the high signal area (Fig. 2).

TABLE 1 Results of neuropsychological evaluation of callosal function

<table>
<thead>
<tr>
<th>Dysfunction</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysarthria or aphasia</td>
<td>Absent</td>
</tr>
<tr>
<td>Somesthetic transfer</td>
<td>Normal</td>
</tr>
<tr>
<td>Tactile naming</td>
<td>Normal</td>
</tr>
<tr>
<td>Visual naming</td>
<td>Normal</td>
</tr>
<tr>
<td>Writing</td>
<td>Normal</td>
</tr>
<tr>
<td>Reading</td>
<td>Normal</td>
</tr>
<tr>
<td>Drawing</td>
<td>Normal</td>
</tr>
<tr>
<td>Praxis</td>
<td>Normal</td>
</tr>
<tr>
<td>Abnormal hand behaviors</td>
<td>Present</td>
</tr>
</tbody>
</table>

FIGURE 1 Unenhanced computed tomographic image at day of onset (a) and enhanced magnetic resonance images 18 days after onset (b–d). Magnetic resonance imaging visualized a high signal area (gadolinium-diethylenetriamine pentaacetic acid enhanced) in the caudal part of the body. b, T2-weighted image; c and d, T1-weighted images.
REHABILITATIVE INTERVENTION AND CLINICAL COURSE

To cope with the clumsiness in her left hand, pegboard exercises, range of motion exercises, and writing were performed as occupational therapy. Clumsiness in the left hand gradually improved, and the abnormal behavior while eating disappeared about 6 wks after onset. However, her left hand still floated purposelessly during walking.

General mobilization, relaxation, and gait exercises with a walker or on parallel bars were performed as physical therapy to cope with the impairment of balance function and hypertonia. Muscle strength in the lower limbs gradually became normal about 5 mos after onset. As a result, her sitting balance, standing balance, and gait function improved. Finally, she was able to walk alone with a T cane.

DISCUSSION

Cause of Hemorrhage in the CC

Hemorrhage in the CC is uncommon and usually found within the context of more extensive cerebral damage, often secondary to bleeding from a vascular malformation. Almost all reported cases have lesions beyond the CC. In our case, however, hemorrhage was restricted to the CC, which is considered to be extremely rare.

Due to the patient’s total gastrectomy for gastric carcinoma 4 yrs earlier, we suspected a metastatic brain tumor. Although magnetic resonance imaging did not provide definitive evidence of a brain tumor, we could not completely exclude the possibility of spontaneous bleeding from a metastatic brain tumor into the CC. Further detailed analysis, including angiography and a lumbar tap, was refused by her family. Because the patient was old, we could not exclude the possibility of amyloid angiopathy as one of the causes of hemorrhage. According to a previous study, hemorrhage due to amyloid angiopathy usually occurs in the subcortical area, especially in the frontal lobe and parietal lobe. Thus, we strongly believe that hypertensive bleeding from a pericallosal artery was the cause of this lesion.

Clinical Features of Extracallosal Damage

Paraparesis is commonly found in cases with callosal hemorrhage. This extracallosal sign may result from pressure of the hemorrhage on the descending precentral and frontal fibers. However, this neurologic finding is mild and transient because the hematoma is gradually absorbed. In cases of a ruptured aneurysm of the distal anterior cerebral artery, paraparesis is typically very severe. As the hemorrhage was restricted to the CC in this case, the paraparesis was transient and quickly recovered. Compared with the hemiparesis due to spinal cord injury, prognosis is relatively favorable.

Clinical Features of Interhemispheric Disconnection

Abnormal behavior of the subject’s left hand manifested in two ways, as disturbance of eating behavior during use of the right hand and as floating in the air during walking. The former was triggered by the right hand’s movement during eating. According to Tanaka et al., diagnosistic dyspraxia should be more appropriately defined as the abnormal motor behavior of the left hand triggered by the voluntary activities of the right hand. Therefore, the abnormal behavior in our case can be considered a manifestation of diagnosistic dyspraxia. This behavior gradually disappeared and no longer disturbed her activities of daily living. This is consistent with the findings of other cases involving diagnosistic dyspraxia.

The latter is similar to the abnormal behavior demonstrated in the case reported by Nishikawa et al. Their patient, aged 23, showed right-hand floating and purposeless movement while lying in bed. This abnormal behavior is similar to groping. Groping is considered a frontomesial hyperkinetic sign. In our case, no significant lesion in the frontomesial cortex was detected. We assumed that the pressure of the hematoma probably produced the dysfunction of the frontomesial cortex. No other disconnection signs were observed in the present case.

Inconsistent relationships between the lesion site in the CC and specific symptoms have been documented in the literature (Table 2). Gazzaniga...
et al.\textsuperscript{5} reported a case of disconnection syndrome after section of the CC for the control of epilepsy. The patient demonstrated left-sided agraphia and hemialexia. Maeshima et al.\textsuperscript{3} reported a case of bilateral crossed optic ataxia due to the compression of the splenium of the CC by a meningioma. Leiguarda et al.\textsuperscript{1} reported a case with hemorrhage in the whole body of the CC, and Watson and Heilman\textsuperscript{15} reported another case with hemorrhage in the same lesion. These two cases demonstrated left-sided apraxia, left unilateral agraphia, paraparesis, and abnormal hand behavior. However, one case demonstrated left hemialexia and the other did not. Lavados et al.\textsuperscript{16} reported another case of hemorrhage with three distinct callosal lesions. The patient showed right hemiparesis and abnormal hand behaviors labeled as “agonistic dyspraxia.” These inconsistent findings among cases with CC lesions may be explained by Yamadori\textsuperscript{19}’s\textsuperscript{19} observation that most cases have additional interhemispheric lesions that influence the symptoms and that the ability to compensate for a lesion differs among individuals. We believe that some patients may regulate these phenomena intentionally, and thus, the subtle or transient phenomena may be overlooked.

In the present case, the hemorrhage was restricted to the posterior part of the CC. The patient demonstrated moderate paraparesis and abnormal behavior by her left hand, but she did not show any other disconnection signs at the initial evaluation at our hospital. We were unable to definitively exclude the presence of other disconnection signs in the acute phase. We presume that when she was transferred to our hospital, the disconnection signs became less prominent due to diminishing of the compression of interhemispheric fibers, resulting from absorption of the hematoma.

**CONCLUSION**

We report a case of a woman with hemorrhage restricted to the CC. She presented with paraparesis and abnormal behavior in her left hand, such as pulling at dishes while eating and purposeless floating of the hand while walking. We believe these behaviors to represent disconnection syndrome. The abnormal hand behavior subsequently resolved, and the patient was able to walk with a cane with disappearance of the hematoma. These findings are compatible with previously reported cases. In cases of a callosal hemorrhage, careful observation from the outset is indispensable to avoid misdiagnosis.

**ACKNOWLEDGMENTS**

We thank Dr. Toshiaki Furukawa and Dr. Mitsuhiko Kodama for their valuable comments.

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**TABLE 2 Relationship between the lesion sites of the CC and disconnection signs**

<table>
<thead>
<tr>
<th>No. of Cases</th>
<th>BCC</th>
<th>Lesion Sites</th>
<th>Main Callosal Disconnection Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RCC</td>
<td>GCC</td>
<td>Ant</td>
</tr>
<tr>
<td>Gazzaniga (6)</td>
<td>1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Maeshima (3)</td>
<td>1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Leiguarda (1)</td>
<td>1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Watson (15)</td>
<td>1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lavados (16)</td>
<td>1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Our case (2004)</td>
<td>1</td>
<td>+</td>
<td>+</td>
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</table>


Ancient Wisdom and Accurate Assessment in the Cost-Conscious Era
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A 91-yr-old woman was referred for a rehabilitation program after osteoporosis was diagnosed. Her presenting complaints were upper back pain beginning around the cervicothoracic junction and radiating down to the mid-thoracic region. She also reported considerable kyphotic posture. Bone mineral densitometry done as part of a standardized work-up before referral to rehabilitation showed T scores of −5.3 for the spine and −3.4 for the hip (World Health Organization guidelines for diagnosis of osteoporosis, T score of −2.5 SD below the peak bone mass for a normal young adult), and lumbar spine radiographs were unremarkable.

The patient’s musculoskeletal examination was notable for thoracic hyperkyphosis and tenderness to palpation in the mid-thoracic and cervicothoracic areas. Her range of motion, strength, reflexes, sensation, and dural tension signs were unremarkable.

Physical therapeutic exercises were provided to the patient, as were educational materials and biomechanical principles for care of the back for a home program. A weighted kypho-orthosis (Posture Training Support, Camp Healthcare, Jackson, MI) also was tried but not prescribed, pending completion of the patient’s work-up (thoracic spine radiographs).

This patient was resistant to additional studies that were recommended, such as thoracic spine radiography, and to the recommended pharmacotherapy because of financial concerns. After much persuasion, she relented to these recommendations. The thoracic radiograph is shown in Figure 1.

Discussion
This case highlights an important aspect of multidisciplinary care—different specialists may focus on different aspects of the disease. Although our case illustrates that the standard work-up was sufficient from the medical perspective for guiding the prescription of antiresorptive agents, one important study from the biomechanical standpoint—thoracic spine radiography—was not done initially.

The patient’s concern regarding finances complicated treatment. She was initially resistant to the thoracic spine studies because of the financial factor and the perception that her work-up was complete. She was also concerned about the cost of all the treatments recommended to her. In the current climate of cost justification, insurers and patients may balk at the “additional” costs of such testing.

In this case, radiography provided valuable anatomic detail of the thoracic hyperkyphosis in that four vertebral compression fractures were discovered. Biomechanical modeling studies of a similar case estimated that these deformities can increase spinal compressive forces 24% and increase the required mid-thoracic paraspinal force by 40%. These forces can substantially alter a patient’s prognosis and could be vital in convincing a patient to comply with the prescribed regimen of treatment.

There is a parable about three blind men examining an elephant. One man felt the ears and reported that the
elephant was like a fan. Another man felt the tusk and reported that the elephant was like a spear. Another man felt a leg and reported that the elephant was like a tree. All of their observations contained an element of truth, but all of them were off the mark. This parable highlights the importance of considering the entire picture, even when providing specialty care.

In patients with osteoporosis, thoracic and lumbar spine radiographs are necessary for accurate assessment of the musculoskeletal status before proper exercise and bracing can be prescribed.

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5. D